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ARTICLE

Effect of Intrahepatic Arterial Delivery of Sorafenib on Normal Liver Tissue of Rabbit: An Experimental Study

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ABSTRACT

Objective: To assess the safety, feasibility and eluting efficiency of intrahepatic arterial delivery of sorafenib on normal liver tissue of rabbit. **Methods:** 24 New Zealand rabbits were randomly divided into three groups: group I (Lipiodol-sorafenid), group II (Lipiodol) and group III (Sorafenib). Group I and II were treated by transcatheter selective hepatic arterial embolization with emulsions of lipiodol and sorafenib or with only lipiodol, while group III was given hepatic arterial infusion with sorafenib. Sorafenib concentration in plasma was determined by HPLC (high performance liquid chromatography) in 0 min, 20 min, 1h, 2h, 4h, 8h, 16h, 32h and 48h respectively. The breathing rate, heart rate, rectal temperature and body weight were measured, as well the blood routine test and the function of liver, kidney, and heart. Two animals of each group were respectively killed in the 3rd day, 1st, 3rd and 6th week after treatment. Histopathologic study was done to liver, heart, kinney, lung, brain, gall bladder and intestine. **Result:** ① The peak sorafenib concentration (Cmax)and AUC(Area under curve) in plasma in group I was 2.46±0.101μg/ml and 945.72 ± 52.3 μg/mL.min respectively, while in group III which was 3.78±0.180 ug/ml and 546.98±21.1μg/mL.min. Compared with group III, the Cmax and AUC of group I had a significant statistics difference ($p<0.05$). ② The breathing rate, heart rate, rectal temperature and AST/ALT,WBC,NEU% of group I and group III has a significant statistics difference($p<0.05$) in the 3rd day. ③ CK ,CK-MB, DB, Cr, BUN,RBC,PLT in plasma did not change in all group. ④ Local necrosis was seen in group I and group II in the 3rd day and 1st week, but they did not seem to be different. Group III showed no necrosis. Granulation tissue with bile duty, portal vein and microfossils hyperplasia were seen in local necrosis area in the 3rd week. No pathological changes were found in brain, heart, kidney, intestine and gallbladder. **Conclusion:** TAE with emulsions of lipiodol and sorafenib is feasible, safe and has some slow-release effect.

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1. Introduction

Transcatheter arterial chemoembolization (short for TACE) is a priority for treatment of advanced liver cancer that cannot be surgically excised. The clinical research has proved that TACE can effectively prolong the patient's long-term survival time. It is a standard treatment method for HCC of Phase B of BCLC. However, tumor recurrence and metastasis are important factors affecting TACE's long-term efficacy. Studies have confirmed that local tissue ischemia and hypoxia after TACE promotes up-regulation of VEGF/VEGFR expression, which promotes neovascularization and is one of the important promoters of tumor recurrence [1-4]. The emergence of novel multi-target molecular targeted drugs, such as Sorafenib, provides a new approach to the treatment of HCC. Combined with oral administration of Sorafenib after TACE can inhibit tumor growth and angiogenesis and prevent tumor recurrence. However, oral Sorafenib has many shortcomings such as long oral administration time, high cost, large side effects, and low response.

Regional local sustained high-concentration slow-release drug technology for treating a variety of diseases has been widely used in clinical, such as local infusion chemotherapy drugs inactivated tumors, giving pancreatic enzyme inhibitors using local indwelling catheter for pancreatitis, local perfusion of pro-angiogenic substances (such as gigaton) to treat femoral head necrosis, continuous direct thrombolysis using local indwelling catheter for treating thrombosis etc. Regional local qualitative delivery of drugs has unique advantages due to its minimally invasive, sustained release of high-concentration drugs and small side effects. Intravascular interventional techniques combined with local molecular targeted therapy have been reported in related experiments and clinical studies [13-15], and achieved good results. Therefore, the local delivery of Sorafenib using intravascular interventional technique is expected to significantly increase the local drug concentration, improve the therapeutic effect, shorten the treatment cycle, reduce the incidence of side effects, reduce the cost, make up for the deficiency of simple interventional therapy, and completely inactivate the tumor, reduce the recurrence rate and prolong the long-term survival time of patients. Based on the above analysis, we propose an experimental research on TACE combined with intravascular delivery of Sorafenib powder with a goal to evaluate the feasibility and safety of intravascular injection of Sorafenib for pharmacokinetics and intravascular injection of Sorafenib.

2. Material & Method

2.1 Material

2.1.1 Animal

Healthy New Zealand white rabbits, a total of 24, 14 females, 10 males, weighing 2.5-3.0 kg, were provided by the PLA General Hospital Experimental Animal Center. Animal experiments were approved by the PLA General Hospital Animal Management Committee.

2.1.2 Drugs

(1) Biological targeting preparation - sorafenib original powder. The tablets were provided free of charge by Bayer and purified by the Biochemical Laboratory of the Academy of Military Medical Sciences. The specific method is as follows. According to the manufacturer's recommendations and our preliminary experiments, the proposed dose is 20mg/Kg [Cancer Res, 2006, 66: 11851].

(2) 40% iodized oil (super liquefied lipiodol produced in France).

(3) Anesthetic with 3% sodium pentobarbital injection (5mg/Kg body weight).

2.1.3 Instruments & Equipment

(1) Digital subtraction angiography (DSA) devices, equipment specification: Philips INTEGRIS, JWYXZ ZI No. DSA07

(2) Super smooth guide wire: RADIFOCUS, TERUMO, Japan

(3) Angiography catheter: 4F Cobra Catheter, Cordis, Johnson & Johnson, USA

(4) 4F arterial sheath: 4F, 24cm long, TERUMO, Japan

(5) Percutaneous puncture suite: Micropunture system, COOK, USA

(6) Agilent 1200 High Performance Liquid Chromatography System 1100 (HPLC), Diode Array Detector

(7) 3F microcatheter (Progreat): TERUMO company, Japan

(8) Optical microscope, type IX51, Olympus, Japan

2.2 Method

2.2.1 Purification of Sorafenib Powder

(1) 20 tablets (4g) of Toluenesulfonic acid Sorafenib were ground to a powder, and 100 ml of methanol was added thereto, and the mixture was heated under reflux for 30 minutes, and decolorized by adding activated carbon. After filtration and concentration of the filtrate, obtain 1.6 g of a solid, which was dissolved by heating with 30 ml of

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ethanol, filtered when it was still hot, and precipitated to crystallize. Filter and drain to obtain 1.3 g of white crystals.

(2) Purification of Sorafenib structure and purity verification: comparison of the melting point, molecular structure and space structure of the purified substance and Sorafenib substance.

① Melting point: compare the melting point of the purified product with the original powder of Sorafenib, the melting point of the purified product is 226-229 ℃ , and the melting point of the original powder is 223-231°C in the literature. The melting point of the purified product is within the melting point of the original powder, and the two have the same possibility of substance.

② Elemental analysis: measured value C H N (theoretical value C of 52.79%, H of 3.80%, N of 8.79%), there was a difference of three thousandths between the measured value and the theoretical value. Compare compounds for the same substance.

③ Nuclear magnetic spectrum (spatial structure, Figure 1)

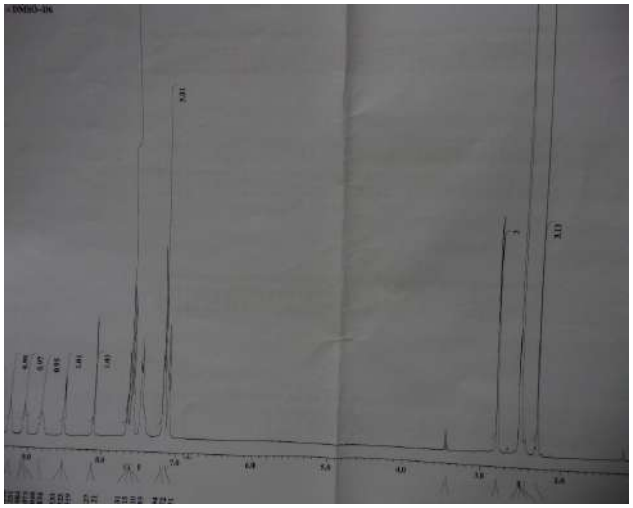

Figure 1. Nuclear magnetic spectrum of Sorafenib powder

Result analysis: 1H-NMR(DMSO-d6,400MHz): δ=2.29(s,3H,CH3); 2.79(d,J=4.8Hz, 3H,NCH3); 5.9(br,s,1H,SO3H); 7.14 (d,J=7.9Hz,2H,2’’’-H,6’’’-H); 7.17-7.22 (m,d,J=8.8Hz,3H,5-H,3’-H,5’-H); 7.44 (d,-J=2.0Hz,1H,3-H); 7.48 (d,J=8.0Hz,2H,3’’’-H,5’’’-H); 7.61 (d,J=8.8Hz,2H,2’-H,’-H); 7.63 (m,1H,5’’-H); 7.67 (m,1H,6’’-H); 8.14 (d,J=2.2Hz,1H,2’’-H); 8.53 (d,J=5.6Hz,1H,6-H); 8.88 (d,J=4.8Hz,1H,NHCH3); 9.1(br,s,1H,NHCO); 9.3 (br,s,1H,NHCO). The analysis by the above method showed that the substance purified by the tablets was Sorafenib.

Figure 2. Purified white Sorafenib powder

2.2.2 Experimental Design

(1)A total of 24 New Zealand white rabbits, 14 females and 10 males were randomly divided into 3 groups according to random number method, group I (iodine-Sorafenib emulsion group) and group II (simple iodized oil group). And group III (Sorafenib only), with 8 in each group. Hepatic artery embolization was performed in group I and group III, respectively, and group S was only treated with Sorafenib arterial infusion. The liver function changes of liver tissue before and after treatment were compared to evaluate the effect of Sorafenib on liver tissue. The drug concentration of iodized oil-Sorafenib emulsion group and Sorafenib group were compared to evaluate the drug loading characteristics of Sorafenib. Sorafenib-iodine was investigated. The change in physiological indexes and pathological examination of the oil group and the Sorafenib group before and after surgery were evaluated to evaluate the safety of Sorafenib.

(2) Hepatic artery catheterization technique: ① three groups of animals before routine experiment with venous blood to check blood routine, liver and kidney function. ② After the experimental rabbits were given intravenous anesthesia, they were inserted on the back of the rabbit plate in the supine position, and the right groin was prepared for skin and disinfection and drape. The local femoral artery was partially incision and separated, and the femoral artery was punctured under direct vision with a 21G micropuncture needle. The guided 4F soft sheath (product of COOK, USA) was inserted into the 4F arterial sheath. ③ Insert a 4F cobra catheter into the celiac artery under fluoroscopy for routine celiac angiography. The contrast agent for contrast was ultravist (370 mg I/ml). The parameters were set to: 4ml per second, a total of 16ml, a pressure of 300PSI. After angiography (DSA) to determine the anatomical details of the hepatic artery, the 3F microcatheter was super selectively inserted into the hepatic artery branch, and then iodized oil was injected according to the experimental needs. iodized oil - sorafenib emulsion, suspension of Sorafenib and phys-

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iological saline. Eight rats in group I were given a bio targeted preparation via a catheter-selective intrahepatic artery—sorafenib powder and iodized oil emulsifier, a total amount of 1.5-2 ml, containing 50-60 mg of Sorafenib powder. In group II, 8 rabbits were used, and iodized oil was administered via a ductal selective hepatic artery with a total amount of 1.5-2 ml. Eight animals were used in group III, and Sorafenib was administered via a transcatheter selective hepatic artery with Sorafenib 50-60 mg. The actual doses of Sorafenib in the survival group I and group III were: group I (53.04±3.209 for lipiodol-Sorafenib group) and group III (54.04±2.409 for Sorafenib group only). There was no statistical difference in the doses of Sorafenib used in the two groups (P=0.49>0.05).

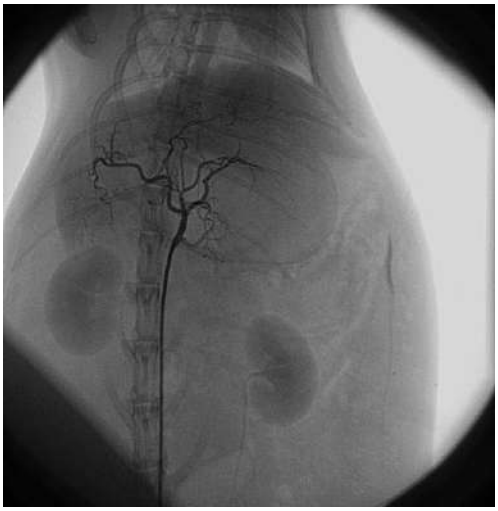

Figure 3. Rabbit celiac angiography

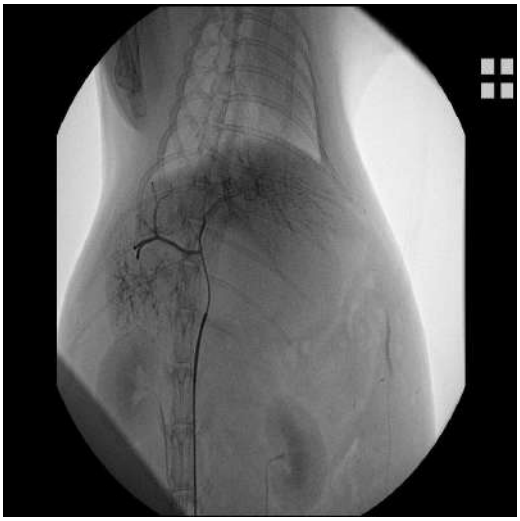

Figure 4. Iodine oil deposition after hepatic artery embolization

④ The catheter and catheter sheath were removed after operation, the right femoral artery was ligated, and the skin was sutured. After the operation, music injection of gentamicin of 20,000 units/Kg was performed for 3 days.

(3) Collection of specimens: Blood samples were collected from experimental animals at 0 hours (before administration) and 10 minutes, 20 minutes, 1 hour, 2 hours, 4 hours, 8 hours, 16 hours, 32 hours, and 48 hours after administration.

(4) Specimen detection: HPLC analysis was measured on rabbit plasma Sorafenib concentration, this part of the work was completed with assistance of the PLA General Hospital pharmacology laboratory. ① Instruments and reagents: Agilent 1200, high performance liquid chromatography. Sorafenib raw materials were provided by our laboratory; acetonitrile and methanol are chromatographically pure; triethylamine and phosphoric acid are of analytical grade. ② HPLC analysis conditions: phenomenex C18 column (5μ, 250mmmx4.6mmx5um); mobile phase: triethylamine phosphate buffer (ultra-pure water of 990ml plus triethylamine of 10ml, adjusted to pH 5.4 with phosphoric acid): acetonitrile = 50:50; flow rate : 1.0 m1/min; detection wavelength: 261 nm; column temperature: 250C. ③ Blood standard concentration determination and linear relationship test: standard solution preparation: precision weighing of 5mg of Sorafenib, placed in a 10ml volumetric flask, dissolved in 75% ethanol, the concentration of 0.5mg/ml; by pipetting from the above solution, it was precisely weighed 5 ml into a 10 ml volumetric flask and dissolved in 10 ml with 75% ethanol at a concentration of 0.25. The following three solutions were prepared in the same manner as above: 0.125 mg/ml, 0.05 mg/ml, and 0.025 mg/ml. Take the above five portions for 400 ul each.

Treatment of blood samples: centrifugation at 3000 r/min for 10 min. Take 100 ul of the supernatant, five portions each. The standard solution and the treated blood were mixed and made in a total of five parts, 500 ul each, and a methanol activated solid extraction cartridge (1x3) was equilibrated with 1 ml of water → 500 ul of the experimental serum was applied to the column, and the impurities were eluted with a 20% methanol solution → and again add 1 ml of methanol, collect the filtrate → dry naturally in a ventilated environment → dissolve the good residue with 200 ul of mobile phase (triethylamine phosphate buffer: acetonitrile = 50:50), centrifuge at 3000 r/min for 10 min → absorb 40 μl of the supernatant was subjected to HPLC analysis. The peak area (Y) was subjected to regression analysis for the corresponding content (X), Y = 0.201X + 0.0921, r = 0.9947. This equation shows that the concentration of plasma Sorafenib has a linear correlation with the peak area determined by the HPLC. The concentration of Sorafenib in the peripheral blood can be obtained from the peak area measured by the

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high-performance liquid phase, and the lowest drug concentration is 0.1 μg/ml.

(5) observation of other indexes after surgery: ① blood routine, liver and kidney functions. ② The experimental animals were sacrificed regularly (3 days, 1 week, 3 weeks, 6 weeks after operation), and the liver and kidney function indexes were taken before blooding. After the sacrifice, the experimental group and the control group were used for liver, heart and kidney diseases. The physical examination was fixed with 10% formalin, and the pathological changes were observed after paraffin sectioning.

2.2.3 Statistical Processing

Using CHISS statistical software, the measured data were expressed by x±s. The data comparison between groups was tested by group t test. When the variance between groups was not uniform or was not in line with the normal distribution, t' test was used.

3. Results

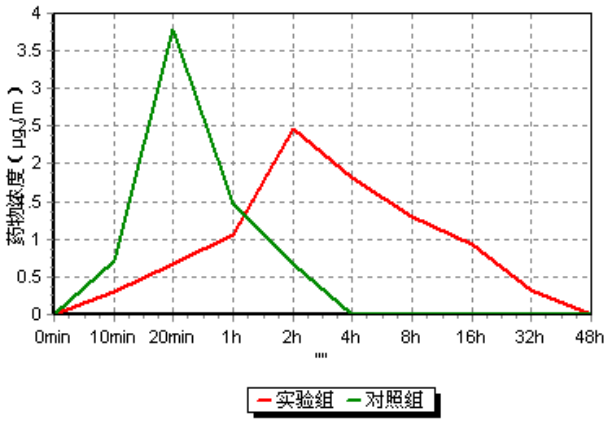
3.1 General Situation

19 survived and 5 died, including 2 in group I, 2 in group II, and 1 in group III. Pathological examinations were routinely performed after all animals died. Except for local necrosis of the liver embolization site, no clear pathological signs were found in other organs. It is considered that the inadequate experience in animal experiments or the possibility of animal intolerance in the early period. Surviving white rabbits had poor appetite, poor mental health, anorexia on the first 1-3 days after surgery, and gradually returned to normal on the 5th day after surgery. Four of the rabbits treated with III had symptoms of diarrhea in addition to the above symptoms, and the symptoms disappeared after 3 days. The other two groups did not show the above phenomenon.

Changes in the concentration of Sorafenib in the transcatheter (see Table 1): Changes in the concentration of Sorafenib of Group I (Iodine oil and Sorafenib emulsion) and Group III (pure Sorafenib group) were shown in the peripheral blood-time curve. The concentration trend of both groups decreased from high, and the concentration peaked at 2 hours after embolization in group I. After that, it decreased slowly for 32-48 hours. In group III (direct intra-arterial infusion of Sorafenib), the concentration peaked and then decreased rapidly. After 4 hours, the concentration of the bleeding drug could not be measured again. Group I (lipid-Sorafenib emulsion group) Cmax (maximum drug concentration, 2.46 μg/mL ± 0.101), AUC (area under the curve of drug time, 945.72 μg/mL.min ± 0.223) and Cmax of Group III (3.78 μg /mL). There was a statistically significant difference ($p<0.05$) between ±0.180) and AUC (546.98 μg/mL.min±21.1).

Table 1. Changes in Sorafenib Time – Blood Drug Concentration after administration in other ways than different than that of Group III (μg/ ml , x ±s)

Group	0 min	10 min	20 min	1h	2h	4h	8h	16h	32h	48h
I	0	0.30± 0.013	0.67± 0.022	1.06± 0.107	2.46± 0.101	1.82± 0.092	1.30± 0.211	0.93± 0.041	0.33± 0.01	0
III	0	0.72± 0.022	3.78± 0.180	1.48± 0.030	0.68± 0.100	0	0	0	0	0



实验组、对照组不同时间点外周血索拉非尼的药－时曲线图

Table 2. Changes in the liver and kidney function indexes before invention operation of the experiment and control groups

Index	Group	Pre-operation	Day 3	Week 1	Week 3	Week 6
ALT (U/L)	I	139.2±27.0	345.2±21.0	133.2±31.0	133.2±29.0	135.7±29.0
	II	140.2±35.7	398.2±40.7	143.2±38.6	139.2±33.2	144.3±36.7
AST (U/L)	I	83.7±35.9	254.7±25.4	86.3±40.9	82.8±32.2	83.4±34.8
	II	85.6±28.0	283.6±27.4	87.2±30.0	85.6±29.1	84.2±26.6
DB (umol/ L)	I	4.6±0.3	4.6±0.2	4.4±0.4	4.5±0.68	4.5±0.6
	II	4.0±0.9	4.1±0.8	3.9±1.0	3.9±0.9	4.1±0.9
ALB (g/L)	I	52.3±3.4	52.8±3.5	53.3±3.0	52.9±3.0	52.6±3.1
	II	50.1±2.9	49.8±1.9	50.3±1.9	51.0±7.6	51.1±8.5
Cr (umol/ L)	I	131.6±12.1	138.4±18.1	133.6±14.2	129.3±8.1	130.6±13.1
	II	140.5±10.7	141.5±20.4	140.3±10.8	141.0±8.4	141.5±23.7
BUN (mmol/ L)	I	10.0±1.3	9.8±1.2	9.6±3.3	10.3±1.6	10.5±1.8
	II	10.8±0.5	10.3±0.2	10.4±0.1	11.0±0.7	11.1±3.0
WBC (10^9/L)	I	4.1±0.9	5.0±0.9	4.0±0.9	4.2±0.1	4.2±0.2
	II	3.3±1.2	4.4±1.2	3.3±1.1	3.4±0.2	3.3±1.4
NEU%	I	39.5±9.4	57.8±9.2	38.5±8.3	38.8±10.3	39.7±8.4
	II	46±10.4	66±9.4	48±10.3	46±9.6	47±8.9
RBC (10^{12}/L)	I	2.3±0.3	2.2±0.8	2.2±0.9	2.3±0.7	2.3±0.9
	II	2.1±0.4	2.0±0.9	2.1±0.8	2.2±0.1	2.1±0.3
PLT (10^9/L)	I	270.2±33.2	269.2±30.2	272.2±34.5	274.2±40.3	269.1±28.2
	II	244.7±28.1	243.8±19.2	243.6±27.6	246.7±30.1	245.1±31.2

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The blood routine, liver and kidney function changes of the three groups of experimental animals before and after operation were shown in the table 2. The AST/ALT levels were significantly increased in the groups I and II 3 days after intervention operation ($p=0.02<0.05$), and the II group continued to recover 1 week after intervention ($p=0.24>0.05$). In group III (Sorafenib perfusion group only), there was no significant change in blood ALT/AST compared with the 3 days after intervention operation. There was no significant change in direct bilirubin between the experiment and control groups ($p=0.35>0.05$).

