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Analysis of the effect of interventional therapy for congenital heart disease complicated with pulmonary artery hypertension

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ABSTRACT

Objective: The diagnosis and treatment process and the follow-up results of 249 congenital heart disease (CHD) patients complicated with pulmonary artery hypertension (PAH) were summarized and analyzed to improve the therapeutic effect.

Methods: The clinical data and related auxiliary examinations of 249 patients with CHD complicated with PAH from January 2014 to December 2018 were analyzed retrospectively. The age of the patients was (24.81±5.78) years old. The patients were followed up regularly after drug treatment and interventional therapy, and their symptoms and signs were monitored.

Results: A total of 175 patients (70.3%) were followed up for 3 months to 5 years. After that, the condition was significantly improved. The cardiac function of 62 patients was significantly improved above grade II, and the cardiothoracic ratio was reduced in varying degrees. Seventeen patients died, including 5 cases of central failure, 4 cases of sudden death, 1 case of postoperative pulmonary hypertension, 4 cases of dyspnea, 1 case of sudden death after cold injection, and 2 cases of unknown cause. Adverse reactions occurred in 73 patients, including hemoptysis, arrhythmia, heart failure, and syncope. The survival time of the patients was 0.78-11.51 years. Pulmonary artery systolic pressure and left ventricular ejection fraction decreased significantly. SpO2 and HGB increased significantly after three treatments, while BNP, total bilirubin, and uric acid levels tended to decrease. In the basic state, the values of Qp/Qs, PVRI, and Rp/RS were 1.02±0.56, 24.86±7.56, 1.01±0.34 respectively. After treatment, the three values changed to 1.34±0.67, 19.98±6.45, 0.77±0.12 respectively.

Conclusion: For patients with CHD complicated with PAH, early diagnosis should be strengthened and appropriate treatment methods and timing should be selected to improve the cure rate and prognosis.

Key words: Congenital heart disease, Pulmonary artery hypertension, Cardiac function, Hemodynamics, Cardiac catheterization.

1. Introduction

Congenital heart disease (CHD) (Bellsham-Revell H. & Burch M., 2002) (Baumgartner H. et al., 2011) (Verheugt C.L. et al.) was a common heart disease, which was mainly caused by the imperfect structure and vascular development of the heart during

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embryonic. According to statistics, in congenital diseases, the incidence of CHD was relatively high, accounting for about 30% (Jing-Jing et al., 2018). There were 200000 new CHD patients in China every year, and about 6/1000 newborns suffer from CHD (Yu kunkun et al., 2014). Thus it can be seen that enough attention should be paid to the CHD treatment. There was an unrestricted left-to-right shunt at the intracardiac/large artery level in patients with CHD, resulting in the increased pulmonary blood flow and the formation of pulmonary arterial hypertension (PAH) (Mclaughlin V.V. et al., 2011) (Galiè N. et al., 2002) (Kelly, M. et al., 2008). PAH was the most common complication in patients with CHD and one of the important factors affecting the timing of the operation, treatment, and prognosis, which was important for the early detection, diagnosis, and treatment of CHD. Hemodynamics was defined as mean pulmonary artery pressure (MPAP)≥25 mmHg, pulmonary artery wedge pressure (PAWP)≤15 mmHg. With the progress of the disease, obstructive PAH (Eisenmanger syndrome) may occur and the opportunity of operation will be lost. In the clinic, cardiac catheterization and acute vasodilator testing were often performed in patients with the dynamic and obstructive marginal state to evaluate whether they can be treated surgically. In this paper, 249 patients with CHD complicated with PAH treated in our hospital from January 2014 to December 2018 were collected, and the diagnosis and treatment were analyzed.

2. Materials and Methods

2.1. Patients

A total of 249 CHD patients complicated with PAH who underwent surgery in our hospital from January 2014 to December 2018 were collected. There were 69 males and 180 females with an age of 24.81±5.78 years. There were 198 cases of simple CHD and 36 cases of complex CHD in all patients. For patients with CHD, the collected data showed that there were 19 cases of anterior tricuspid shunt CHD, 172 cases of posterior tricuspid shunt CHD, and 58 cases of mixed shunt CHD. The chest X-ray before treatment showed that the pulmonary blood was increased, and the cardiothoracic ratio was 0.4-2. The level of SpO2 was 65%-94%, HGB was 91-244 g/L, BNP was 32-577.2 pg/ml, uric acid was 19.3-653.5umol/L, SPAP was 20-249mm, left ventricular ejection fraction (LVEF) was 40%-87%.