Pathological changes: (1) changes in liver tissues: liver tissue 3 days after intervention operation of Groups I, II, and 1 week after embolization were focally necrotic to varying degrees, showing hemorrhagic and coagulative necrosis, and the local liver structure completely disappeared (Figure 5, 6). Microscopically, there was no significant difference between the two groups in the extent of necrosis and necrosis. Three weeks after interventional embolization, the localized granulation tissue regeneration was observed in the embolized areas of group I and II. There were macrophage reaction of foreign bodies and neovascularization of capillaries, bile ducts and hepatocytes. Local fibrosis appeared after 6 weeks. Hyperplastic bile ducts, blood vessels, hepatocytes and fibrous tissues showed no manifestations of bile duct necrosis and cholestatic (Figure 7). In group III, there was no significant change in liver tissue after treatment. There was no abnormality in the structure of liver tissue in the unembedded area of the three groups. The central vein, bile duct, hepatocytes and micro-arteries were arranged normally. (2) The histopathological examination of the three groups of heart, kidney, lung, brain, intestine, gallbladder, etc. with no abnormal findings (Figure 8,9,10).

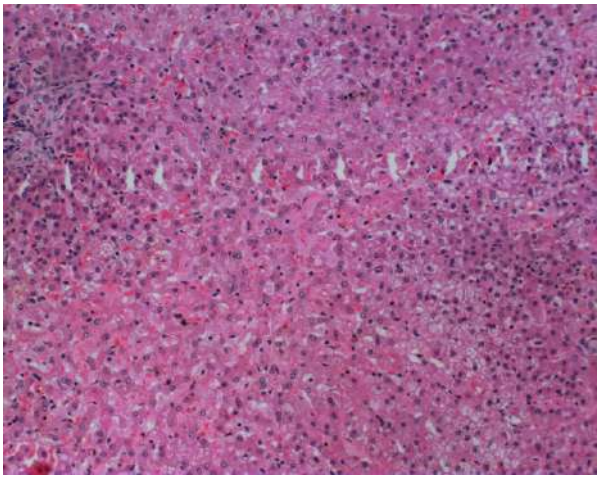

Figure 5. (x40): Normal liver

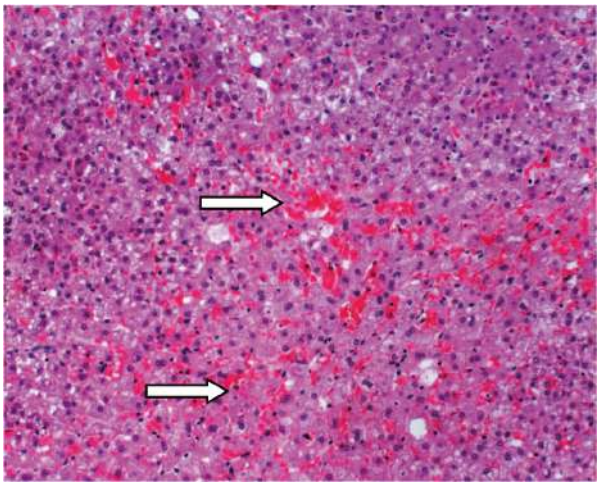

Figure 6. liver tissue (x40) 1 week after embolization: hemorrhagic necrosis, local hepatocyte necrosis surrounding the normal liver tissue (→)

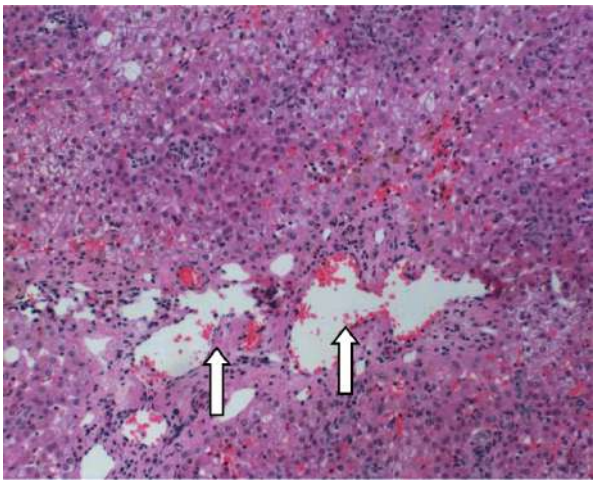

Figure 7. Liver tissue 3 weeks after embolization (x40 times): Local necrotic tissue and granulation tissue formation, visible hyperplastic vessels (↑).

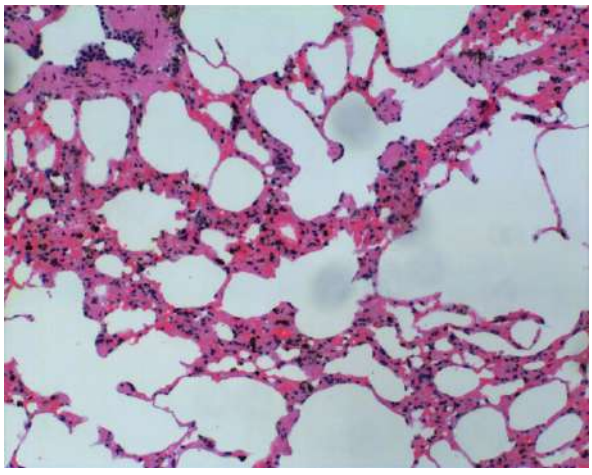

Figure 8. lung tissue, no abnormal manifestations

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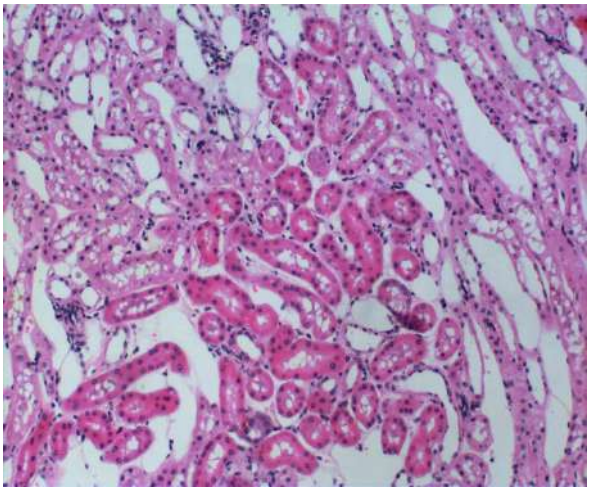

Figure 9. kidney tissues (x40), no abnormal manifestations

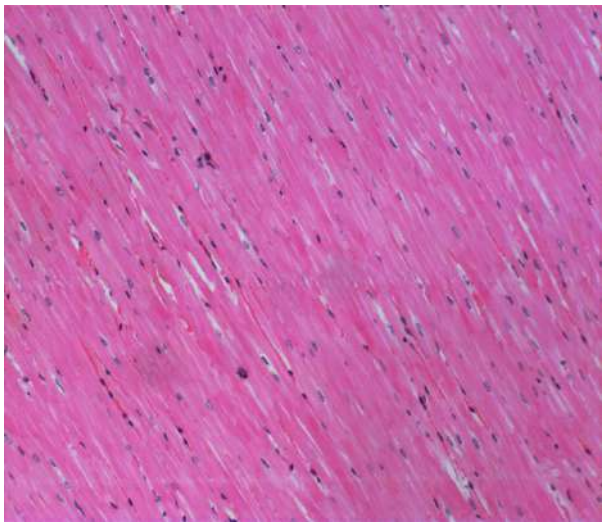

Figure 10. cardiac muscle tissue (x40): no abnormal manifestations

4. Discussion

TACE is currently one of the first measures to treat unresectable primary liver cancer. The principle of treatment is to completely inactivate the tumor through the synergistic effect of chemotherapy and embolization, and residual tumor recurrence and metastasis are one of the important factors affecting the long-term efficacy. Tumor recurrence and metastasis are associated with angiogenic factors such as VRGF and are the initiators of tumor recurrence and metastasis [1-5]. The emergence of molecular targeted agents provides a new means to control tumor recurrence and metastasis. Sorafenib is a multi-target multi-kinase inhibitor of the Raf/MEK/ERK signaling pathway that inhibits tumor growth and angiogenesis. Clinical studies have demonstrated that combined TACE and oral molecular targeted therapy can inhibit tumor growth and tumor angiogenesis. Our clinical application found that for long-term oral administration of Sorafenib in patients with primary liver cancer, angiography showed that the diameter of the hepatic artery was significantly thinner than that before administration. The above performance is related to the effect of Sorafenib on normal tissues. Therefore, the high selectivity of Sorafenib's target of action is relative. The TACE combined with local transcatheter delivery of the molecular targeted preparation not only makes the target of the targeted drug more selective, achieves the purpose of precise guidance, improves the tumor suppressing ability, but also reduces or avoids side effects caused by oral administration. In addition, the use of local intra-arterial delivery of Sorafenib also has the advantage of fully improving the bioavailability of Sorafenib. The bioavailability of conventional oral Sorafenib tablets is only 38-49%.

At present, domestic and foreign scholars have carried out beneficial explorations on TACE combined with molecular targeted drug therapy for HCC, laying a foundation for its clinical application[15~18]. The basic research on angiostatin gene fragments was performed by localized delivery of recombinant human endostatin injection (Endostar), fumagillin derivative (TNP-470), reaction stop (thalidomide) and other tumor angiogenesis inhibitors and angiogenesis by interventional techniques. Preliminary results showed that compared with the TACE group, the expression of VEGF, local tumor volume, VEGF and MVD around the tumor was significantly lower in the TACE combined with the local targeted drug group than in the control group. The combination therapy was more than a single technique. Significant inhibition of tumor growth. Foreign scholar Maataoui et al found that in animal models of liver cancer, TACE combined immunotherapy (OK-32) and anti-angiogenic therapy (TNP-470) can significantly delay tumor growth compared with TACE treatment alone but the combined anti-angiogenesis treatment effect is more significant. Antoine et al first performed percutaneous local radiofrequency ablation combined with oral multi-targeted drug Sorafenib in the treatment of renal cell carcinoma in mice. The results showed that the tumor tissue micro vessel density (MVD) was significantly reduced in the treatment group compared with the control group. Our experimental studies found that the side effects of the experimental animals after embolization with iodized oil-Sorafenib emulsion (group I) were not significantly different from those of simple iodized oil embolization (control group), and Sorafenib was directly perfused through the trans arterial artery. After (III), the side reaction was mild. In the control group, 4 of the experimental animals were

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directly perfused with Sorafenib, and there were 4 cases of recent diarrhea and other discomforts. Considering the relative sustained release of Sorafenib with iodized oil as a carrier, our pharmacokinetics was further verified. Our hypothesis is that the peak of drug concentration is reached in 20 minutes when Sorafenib is perfused alone, and the peak is reached 3 hours after intervention with lipiodol as a carrier, and there is a significant difference between the peak concentration and AUC. We consider the high drug concentration results in the production of Sorafenib toxicity.

Both combined TACE and transcatheter arterial delivery of Sorafenib formulations can exert synergistic anti-tumor effects [19-23]. There is synergy between anti-tumor and tumor angiogenesis between commonly used chemotherapeutic drugs and molecularly targeted drugs in TACE. Recent studies have shown that molecularly targeted drugs (such as endostatin, bevacizumab, Sorafenib, etc.) and chemotherapeutic drugs (such as doxorubicin, cisplatin, gemcitabine, etc.) have a certain synergy, providing basic theoretical support for its joint application. Therefore, the combination of previous academic and clinical research and our recent animal studies have shown that TACE combined with the local delivery of Sorafenib in the hepatic artery is operative and feasible. Local delivery of Sorafenib has significant advantages over systemic treatment.

The effect and deficiency of carrying Sorafenib powder with iodized oil as carrier [24-26]. Local routes of intra-arterial injection of molecularly targeted pharmaceutical agents are direct perfusion and indirect release of emulsions with lipiodol. Our studies found that the peripheral blood reached the peak concentration of the drug after 20 minutes of direct perfusion, and the concentration of the bleeding was not measured in the peripheral blood for 4 hours. The release of the iodized oil emulsion for 2 hours showed a peak drug concentration, and the peak value was significantly smaller than that of the direct perfusion drug, and lasted for 48 hours, indicating that the lipiodol emulsion can be used as a drug carrier to continuously release the molecular targeted agent, thereby continuing to inhibit tumor growth and angiogenesis. Compared with the literature reports, we used Solafenib and lipiodol as embolization of the hepatic artery to release the drug for a long time. Our analysis may be related to the dense emulsification of Sorafenib and lipiodol, both of which are insoluble in water, and can be formed more stable. Related to the emulsion. However, there are certain deficiencies in the use of lipiodol as a carrier. We found in the experiment that compared with the arterial infusion of Sorafenib, although the experimental group of lipiodol-Sorafenib emulsion can be relatively slow release after hepatic artery embolization, the drug concentration was not detected on the third day after the intervention, and the concentration of the drug at different times during the process of releasing showed some volatility. Our analysis may be related to the following factors: ① Iodine oil is a liquid terminal embolic agent, so its clearance is affected by high dynamic hepatic artery blood flow. In Kan et al., in the experiment of living arterial liver tumor, the arteriovenous shunt of ultra-liquefied lipiodol was observed under microscope, that is, the super-liquefied lipiodol was shunted to the small portal vein before entering the tumor vascular bed, and then the high-pressure hepatic artery blood flow was cleared up. Therefore, in order to prevent this from happening, it is often used to block arterial blood flow by combining other embolic substances, prolonging the time when the drug and super-liquefied lipiodol are cleared, super-liquefied lipiodol with chemotherapy drugs, embolization of portal vein, absorbable gelatin sponge Or polyvinyl alcohol embolization of the hepatic artery, this method is called "sandwich" therapy. The "sandwich" method is adopted to significantly increase the rate of tumor necrosis. We did not use the above embolic material in the experiment that is normal liver tissue, so its release rate should be significantly increased; ② Different from the liver tumor tissue structure, there are Kupffer cells in the normal liver, which enhances the clearance rate of lipiodol. The tumor tissue is unique. There is no Kufu's cell in the tumor tissue, and the microvascular basement membrane is incomplete in the tumor. It consists only of a single layer of endothelial cells and a sheath lacking an elastic membrane. The blood vessels are fragile and easily broken with high permeability, and it is lacked of neurological conditions, enabling iodized oil and Sorafenib emulsion easier to enter into tumor tissues; ③ iodized oil itself as a carrier has instability and uncontrollable drug release. The main reason is that lipiodol as a carrier releases the drug through passive release rather than active release, so its release rate is first affected by various factors such as blood flow velocity. TACE combined with transcatheter arterial infusion of Sorafenib is safe. After interventional operative observation, it was found that there were different degrees of anorexia and other discomforts in the surviving rabbits. It is important to pay attention to that in 4 cases in the Sorafenib perfusion group alone, symptoms of diarrhea occurred for 3 days. However, there was no diarrhea in the iodized oil Sorafenib emulsion group and the simple lipiodol embolization group. We speculated that it may be related to the local perfusion of high concentration Sorafenib. Compared with preoperative, the basic physiological indexes of each group returned to normal

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one week after intervention. In the Surafenib emulsion group and the simple lipiodol group, the percentage of routine white blood cells and neutrality increased after 3 days, but the Sorafenib perfusion group did not change much, considering the post-embolization response. Regarding the effect of Sorafenib on liver function. The study showed that there was a transient increase in ALT/AST between the Sorafenib lipiodol emulsion group and the simple lipiodol group. There was a statistically significant difference between the two groups (P=0.002 <0.05). There was no significant difference in ALT/AST between the two groups (P=0.13>0.05). The ALT/AST was normal after intervention in the Sorafenib infusion group. There was no significant difference compared with preoperative. (P = 0.2 > 0.05). Five days after intervention, the ALT/AST of the simple lipiodol group returned to normal, and the ALT/AST of the Sorafenib lipiodol emulsion group was still at a high level, and the two were statistically different (P=0.04<0.05). This shows that the elevation of transaminase after liver intervention is related to the lipiodol used in the intervention, but not related to Sorafenib, but Sorafenib has a certain effect on the recovery of liver transaminase. Our analysis may be related to the characteristics of Sorafenib: ① Unlike chemotherapeutic drugs, Sorafenib is a molecularly targeted preparation with high target selectivity and does not directly cytotoxic to normal tissues, so it carries Sorafenib's lipiodol. It does not aggravate the toxicity to normal liver; ② The slower rate of ALT/AST recovery in the Sorafenib lipiodol emulsion group may be related to the involvement of Sorafenib in inhibiting liver microvascular regeneration. The mechanism of action may be due to tissue ischemia and hypoxia-induced VEGF expression after interventional embolization, while the sustained release effect of Sorafenib inhibits microvascular regeneration of liver tissue, resulting in slower recovery of liver function. ③ Because the expression of VEGF in normal liver tissue is very low, and Sorafenib drug metabolism is fast at local perfusion (up to 30 minutes, peripheral blood cannot be detected after 2 hours), so Sorafenib has a weaker inhibitory effect. When the hepatic artery was directly perfused on a normal liver, the changes in ALT/AST were not obvious. Our pathological examination further confirmed this phenomenon, and the liver pathology was normal after local perfusion of Sorafenib group. From a long-term perspective, ALT/AST in the lipiodol Sorafenib emulsion group and the simple lipiodol group returned to the preoperative level 1 week after intervention, and the liver pathology was compared between 1, 3, 6, and 12 weeks. Ischemic necrosis was the main manifestation in 1 week. The granulation tissue began to appear in the local necrosis area at 3 weeks after operation, and the fibrous regeneration nodules appeared in 6 and 12 weeks, which showed hyperplasia of bile duct, small blood vessel and portal vein. There was no significant difference in the extent, extent, and tissue proliferation of tissue necrosis. It shows that Sorafenib has little effect on the repair of tissue necrosis after liver embolization, and may also be related to the failure of the iodized oil as a carrier to fully exert sustained release drugs, and thus play a pharmacological role, needing to be further studied.

Shortcomings of this research: (1) due to the limitations of experiment time and conditions, sufficient radiology detection cannot be made; (2) Failure of detecting VEGF expression: the relationship between the drug concentration Sorafenib and blood VEGF cannot be studied; (3) the concentration of Sorafenib in tissue cannot be determined; (4) Due to the choice of normal animal as a model, the efficacy of local percutaneous delivery of Sorafenib on tumor cannot be completely evaluated, which needs further research and evaluation of local delivery of Sorafenib preparation on tumor.

5. Conclusions

The transcatheter delivery of Sorafenib Technique liver artery has high feasibility and safety, having significant injury of important organs such as liver. Iodipin-emulsified Sorafenib has certain sustained release, which can avoid adverse effect arising from transient concentration caused by perfusion. It still is affected by such factors as liver blood flow, removal of kuffer cells when released, and the sustained duration of release is still short.

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ARTICLE

Clinical Efficacy of Mixing Natural Teeth and Implant Supported Denture Sleeve

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ABSTRACT

Objective: To analyze the clinical efficacy of Mixing natural teeth and implant supported denture sleeve, and provide reference for clinical treatment. **Methods:** 46 patients with Molarless in hospital from December 2010 - December 2014 were selected, patients were randomly divided into observer group and control group, two groups of patients were designed and planted natural teeth fixed bridge and natural teeth and implants mixed support sleeve denture, regular follow patients and the surrounding alveolar bone height changes, 5-year cumulative retention rate, clinical efficiency and other indicators. **Results:** During clinical observation, patients with no obvious symptoms, the use of feel good, no loose superstructure situation. Two groups of patients were 2 cases of patients with implant loosening occurs, the amount of bone resorption annual observation group (0.22 ± 0.10) mm less than the control group (0.24 ± 0.08) mm, but no significant difference (P> 0.05), clinical observation group efficiency (100%) was significantly higher (72.3%) (P <0.05), the observation group study implants 5-year cumulative retention rate was 94.4%. **Conclusion:** Mixing natural teeth and implant - supported telescopic denture success rate of 100% was observed during the clinical results were satisfactory, with use value.

1. Introduction

At present, the research on the restoration of the natural tooth-implant combined support is controversial, and the focus of the controversy is that the biomechanical properties of the two are different. The three-dimensional finite element test shows that it is feasible to use a reasonable design for the joint support scheme as long as the resultant force can be evenly distributed on the abutment[1], however, such dentures often have excessive loosening, absorption of the alveolar bone of the implant, and the like. The sleeve crown retainer consists of an inner crown and an outer crown. The force of the abutment between the inner and outer crowns is used to cushion the abutment, and the denture is well retained and stabilized, such telescopic dentures are often used for fixed-to-active joint repair of most missing teeth and a few residual teeth, which can protect the remaining teeth and the surrounding supporting tissues, which can also reduce the stress on the restoration and help to maintain the health of the abutment and its surrounding tissues in isolated orthodontic patients. In this study, the cushioned

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telescopic crown was used as the upper structural retainer of the implant in the natural dental-implant-supported restoration. The aim is to explore whether the clinical efficacy of placing the telescopic crown on the implant is superior to that of the natural dental-implant combined support prosthesis and can be widely used in oral clinical practice. The patients who have undergone dentition defect in our hospital are the subjects of the study. The report is as follows:

2. Data and Methods

2.1 Case Selection

46 patients with dentition defects of the mandibular molars who were admitted to our hospital from January 2010 to December 2014 were selected as subjects. Patients with good general condition, no systemic disease, implant surgery, good compliance, and missing molars were required to be divided into observation group and control group, respectively. There were 15 males and 8 females in the observation group, aged 58-76 years, with an average of (70.3±5.6) years old; there were 14 males and 9 females in the control group, aged 60-78 years, with an average of (71.6±6.0) years old. The general data of the two groups were comparable (P>0.05).

Table 1. Case selection

Group	Observation Group	Control Group	P
Gender (male/female)	15/8	14/9	0.7600
Age	70.3±5.6	71.6±6.0	0.0603

2.2 Experimental Materials

There were 36 implants in the observation group and 38 implants in the control group. The materials and instruments used in the observation group mainly include: strauymann implant (4mm in diameter, 10mm in length), abutment, cobalt-chromium alloy, zirconia, pure titanium inner crown, cobalt-chromium alloy, gold deposit, pure titanium sleeve crown, cobalt-chromium alloy, pure titanium bracket, metal baked crown, dental CT, digital imaging machine, etc. The control group was fixed with conventional fixed bridge. The main instruments included strauymann implant (4mm in diameter, 10mm in length), abutment, cobalt-chromium alloy, pure titanium porcelain crown, zirconia crown, dental CT, digital imaging machine, etc.

2.3 Experimental Methods

The patients in the observation group and the control group were routinely prepared for natural teeth, and the implants in the edentulous region were routinely implanted, and the second premolar and the second molar implant were used as the abutment. In the observation group, the implant was implanted in the edentulous area, and the implant was healed without force for more than 3 months. After the healing was confirmed to be good, the upper structure was repaired, and the sleeve crown was fixed in the implant segment. The traditional tooth preparation for the natural tooth is completed, and the natural tooth and implant mixed support sleeve crown is repaired, and the patient is regularly reviewed after 3, 6 and 12 months. Healed for more than 3 months without stress, after healing, repair the upper structure and check regularly at 3, 6, and 12 months. The two groups of patients were examined for implants before repair, requiring no inflammation, looseness, healthy surrounding soft tissue, good bone healing on X-ray examination, good bone binding standard, silicone rubber modulo, fixed bridge and sleeve crown, try on, bonding.

2.4 Observation Index

Evaluate the patient's self-conscious symptoms, determine the natural tooth and implant looseness, X-ray examination after implant denture repair, determine the actual bone resorption (Measure the distance of bone resorption with ODIS image analysis software and eliminate the magnification of X-ray film by mathematical calculation).

2.5 Clinical Efficacy Evaluation

The clinical efficacy evaluation is divided into three grades. The natural abutment has no gingival hemorrhage, periodontal pocket, and X-ray without alveolar bone resorption. The patient's subjective feeling is good and does not affect chewing. The natural gums have no redness and no periodontal pockets. The X-ray shows that the implant's gingival bone absorption is less than 2mm. It is effective that the patient's subjective feeling is good but can't chew hard food, and it is ineffective to loosen the implant or absorb the natural alveolar bone more than 2mm, clinical efficiency = marked effective rate + effective rate.

2.6 Statistical Analysis

Using SPSS19.0 statistical software, the bone resorption amount accorded with the normal distribution using t test, the clinical evaluation and the cumulative retention rate were tested by x2 test, and the difference between groups was significantly indicated by P<0.05.

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3. Results

3.1 Patient Satisfaction Survey and Clinical Examination

Through the form of questionnaire survey, the patients were included in the clinical observation period, including chewing efficacy, comfort and aesthetics. The results were divided into dissatisfaction, general satisfaction and satisfaction. Perform a systematic clinical examination of the patient, including the alveolar ridge and mucosa of the dentition-deficient area, whether the implant is loose and the absorption of the surrounding alveolar bone, the periodontal and periodontal tissue of the natural abutment, the retention and stability of the denture.

3.2 Annual Average Bone Resorption of Implants

There were 2 cases of implant loosening in the two groups. The other cases showed no obvious bone resorption and good function. The average annual bone resorption of the observation group was smaller than that of the control group, but the difference was not obvious (P>0.05). See Table 2 for details.

Table 2. Comparison implant bone loss annually

Group	Implants	Bone Resorption(mm)
Observation Group	36	0.22±0.10
Control Group	38	0.24±0.08
P		0.4579

3.3 Comparison of Clinical Evaluation

All patients were successfully followed up for more than 5 years. The clinical effective rate of the observation group was significantly higher than that of the control group (P<0.05). See Table 3 for details.

Table 3. Clinical Efficacy Evaluation

Group	Excellent	Effective	Ineffective	Total efficiency (%)
Observation Group (n=36)	29(80.6)	7(19.4)	0	100
Control Group (n=38)	18(47.4)	11(28.9)	9(23.7)	72.3
P				0.0018

4. Discussion

There are many methods for planting and repairing. In the clinical, especially after the treatment of missing teeth, sometimes the use of natural tooth and implant combined support denture repair program is considered. For example, under certain clinical research conditions, such as patients with insufficient bone loss in the posterior teeth or due to the economic factors of the patient, or implants with short implants, the prognosis is not good; therefore, it is of great practical significance to study the fixed restoration method of natural tooth-tooth implant support[2,3].

The combination of natural teeth and implants can avoid areas with poor planting conditions and alleviate patient suffering. It is a relatively simple method of planting and repairing clinical operations. Many scholars believe that the joint support of fixed repair can make full use of the feedback regulation of natural periodontal ligament[4], to reduce trauma. Initial research suggests that the support of natural teeth and implants will affect the soft and hard tissues of natural abutments, and it is prone to the loss or breakage of the prosthesis. In recent years, it has been found that combined with the joint-supported fixed repair, the natural tooth can play a proprioceptor role, improve the sensibility, and at the same time, can also use the periodontal reserve capacity of the natural tooth to avoid the bite force and lead to the wound.

There are some differences in the mechanical properties of implants and alveolar bones in the design of joint support and restoration of implants, including rigid joints and non-rigid joints. In theory, it is considered that the use of a non-hard connection method can reduce the difference in physiological mobility between the two. Some scholars have designed the IMZ planting system to make the implants have physiological kinetics similar to those of natural teeth, meeting the requirements of uniform stress distribution. Domestic scholar Yina Lin [5] and other researches have pointed out that there is no significant difference in bone resorption between different combinations, and there is no significant difference in stress size and distribution. More and more studies have pointed out that the rigid connection between implants and natural teeth is a more feasible method of repair[6], in this group of studies, the natural tooth and implant mixed support socket denture rigid connection was used, and the connection was rigidly connected. The sleeve crown is composed of an outer crown and an inner crown, and the gap between them can buffer the stress on the abutment. In this study, the design of the sleeve retainer in the anterior segment of the implant, buffering the stress level of the implant, can improve the different support bone histological responses between the two, and reduce the possible damage of the supporting tissue [7]. At present, there are many researches on the joint restoration of natural teeth and implants in China. Most of them focus on the analysis of finite element models, and analyze the stress distribution of supporting tissues and teeth. Guangping Xie [8] and other studies have analyzed the stress analysis of nat-

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ural tooth and implant combined support sleeve crown, and found that there is no significant difference in stress values between vertical distribution and lateral distribution, and the effect of natural dental bone tissue is not obvious. The opposite is true for cushioned sleeve crowns, the soft tissue covered by the alveolar ridge can share the partial load to reduce the burden on the implant, suggesting that measures such as expanding the base area and reducing the length of the free end should be taken during the clinical design to prevent the alveolar ridge from being overstressed. During the clinical observation period, the patients had no obvious discomfort, and felt good when used, and the upper structure was not loose. Two groups of patients had implant loosening in 2 cases. The annual average bone resorption capacity of the observation group (0.22±0.10) mm was smaller than that of the control group (0.24±0.08) mm, but the difference was not obvious ($P>0.05$); the clinical effective rate (100%) of the observation group was significantly higher than that of the control group (72.3%) ($P<0.05$). The cumulative retention rate of the implants in the observation group reached 94.4%. It can be seen that in a short period of time, the success rate of the support of the natural tooth and implant mixed support denture is 100%, which is feasible in the short term. For the long-term efficacy, it is necessary to extend the follow-up time for further observation. Natural tooth and implant mixed support telescopic denture need to pay attention to the coordination of bite force conduction, reduce the lateral stress on the implant; the bite force needs to be restored within the physiological range, reduce the span of the bridge, and reduce the buccal diameter of the restoration, the stress on the upper restoration should not exceed the baseline, and the implant should be of sufficient length to be reviewed periodically after repair. When the implants are in different orientations, adjust the position in time to avoid improper stress. The implant surface should be highly polished to avoid plaque adhesion. Natural teeth are preferably healthy teeth. Patients should be reviewed at least once every six months to remove plaque and maintain the health of soft and hard tissues.

5. Conclusion

At present, there is still much controversy about the support of fixed bridges supported by natural teeth and implants. In this study, it can be seen that the success rate of natural tooth and implant mixed support telescopic dentures is 100%, the effect is obvious, and it has useful value.

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ARTICLE

Therapeutic Effect Observation of Tiotropium Bromide in the Treatment of Overlap Syndrome

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ABSTRACT

Objective: To study the M receptor blocker on inhalation in patients with overlap syndrome (chronic obstructive pulmonary disease and Obstructive sleep apnea syndrome) curative effect analysis. **Methods:** 25 patients with overlap syndrome as the experimental group, chronic obstructive pulmonary disease patients (30) as control group, patients with overlap syndrome use inhaled tiotropium powder treat 30 days, to observe the changes of pulmonary function, polysomnography, and other indicators after treatment. **Results:** Overlap syndrome were treated by tiotropium bromide inhalation powder, has improved the pulmonary function, the sleep apnea index and lowest nocturnal oxygen saturation after treatment. **Conclusion:** tiotropium bromide has a preferable effective in treatment of overlap syndrome, COPD and OSAHS are interacting with each other.

1. Introduction

"Overlap syndrome (OS)" refers to patients with chronic obstructive pulmonary disease (referred to as COPD) with obstructive sleep apnea hypopnea syndrome (OSAHS). Patients with OSAHS have recurrent apnea and hypopnea during sleep, leading to hypoxemia. Patients with COPD have persistent airflow limitation and hypoxemia for a long time, which causes more severe hypoxia in OS patients. The coexistence of the two aggravates the patient's condition, and is more likely to cause increased risk of hospitalization and mortality due to risk factors such as respiratory failure, heart failure, and arrhythmia.

Experiment with the pharmacological effects and effects of anticholinergic drugs (tiotropium bromide), and treat patients with OS with tiotropium bromide powder inhaler. The changes of lung function, AHI index and nocturnal minimum oxygen saturation (SaO2) in OS patients before and after treatment were observed. The efficacy of inhaled tiotropium bromide powder inhalation in OS patients was analyzed.

2. Materials and Methods

2.1 Research Objects

30 patients with chronic obstructive pulmonary disease and 25 patients with OS were enrolled from 2016 to 2018. Patients with COPD were in clinical remission.

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There were no significant differences in gender, age and height between the study groups (P>0.05). In the past two months, there was no acute exacerbation. In the past month, no history of taking psychotropic drugs and inhaling corticosteroids and β-agonists was used. There was no history of drinking in the week before the experiment. The included study population excluded tonsil enlargement, thoracic deformity, and other respiratory diseases such as pulmonary infection, bronchial asthma, and pulmonary interstitial fibrosis.

2.2 Research Methods

Night polysomnography and pulmonary function tests were performed in the chronic obstructive pulmonary disease patients included in the study. The results were grouped according to the results of FEV1/FVC in pulmonary function and apnea hypopnea index (AHI) in polysomnography, as follows:

1. COPD group (30 cases): FEV1/FVC <70%, AHI<5 times/h, and chronic obstructive pulmonary disease group as control group.

2. OS group (25 cases): FEV1/FVC <70%, AHI>5 times/h.

For patients with OS, a 30-day treatment with tiotropium sulphate powder inhalation, 1 inhalation, 1 inhalation per morning, 1 day after treatment, 30 days after treatment, return to hospital for nighttime sleep monitoring and pulmonary function tests. The changes of AHI, night minimum SaO2, FEV1%, FEV1/FVC and other related indicators were observed before and after treatment.

2.3 Statistical Methods

Statistical methods Statistical analysis was performed using the SPSS 19.0 statistical software package. The t test was used between the two sample means. The difference was statistically significant when the test standard P < 0.05.

Table 1. Comparison of pre-treatment data between OS group and chronic obstructive pulmonary disease group (* P<0.05)

Group	n	Minimum night SaO2 (%)	FEV1% (%)	FEV1/FVC (%)
COPD group	30	90.82±4.23	60.34±7.52	62.53±4.24
OS group	25	64.74±4.72*	56.34±5.86*	60.54±3.36

Table 2. Comparison of sleep monitoring and lung function data after OS treatment in OS group

OS group	AHI (times/h)	Minimum night SaO2 (%)	FEV1% (%)	FEV1/FVC (%)
Before treatment	27.30±7.32	64.74±4.72	56.34±5.86	60.54±3.36
After treatment	25.53±7.58	68.26±5.85	59.65±6.41	62.24±4.23
t value	3.68	5.805	6.341	1.672
p value	0.003	0	0	0.105

3. Discussion

Overlap syndrome (OS) is involved in multiple systems and is a generic term for two different diseases in the same discipline. In respiratory medicine, OS refers to patients with both chronic obstructive pulmonary disease and OSAHS. According to foreign research statistics, the overall population prevalence of OS is 0.5%[1], and the prevalence rate in males is 1%[2]. Airway stenosis in patients with chronic obstructive pulmonary disease occurs in the lower respiratory tract, especially in the bronchioles and distal end, and hypoxemia occurs after the airflow limitation is gradually aggravated; the airway stenosis in patients with OSAHS is the upper airway, intermittent apnea and hypopnea during sleep, characterized by intermittent hypoxemia. Although the two diseases have different pathogenesis, there are many similarities between the adverse consequences and the impact on the body, which result in OS patients with concurrent disease with more severe hypoxemia and ventilatory dysfunction, and the two diseases can interact at multiple levels: Patients with chronic obstructive pulmonary disease are susceptible to upper respiratory tract infection, and the upper airway obstruction is aggravated when infected; smoking can aggravate upper airway collapse and promote the increase of OSAHS[3]; during sleep, the diaphragm muscle shifts upward, resulting in a decrease in functional residual capacity and supplemental expiratory volume, and patients with OSAHS often have restrictive ventilation dysfunction due to obesity, further affecting the ventilation function of the lung[4] and so on. The interaction between the two will inevitably aggravate the patient's hypoxia and sleep disorders[5].

4. Conclusion

This study looked at the efficacy of inhaled tiotropium bromide in patients with OS. Tiotropium bromide is a M1 and M3 antagonist in the respiratory tract, and the dissociation rate is significantly lower than that of the M2

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receptor when combined with the M1 and M3 receptors[6]. It has high selectivity for airway receptors, and the effect of expanding airway is continuous and powerful, reducing respiratory secretions. It is recommended for the treatment of chronic obstructive pulmonary disease in the treatment of patients with chronic obstructive pulmonary disease[7]. Tiotropium bromide also inhibits mucin secretion, anti-inflammatory, and reduces airway remodeling[8]. Chronic obstructive pulmonary disease has local and systemic inflammatory responses in the airways, as does OSAHS[9]. Both of them have pathogenic factors such as increased parasympathetic tone and oxidative stress. OS patients have improved sleep monitoring and lung function indicators after treatment, which may be related to the mechanism of action of tiotropium to improve hypoxia[10], reduce airway inflammation[11], and reduce parasympathetic tone[12]. At present, the treatment of OS is mainly oxygen therapy and non-invasive ventilation, and has achieved good results[13]. However, there is still no clinical guidance for the drug treatment of OS. The current research is mainly based on ICS+LABA, which provides a new idea for clinical drug treatment of OS patients. At the same time, clinicians should pay attention to the diagnosis and treatment of OS, and timely treatment and rehabilitation guidance for OS patients.

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ARTICLE

Therapeutic Effect of Common Goldenrop Decoction Combined With Ramuli Cinnamomi Decoction in the Treatment of Patients with Insomnia during the Period of the Day from 11 PM to 3 AM

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ABSTRACT

Objective: To observe the clinical efficacy of common goldenrop decoction combined with ramuli cinnamomi decoction in the treatment of patients with insomnia during the period of the day from 11 PM to 3 AM. **Methods:** 80 patients with insomnia during the period of the day from 11 PM to 3 AM were randomly divided into control group and intervention group. The control group was treated with 1 mg of estazolam tablets at 9 PM every night; while the intervention group was given common goldenrop decoction combined with ramuli cinnamomi decoction based on the estazolam tablets. After 2 weeks of treatment and after 2 weeks of withdrawal, the improvement in sleep was observed. **Results:** After 2 weeks of treatment, the efficacy of the intervention group (97.5%) was significantly higher than that of the control group (75.0%). The difference was statistically significant. After 2 weeks of withdrawal, the intervention group still had an effective rate of 87.5%, which was significantly higher than that of the control group (55.0%). **Conclusion:** common goldenrop decoction combined with ramuli cinnamomi decoction can improve the short-term and long-term sleep quality of patients with insomnia during the period of the day from 11 PM to 3 AM.

1. Introduction

Sleeplessness, Traditional Chinese Medicine called "insomnia", patients in less severe cases fall asleep with difficulty, and even if fall asleep, they are easy to wake up, cannot fall asleep again after waking up, and sometimes fall asleep sometimes wake up; patients in severe cases cannot fall asleep all night. During the period of the day from 11 PM to 3 AM, the human body is in the charge of liver meridian and gallbladder meridian. It is found clinically that some patients are easy to wake up during the period of the day from 11 PM to 3 AM, and it is not easy for them to fall asleep again after waking up. In recent years, the author team draws on the experience of the predecessors, and actively summarizes the clinical experience, using common goldenrop decoction combined with ramuli cinnamomi decoction to treat this type of insomnia patients, found that there is a curative effect, summarized as follows:

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2. Materials and Methods

2.1 General Information

80 outpatients and inpatients during the period from January 2017 to July 2018 in the department of encephalopathy in our hospital were selected. These patients meet the characteristics that when fall asleep, they are easy to wake up, cannot fall asleep again after waking up. Randomized digital table method was divided into control group and intervention group, 40 cases in each group, the course of disease was half a year to 5 years. The control group was 29-75 years old with an average of (42.21±2.23) years old; the intervention group was 29-74 years old with an average of (42.67±2.21) years old. There was no significant difference in the general age and duration of the two groups (P>0.05), which was comparable.

2.2 Case Selection Criteria

2.2.1 Diagnostic Criteria

Western medicine diagnosis refers to the diagnostic criteria for "sleeplessness" in the "Chinese Classification and Diagnostic Criteria for Mental Disorders".[1] The diagnosis of TCM (Traditional Chinese Medicine) refers to the diagnostic criteria and dialectical criteria of "insomnia" in the "Diagnostic and Efficacy Standards for TCM Syndrome" of the State Administration of TCM.[2]

2.2.2 Inclusion Criteria

In line with the above-mentioned Western and Chinese diagnostic criteria, The patients who are easy to wake up and cannot fall asleep again after waking up during the period of the day from 11 PM to 3 AM, aged 18-75, were chosen and the informed consents were signed.

2.2.3 Elimination Criteria

Exclude secondary sleeplessness caused by other physical illnesses or mental disorders; and exclude the use of anti-anxiety, depression, psychotropic drugs, such as lorazepam tablets, deanxit, serotonin reuptake inhibitors and other drugs.

2.3 Methods

2.3.1 Therapeutic Method

The patients in the control group were treated with estazolam tablets (Beijing Yimin Pharmaceutical Co., Ltd., State Food and Drug Administration Approval No.: H11020891), 1 mg each time, orally at 9 PM every night for 2 weeks. The intervention group was given common goldenrop decoction combined with ramuli cinnamomi decoction based on the estazolam tablets. The prescription is as follows: Bupleurum sinenses DC. 12g, Scutellaria baicalensis 10g, Codonopsis pilosula 10g, Pinellia ternate 9g, Licorice 9g, Ginger 6g, Jujubae 10g, Cassia twig 10g, Paeonia lactiflora pall 15g, one dose per day, decoction 2 times, morning and evening, also taken orally for 2 weeks.

2.3.2 Observation Method

The improvement in sleep was observed after 2 weeks of treatment and after 2 weeks of withdrawal.

2.4 Efficacy Judgment Criteria

Adopt the sleeplessness efficacy judgment criteria in "Guidelines for Clinical Research of New Drugs in Traditional Chinese".[3] Recovery: sleeplessness disappeared, able to sleep for more than 6h, with good sleep quality, good spirits after waking up; significant effect: sleeplessness improved, sleep time increased by more than 3h, and the depth of sleep increased; valid: sleeplessness has improved, sleep time increased by less than 3h; invalid: sleeplessness has no obvious improvement or even worse.

2.5 Statistical Processing

Use SPSS18.0 software statistics, t-test (metering data) and x^2 test (counting data) were performed separately, and P<0.05 was considered as significant difference.

3. Results

3.1 Comparison of Therapeutic Effects between the Two Groups

After 2 weeks of treatment, the effective rate of the control group was 75%, and the effective rate of the intervention group was 97.5%. The difference was statistically significant (P<0.05), as shown in Table 1 below.

Table 1. Comparison of efficacy between the two groups [n (%)]

Group	Total Number of Cases (n)	Recovery (n)	Significant Effect (n)	Valid (n)	Invalid (n)	Total Effective Rate [n (%)]
Control Group	40	4	16	10	10	30 (75.0)
Intervention Group	40	6	19	14	1	39 (97.5)

3.2 Comparison of Efficacy after 2 Weeks of Withdrawal

After 2 weeks of treatment, the control group discontin-

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ued estazolam tablets; the intervention group discontinued estazolam tablets and common goldenrop decoction combined with ramuli cinnamomi decoction. After 2 weeks of withdrawal, the effective rate of the control group decreased to 55%, and the effective rate of the intervention group was 87.5%. After 2 weeks of withdrawal, the effective rate of the intervention group was significantly higher than that of the control group, suggesting that the control group is more likely to relapse, see Table 2 below.

Table 2. Comparison of efficacy after 2 weeks of withdrawal [n (%)]

Group	Total Number of Cases (n)	Recovery (n)	Significant Effect (n)	Valid (n)	Invalid (n)	Total Effective Rate [n (%)]
Control Group	40	2	11	9	18	22 (55.0)
Intervention Group	40	5	18	12	5	35 (87.5)

4. Conclusion

The normal sleep of the human body depends on the "yin and yang in equilibrium", "Miraculous Pivot·Big Confusion Theory" believes that "Defensive Qi cannot enter the Yin, often stays in the Yang. Staying in the Yang, the Yang Qi is full and then the Yang Qiao meridian is vigorous; Defensive Qi cannot enter the Yin, and the Yin Qi is deficient, and then the eyes cannot close", "The pathogenesis of insomnia is that the Yang is not intersected with the Yin". The Defensive Yang is vigorous outside; while the Nutritive Yin is deficient inside, the Defensive Yang cannot enter the Yin, thereby cause insomnia. The normal sleep depends on the normal operation of the Defensive Qi and the Nutritive Qi. The ramuli cinnamomi decoction is a famous prescription for the reconciliation of Defensive Qi and the Nutritive Qi, and it is also called the "cinnamon twig decoction", which consists of five kinds of medicines: cassia twig, peony, radix glycyrrhizae preparata (honey-fried licorice root), ginger and jujube. In the prescription, the compatibility of liquorice and peony, jujube nourish the Yin with sour and sweet to assist the Nutritive Yin, which can better moisten and nourish the viscera, making the viscera in harmony and then the insomnia is eliminated,[4] based on these theoretical foundations, many experts conditioned insomnia based on ramuli cinnamomi decoction.[5]

During the period of the day from 11 PM to 3 AM, the human body is in the charge of liver meridian and gallbladder meridian. And fall asleep during this period, "the human lies on the bed, and then the blood goes back to the liver", when the blood goes back to the liver, the liver is nourished by blood, the so called "liver being the resolute viscera, when the human body is under the Yin, use the Yang to accomplish reconciliation", when the blood in the liver is enough, the liver Qi can be in normal free coursing, thereby the Qi and the blood accomplish unobstructed flow. The gallbladder is the "viscera with decisive character", and is also the viscera with pureness, is in charge of decision making, the gallbladder and the liver are mutual outside and inside, and if the gallbladder is not cleared, the liver will not be unobstructed, thereby cause the liver Qi and gallbladder Qi in an obstructed situation, and form stagnation leading to inflammation, the gallbladder inflammation with internal disturbance on state of mind which finally cause the insomnia, and even emotional restlessness, depression and other symptoms. In addition, the Shaoyang gallbladder meridian is the pivot, is in the charge of opening and closing, when the Shaoyang gallbladder meridian opening and closing are abnormal, the Yang is not intersected with the Yin, which can also cause the insomnia. Many studies and clinical work have found that, patients with insomnia during the period of the day from 11 PM to 3 AM In addition to poor sleep, patients often have emotional symptoms, such as upset, irritability, and even anxiety and depression, in addition to poor sleep,[6] which have laid the foundation for liver and gallbladder treatment of insomnia, in summarizing Ronglin Gao's insomnia treatment experience, Zonglian Liu[7] put forward insomnia treatment from the liver meridian and gallbladder meridian. Common goldenrop decoction comes from the medical sage Zhang Zhongjing's "Treatise on Febrile Diseases" and "Synopsis of Golden Chamber", involved in many of the provisions, which is a famous prescription for harmonizing Shaoyang gallbladder meridian, widely used in clinical application. In the prescription, radix bupleuri can play the role of solving pathogenic heat and dredging meridians and Qi. Scutellaria baicalensis clears the pathogenic heat and can clear and reduce the Yang inflammation. Pinellia ternate has the effect of harmonizing the stomach, calming the adverse-rising energy, and preventing or arresting vomiting. Codonopsis pilosula can regulate the Qi and blood, licorice and jujube have the effect of benefiting the Qi and stomach.[8] Common goldenrop decoction combined with ramuli cinnamomi decoction, the two can be used together to reconcile Shaoyang gallbladder meridian and accomplish the reconciliation of Defensive Qi and the Nutritive Qi, Not specializing in the treatment of insomnia and the symptom of sleeplessness is eliminated.

Due to various pressures such as work, life, and disease, many people are now prone to abnormal emotions such as anxiety and irritability, often resulting in insomnia due to poor venting, and it is not easy for some people to

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fall asleep again after waking up during the period of the day from 11 PM to 3 AM. This part of the patient is often accompanied by mental and psychological disorders such as anxiety and depression. In patients who wake up in the middle of the night and are not easy to fall asleep again, simple sedative drugs are often ineffective. After years of clinical exploration, the author team used the experience of predecessors to apply TCM classical prescription "common goldenrop decoction combined with ramuli cinnamomi decoction" in the treatment of patients with insomnia during the period of the day from 11 PM to 3 AM., and the clinical efficacy is more precise, based on which the study was developed. The results of the study showed that the clinical efficacy (97.5%) of the common goldenrop decoction combined with ramuli cinnamomi decoction group was significantly higher than that of the simple sedation group (75.0%), the difference was statistically significant, which suggests that the common goldenrop decoction combined with ramuli cinnamomi decoction does improve the sleeping status of patients with insomnia during the period of the day from 11 PM to 3 AM. Not only that, after 2 weeks of treatment, the sedative drug and common goldenrop decoction combined with ramuli cinnamomi decoction, after another 2 weeks of observation, it was found that the simple sedation group increased the inefficiency by at least 20% (75%-55%=20%), suggesting that it is easy to relapse after stopping the drug, the quality of sleep is easily deteriorated, and the drug dependence is high. The common goldenrop decoction combined with ramuli cinnamomi decoction group increased the inefficiency by about 10% (97.5%-87.5%) after 2 weeks of withdrawal, compared with 20%, the difference is more significant, suggesting that common goldenrop decoction can not only improve the patient's recent sleep, but also improve their long-term sleep, which may be less dependent on sedative drugs.

Due to limited geographical and time, the number of cases in this study is small and non-multi-center research is a deficiency. The author hopes to further expand the number of cases and geographical scope in the future, and conduct a more in-depth research on the patients whose incommnia during the period of the day from 11 PM to 3 AM, and inherit the classics of TCM.

In a broader sense, from the perspective of TCM health, we have been promoting a healthy lifestyle of "early to bed, early to rise", falling asleep during the period of the day from 11 PM to 3 AM make the blood goes back to the liver the liver Qi can be in normal free coursing, thereby the Qi and the blood accomplish unobstructed flow, but sleeping late (after 11 PM) has become the norm for many people, especially university and college students. Not falling asleep when one should go to bed, the Yang Qi doesn't enter the Yin when it supposed to do, thereby on the next day, the yang Qi will not raise, therefore, when one should be awake, he would be sleepy. Some scholars have studied that,[6] late sleep is one of the main culprits of the depression and aggravation of many people, and now many people's sub-health status has a certain relationship with this. Chinese medicine has the theory of "treating different diseases with the same method", for many patients with emotional disorders derived from the insomnia during the period of the day from 11 PM to 3 AM, the author found that common goldenrop decoction combined with ramuli cinnamomi decoction also has a certain effect in the clinical application, looking forward to doing more research on this area.

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ARTICLE

Exploration and Discussion on the Clinical Therapeutic Effects of the Application of Cross-Injury Vertebral Fixation and Via-Injury Vertebrae Fixation in the Treatment of Bone Tumor with Thoracolumbar Spine Fracture

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ABSTRACT

Objective: To explore and discuss the clinical therapeutic effects of the application of cross-injury vertebral fixation and via-injury vertebrae fixation in the treatment of bone tumor with thoracolumbar spine fracture. **Methods:** A total of 58 patients with bone tumors and thoracolumbar spine fractures admitted to our hospital from February to February 2019 were selected as the study subjects. They were randomly divided into control group and observation group, with 29 cases in each group. The patients in the control group received cross-injury vertebral fixation treatment, while the patients in the observation group were treated with via-injury vertebral fixation. The therapeutic effects of the two groups were compared. **Results:** The operation time and hospitalization time of the observation group were significantly shorter than those of the control group (P<0.05), and the postoperative drainage volume of the intraoperative blood loss was significantly less than that of the control group (P<0.05). There was no significant difference in postoperative pain and spinal JOA scores between the two groups (P>0.05); there was no significant difference in the compression ratio of the injured vertebrae and the kyphosis Cobb angle between the two groups (P>0.05), after the operation, the two groups of patients were significantly reduced, and the compression ratio of the injured vertebrae and kyphosis Cobb angle of the observation group were more obvious (P<0.05); the vertebral height loss and Cobb angle loss in the observation group were significantly lower than those in the control group (P<0.05). **Conclusion:** In the treatment of bone tumor with thoracolumbar spine fracture, compared with cross-injury vertebral fixation, via-injury vertebral fixation has a more significant clinical effect and is more suitable for clinical application and promotion.

1. Introduction

Bone tumors and spinal fractures are clinically serious orthopedic diseases, often accompanied by symptoms such as pain, swelling and dysfunction, which greatly affect the patient's physical health and quality of life[1]. At present, the main clinical treatment of plate screw fixation is the preferred treatment for thoracolumbar spine fractures, which not only effectively promotes the reduction and fixation of the spine, but also helps patients

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with bone tumor resection to enhance the stability of their spine. It has important clinical significance for patients with bone tumor with thoracolumbar spine fracture[2-4]. However, in the treatment of thoracolumbar spine fractures, the choice of surgical approach and the determination of fixed segments have been controversial[5], Here, the application effects of cross-injury vertebral fixation and via-injury vertebral fixation in the treatment of bone tumor with thoracolumbar spine fracture were explored and discussed in this paper, reported as follows.

2. Data and Methods

2.1 Data

A total of 58 patients with bone tumor with thoracolumbar spine fracture admitted to our hospital from February to February 2019 were enrolled in this study. They were randomly divided into control group and observation group, with 29 cases in each group. In the control group, there were 19 male patients and 10 female patients; the age ranged from 25 to 58 years, with average age of (32.5 ± 2.3) years old; according to the fracture sites, 8 cases were T_{11}, 7 cases were T_{12}, 11 cases were L_1, 2 cases were L_2, and 1 case was L_3. There were 18 male patients and 11 female patients in the observation group; the age ranged from 26 to 58 years, with average age of (32.6±2.5) years old; according to the fracture site, 9 cases were T_{11}, 8 cases were T_{12}, 10 cases were L_1, 1 case was L_2, and 1 case was L_3. There was no significant difference in the comparison of the basic clinical data between the two groups, $P>0.05$.

Inclusion criteria: (1) All participating patients were clinically diagnosed by imaging examination, all patients with bone tumor with thoracolumbar spine fracture; (2) All patients underwent tumor resection in our hospital; (3) All patients voluntarily participated in the study under informed consent and signed consent forms.

Exclusion criteria: (1) Exclude patients with severe spinal cord injury and coagulopathy; (2) Exclude patients who do not meet the indications for surgery and who have no surgical contraindications; (3) Exclude patients with other major diseases and mental disorders.

2.2 Methods

All patients underwent general anesthesia and underwent surgery in the prone position. The patient's sternum stem and pelvis position are raised, and the patient's injured vertebra is set as the center from the posterior middle part of the patient, and the patient's injured part is exposed by a minimally invasive approach.

Patients in the control group underwent cross-injury vertebral fixation treatment, and pedicle screws were placed in the pedicles on both sides of the upper and lower vertebrae of the injured vertebrae. The pre-bent longitudinal link is placed and then opened to help the patient's injured vertebrae height to be restored, and the kyphosis and the like are corrected.

Patients in the observation group were treated with via-injury vertebral fixation, on the basis of postoperative follow-up of the control group, two pedicle screws were placed at the bilateral pedicle position, then the pre-bent iron rod was placed and the injured vertebra was tightened. The longitudinal side of the patient whose vertebral body endplate is seriously injured is longitudinally opened. After the height of the injured vertebra is restored, the nut on the side is tightened, and the other side can be appropriately opened according to the actual situation, finally, carefully check and fix the nut after tightening.

2.3 Observation Indexes

(1) Compare the operation and hospitalization of the two groups, including the operation time, intraoperative blood loss, postoperative drainage and hospitalization time.

(2) Compare the postoperative pain level and spinal function in the two groups. VAS and JOA scores were used to assess the degree of postoperative pain and spinal function in patients. The higher the VAS score, the lighter the patient's pain, and the higher the JOA score, the better the spine function.

(3) Compare the compression ratio and kyphosis Cobb angle of the two groups of patients before and after surgery.

(4) Observe and record the fracture recovery of the two groups of patients within six months after surgery, including the height of the vertebral body and the loss of Cobb angle.

2.4 Statistics

The data of 58 patients were all processed by statistical software (SPSS20.0). The counts and measurement data were compared and analyzed by chi-square test and t-test respectively. $P<0.05$ indicated that the comparison data was very different.

3. Results

3.1 The operation time and hospitalization time of the observation group were significantly shorter than those of the control group ($P<0.05$), and the postoperative drainage volume of the intraoperative blood loss was significantly less than that of the control group ($P<0.05$).

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Table 1. Surgery and hospitalization of the two groups of patients (`x±s)

Group	Control group (n=29)	Observation group (n=29)	*t*	P
Operation time (min)	87.4±7.1	71.2±6.8	8.87	0.00
Intraoperative blood loss (ml)	265.3±16.8	221.5±15.7	10.26	0.00
Postoperative drainage (ml)	146.5±19.6	115.5±19.5	6.04	0.00
Hospital stays (d)	18.9±2.9	17.4±2.6	2.07	0.04

3.2 After recording and observation, there was no significant difference in postoperative pain and spinal JOA scores between the two groups (p>0.05).

Table 2. Postoperative pain and spinal function in both groups (`x±s)

Group	Cases (n)	VAS score	JOA score
Control group	29	2.5±0.8	23.9±2.0
Observation group	29	2.4±0.7	23.5±1.8
t	-	0.51	0.80
P	-	0.61	0.43

3.3 There was no significant difference in the compression ratio of the injured vertebrae and the kyphosis Cobb angle between the two groups (p>0.05), after the operation, the two groups of patients were significantly reduced, and the compression ratio of the injured vertebrae and kyphosis Cobb angle of the observation group were more obvious (P<0.05).

Table 3. Compression ratio of the injured vertebrae and kyphosis Cobb angle (`x±s) before and after surgery in both groups

Group	Time	Control group (n=29)	Observation group (n=29)	*t*	P
Compression ratio of the injured vertebrae (%)	pre-operation	44.6±4.6	43.4±4.4	1.02	0.31
	post-operation	6.8±1.6	3.3±1.2	9.42	0.00
kyphosis Cobb angle (°)	pre-operation	22.3±2.7	22.4±2.8	0.14	0.89
	post-operation	6.8±1.2	4.5±0.8	8.59	0.00

3.4 After follow-up observation and records, the vertebral height loss and Cobb angle loss in the observation group were significantly lower than those in the control group (P<0.05).

Table 4. Fracture recovery in the two groups of patients within six months after surgery (`x±s)

Group	Cases (n)	Vertebral height loss (%)	Cobb angle loss (°)
Control group	29	6.2±0.7	3.8±0.5
Observation group	29	1.3±0.3	0.8±0.3
t	-	34.65	27.71
P	-	0.00	0.00

4. Discussion

Spinal fractures are clinically common orthopedic diseases. The incidence of thoracolumbar fractures is the highest[6-8], mostly caused by indirect external forces, which have adverse effects on patients' physical and mental health and quality of life. In addition, according to clinical studies, most patients with thoracolumbar fractures are accompanied by nerve damage and spinal cord damage[9-11], therefore, surgery should be performed in time to promote rapid recovery of spinal function, especially for patients with bone tumor with spine fracture, the cause of spinal cord and nerve damage should be relieved as soon as possible[12,13].

Commonly used surgical methods are mainly cross-injury vertebral fixation and via-injury vertebral fixation[14-16]. Among them, cross-injury vertebral fixation can achieve certain clinical effects; however, its drawbacks are also obvious. The postoperative spinal stress is more concentrated, which can easily lead to various complications, which affects the rehabilitation effect[17]. In addition, cross-injury vertebral fixation mainly concentrates the screws on the upper and lower parts of the patient's injured vertebrae, resulting in lack of effective support in front of them, resulting in the patient's anterior column being unable to be effectively restored and reconstructed, even losing its correction has a serious impact on the patient's recovery and prognosis[18], moreover, the anti-rotation ability of the pedicle screw internal fixation system is not good, so its lateral stability is usually poor, so that the fracture site and the surrounding intervertebral disc and ligament are not well repaired, even due to the short distance between the leading edge of the upper and lower vertebral bodies and the kyphosis of the vertebral body, the suspension effect appears[19], which has a serious impact on the patient's corrective effect. Via-injury vertebral fixation is a new derivative of cross-injury vertebral fixation. Two pedicle screws were added on the basis of cross-injury vertebral fixation, and the pedicle screws were properly optimized to strengthen the top thrust of the injured screw and the firmness of the fixed segment, which greatly improved the patient's reduction effect,

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at the same time, the burden on other screws is reduced, which effectively reduces the incidence of adverse reactions in patients[20].

5. Conclusion

In the above study, the duration of surgery and hospital stay in patients treated with via-injury vertebral fixation were significantly shorter than those treated with cross-injury vertebral fixation (P<0.05), moreover, the postoperative drainage volume of intraoperative blood loss was significantly less than that of patients treated with cross-injury vertebral fixation (P<0.05). In addition, the compression fracture rate and kyphosis Cobb angle of the two groups were significantly improved after surgery, and the improvement of patients with via-injury vertebral fixation was more obvious (P<0.05), the loss of vertebral height and the loss of Cobb angle in patients treated with via-injury vertebral fixation were significantly less than those treated with cross-injury vertebral fixation (P<0.05). It can be seen that in the treatment of bone tumor with thoracolumbar spine fracture, via-injury vertebral fixation has a more significant clinical effect than cross-injury vertebral fixation, and is more suitable for clinical application and promotion.

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ARTICLE

Comparison on Detection Results of Pathogen Nucleic Acids for Bronchoalveolar Lavage Fluid of Lung Infection Infants Between Uighur Nationality and Han Nationality

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ABSTRACT

Objective: To analyze the detection results of pathogen nucleic acids for bronchoalveolar lavage fluid (BALF) of lung infection infants from Uighur nationality and Han nationality. **Methods:** A retrospective analysis was performed on the 318 infants with lung infection who were admitted to the hospital from April 2018 to April 2019. According to their nationality, they were divided into Uighur nationality group (190 cases) and Han nationality group (128 cases). The BALF specimens were collected to test pathogen nucleic acid. The distribution and positive rates of [respiratory syncytial virus (RSV), adenovirus (ADV), influenza virus A (IFA), influenza virus B (IFB), parainfluenza virus type 1 (PIV I), parainfluenza virus type 2 (PIV II), parainfluenza virus type 3 (PIV III)], bacteria (Streptococcus pneumoniae, Haemophilus influenzae, staphylococcus aureus, Pseudomonas aeruginosa, klebsiella pneumoniae), Mycoplasma pneumoniae (MP) and Chlamydia pneumoniae (CP) in both groups were observed and compared. **Results:** The virus detection for RSV, ADV and PIV III were on the top three in BALF from the children in both groups. The total positive rate of virus examination in Uighur nationality group was higher than that in Han nationality group ($P<0.05$). BALF in both groups was mainly on Streptococcus pneumoniae. The total positive rate of bacteria, MP and detection rate of chlamydia were higher in Uighur nationality group were higher than those in Han nationality group ($P<0.05$). **Conclusion:** The pathogen nucleic acid examination for bronchoalveolar lavage fluid in infants with lung viral infection is in the majority, mainly on RSV virus infection. The positive rates of virus, bacteria, MP and CP of children in Uighur nationality are high than those in Han nationality.

1. Introduction

Lung infection, as one of the most common respiratory diseases in infants and young children, is a multi-infectious disease caused by viruses, bacteria, mycoplasma, chlamydia, etc. Its main clinical symptoms include wheezing, shortness of breath, cough, expectoration, etc. With the progression of disease, lung infection is easily to be turned into severe pneumonia, which is a serious threat to the health of infants [1]. Clinically, the virus test, bacteria test and other tests are mainly carried out by examining blood, sputum and nasopharyn-

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geal swabs of the sick children. In recent years, studies have found that clinically collected samples are easily contaminated, and the positive rate of isolated culture is low, limiting etiology diagnosis to a certain extent [2]. Bronchoalveolar lavage (BAL) is a pulmonary segment lavage measure through the use of fiber bronchoscope, and the examination and treatment are carried out by recycling the small airway and bronchoalveolar lavage fluid, and the analysis of bronchoalveolar lavage fluid (Bronchoalveolar) Lavage fluid, BALF) can help to understand the immune process of lung disease [3]. BAL has a higher application value in the pathogenic diagnosis of lung infection and can accurately reflect the pathogens of the lungs, because that it obtains more pathogens on the basis of the direct taking of lesion specimen and the reduction of oropharyngeal contamination specimen [4]. Based on this, this study compared the detection results of pathogen nucleic acids for bronchoalveolar lavage fluid of lung infection infants between Uighur nationality and Han nationality. The results of the study are reported below.

2. Data and Method

2.1 General data

With a retrospective analysis of 318 infants with lung infection admitted to our hospital from April 2018 to April 2019, the infants were divided into Uighur nationality group (190 cases) and Han nationality group (128 cases) according to their nationalities. There were 117 males and 73 females in the Uygur nationality group; the infants' ages ranged from 1 month to 12 months, and the average age was (6.35±3.12) months; there were 75 males and 53 males in the Han nationality group, the infants' ages ranged from 1 month to 12 months, and the average age was (6.77±3.30) months. There was no statistical difference in the general data of the patients in the two groups (P>0.05), which was comparable.

Inclusion criteria: ① consistent with the diagnostic criteria for infant lung infection in Obstetrics and Gynecology[5], and confirmed by X-ray chest radiography; ② 4in line with the indications for fiberoptic bronchoscopy, no contraindications for examination; ③ first bronchoalveolar lavage with fiber bronchoscope was performed with permission of infants' family members within 1-5 days after being hospitalized; ④ the guardians of the infants were informed and volunteered to participate in the study; ⑤ the study was approved by the Medical Ethics Committee of our hospital.

Exclusion criteria: ① synchronously suffered from severe organ dysfunction (such as hypohepatia, renal insufficiency, etc.), spontaneous hemorrhage, coagulopathy, etc.; ② there is a history of hormone use; ③ infants cannot cooperate to complete the work related to specimen collection; ④ clinical and examination data are incomplete.

2.2 Method

2.2.1 Specimen Collection

BAL was implemented in both groups. The instruments were produced by Olympus, a Japanese company, and the model numbers were BF-XP60 (outer diameter: 2.8mm, inner diameter: 1.2mm), BF-3C40 (outer diameter: 3.6mm, inner diameter: 1.2mm), and BF-MP60 (outside diameter: 4.0mm, inner diameter: 2.2mm). The specific operation is as follows: routine preoperative preparation (including blood routine examination, blood clotting time examination, prothrombin time examination, liver and kidney function tests, etc.), choosing the appropriate model for surgery based on the infant's condition, using nasal insertion method and performing airway local anaesthesia, examining non-lesioned site, and then performing lavage and examination for the diseased region and conducting alveolar lavage (3 times) with about 5 ml of normal saline (37 ℃), and then collecting and sealing the lavage fluid. Note that lidocaine should not be used before the lavage fluid is taken to avoid reducing the positive rate of bacterial culture in the lavage fluid.

2.2.2 Specimen Detection

The lavage fluid is stored in a refrigerator with temperature at 4 ℃ , and the ice box is sent to the laboratory for inspection within 20 minutes. The Wright stain smear was conducted at first, and the specimen would be stored in a refrigerator with temperature at 4 ℃ after being qualified, and the inspection was completed within 48 hours. Standard: squamous epithelial cells <10/low power field, Leukocytes >10-25/low power field, or the ratio of the two is 1:25.

Qualified specimens were examined by real-time fluorescence quantification polymerase chain reaction (PCR). The instrument was produced Applied Biosystems, an American company, and the model number is 7300, including: Respiratory syncytial virus (RSV), Adenovirus (ADV), Influenza virus A (IFA), Influenza virus B (IFB), Parainfluenza virus 1 (PIV I), Parainfluenza virus 2 (PIV II), Parainfluenza virus 3 (PIV III), Mycoplasma pneumoniae (MP), Chlamydia pneumoniae (CP); and followed by bacterial inoculation and selection of dominant strains for pure culture, using the API system for strain identification, including streptococcus pneumoniae, haemophilus influenzae, staphylococcus aureus, pseudomonas aeruginosa,

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klebsiella pneumoniae.

2.3 Observation Index

The detection results of pathogen nucleic acid for bronchoalveolar lavage fluid of the two groups were observed and compared, and the positive rate of diagnosis was prepared according to the Chinese Expert Consensus for the Detection of Bronchoalveolar lavage Pathogens in Lung Infectious Diseases (2017 Edition)[6].

2.4 Statistical Method

All the data in this paper were entered into EXCEl form without exchange, and was processed by statistical software SPSS17.0. The measurement data was expressed by Mean±SD(±s), and when the data were consistent with normal distribution and equal variance, a t-test was used between the two groups. The enumeration data was expressed by the number of cases (%), and the unordered categorical data was analyzed byχ^2 test. All tests were two-sided tests, and the difference was statistically significant when P was less than 0.05 (P<0.05).

3. Results

3.1 Comparison of Detected Virus Component Ratio and Detection Rate Between the Two Groups

The virus detection for RSV, ADV and PIV III were on the top three in bronchoalveolar lavage fluid (BALF) from the children in both groups. The total positive rate of virus examination in Uighur nationality group was higher than that in Han nationality group (P<0.05), as shown in table 1.

3.2 Comparison of Component Ratio and Detection Rate of Bacteria, MP And Chlamydia Between the Two Groups

Bronchoalveolar lavage fluid (BALF) in both groups was mainly on Streptococcus pneumoniae. The total positive rate of bacteria, MP and detection rate of chlamydia in Uighur nationality group were higher than those in Han nationality group (P<0.05), as shown in table 2.

4. Discussion

It is easier for infants to suffer from lung infection for their narrow trachea and bronchial lumen, less mucus secretion, poor ciliary movement ability, stunted lung elastic tissue, rich and easily congestive pulmonary blood vessels, vigorous pulmonary interstitial development, less number of pulmonary alveoli and less Lung Qi concentration, susceptible to mucus choke, and incomplete-developed immunity, and lung infection can be turned into pneumonia and severe pneumonia, etc., which seriously threaten the health of infants[7]. With the continuous development of medical technology, the cure rate of lung infection in children is greatly improved, and the patients mainly are cured by clearing airway secretions, preventing airway obstruction and hypoxia caused by airway obstruction, and simultaneously administering local drug-targeted lavage, etc. [8]. Therefore, a reasonable and effective analysis of the composition of the lavage fluid is helpful to diagnose the cause of the disease, confirm the pathogen, and choose the drug properly.

Table 1. Comparison of virus component ratio and detection rate between the two groups [case (%)]

Groups	RSV	ADV	IFA	IFB	PIV I	PIV II	PIV III	Total positive rate
Uighur nationality group(n=190)	46 (24.21)	23 (12.10)	5 (2.63)	2 (1.05)	2 (1.05)	5 (2.63)	10 (5.26)	93 (48.95)
Han nationality group	23 (17.97)	11 (8.59)	3 (2.34)	1 (0.78)	1 (0.78)	3 (2.34)	6 (4.69)	48 (37.50)
χ^2	1.753	0.988	0.026	0.060	0.060	0.025	0.053	4.061
P	0.185	0.320	0.872	0.806	0.806	0.872	0.818	0.044

Table 2. Comparison of component ratio and detection rate of bacteria, MP and chlamydia between the two groups [case (%)]

Groups	Bacteria						MP	CP
	Streptococcus pneumoniae	Haemophilus influenzae	staphylococcus aureus	Pseudomonas aeruginosa	klebsiella pneumoniae	Total positive rate		
Uighur nationality group(n=190)	10(5.26)	8(4.21)	4(2.10)	3(1.58)	6(3.16)	31(16.32)	33(17.37)	25(13.16)
Han nationality group(n=128)	3(2.34)	3(2.34)	1(0.78)	1(0.78)	3(2.34)	11(8.59)	12(9.38)	8(6.28)
χ2	1.662	0.337	0.222	0.013	0.007	3.978	4.022	3.924
P	0.197	0.562	0.637	0.910	0.933	0.046	0.045	0.048

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BAL is one of the most effective methods for the diagnosis and treatment of lung infection in infants and young children in recent years. The method is to inject saline into the bronchoalveolar of infants through fiber bronchoscope, and then collect the surface fluid of alveoli for diagnosis and remove impurities in the alveoli [9]. BAL can effectively obtain the cells and biochemical components from the lower respiratory tract (mainly alveoli), and then know the characteristics and activity of the lower respiratory tract lesions, and effectively analyze and explore the lung lesions [10]. BAL can directly obtain lavage specimens from the lung infection site. The sampling range is wide, and it can accurately reflect the lung infection lesions. But it is an invasive operation, a strict safety evaluation should be performed on the infant in the actual operation for that there are more surgical contraindications and preoperative and postoperative complications in the BAL operation [11].

At present, there are different reports on the causes of lung infection in young children. The causes of the disease are closely related to viruses, bacteria, mycoplasma and chlamydia infections, etc., of which, the common virus include RSV, IFV, PIV, ADV, etc., and the bacteria mainly include Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumoniae, etc. Virus is a common cause of lung infection, and the infection is mainly related to immune function status, patient's age, route of infection, etc., and the incidence of lung infection of young children is slightly higher than that of adults [12]. Bacteria are an important cause of pneumonia in infants and young children, the incidence of pneumonia is closely related to the pathogen and patient's status. Clinically, pneumonia can be properly treated through pathogenic diagnosis and selection of sensitive drugs [13]. MP and CP, widely distributed in nature, can be spread by droplets, and they both are pathogens of respiratory tract infection, which have certain destructive effects on respiratory ciliated epithelial cells and respiratory mucosa, and can cause respiratory diseases such as pneumonia and bronchitis [14].

According to the results of this study, pathogen nucleic acids examination for bronchoalveolar lavage fluid of lung infection infants found that the lung infection was mainly caused by virus and was mainly infected with RSV virus, and the study result is similar to that of severe pneumonia (written by Ding Lin et al [15]). RSV is the most common cause of bronchiolitis and pneumonia for infants who are less than 12 months old, and the infection is related to patient's age, season and climate, etc., e.g. in northern China, the incidence is higher in the season when autumn and winter alternates. This research also studied the lung infection conditions of infants of Han nationality and Uygur nationality, the results showed that the infection rates of virus, bacteria, MP and CP of children in Uighur nationality are high than those in Han nationality, this may have a certain relationship with their growth environment. Compared with the Han nationality, the geographical environment and living environment of Uygur nationality are relatively poor, the infectious factors are more and the level of education and attention to disease are relatively low.

5. Conclusion

In summary, the detection of pathogen nucleic acids for bronchoalveolar lavage fluid of lung infection infants found that virus is the majority cause of lung infection, and RSV virus infection is common. Through the comparison of detection results of the Uyghur nationality group and the Han nationality group, it is found that the infection rate of virus, bacteria, MP, CP in the Uyghur infants are higher than those of Han infants. Therefore, more attention should be payed to the Uyghur infants in the diagnosis and treatment of lung infection in the later stage, and diagnosis and cure rate of pathogens should be effectively improved.

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REVIEW

Treatment of Dilated Cardiomyopathy with Qilan Qiangxin Capsule Combined with Sakubatra and Valsartan: A Case Report

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ABSTRACT

A case of dilated cardiomyopathy was reported, including the course of onset and long-term application of Qilan Qiangxin Capsule combined with a new anti-heart failure drug, Sakubatril Valsartan, in order to improve the symptoms of heart failure, increase the LVEF (left ventricular ejection fraction), and reduce the plasma NT-proBNP (N-terminal B-type natriuretic peptide) level. The effect of improving ventricular remodeling is obvious, and the quality of life of patients is improved.

1. Introduction

Dilated cardiomyopathy (DCM) is a primary cardiomyopathy of unknown cause. The disease is characterized by enlargement of left or right ventricles or bilateral ventricles, accompanied by decreased ventricular systolic function, and congestive heart failure. The incidence of the disease is relatively common, with the incidence of 13-84/100,000 in China. The disease is progressively aggravated, and death can occur at any stage of the disease. At present, comprehensive treatment including beta-receptor antagonist, angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor antagonist (ARB) is mainly used to slow down ventricular remodeling and further myocardial damage and delay the development of lesions[1]. However, some patients still have poor prognosis. Qilu Qiangxin Capsule is a Chinese patent medicine for heart failure based on collateral

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disease theory of traditional Chinese medicine[2]. This medicine has the merits of benefiting the temperature and yang, promoting blood circulation and dredging collaterals, promoting water and reducing edema. It has a good curative effect for patients with heart failure syndrome which belongs to deficiency of yang-qi and stagnation of collaterals and blood stasis. Sakubatril valsartan is the first angiotensin receptor enkephalin inhibitor, which can improve cardiac systolic and diastolic function, better reverse ventricular remodeling and improve left ventricular ejection fraction (LVEF) [3]. This patient was treated with Qilu Qiangxin Capsule combined with Sakubatra and Valsartan. The curative effect is good. The report is as follows.

2. Summary of Medical Records

The patient, a 22-year-old woman, was hospitalized on February 01, 2018. Complaint: Paroxysmal shortness of breath, edema of both lower limbs for 1 month, aggravation with cough and sputum for 1 week. History: Before January, the patient began to suffer from shortness of breath during night supine rest, reduced shortness of breath in high pillow or sitting position, affecting sleep, concomitant depressed edema of lower limbs, no fever, chills, dizziness, headache, abdominal pain, abdominal distension and other symptoms. Then he went to the local hospital to see a doctor and improve the relevant examinations. B-type brain natriuretic peptide showed 1646 pg/ml, electrocardiogram showed myocardial ischemia, echocardiography showed abnormal segmental motion of left ventricular wall and bilateral enlargement. Considering heart failure, Digoxin was given, spironolactone diuretic was given, beta-blocker inhibited sympathetic excitation, and Benazepril reversed heart function. Symptomatic supportive treatment such as ventricular remodeling is ineffective. 1 weeks ago, the patient developed sudden shortness of breath, aggravated breathing, difficulty breathing, especially slight movement and supine position, with cough, expectoration, white foam sputum, and fatigue when resting. Then he came to the First Affiliated Hospital of Shaanxi University of traditional Chinese medicine. Mild reflux, a small amount of pericardial effusion (left ventricular end-diastolic diameter: 57 mm, left atrial anteroposterior diameter: 55 mm, right ventricular anteroposterior diameter: 27 mm, right atrial transverse diameter: 54 mm, EF: 30%). The outpatient clinic was admitted to the hospital with "Class IV Cardiac Function of Dilated Cardiomyopathy". Admission symptoms: shortness of breath, dyspnea, limited lying time, cough, sputum, fatigue, no fever, no nausea and vomiting, poor appetite, bad night rest, no abnormal stool and urine. Physical examination: body temperature 36.4, pulse 103 times per minute, breathing 24 times per minute, blood pressure 124/84 mmHg, young women, clear mind, poor mental state, cyanosis of lips, jugular vein enlargement, chest symmetry and no deformity, bilateral respiratory mobility consistent, bilateral pulmonary percussion was voiced, bilateral pulmonary respiratory sounds were thick, bilateral lung floor was covered with moist rales, no protuberance in the anterior heart region, Apical enlargement, heart rate 103 beats/min, rhythm, blunt heart sounds, diastolic galloping rhythm can be heard in mitral stethoscope, systolic murmurs of grade 2/6 can be heard in apex, and pathological murmurs cannot be heard in remaining valves stethoscope. The lower extremities were moderately depressed edema with obvious edema on both feet. The tongue is pale, the fur is white and greasy, and the pulse is fine. Auxiliary examination: ECG: sinus rhythm ventricular rate 110 times per minute myocardial ischemia; B-type brain natriuretic peptide (BNP) 2249pg/ml, NT-proBNP 614pg/ml; myocardial enzymes, blood routine, urine routine, fecal routine, liver function, kidney function, electrolyte, blood lipid, fasting blood sugar were not significantly abnormal. Chest X-ray: The texture of both lungs became thicker. Heart shadow enlarged to both sides, which accorded with cardiomyopathy. Western medicine diagnosis: dilated cardiomyopathy heart function IV; Chinese medicine diagnosis: chest arthralgia (Qi deficiency, blood stasis and water obstruction syndrome). After hospitalization, western medicine was given oxygen inhalation, the mixture of sodium nitroprusside 50 mg and 50 ml 5% glucose injection was injected by light-avoiding micro-pump to reduce the pre-and post-cardiac load, metoprolol succinate sustained-release tablets 23.75 mg once a day inhibited sympathetic nerve, furosemide tablets 20 mg once a day, spironolactone 20 mg once a day diuretic to reduce the pre-cardiac load, and Shakuba. Trivalsartan sodium tablets 50 mg twice a day corrected heart failure and inhibited ventricular remodeling. Coenzyme Q10 capsules 20 mg 3 times a day, trimetazidine hydrochloride tablets 20 mg 3 times a day, isosorbide mononitrate sustained-release capsules 50 mg once a day, intravenous infusion of levocarnitine 6 g and 250 ml 0.9% sodium chloride mixed solution nourished myocardium, protected heart, and properly supplemented potassium vitamin. Keep electrolyte balance. The mixture of 60 ml Shenmai injection and 100 ml 5% glucose injection was given intravenously and three capsules of Qilanqiangxin capsule were taken orally three times a day. On the 6th day after admission, shortness of breath, dyspnea, cough and phlegm were relieved obviously. The patient could lie on his back and rest. Blood pressure was 112/76 mmHg,

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heart rate was 83 beats/min, jugular vein was not full, and edema of both lower limbs was obviously relieved. On the 14th day after admission, the patient had no shortness of breath, dyspnea, cough and sputum, and his fatigue was significantly alleviated. He took cocoa, had nighttime rest and had no abnormal stool and urine. Blood pressure 110/78 mmHg, heart rate 77 times/min, lip no cyanosis, jugular vein no filling, bilateral lung percussion was clear, bilateral lung breathing sounds clear, no moist rales, apex can be heard 2/6 systolic murmur, bilateral lower limbs, bilateral feet no edema, pale tongue, thin white coating, fine pulse. The NT-proBNP403.05 pg/ml was reexamined. The electrocardiogram showed that the T-wave of low level had risen, suggesting that heart failure had been corrected. Sakubatroxol valsartan sodium tablets were adjusted to 100 mg twice a day, and metoprolol succinate sustained-release tablets were increased to 47.5 mg once a day. The patient was diagnosed clearly and his symptoms improved. He was ordered to discharge. After discharge, he was given oral drugs: coenzyme Q1020 mg 3 times a day, trimetazidine hydrochloride tablets 20 mg 3 times a day, metoprolol succinate 47.5 mg 1 time a day, spironolactone tablets 20 mg 1 time a day, furosemide tablets 20 mg 1 time a day, sakubatrovalsartan 100 mg 2 times a day, Qiqiangxin capsules 3 times a day./ Day.

On March 05, 2018, the patient's first visit showed no obvious shortness of breath, difficulty in breathing, lying on his back at night, no restrictions on daily activities, no cough, sputum, general fatigue, no edema of lower limbs, dim tongue, thin white coating, fine pulse, 110/72 mmHg of blood pressure, 68 beats/min of heart rate. Chest X-ray reexamination showed that the heart shadow was larger (smaller than before), which was consistent with the manifestation of dilated heart disease. Color Doppler echocardiography showed that left ventricular diastolic function was normal, systolic function was reduced by 39%, mitral regurgitation was moderate, tricuspid regurgitation was mild. Compared with the admission date on February 01, 2018, the patient had no obvious symptoms of heart failure, grade II of heart function, decreased heart function, increased left ventricular ejection fraction, blood pressure and heart rate, increased metoprolol succinate to 95 mg once a day, valsartan to 200 mg twice a day, continued to take Qiqiangxin capsule 3 times a day, the rest. The medicine remains unchanged.

On June 25, 2018, the patient's third visit showed stable symptoms, no shortness of breath, no edema of lower limbs, dim tongue, thin white fur, fine pulse, 114/70 mmHg of blood pressure and 74 beats/min of heart rate. Color Doppler echocardiography showed changes in myocardial involvement, left ventricular enlargement with minor mitral regurgitation, left ventricular systolic function decreased by LVEF45%, coronary sinus widened (persistent left superior chamber may be). ECG showed improvement of myocardial ischemia and discontinuation of trimetazidine hydrochloride. Re-examination of NT-proBNP334.04 pg/ml showed that metoprolol succinate had been increased to 190 mg once a day and sakubatrovalsartan to 200 mg twice a day, which had reached the maximum dose tolerated by patients. The patients' liver function, kidney function, blood potassium, blood pressure and heart rate were monitored regularly. Qiqiangxin capsules were still taken orally three times a day, while the rest drugs remained unchanged.

On January 08, 2019, the fifth visit of the patient showed no obvious shortness of breath, edema of both lower limbs, pale red tongue, thin white fur and fine pulse. Blood pressure 116/76 mmHg, heart rate 72 times/min. Color Doppler echocardiography showed that left ventricle enlarged, left ventricular anterior septum and anterior wall motion decreased, left ventricular wall motion was uncoordinated, left superior chamber persisted, tricuspid regurgitation was mild (left ventricular end-diastolic diameter: 56 mm, left atrial anterior and posterior diameter: 36 mm, right ventricular anterior and posterior diameter: 21 mm, right atrial transverse diameter: 37 mm, EF: 51%). NT-proBNP 74pg/ml was reexamined. Up to now, the patient's condition has been stable. Continue to observe and adjust the medication.

3. Discussion

Dilated cardiomyopathy has no specific name in traditional Chinese medicine. According to its clinical manifestations, it can be classified as "chest pain", "edema", "palpitation", "asthma syndrome" and "heart distention". The disease is mostly seen in young and middle-aged people, and its location is in the heart. It often involves the lungs, spleen, liver, kidney and other organs[4]. Due to the lack of innate endowment, acquired loss of nutrition, chronic illness, deficiency of Yang Qi, unstable external defense, warm heat and toxic pathogens, heart sinking, heart-Yin depletion, and eventually a series of symptoms of heart loss and nourishment. The main pathogenesis is the mixture of deficiency and excess, deficiency of yang-qi as the basis, phlegm and drink, blood stasis, water and dampness as the criteria. According to the different stages and clinical manifestations of the disease, the disease can be divided into three stages [5]: in the early stage, the deficiency of cardiopulmonary Qi is dominant, phlegm and blood stasis is relatively light, mainly manifested as panic, shortness of breath and fatigue; in the middle stage, the deficiency of heart and kidney yang can cause palpitation fatigue,

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fear of cold limbs, edema and other symptoms; in the late stage, the deficiency of yin and Yang is dominant, and the patients appear mental fatigue, dyspnea, palpitation, and depression of Now. The disease is based on deficiency and excess, and is treated according to syndrome differentiation of qi, blood and body fluid. Clinically, they are divided into Qi deficiency and blood stasis type, Qi deficiency and Yin deficiency and blood stasis type, Qi deficiency and blood stasis and water stasis type, Yang deficiency and blood stasis and water stasis type, etc[6]. According to the symptoms and signs of the patients, the patients are mostly due to Pingyu deficiency, combined with inappropriate regulation and nourishment, insufficient Yang Qi in the heart, heart loss, poor blood circulation, obstruction of the heart vein, stasis and water stoppage, and chest obstruction, which is suitable for warming yang and invigorating qi, activating blood circulation and dredging collaterals, and reducing edema. Qilu Qiangxin Capsule is the first Chinese patent medicine to treat chronic heart failure established under the guidance of collateral disease theory in China[7]. The theory of TCM venation explores the pathogenesis of chronic heart failure from the aspects of qi, blood and water. Qi, blood and water cemented each other, blood stasis can not only directly block the veins, leading to obstacles in water circulation, but also block the movement of Yingwei Qi, aggravating the dysfunction of Yingwei Qi; water pathological changes also block Yingwei Qi, causing abnormal blood flow and blood stasis; Qi, blood and water are mutually harmful, forming a vicious pathological cycle, and eventually leading to the accumulation of heart collaterals. This is consistent with the long-term over-activation of neuroendocrine system in Western medicine, which directly damages the heart and blood vessels, leads to myocardial hypertrophy and deterioration of cardiac function, and aggravates the activation of neuroendocrine system, thus forming a vicious cycle process [8]. Aiming at the pathogenic characteristics of chronic heart failure such as deficiency of Qi and yang, stagnation of collateral stasis and accumulation of collateral interest, this paper puts forward the treatment principle of "treating qi, blood and water together, dividing and dispelling" guided by the theory of collaterals, and determines the treatment method of "benefiting temperature and yang, promoting blood circulation and dredging collaterals, promoting edema and eliminating edema". On this basis, an innovative prescription of Qilu Qiangxin Capsule is developed. It mainly consists of safflower, Salvia miltiorrhiza, Astragalus membranaceus, cinnamon twig, ginseng, Alisma orientalis, aconite, incense peel, orange peel, Yuzhu and amaranth. Among them, Astragalus membranaceus and aconite are the monarch drugs. Astragalus membranaceus is beneficial to Qi deficiency and Yang deficiency, and it is also beneficial to water and swelling [9]. It is especially suitable for those who are weak in Qi and Yang and have more than weak in sweat. Ginseng, Salvia Miltiorrhiza, Amaranthus Chinensis, Ginseng Dabu Yuanqi, Heart and Lung Tongjing Huoxue, Ginseng participates in the combination of astragalus, Astragalus partially supplements Wei Qi, Ginseng is the main tonifying Qi and Yang, Gubiao Zhituo Gong [10]; Salvia Miltiorrhiza Huoxue Huayu; Amaranthus Chinensis purging lung and circulating water, three drugs Qi, blood and water are used as courtier drugs. The adjuvant medicine safflower activates blood circulation and dissipates blood stasis, orange peel regulates Qi and dampness, Alisma orientalis and incense plus peel slightly permeate water, and Yuzhu nourishes Yin to maintain healthy qi. It warms up the Yang and turns the gas into the air of Cinnamomum cassia twig. All medicines are used to treat dilated cardiomyopathy by warming Yang Qi, activating blood circulation and promoting blood circulation, promoting water retention and detumescence. Modern pharmacology believes that Salvia miltiorrhiza can dilate coronary artery and increase coronary artery blood flow [11]; ginseng can dilate blood vessels, enhance myocardial contractility, cardiac output and anti-ischemic ability of myocardium will also be enhanced; purslane can reduce phlebitis and reduce cardiac load [12]; Astragalus can reduce renin and angiotensin in patients, reverse ventricular remodeling, and reduce oxygen self-regulation. The damage of cardiac myocytes by radicals increases their oxygen tolerance [13]. Therefore, Qilu Qiangxin Capsule can improve the cardiac function of patients with chronic heart failure and prevent chronic heart failure, which is closely related to its effects of enhancing myocardial contractility, diuresis, inhibiting the over-activation of neuroendocrine system such as RASS, inhibiting inflammation, myocardial fibrosis, apoptosis and autophagy, improving myocardial energy metabolism, promoting angiogenesis and improving endothelial function [14]. Other studies have shown that Qilu Qiangxin Capsule does not cause electrolyte disturbance, but can reduce the occurrence of arrhythmia without significant impact on liver function, renal function and myocardial enzymes [15]. It is also the only recommended Chinese patent medicine in China's guidelines for the diagnosis and treatment of heart failure. This case was treated with western medicine and Qilu Qiangxin Capsule. It can warm yang and invigorate qi, activate blood circulation and dredge collaterals, relieve edema, treat both symptoms and symptoms, and has a good effect.

At present, there is no specific treatment for dilated cardiomyopathy in Western medicine. Early drug interven-

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tion is still the basic treatment of dilated cardiomyopathy, including the use of ACEI or ARB, beta blockers, aldosterone receptor antagonists, diuretics, vasoactive drugs and other drugs [16]. The main purpose is to slow down ventricular remodeling and further myocardial damage and delay the development of lesions. ACEI or ARB, beta-blocker and aldosterone receptor antagonist are called "golden triangle" drugs for heart failure. They should be used as early as possible without contraindication. Starting from small dosage, the dosage should be gradually increased to reach the maximum dose that different patients can tolerate. However, in the actual use process, most patients are difficult to reach due to various adverse reactions. At the target dose, the 5-year mortality rate is still over 50%[17]. In recent years, new angiotensin receptor enkephalin inhibitors (ARNI) have emerged, forming a "new golden triangle" based on ARNI with beta blockers and aldosterone receptor antagonists. Sakubastral valsartan is the first angiotensin receptor brain natriuretic peptide inhibitor in the world, and has the drug properties of Sakubastral and Valsartan [18]. Damage of cardiac myocytes in patients with heart failure causes changes in size, shape and function of cardiac myocytes, resulting in overactivation of RASS and sympathetic nervous system, ventricular remodeling and hemodynamic changes. While RASS and sympathetic nervous system are activated, natriuretic peptide system is also activated. Natriuretic peptide has the functions of dilating blood vessels, lowering blood pressure, lowering sympathetic nerve activity, lowering vasopressin, reducing aldosterone, and inhibiting ventricular remodeling [19]. Natriuretic peptide metabolism is mainly through two processes: self-receptor mediated scavenging and enkephalin degradation. Sakubattral is a precursor drug, which is metabolized into a kind of active NEPI (neutral endopeptidase inhibitor) in vivo. It can inhibit enkephalin, enhance the effects of natriuretic peptide, bradykinin, adrenomedullin, angiotensin I / II and other vasoactive activities. However, the emergence of NEPI also increased the concentration of angiotensin I, II and endothelin-1, which counteracted each other. Therefore, the use of enkephalin inhibitors alone had little effect on heart failure and offset its potential benefits. To inhibit enkephalin, RASS must be blocked in order to avoid the elevation of angiotensin I, II and endothelin-1. Valsartan is the AT1 R blocker, which can block the RASS system. Therefore, ARNI has dual effects of ARB and NEPI, which can inhibit both RASS and natriuretic peptide system, and inhibit ventricular remodeling [20]. In addition, PARADIGM-HF results showed that compared with the traditional golden triangle drug ACEI, sakubatroxatan could reduce the risk of cardiovascular death, hospitalization risk of heart failure and all-cause death risk. It can also improve the common daily activity limitation of patients with heart failure and almost all physical and social activity items in the total score of the Kansas Cardiomyopathy Questionnaire (KCCQ). The greatest improvement is in sexual relations. At the same time, the adverse reactions such as renal function damage, hyperkalemia and cough in the Sakubatra and Valsartan group were less [21]. This study provides high-level evidence-based support for ARNI's position in the guidelines. The new edition of heart failure guidelines in Europe and the United States strongly recommended ARNI for the treatment of patients with symptomatic decreased ejection fraction. The latest guidelines for diagnosis and treatment of heart failure in China also recommend that ARNI should be used instead of ACEI/ARB in order to further reduce the incidence and mortality of heart failure if NYHA has symptomatic Ejection Fraction (Ejection Fraction) decline and can tolerate ACEI/ARB.

The initial treatment of this patient was based on the traditional "golden triangle" drug of ACEI or ARB, beta-blocker and aldosterone receptor antagonist, and the effect was not good. According to the guideline of medication for heart failure, ARNI was used as the cornerstone and the new "golden triangle" drug of beta blocker and aldosterone receptor antagonist was added. Combining with Qi'an Qiangxin Capsule, the curative effect was very good.

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REVIEW

Praziquantel and Albendazole Pills Can Cure Cancer

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ABSTRACT

Objective: To prevent and treat various types of cancer safely, reliably, and at low cost. Method: Early and mid-stage cancer patients took praziquantel and albendazole every day, late cancer patients only took albendazole every day, while with the traditional Chinese medicine "ginseng jade bamboo particle" to eliminate the adverse reactions and side effects caused by the above two western medicines, continue for more than three months. **Conclusion:** Praziquantel and albendazole have good therapeutic and cancer prevention effects in actual clinical trials.

1. Introduction

With the continuous development of human society and more civilized progress, through a variety of science and technology power over human nature many originally can't overcome natural disasters, to human survival on the earth have developed more comfortable and elegant living environment. However, cancer is all about the color change of subject, to a lot of families bring heavy economic burden and mental stress. A people, both rich and poor alike, seniority, and once cancer is sentenced to death, fear, the fear of death and cancer patients a heavy economic burden to cancer patients and their family members out of breath, but western medicine means of radiation and chemotherapy can completely destroy the cancer patient's own immune system, cause a cancer patient's own immunity and disease-resistant ability all return to zero, a direct result of the cancer cells without any immunity and disease resistance of cancer patient again, to speed up the death of the cancer patients, resulting in cancer patients whose families.

The goal of this study is: Can humans be safe, reliable, and cost effective? How to cure all kinds of early, middle and advanced cancers? The answer is yes, it can be cured! Because I'm in 15 years of clinical research of traditional Chinese medicine theory and the process, found that no one in India was cancer, explore the result is: in the daily habits of people in India, to mix up the turmeric as a food flavoring food every day to eat, and turmeric contains curcumin has the function of blood, it can destroy the cancer cells of blood system, prevented cancer cells from a cancer patient's body organs absorption into the blood and the glucose, the cancer cell cancer caused by ischemia of sugar was starved to death, this is the same with India

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circulating in recent years.[1]

In a further study of the process, I accidentally discovered praziquantel and albendazole pills has the effect of curcumin such: it can effectively destroy cancer cells of blood system, prevented cancer cells from a cancer patient's body organs absorption into the blood and the glucose, the cancer cell cancer caused by ischemia of sugar was starved to death, and is not affected by any normal cells, cancer patients in this way, people have been without radiation and chemotherapy to treat cancer means to destroy the cancer patient's own immunity and disease resistance, and can completely by taking drugs praziquantel and albendazole pills effectively destroy cancer cells of blood supply, prevented cancer cells from a cancer patient's body organs absorption into the blood and the glucose, the cancer cell cancer caused by ischemia of sugar was starved to death, causing cancer gradually shrink, wither and fall off, the cancer patient body organs to restore the original organ function, cancer patients to restore health!

So how humans to good use drugs praziquantel and albendazole piece of safe and reliable, low effective cure for a variety of middle-late early cancer? Using drugs praziquantel and albendazole cure all sorts of middle-late early cancer specific methods:

2. Why do Human Organs become Cancerous

During the fifteen years of theoretical research and clinical trials of traditional Chinese medicine, through years of comparative analysis of the physical condition, living habits, working conditions and living environment of various cancer patients, I found that the main reasons why human beings get cancer are as follows:

First, the patient's parents have excessive physical weakness during the pregnancy and pregnancy, and the physical condition of the child is inherently weak. The child's natural immunity and disease resistance are poor, and there is no normal health group. Immunity and disease resistance, cancer cells are the easiest to take advantage of, to overcome the weak human immunity and disease resistance, occupy the territory of human organs, and continue to grow and develop.

Second, the patient's living habits are too bad, the diet is irregular, eating is not at the meal for many years, gluttony, drinking, drinking and drinking for a long time, all night long, no adequate sleep time, long-term health, serious overdraft, resulting in self-immunity and The disease resistance is obviously reduced. Cancer cells will also take advantage of this, and overcome the weak human immunity and disease resistance, and occupy the territory of human organs and continue to grow and develop.

Third, in order to obtain an unimaginable reputation or status, or to survive a high level of life, the patient is working hard all day beyond the limit of his ability, working overtime and staying up late for a long time, and his health is seriously overdraft, resulting in his own immunity and disease resistance. The rapid decline, cancer cells take advantage of the virtual, overcome the weak human immunity and disease resistance, occupy the territory of human organs, continue to grow and expand, spread and spread.

Fourth, the patient's living environment is too poor, cold and humid, air pollution is serious, there is no basic warmth measures, starving and freezing, the body is extremely lack of nutrition, resulting in a significant decline in autoimmune and disease resistance, cancer cells will also Take advantage of the virtual, overcome the weak human immunity and disease resistance, occupy the territory of human organs, continue to grow and expand, spread and spread. [4]

3. Why Indians Don't Have Cancer

I was fifteen years of clinical research of traditional Chinese medicine theory and the process, found that no one in India was cancer, explore the result is: in the daily habits of people in India, Indians in order to dispel the smell of seafood, to mix up the turmeric as a food flavoring food every day to eat, after verification, turmeric contains curcumin has the function of blood, it can destroy the cancer cells of blood system, prevented cancer cells from a cancer patient's body organs absorption into the blood and the glucose, the cancer cell cancer caused by ischemia of sugar was starved to death, this is the same with India circulating in recent years.[1]

I used in my "ginseng jade bamboo particles" of traditional Chinese medicines inside join turmeric, for cancer patients, taking three months after the tumor showed signs of shrinking, but reduce speed is slow, I have to find a of curcumin on the efficacy of the drug, accidentally discovered praziquantel and albendazole pills has the effect of curcumin such: it can effectively destroy cancer cells of blood system, prevented cancer cells from a cancer patient's body organs absorption into the blood and the glucose, the cancer cell cancer caused by ischemia of sugar was starved to death, and is not affected by any normal cells, cancer patients in this way, people have been without radiation and chemotherapy to treat cancer means to destroy the cancer patient's own immunity and disease resistance, and can completely by taking drugs praziquantel and albendazole pills effectively destroy cancer cells of blood supply, prevented cancer cells from a cancer patient's body organs absorption into the blood and the

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glucose, the cancer cell cancer caused by ischemia of sugar was starved to death, causing cancer gradually shrink, wither and fall off, the cancer patient body organs to restore the original organ function, cancer patients to restore health!

Many people will question: why haven't found take praziquantel and albendazole pills can kill cancer cells, can completely cure cancer? Reason is: in the past, people take praziquantel and albendazole pills to kill worms, parasites, blood-sucking worm, take 3 to 5 days work immediately after drug withdrawal, there is no long-term use, and lifetime consumption of turmeric, Indian children aged two to eventually died, a day of food have turmeric, curcumin efficacy of accumulated for a long time, if you keep eating every day can destroy the cancer cells of blood supply system effectively, make cancer cells cannot be absorbed into the blood from the human organs and glucose, causing cancer cells caused by ischemia of sugar was starved to death, so the Indians did not have cancer.

Inspired by this event, I try to cancer patients take praziquantel and albendazole pills adhere to long-term use, in order to eliminate take praziquantel and albendazole pills on the human body may produce adverse reactions and side effects, I put my traditional Chinese medicine "ginseng jade bamboo particles with praziquantel and albendazole pills taken together, completely eliminates the take praziquantel and albendazole pills on the human body may produce adverse reactions and side effects of cancer patients can be long-term use, completely every day for more than three months' time, tumor gradually narrowing, wither and fall off, the cancer patient body organs to restore the original organ function, cancer patients to restore health! Can cure various human middle-late early cancer completely.

4. What Is the Principle of Praziquantel and Albendazole?

Praziquantel have therapeutic effects on schistosomiasis, tapeworm, cysticercosis, Clonorchis sinensis, paragonimiasis and Fasciola ginger. There are two main pharmacological effects on the worms:

(1) Spastic paralysis occurs when the muscles of the worms contract rigidly. The body tension of Schistosoma japonicum increased only 20 seconds after exposure to praziquantel at low concentration. When the concentration of praziquantel was above 1 mg/L, the body contracted intensely instantaneously. The contraction of worm muscle is related to the increase of membrane permeability by praziquantel and the loss of intracellular calcium ions.

(2) Cortical damage and immune function are involved in killing the worms. Praziquantel has a rapid and obvious damage to the body cortex, causing the syncytial outer skin to swell, appear vacuoles, form bullae, protrude the body surface, eventually the epidermis erosion and ulceration, almost all the secretions disappeared, and the circular and longitudinal muscles also dissolve rapidly and successively. In human body, vacuolar degeneration of the epidermis was observed 15 minutes after administration. After the destruction of the cortex, the absorption and excretion of the parasite are affected. More importantly, the exposure of its surface antigen makes it vulnerable to human immune attack. A large number of eosinophils attach to the lesion and invade it, which leads to the death of the parasite. In addition, praziquantel can also cause secondary changes, depolarize the surface membrane of the parasite, decrease the activity of alkaline phosphatase in the cortex, inhibit the uptake of glucose and deplete endogenous glycogen. Praziquantel can also inhibit the synthesis of nucleic acid and protein.[2]

Albendazole derivatives of benzimidazole derivatives are rapidly metabolized to sulfoxide, sulfone alcohol and 2-aminosulfonol in vivo. It selectively and irreversibly inhibits the aggregation of cytoplasmic microtubules in intestinal wall cells of parasites, blockades their uptake and absorption of various nutrients and glucose, leads to the depletion of endogenous glycogen, inhibits the fumaric acid reductase system, prevents the production of adenosine triphosphate, and makes the parasite unable to survive and reproduce. Albenda contusion tablets can also cause the denaturation of cytoplasmic microtubules in intestinal cells of the worms, and bind to their microtubule proteins, resulting in blockage of intracellular transport, accumulation of Golgi endocrine granules, gradual dissolution of cytoplasm, complete degeneration of absorption cells, and death of the worms. Albenda fruits can completely kill hookworm eggs and whipworm eggs and partially kill Ascaris eggs. Besides killing and repelling all kinds of nematodes parasitic in animals, it also has obvious killing and repelling effects on tapeworm and cysticercus.[3]

Praziquantel is born at the same time has the function of three kill cancer cells is a tonic contraction, resulting in the cancer causing spastic paralysis, kill cancer cells. 2 it is broken cause cancer cells to the cortex, cooperate with the body's own immune function against cancer cells, kill cancer cells. 3 it is cause cancer cells to form membrane depolarization, cortex alkaline phosphatase activity significantly decreased, the cancer cells by inhibiting the uptake of glucose and endogenous glycogen depletion starve the cancer cells. Albendazole born at the same time also has the function of three kinds of killing cancer cells is a block cancer cells in a variety of nutrition and intake

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and absorption of glucose, lead to cancer cells endogenous glycogen depletion, starve the cancer cells; Second, inhibition of fumaric acid reductase system, prevent the generation of adenosine triphosphate, causing cancer cells cannot survive and reproduce, and kill cancer cells. 3 it is to cause cancer cell cytoplasm microtubules degeneration, and wed tubulin and cause cancer cells to transport congestion, the golgi secretory granules accumulated inside body, cytoplasm gradually dissolve, absorb the cell degeneration, cause cancer cell death. Praziquantel and albendazole kill cancer cells method is different, but the result is the same, can help kill cancer cells. But: praziquantel in kill cancer cells, can give a cancer patient cause slight difficulty in breathing, but the symptoms disappeared soon. So: have difficulty breathing symptoms of cancer patients had better not take praziquantel tablet, however: no breathing difficulties of cancer patients can take praziquantel, take praziquantel tablet in treatment of cancer, must protect liver and kidney shot, at the same time so as not to hurt the liver kidney damage! If the praziquantel and albendazole pills with together to eat, take praziquantel pills in the morning and evening eat albendazole tablets, so the effect of killing cancer cells than take praziquantel pills alone or single albendazole tablets is a drug effect to increase 3 to 4 times. [2,3]

5. Application of Praziquantel and Albendazole in Early, Middle and Advanced Cancers

Praziquantel and albendazole were used in patients to damage the corpus and participate in killing the corpus, inhibiting the synthesis of nucleic acid and protein, depolarizing the surface membrane of the corpus, significantly reducing the activity of alkaline phosphatase in the cortex, inhibiting the uptake of glucose, and depleting the endogenous glycogen to starve the corpus. It can also cause the degeneration of cytoplasmic microtubules in intestinal cells of worms, and combine with their microtubule proteins, resulting in blockage of intracellular transport, accumulation of endocrine granules in Golgi apparatus, gradual dissolution of cytoplasm, complete degeneration of absorbed cells, and the pathogenesis of death of worms. Cancer cells are directly regarded as worms and parasites in cancer patients. The worm, the schistosome, kills like that, starves to death. First, long-term administration of Praziquantel destroys the parasite cortex of cancer cells and lets human immune function participate in killing cancer cells. Secondly, long-term administration of Praziquantel and albendazole inhibits the synthesis of nucleic acid and protein in cancer cells, depolarizes the surface membrane of cancer cells, and significantly reduces the activity of alkaline phosphatase in the cortex, resulting in cancer cell attachment. Inhibition of glucose uptake in human organs leads to the depletion of endogenous glycogen and starvation of cancer cells. Thirdly, long-term administration of Albenda contusion can also cause the degeneration of cytoplasmic microtubules in cancer cells, which binds to their microtubule proteins, resulting in blockage of intracellular transport, accumulation of Golgi endocrine granules and gradual dissolution of cytoplasm. It causes complete denaturation of cancer cells and death of cancer cells. In accordance with the above measures, Praziquantel and albendazole are taken alternately every day for more than three months. If they are taken for a long period of time, they can completely gradually kill and starve cancer cells, resulting in the gradual shrinkage of cancer tumors, withering and shedding, so that human organs are no longer engulfed and eroded by cancer cells, and recover. Restore the original organ function of human organs, eliminate the damage of cancer to human organs, so as to restore the health of cancer patients. [2,3]

Methods of taking Praziquantel and albendazole to cure various early, middle and late cancers:

(1) Every morning on an empty stomach praziquantel 100 mg + albendazole 400 mg +1 grain of Ve, the ginseng of jade bamboo particle 40 grains.

(2) Before supper on an empty stomach praziquantel 100 mg + albendazole 400 mg +1 grain of Ve, the ginseng of jade bamboo particle 40 grains.

(3) Fluids or cancer patients have difficulty eating, can put the medicine pressed into powder, with warm boiled water a blunt down, as long as can do more than one thousand ways to eat medicine, there must be some effect for the treatment of cancer.

(4) Of liver cancer patients must take the soybean phosphatide, pancreatic cancer, and gastrointestinal digestion and absorption function for severe cancer patients have problems, during the period of drugs to treat cancer must be nutritional injection to sustain life, to prevent accidental phenomenon.

Why should we take Ginseng Yuzhu Granule simultaneously when taking Praziquantel and albendazole to treat all kinds of early, middle and late cancer? Because: although the Chinese medicine "Ginseng Yuzhu Granule" alone cannot kill cancer cells, but: Chinese medicine "Ginseng Yuzhu Granule" has the effects of tonifying kidney, invigorating blood and qi, reducing inflammation and diuresis, calming and tranquilizing mind, strengthening muscles and bones, and strengthening the body. At the same time, taking Chinese medicine "Ginseng Yuzhu Granule" can eliminate Praziquantel and albendazole. All kinds of adverse reactions and toxic side effects caused by

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Albenda frustrated tablets, because the traditional Chinese medicine "Ginseng Yuzhu Granule" contains special Chinese medicine ingredients to relieve Baidu! Taking Praziquantel and albendazole has some side effects which are quite normal. It is 100 times stronger than death caused by cancer. In addition, the traditional Chinese medicine "Ginseng Yuzhu Granule" has the effect of tonifying kidney, invigorating blood and qi, replenishing energy and improving immunity. It can be obvious that Praziquantel and albendazole are taken together with the traditional Chinese medicine "Ginseng Yuzhu Granule". Reduce adverse reactions, eliminate toxic side effects! Therefore, the Chinese medicine "Ginseng Yuzhu Granule" with Praziquantel and albendazole frustrated tablets to eat together, in order to kill cancer cells, and make the tumor gradually shrink, wither and fall off, fundamentally cure cancer! If only Praziquantel and albendazole were taken alone, and the Chinese medicine "Ginseng Yuzhu Granules" was not taken, cancer patients would definitely have obvious adverse reactions, toxic side effects and serious harm to the health of cancer patients! Only when the traditional Chinese medicine "Ginseng Yuzhu Granule" is eaten together with Praziquantel and albendazole, can cancer be effectively cured, and all kinds of early, middle and late cancer patients can be cured!

Clinical case: three years ago, there was a bone cancer patients taking Chinese traditional medicine alone "ginseng jade bamboo particles in the treatment of bone cancers, cancers of the take three months later, the shaded part of filmmaking tumor from 24 mm to 21 mm in diameter, the patient felt sure can eliminate tumor, so I stopped to be your own boss, after six months of the shaded part of filmmaking tumor from 21 mm to 32 mm in diameter, the patient was worried, find my request again to continue taking Chinese traditional medicine" ginseng jade bamboo particle to treat cancer, this time I take praziquantel and albendazole pills together with Chinese traditional medicine "ginseng jade bamboo particle" to the bone cancer patients to treat cancer, continue taking three months after the tumor significantly narrowed, and continue to take two months' time, tumor completely disappeared. In the clinical cases, there are many cancer patients are taking praziquantel and albendazole with traditional Chinese medicine "ginseng jade bamboo particle to treat cancer, a high efficient. [4]

6. Conclusion

Taking praziquantel and albendazole pills alternately every day for more than three months, can gradually kill and starve cancer cells. It can gradually shrink, wither and fall off cancerous tumors, so that human organs are no longer devour and eroded by cancer cells, restore the original organ functions of human organs, eliminate the damage of cancer to human organs, and make patients back to health. At the same time, taking the traditional Chinese medicine "ginseng jade bamboo particle" can completely eliminate various adverse reactions and side effects caused by praziquantel and albendazole pills.

After repeated clinical trials, the following conclusions were drawn: all patients with advanced cancer, cancer patients with liver and kidney dysfunction, lung cancer, laryngeal cancer, and esophageal cancer patients with respiratory-related body organs have been banned with praziquantel. Benazol and "ginseng jade bamboo particle" can be used, and taking longer time can completely cure cancer! Although praziquantel works quickly, it is only suitable for early and mid-stage cancer patients under 50 years of age. Praziquantel tablets must be eaten in the morning, it is best not to eat praziquantel tablets in the evening, so as not to affect the breathing. Praziquantel must be eaten in the morning. It is best not to take praziquantel in the evening to avoid affecting your breathing.

I eat western medicine and Chinese medicine cooperate together to treat cancer, is a major breakthrough and innovation of human medicine, because of all the western medicine will hurt liver kidney damage, the patient can't eat for a long time. However, with praziquantel and albendazole pills to treat cancer must be more than three consecutive months of time to shrink the tumor, wither and fall off, so with praziquantel and albendazole tablets to treat cancer, must protect liver and kidney shot, at the same time so as not to hurt the liver kidney damage! So, I didn't take praziquantel and albendazole tablets and traditional Chinese medicine ginseng jade bamboo particle distribution together to eat, eliminate the long-term use of praziquantel and albendazole tablets produced side effects! Ensure that no damage in cancer patients healthy!

I hope that my research results and new findings, like the LED lights developed by Japanese scholars, can save a lot of manpower, material resources and treatment costs, and prolong the life expectancy of cancer patients.

7. Prospects for the Future

Some cancers are deeply hidden, usually cannot be found, and cannot be detected by physical examination. Once found, it is late, and the best time period for treatment is missed, and the cancer patient died quickly.

Normal before cancer did not appear should take praziquantel and albendazole and "ginseng jade bamboo particles" with Chinese herbal medicine to prevent cancer, immunity and disease resistance of the everyone's different, when the human organs with parasites or cancer cells ap-

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peared, people's own imperceptible, physical examination and check out, such as cancer cells to spread it is too late. Normal person can eat before the cancer did not appear and diffusion praziquantel and albendazole and "ginseng jade bamboo particles" with Chinese herbal medicine to prevent cancer, all the potential of the parasite and cancer cells to kill education body outside, praziquantel and albendazole like the scavenger in the human body clean up human body trash, parasite prevention and cancer cells in the human body growth and development, the spread of spread, so as to prevent the emergence and spread of cancer.

After repeated trials concluded that all of the normal human cancer prevention disables praziquantel and albendazole only chips and the ginseng jade bamboo particles can prevent cancer, some take a long time can also be very good to prevent cancer. If you take praziquantel to prevent cancer, must protect liver and kidney shot, at the same time so as not to hurt the liver kidney damage!

8.The Moral, Funds, Data Sharing and Related Statements

8.1 Solemnly Declared

My manuscript entitled: 'Praziquantel and Albendazole Pills Can Cure Cancer' and research was done I am a man, I am the only one of the authors, not involved with the second author, absolutely won't have any economic interests of the copyright disputes and disputes. At the same time, my research results have no sponsor or any organization and institutions to provide financial support, no organizations and institutions with me any more rights and interests conflict. My research and thesis writing is done I a person, clinical trial data and theoretical basis is reliable, the thesis writing in line with the scientific reason, regardless of any medical disputes and legal responsibility, all by my a person to assume, without conceit.

Cancer patients and their relatives in the QQ group or WeChat friends see my advertising of the treatment of cancer drugs, then cancer patients and their relatives to buy my four kinds of drugs for cancer patients to eat, eat have effect for the treatment of cancer will continue to eat, eat until three months after the radical cure cancer, the cancer cure, cure cancer patients to other cancer patients, promote my four drugs for the treatment of cancer, news and propaganda out like that!

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REVIEW

Research on the Related Factors of the Second Molar Dislocation and Orthodontic Erect Method

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ABSTRACT

The second molar dislocation is more common clinically. To investigate the related factors of the second permanent molar dislocation, and provide reference for the clinical diagnosis and treatment of orthodontics. From the current clinical research, the clinical methods of orthodontic erect secondary molars are also diverse and clinical.

The narrower first molar alveolar arch width, smaller ANB angle, and crowded maxillary posterior segment arch are the factors that cause the maxillary second permanent molar dislocation. The narrow alveolar arch width, the smaller SNB angle, the larger ANB angle, and the crowded lower mandibular arch are the factors leading to the dislocation of the mandibular second permanent molar. In addition, for the second mandibular molar malposition, it is particularly important to select the corrective treatment plan. It is especially important to improve the treatment.

1. Introduction

During human evolution, due to changes in food, it causes degradation of the chewing organs. The alveolar and jaw are degraded faster than the teeth, so the length of the entire jaw is relatively short, making it difficult to accommodate all the teeth, resulting in crowded teeth, malocclusion, and impact, and the second molar is no exception. In recent years, in the clinical work, the second permanent molar dislocation is more and more common [1]. It is widely believed that tilting molars can cause or at least aggravate the periodontal tissues damage [2]. There are two most common clinical ones: one is the dentition period the second molar is nearly tilted due to factors such as eruption. There are imaging studies reporting that the former incidence rate is in all the impacted teeth. Occupy 0.3% to 0.6% ridicule [3]. This study aims to summarize the incidence of second permanent molar dislocation and its related factors, in order to provide reference for orthodontic clinical treatment.

2. Relevant Factors

With the evolution of human race, modern people's chewing organs have a deteriorating trend, and the imbalance of tooth volume and bone mass is one of the main causes of malocclusion [4]. The related research results show that the incidence of dislocation of the second permanent molar is 52%, which provides a certain data reference for orthodontic treatment. The result of the study is higher than

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that of Han Chun [8] in 2006, which is slightly higher than 51.5% of the survey results of Cai Huibin [9] in 2015. The reason may be that the inclusion conditions of the samples are different.

Wang et al [10] measured the projection of the most prominent point of the maxillary first molar in the lateral plane of the skull and the projection of the maxillary fissure in the anterior skull base plane in 23 patients with second molar occlusion. The distance between the two molars was found to be significantly smaller than the normal occlusion of the maxillary first molar to the posterior wall of the maxilla. Therefore, it is considered that the second molar is closely related to the posterior gap of the dental arch. Soonshin et al [11] in the study of 40 patients with maxillary second permanent molar dislocation, that the dislocation of the maxillary second permanent molar is related to the length of the arch, the ANB angle and the distance from the distal to maxillary nodules of the maxillary first molar.

The cephalometric measurements, SNA angle, SNB angle, ANB angle and SN/MP reflect the sagittal plane and vertical bone type. Different bone type jaws grow differently, and the second permanent molars erupt. The situation may be different, so this study will analyze it. Zhang Jianhang [12] studied that vertical bone type and sagittal plane type had no effect on the malposition of the second permanent molar during orthodontic treatment. Soonshin et al [13] study that the dislocation of the maxillary second permanent molar is closely related to the ANB angle.

The related research results show that the dislocation of the maxillary second permanent molar is related to the width of the maxillary first permanent molar. The dislocation of the maxillary second permanent molar is related to the size of the maxillary ANB angle, and is independent of the vertical bone type (SN/MP). This is consistent with Soonshin:s findings. The misalignment group showed a smaller ANB angle, the average value of the SNA angle was smaller, and the position of the A point was relatively posterior, which means that the position of the maxilla was relatively posterior, in accordance with the previous Pulver [15] study.

The dislocation of the mandibular second permanent molar is related to the width of the alveolar arch between the first and second molars of the lower jaw and the crowdedness of the posterior segment of the mandibular arch, which is consistent with the results of Ma Haiqing [16]. The dislocation of the mandibular second permanent molar is also related to the SNB angle and the ANB angle. In patients with larger ANB angles, the mandibular arch and alveolar arch are narrower than the normal arch [21], and the posterior segmental arch and alveolar arch form a suitable occlusal environment and dynamic balance [17], mandibular The eruption of the second molar may be affected by these local factors, and the probability of misalignment increases. The increase in mandibular length is achieved by the growth of the posterior condyle and the absorption of the new bone of the posterior margin of the mandibular branch. Different vertical bone types have different growth directions of mandible. LAUCK [21] found that patients with mandibular third permanent molars had more high-angle features. Tsai [20] found that the maxillary second molar was in the early stage of development, and the crown was oriented to the far center. After that, the axis of the lower molar gradually erected with eruption. The second molar of the mandible was in the early stage of development, and the crown was tilted to the middle, and there was no significant difference in the developmental stages. Most of the maxillary molars have a long-term tilt, while the mandibular molars have a near-middle tilt which is consistent with the direction of the dip angle of the upper and lower jaw second molars, suggesting that there is a correlation between the tilt angle of the second molar and the malocclusion. This is for further study.

3 The Purpose and Clinical Practice of Vertical Second Molars

The purpose of vertical molars is to improve the health of the periodontal tissue and the function of the jaw by adjusting the position of the teeth, facilitating the eruption of the impacted teeth in the near-middle tilt or facilitating the repair of the edentulous area.

In 1973, Brown proposed that the orthodontic process may create a more appropriate degree of dental tilt for patients with periodontal disease, restore normal sacral plane, and improve occlusion [18]. He uses thin orthodontic arch wires to reduce the undesired movement of the teeth, using accessories such as upright springs and spiral-opening springs to achieve the desired molar movement. Although the proximal alveolar bone loses 0.5 to 1 mm, the vertical molar is still considered a routine step in the treatment of periodontal disease sequences. Upright molars reported from the current literature, and there are two main categories of methods.

The first type of surgical replantation: although simple and convenient, it may cause loss of tooth pulp vitality, root resorption and root adhesion.

The second type is orthodontic assisted upright: orthodontic treatment is currently a relatively safe treatment, mainly using the principle of arch wire suspension arm, which mainly includes full-mouth fixed appliance or fragment with auxiliary spring or auxiliary arch. In addition,

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there are also implant-supporting traction erect or indirect anchorage with auxiliary springs, movable appliances and belt loops with far-reaching hooks [22]. The traditional orthodontic erect mandibular second molar is mainly the primary tooth. The full-mouth fixed appliance or segmental arch technique is used together with the auxiliary spring or the push spring to erect the mandibular second molar, which has higher requirements on the collar, but with the rise of temporary anchorage devices (TADs) will slowly be discontinued. The nailing technique is a representative of the TADs technology that has emerged in recent years. Although it follows biomechanics, it has some characteristics of its own, such as strong anchorage, low pressure effect and high efficiency mechanics [6]. These features are more effective and effective in the application of traditional methods, improve treatment efficiency, and expand the application of orthodontics. The implant is used as a direct or indirect anchorage with an auxiliary spring or an elastic orthodontic attachment [22]. The erect mandibular second molar is simple and efficient.

4 Develop a Plan

As mentioned above, due to individual differences, the development of correctional treatments needs to be different from individual to individual to improve efficiency. Firstly, according to relevant research, the mandibular second molar is gently tilted forward. The simplest method is to place a separate device between the first molar and the second molar to loosen the contact points of the two teeth, so that the second molar can erupt. If the slanted mandibular second molar is lower than the functional sacral plane, the mandibular molar needs to be extended, and the torque is about 2000~3000 gm. Secondly, If the posterior teeth need significant elongation, then the force applied in the anchorage should be larger. If elongation is not required, the force needs to be smaller, and the forearm of the suspension arm should be as long as possible. At this time, the full-back fixed appliance technology or the segment bow technique can be used with the auxiliary spring (such as the scorpion, the Tip. back device, the modified slider, the "T" shape, etc. At last, When the distal crown of the oblique molar is higher than the functional fetal plane, the molars need to be lowered, and the biomechanics becomes more complicated. According to the balance principle, the torque required to be loaded onto the molar is smaller than the torque applied to the anchor. However, a straight spring similar to a backward tilt has side effects, that is, the molars are elongated during the erecting process. Therefore, in the past, the sputum should be constantly adjusted or used to avoid severe trauma. At this time, the implanted nails can be avoided by indirect anchorage with Sander. The pre-formed Sander spring, the rear part of the spring is a 0.016 × 0.022-inch super elastic arch wire connected to a straight 0.017 x 0.025 inch stainless steel bow with a flexible tube Composed on the silk fragments. The front part is inserted into a prefabricated vertical cross tube. In order to make the molars stand upright and depressed, the angle of the anterior teeth should be 135[23].. The angle of the posterior teeth should be 90°

5. Conclusion

In summary, due to the high incidence of dislocation of the second permanent molar, it is recommended that the second permanent molar be included in the correction at the initial stage of correction, combined with the type of dislocation, to shorten the treatment time and reduce the patient's pain. Clinically, patients who are newly diagnosed should not only pay attention to the anterior segment of the arch, but also pay attention to the analysis of the gap of the posterior arch. Patients with dislocation of the second molar due to insufficient posterior interdental space should first develop a gap in the correction process. The condition of the dislocation of the second molar is provided. For the pusher teeth to the distal patient, the amount of jaw bone growth should be combined with the growth of the jaw before the correction. Be careful not to transfer the crowd in the anterior region to the posterior region, artificially causing the dislocation of the second permanent molar or even locking the teeth. At the same time as the correction of the mandibular relationship in patients with different sagittal planes, attention should be paid to the correction of the dislocation of the second permanent molar. The best method of correcting the molars must be based on the individual:s condition, and the best method should be chosen to improve the corrective effect of the vertical molars. Although there are clinical reports, patients with bifurcation lesions, near-middle edge bone loss, increased tooth mobility, mainly because the previous appliance is too simple, without considering individual differences, we should design according to individual circumstances Appliances, micro-planting nail technology is the future development trend, we should give full play to its advantages to achieve the best results.

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REVIEW

The Role of Blood Station Quality Management System in the Quality Control of Blood Collection

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ABSTRACT

With the continuous development of China's medical industry in recent years, relevant staff has also paid more attention to the quality management of blood stations, and China has gradually improved during the setting of laws and regulations for blood station quality management. The policies set by the Chinese government have been fully implemented through the reasonable implementation of relevant staff. With the continuous development of China's medical industry in recent years, relevant staff have also paid more attention to the quality management of blood stations, and China has gradually improved during the setting of laws and regulations for blood station quality management. The policies set by the Chinese government have been fully implemented through the reasonable implementation of relevant staff. On this basis, the management model of the Chinese blood station has been continuously innovated in the application process, and the blood collection work of the Chinese blood station has been greatly developed. However, when the blood station in China is conducting blood collection, its quality control program is still not fully mature. Therefore, in this context, it is necessary to do a good job in the construction of the corresponding blood station quality management system and make effective adjustments, which will give full play to the role of the management system in the quality control process of blood collection. In this paper, the construction plan of the blood station quality management system is analyzed to explore the role of the blood station quality management system in the process of blood collection quality control, aiming to provide assistance for the quality management of blood collection in China.

1. Introduction

Blood collection plays an important role in the modern medical industry, and the main purpose of blood collection is to provide healthier and better blood sources for patients who need blood transfusions in clinical settings. Under normal circumstances, in the quality management of blood collection, it is necessary to measure the actual working condition of the blood station, clarify the different problems presented by the blood standing in the work process, and establish a perfect blood station quality management system according to the needs in the blood station, which can effectively strengthen the quality control of blood collection, thereby promoting the substantial improvement of blood collection quality and work efficiency, and improving the quality of modern

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clinical medical blood. Blood collection is an important part of clinical medical work, not only to provide a good blood source for clinical patients, but also to a certain extent to show the level of China's medical industry. In this context, it is necessary to actively carry out the construction of the blood station management system, thereby improving the quality management effect of the blood station, and has a positive effect on the development and reform of China's medical industry.

The blood station quality management system is the core content of the blood station management work, and also the focus of the blood station management work. In the case of various management tasks, if you leave the quality control, it means that the management work is completely out of control, therefore, quality control is not only the key to ensure the blood collection effect, but also the basis for improving the management effect, and is the lifeline of blood collection work. The quality of blood collection at the blood station in clinical work is directly related to the life safety and treatment effect of clinical blood donors. Therefore, in order to ensure a good blood station quality management system, it is necessary to take practical measures when conducting blood station management, so as to ensure that the blood collection work is carried out in an orderly manner, and the blood collection goals of different patients have been completed. Therefore, it is necessary to strengthen the management and continuous improvement of the blood station quality management system at work, and clarify the problems existing in it to ensure the blood collection effect.

2. The Construction Plan of Blood Station Quality Management System

2.1 Organization and Management

First of all, in order to ensure the quality control effect of blood collection in China, it is necessary to do a good job in quality management of blood stations, so as to help ensure the quality of blood collection and ensure the effect of blood in clinical use. In the first place, it is necessary to establish a perfect blood station quality management system according to the specific working status and operation form of the blood station. The relevant management departments need to first clarify the existing personnel omissions and strengthen the technical training of the staff in the blood station, which can improve the overall quality of the staff, and the qualified blood stations can carry out corresponding intensive education and training in the blood station, and some blood collection personnel with rich experience can be selected as the staff, and will greatly improve the quality of the work of the staff in the blood station, and establish a better and more efficient blood station work team. Relevant departments should first pay attention to and deeply understand the necessity of blood station quality management, and set up a corresponding management system according to the management status in the blood station and the postal authority of the staff, which can help the construction of the blood station quality management system. Before the blood station carries out various blood collection works, the blood station management personnel need to clarify the way of human resource allocation and select the appropriate staff according to the relevant requirements. Blood collection personnel with different working years and different qualifications need to be managed separately to ensure the coordination and rationality of personnel deployment. A staff member with strong professional ability and rich work experience can also be selected as the supervision team leader of blood collection work, which will enable the responsibility to be implemented to ensure the smooth progress of blood collection.

The blood station that successfully implements blood station organization management has a characteristic, that is, blood station management personnel are actively promoting blood station organization management. Such managers have not only good knowledge and attitude towards the management of blood stations, but also willing to accept relevant learning and knowledge for a long time, and constantly strengthen himself in his daily work, and apply the learned content to the actual implementation of the blood station quality control system. So it can be seen that blood station management personnel and leaders need to pay attention to the rational application of the blood station quality control system and the modern reform method in daily work, and set up an effective blood station quality control system management mode and system in combination with the specific professional direction and working conditions of the blood station, which will greatly improve the feasibility and effectiveness of the implementation of the blood station quality control system. If the blood station quality control system management method of other blood stations is completely copied, it is not only difficult to achieve the effect of adapting to local conditions, but it may also be completely counterproductive and affect the smooth progress of blood collection work.

2.2 Establish a Good Blood Collection System

When the blood collection personnel write the blood collection record, they should ensure the writing specifications, do the corresponding blood collection record operation, and formulate the perfect writing content according

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to the actual situation of the profession. Make the record of the blood donor's situation clear and record the change status and the treatment form, and record the basic data of the blood donor objectively and truthfully and record the blood collection status. By writing the contents of the record sheet, not only the monotonous and empty recording of the clinical blood collection personnel can be avoided, but also the writing content can be prevented from being overlooked. When carrying out continuous improvement work on the quality management of the blood collection system in the blood station, relevant management personnel may regularly check or irregularly check the written list, and reward the blood-collecting personnel who are well-written and well-organized, and the blood-collecting personnel who have omissions should also promptly correct and, if necessary, give certain punishments, which can improve the subjective initiative of the blood collectors and avoid the situation.

Whether it is reward or punishment, the ultimate goal is to promote the smooth development of blood collection work. Therefore, when setting up the reward and punishment system, punishment and rewards cannot be set too heavy, this will dampen the enthusiasm of blood collection personnel. It is recommended that when setting up rewards, do not link with the performance of blood collection personnel, and separate the reward and punishment system separately, which can help improve the quality of blood collection staff. However, when summarizing the problems that are easy to occur in the blood station quality control system, it is necessary to clarify the severity of different problems and give objective evaluations. It is reasonable to set up the reward and punishment system for the work omissions of blood collection personnel and to enhance the responsibility of blood collection personnel for work. In the daily work, the existing problems are criticized and punished. If the same problem is found again during the strict inspection, the punishment should be aggravated. The intensity should be reduced at the time of the initial punishment, so as to avoid the enthusiasm of the blood collection personnel; while medical staff who have excellent work performance and no occupational omissions need to be rewarded accordingly, which can encourage the blood enthusiasm's work enthusiasm to exert subjective initiative.

2.3 Establish Sound Rules and Regulations, and Implement Responsibility System

At work, managers need to develop patient-compliant workflows based on different job characteristics within the blood station and the characteristics of the blood collection personnel in different shifts. In this way, it is possible to formulate rules and regulations with clear responsibilities and operational rules in the process, and ensure that blood collection personnel can have rules to follow in their daily work. In actual work, the blood collection personnel need to provide corresponding feedback and suggestions to the system according to their own conditions, and the blood station manager needs to collect and summarize the feedback and suggestions to understand the problems that most blood collection personnel will have. In this situation, the effect of continuous improvement is ensured by constantly revising the system.

Most blood stations conduct quality inspections and inspections in the first quarter or one month, and they are easy to flow in the form during the inspection process. This situation is the status quo of most blood stations when performing blood collection management. Not only can the quality of blood collection be improved, but also the blood collection operation cannot be supervised and affect the actual work quality. In this context, the inspection work for blood collection personnel needs to be carried out as frequently as possible, so that a large check every week, three days a small check. Through random inspection to ensure the availability of supervision and inspection work, this can greatly improve the working attitude and seriousness of blood collection personnel in daily blood collection, and will strictly instill their psychological state into daily work. On the basis of irregular sampling and regular inspections, the supervision and inspection of blood collection quality will be strengthened, which will ensure the effectiveness and management effect of daily work quality.

2.4 Establish a Blood Station Management System with Humanities Management

Because the blood collection work needs to face different blood donors, and the blood collection personnel have a large daily workload, mainly in the basic operations such as blood collection, blood preservation, and blood donor data analysis of blood donors. Under such circumstances, the conventional management method has been difficult to meet the blood collection needs of modern blood stations, so the main content of blood collection services has gradually changed from providing high-quality blood collection operation services to active communication and communication with blood donors. In order to achieve this goal, blood collection personnel need to ensure a smile, thoughtful and civilized service attitude in their daily work. In order to achieve such a goal, it is necessary to establish a good humanistic management improvement direction in the ward, which can be based on basic humanistic care methods such as "a smiley face", "a kind

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greeting," and "a cup of hot water". A quiet and clean environment can make people feel comfortable, and good blood collection personnel can ensure the communication quality between blood donors and blood collection personnel is good, therefore, blood collection personnel need to implement a good job responsibility system, and establish a sound humanistic communication system in the hospital, requiring blood collection personnel to continuously improve their humanistic qualities in their daily work. Regular and excellent technical operation, high-quality service quality, and strict implementation of rules and regulations can improve the humane care and effectiveness of blood collection personnel. In this way, the work of blood collection service management can be refined.

Although the humanized construction of the blood station management system has a good effect and is suitable for use in a variety of medical environments, even if the relevant reform staff is not willing to actively participate in the reform activities, they will lose their proper meaning. The blood station management system is also such. Therefore, in the process of improving the blood station management system, it is necessary to put the focus of work on the enthusiasm of the blood station management personnel. On the one hand, it is necessary to allow as many bone blood collection personnel as possible to participate in the activities of the blood station management system construction, In the blood station, mainly including management personnel and blood collection personnel with long-term seniority, exert their ability to subjective initiative and solve problems, and constantly strengthen their own blood collection techniques. On the other hand, it is also necessary to mobilize the enthusiasm of the general staff to enable all blood collection staff to experience the corresponding sense of accomplishment in the management process, strengthen the awareness and ability of the blood collection staff to solve problems, and improve their participation, which can greatly improve the practical application value of the blood station management system.

3. The Role of Blood Station Quality Management System in Blood Collection Quality Control

3.1 Guarantee the Orderly Development of Blood Collection Work

The construction of the blood station quality management system can enable the blood collection work to be carried out smoothly and orderly. Through the effective quality system construction, all the links in the blood collection can be smoothly carried out, in particular, the blood test and blood transfusion work need to have high standardization, and the blood station quality management system can effectively restrain and standardize various operations. The blood station quality management system can ensure that the blood collection work strictly follows the relevant rules and regulations and regulations when it is carried out, which greatly reduces the occurrence of various infectious events and helps to ensure the quality of blood collection.

3.2 Ensure the Professional Quality and Comprehensive Quality of Blood Collection Personnel

The blood station quality management system can enhance the professional quality and comprehensive quality of relevant management personnel in the management process, and help guide relevant medical staff to recognize the importance of blood collection. In addition, this management method enables the blood station staff to strictly follow the rules and regulations in carrying out various operations to further ensure the smooth collection of blood. It has greatly enhanced the vigilance and prevention awareness of medical staff on risks, and further strengthened the professional skills and social responsibility of medical staff.

3.3 Improve the Treatment of Blood Collection Work

The blood station quality management system can help to improve the quality of the blood collection work, and at the same time greatly enhance the technical management capabilities of the relevant staff, thus improving the quality of blood collection in China, which guarantees the quality of work in all aspects of blood collection, helps to enhance the scientific and efficient blood collection, and achieves the quality assurance of blood collection activities.

4. Conclusion

In summary, the main purpose of the blood station quality management system is to strengthen the quality control of blood collection, which can help optimize the management of blood quality collection. Therefore, the relevant medical staff needs to establish a sound blood quality management system. When conducting blood collection work, strictly follow the relevant systems and conduct orderly operations to ensure that the accuracy of blood collection is high. At the same time, it can also strengthen the supervision quality of blood collection work, improve the quality control effect of blood collection in China, ensure the quality of blood collection in China, and make China's

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blood collection contribute to the medical industry.

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REVIEW

Improve the Center Supply Room to Ensure the Quality System for Disinfection and Sterilization

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ABSTRACT

The disinfection supply room is a very important department of the hospital. Its main job is to provide sterile equipment and dressings for various activities in the hospital. It is an important department in the hospital infection management process. Doing a good job in the control and management of the disinfection supply room is the main link to ensure the prevention and control of hospital infections. The quality of management directly affects modern clinical medical work. Therefore, the hospital supply room should be strengthened and improved to ensure that all items can be safely used in the work process, which can effectively avoid the occurrence of cross-infection incidents in the hospital.

1. Introduction

Infections in hospitals have been paid attention to by modern society and related medical staff, and high-quality disinfection and sterilization in hospitals can help control hospital infections. In different hospitals, there are more patients and related medical personnel, so this has higher requirements for the staff and work quality of the central supply room. However, it is worth noting that in the investigation and research, the supply quality of the central supply room is a relatively weak link in the overall development of China's medical industry[1]. In order to further promote the control of infections in hospitals, it is necessary to analyze the advanced management experience at home and abroad, understand the management techniques, and establish a complete and advanced central supply system according to the specific characteristics of different hospitals. In this way, the hospital center supply room will be reformed, so as to help prevent infections and prevent hospital infections.

2. Reasonable Layout Facilities Can Ensure the Effect of Infection Control in the Hospital

Since the central supply in different hospitals is a relatively independent area, different sections can be divided according to their cleanliness and work functions, and they can be divided into contaminated areas, clean areas, sterile areas and general working areas. First of all, when managing different areas, strict boundaries should be set in different areas, when medical personnel enter and leave different areas, they need to do protective operations such as changing clothes and changing shoes[2]. It is necessary to set clear labels at different doorways and establish a perfect isolation barrier. A conventional fully automatic cleaning and disinfecting machine is required between the contaminated area and the clean area as a physical barrier; relevant staff members need to carry out

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maintenance analysis on the working status of the disinfection washing machine on a regular basis to ensure that the areas can have corresponding cleaning and disinfection effects. The high-pressure steam sterilizer needs to be used as a physical barrier between the cleaning area and the aseptic area. It is also necessary for the corresponding staff to manage their operating conditions reasonably. Air purifiers can also be installed inside different areas to keep the air in the room clean. In order to avoid contamination of the aseptic zone or the cleaning zone in other areas during the working process, the air pressure in the sterile zone can be set to a slight positive pressure, and the contaminated zone needs to be set to a micro-negative pressure, which ensures air circulation between the sterile and contaminated areas, from the sterile area to the contaminated area rather than the contaminated area to the sterile area[3]. In the daily work process, the room temperature in the central supply room needs to be controlled at about 20 degrees Celsius, and the relative humidity is set at about 50%, while ensuring the supply of water and charge compressed air.

In the environmental management of the central supply room, it is necessary to set up relevant rules and regulations to ensure that different items are placed in the corresponding positions, and the daily staff needs to be properly managed and inspected, and checked regularly. At the same time, random inspections are carried out, which ensures that the layout facilities in the central supply room are in a normal state. It is worth noting that when a certain equipment or equipment in the center supply room is aged or damaged, it needs to be repaired or replaced immediately. This is the key to ensuring environmental sanitation in the aseptic area and the clean area, which avoids contamination of the sterile field without the support of the facility. When setting up the environment, a prominent label should be posted everywhere, and the writing on the label should be clear. If it is out of paint or discoloration, it needs to be replenished or replaced immediately, which will ensure that medical personnel can follow the signs when conducting various medical activities.

3. The Various Workflows Need to Be Consistent with the Requirements of the "Three Workflows" in the Central Supply Room

In the disinfection supply room, the workflow needs to include: accepting the dirt "recycling equipment→classification→cleaning→disinfection→drying→inspection, maintenance→packaging→sterilization→storage→distribution".

When the circulation of various items is carried out, the circulation of the personnel in the department in the disinfection supply room and the circulation of the articles shall be carried out separately, and the topography or shuttle phenomenon in different areas may not occur, so as to ensure the quality of the aseptic. When the department handed over the goods, it should first enter the contaminated area to hand over the contaminated items to the relevant receiving personnel. After the two parties have verified the correctness, the receiving party may notify the dispensing office of the sterile article and issue the sterile goods to the handover personnel to ensure the rationality of the exchange of the articles. After the items are recycled, the relevant staff should first record and classify the items, and disinfect them accordingly. After the objects are disinfected, they need to be properly packaged according to the characteristics of the items and the needs of the equipment. After the packaging is completed, the sterilization operation is carried out and tested to check whether the sterilization effect is qualified. After confirming the qualified, it is placed in a sterile cabinet for storage, and then distributed when necessary[4]. By carrying out the item handover and management operations in strict accordance with such a process, it is possible to make the item management meet the requirements and avoid the contamination of the item.

Since the various items in the operating room are particularly specific in application, it is necessary to operate according to the surgery in the disinfection supply room[5]. A separate channel is set for each item in the room. If the operating room is close to the disinfection supply, an elevator can be placed directly in the aseptic area and the contaminated area to directly connect the contaminated area and the sterile area to the operating room. In the polluted area, the contaminated items after the operating room are directly sent to the supply through the pollution elevator. The disinfection personnel in the polluted area collect and record them, and then put them into the cleaning box and send them to the cleaning and disinfecting machine for cleaning and disinfection, After entering the cleaning area, the articles are effectively sorted and sterilized, and the articles are directly delivered to the operating room through the aseptic elevator or stored in the aseptic storage cabinet until the next operation. After the surgery on the day is completed, the roving nurse needs to contact the staff in the disinfection supply room to analyze the omissions and adjust them, and then deliver the items involved to the operating room through the aseptic elevator. This kind of workflow enables the nursing staff in the operating room to concentrate on the operation of cleaning, maintenance and disinfection of the instruments during the operation, so that the nursing staff can more actively understand the patient's condition and achieve the effect of doctor-patient handover[6].

It is worth noting that during the various workflows, monthly or quarterly, the omissions of operations in each process need to be clarified and summarized to understand the omis-

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sions between the workflows and adjusted through reasonable management and adjustment, which ensures continuous improvement in the operations in the sterilization supply room.

4. Supporting Application of Equipment

In the process of disinfection supply operation, it is necessary to clarify the supporting application and management of the equipment, which can improve the disinfection efficiency as much as possible, avoid the situation of excessive workload, and reduce the cross-infection caused by the flow of personnel in the disinfection supply room to reduce the incidence of nosocomial infections[7].

4.1 Equipment Cleaning and Disinfection Management

With the continuous development of new disinfection and cleaning technologies in recent years, it is necessary to clean and disinfect the various medical operations in order to ensure complete sterilization[8]. This is because any residual organic matter may affect the effective contact between the microorganism and the sterilization medium during the sterilization operation. Common organic substances include blood clots, proteins, and mucus, and this condition produces a protective film against bacteria that ultimately affects the sterilization effect. Therefore, it is extremely important to perform appropriate cleaning operations before sterilization.

For the time being, clinical cleaning operations mainly include manual cleaning and mechanical cleaning.

In the process of manual cleaning, the instruments are mainly cleaned and disinfected by hand. The main components include precision and sharp instruments, instruments that cannot be immersed in water and serious pollution or blood stains on the instruments that cannot be cleaned by the machine. The main purpose of manual cleaning is to protect the equipment, and at the same time, it cannot be processed by various kinds of machinery, or the materials of the machine will be cleaned during the cleaning process. This can ensure the cleaning effectiveness of the equipment and ensure the reasonableness of the equipment of different contents. Clean[9]. But it is worth noting that manual cleaning has certain limitations. This is because manual cleaning may be affected by many factors, resulting in incomplete cleaning. Even sharp and sharp items in the cleaning process can damage the relevant medical personnel. Therefore, it is necessary to pay attention to self-protection when applying manual cleaning to avoid occupational exposure.

In the process of cleaning the contaminated device during mechanical cleaning, even if the cleaning cannot remove the dirt, however, it is possible to directly heat the device to above 90 degrees Celsius, which can kill most of the bacteria and viruses. The disinfection effect is an ideal operation for infection control in hospitals. At the same time, the use of water and detergent as a disinfecting medium in the mechanical cleaning process can avoid the brushing during the manual cleaning process, and minimize the wear and damage caused to the equipment. Due to the extremely high fluidity of the water, it is possible to remove the parts that are difficult to clean in the artificial environment when the machine is used for disinfection. For example, the gap between the instruments and the position of the joints can greatly reduce the occurrence of sanitary corners. When cleaning is performed, since the operations are performed by machinery, the possibility of occupational exposure of the operator is reduced. The machine can fully automate the treatment of the items, effectively isolating different areas to minimize the incidence of re-contamination events. During the disinfection process, the machine can be adjusted through effective physical monitoring parameters and set with appropriate monitoring standards. It is more scientific than the visual inspection of manual cleaning, and can more accurately judge the cleanliness. Different hospitals can be equipped with automatic cleaning and disinfection machines according to their own conditions.

4.2 Item Packaging

At present, China's domestic high-pressure steam sterilization packaging mainly chooses cotton cloth, and after each application of the cloth, it is necessary to thoroughly clean the cloth and check whether there is a hole in the surface of the cloth[10]. In order to manage and control the cloth, it is necessary to irradiate the packing table with the corresponding inspection lamp during the inspection, so as to confirm whether the cloth is of good quality. If the vulnerability of the package is found during the application process, it needs to be replaced in time, and it cannot be repaired. This is because the quality is passed through the production process, and the quality is passed through the repair method. If the cloth is reapplied, it may affect the quality of the package and cause contamination.

For the time being, ethylene oxide sterilized packaging materials mainly choose finger-based tapes, which can be packaged by a special sealing and packaging machine with printing function. In the packaging process, the packaging date, expiration date and staff code can also be packaged and printed, which will avoid artificial changes, make the packaging more standardized, and implement the responsibility to the people, further ensuring strict implementation of the rules and regulations for disinfection operations.

4.3 Item Sterilization

The central supply room often has various types of steril-

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izers such as a pre-vacuum high-pressure steam sterilizer, an ethylene oxide sterilizer, and a dry heat sterilizer. The main purpose is to ensure that when the article is sterilized, according to the type and characteristics of the article, a suitable solution is selected for sterilization, which can ensure the rationality of the sterilization of the article and avoid damage to the device. In order to further distinguish between sterilized and non-sterile items, the loading and unloading should be separated in the sterilizer, the loading side is unloaded in the cleaning area, and the side is the sterile area. In the sterilization room, it is necessary to minimize the flow of the sterilizer, and the same group of personnel can effectively sterilize, so as to avoid cross-infection, and in order to ensure the sterilization effect, strict physical, chemical and biological monitoring is required.

During the sterilization process, high-pressure steam sterilization should be the first to be the main sterilization solution. This sterilization method has good killing effect on a variety of bacteria, and has fewer side effects, and can be applied to sterilization of various high-temperature resistant articles. However, it is worth noting that many medical devices used in clinical practice have the characteristics of being incapable of high pressure and high temperature, so it is necessary to select a low temperature sterilization technology, which is extremely important for the control of infection events in hospitals. For the time being, the cryostat sterilization method applied in the clinic is mainly based on plasma hydrogen peroxide sterilization. Plasma hydrogen peroxide is the most penetrating broad-spectrum sterilizing agent reported in modern clinical practice. This sterilant penetrates many tiny holes in the device, reaches the depths of the item, and is extremely biodegradable. Applying it to the sterilization of the device can protect the equipment from damage while ensuring the sterilization effect. At the same time, it can keep the articles sterile for 180 days while being sterilized with packaging materials. It can be used for emergency storage of first-aid items and unusable items. The plasma hydrogen peroxide sterilizer used in modern clinical practice has a high degree of automation, and the vacuum can be automatically extracted and the temperature and humidity can be automatically adjusted during the sterilization process, at the same time, according to the state and shape of the article to adjust the sterilization time, there are fewer factors that require human intervention, and the influence of human factors on it can be reduced as much as possible to ensure the sterilization effect. In the detection process, this detection method is also more standardized, and various detection schemes such as physical and biological can be used, and the use is strong at the same time, it does not pollute the sterilized items. Equipments for sterilizing such sterilizers can be selected in the operating room and in various departments.

5. Conclusion

In addition to the management of various items and equipment, relevant practitioners in the department need to actively participate in clinical trials and research in the hospital. Identify the omissions in the sterilization operation and improve them, and confirm the quality system of disinfection and sterilization to ensure the smooth operation of various sterilization operations and surgical operations inside the hospital.

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