2.2. Methods

The preoperative examination included the physical examination, echocardiography, chest X-ray, laboratory examination, cardiac catheterization, acute vasodilator testing. The surgical related indexes such as the ratio of pulmonary flow to systemic blood flow (Qp/Qs), pulmonary arteriolar resistance index (PVRI), and the resistance ratio of pulmonary circulation to the systemic circulation (Rp/Rs) were calculated by FICK method. The contents of the telephone interview and outpatient follow-up included symptoms and signs.

2.3. Statistical analysis

All data were processed by SPSS 20.0 software. The measurement data were expressed by x±s, the comparison between groups was expressed by the t-test. The counting data was expressed by percentage, and the comparison was expressed by χ^2 test. $P<0.05$ indicates that the difference was statistically significant.

3. Results

3.1. General

All patients received interventional therapy and then cured and discharged. A total of 175 patients (70.3%) were followed up for 3 months to 5 years, and the prognosis was significantly improved. The cardiac function of 62 patients was significantly improved above grade Ⅱ, and the cardiothoracic ratio was reduced in varying degrees. Seventeen patients died, including 5 cases of central failure, 4 cases of sudden death, 1 case of postoperative pulmonary hypertension, 4 cases of dyspnea, 1 case of sudden death after cold injection, and 2 cases of unknown cause. Adverse reactions occurred in 73 patients, including hemoptysis, arrhythmia, heart failure, syncope. The survival time of the patients was 0.78-11.51 years. Finally, the cardiac function grades of follow-up were grade Ⅰ in 8 cases, grade Ⅱ in 122 cases, grade Ⅲ in 12 cases, grade Ⅱ-Ⅲ in 1 case, and grade Ⅳ in 2 cases.

3.2. Changes in cardiac function

The cardiothoracic ratio of the patients before and after treatment was analyzed. The results showed that the cardiothoracic ratio of the patients

before treatment was 0.57±0.08. After the first treatment and the second treatment, the cardiothoracic ratio decreased to 0.51±0.04 and 0.53±0.05 respectively. There was a significant change in the cardiothoracic ratio before and after treatment (P<0.05) (Table 1). After the first treatment and the second treatment, the SPAP of the patients were 96.00±16.78mmHg and 51.20±10.34 mmHg respectively, which were significantly different from those before treatment (99.54±21.65 mmHg). The LVEF before treatment was 66.7±12.63%, and the results after the first treatment, the second treatment, and the third treatment were 61.83±9.45%, 66.00±10.43% and 62.00±8.65% respectively, which decreased significantly before and after treatment (P<0.05) (Table 2).

Table 1: **Changes of cardiothoracic ratio before and after treatment ($\bar{x}$±s)**

Treatment	Cardiothoracic ratio	P Value
Before treatment	0.57±0.08	<0.05
First treatment	0.51±0.04	
Second treatment	0.53±0.05	
Third treatment		

Table 2: **Changes of cardiac function before and after treatment ($\bar{x}$±s)**

Treatment	SPAP (mmHg)	P Value	LVEF (%)	P Value
Before treatment	99.54±21.65	<0.05	66.7±12.63	<0.05
First treatment	96.00±16.78		61.83±9.45	
Second treatment	51.20±10.34		66.00±10.43	
Third treatment			62.00±8.65	

3.3. Changes in serum biochemical indexes

The changes of the serum biochemical indexes before and after treatment were analyzed. The results showed that before treatment, the values of SpO2 and HGB were 86.82±12.65 and 172.71±26.86 g/L, respectively. After three times of treatment, the values of the two variables were 89.56±9.67% and 177.81±47.85 g/L, respectively. There were significant differences in the values of the two variables before and after treatment (P<0.05). Before treatment, the levels of BNP, total bilirubin, and uric acid were 172.96±34.76 pg/ml, 20.10±4.85 umol/L, and 382.80±74.84 umol/L, respectively. After three times of treatment, the values of the three variables were 70.25±3.56 umol/L, 11.36±3.56 umol/L, and 328±30.65 umol/L, respectively. There were significant differences in the values of the two variables before and after treatment (P<0.05)（Table 3）.

3.4. Cardiac catheterization

The results of cardiac catheterization in patients with CHD complicated with PAH showed that in the basic state, the values of Qp/Qs, PVRI, and Rp/RS were 1.02±0.56, 24.86±7.56, 1.01±0.34, respectively. After treatment, the three values were 1.34±0.67, 19.98±6.45, 0.77±0.12, respectively（Table 4）.

Table 3: **Changes in serum biochemical indexes ($\bar{x}$±s)**

Treatment	SpO2 (%)	HGB (g/L)	BNP (pg/ml)	Total bilirubin (umol/L)	Uric acid (μmol/L)
Before treatment	86.82±12.65	172.71±26.86	172.96±34.76	20.10±4.85	382.80±74.84
First treatment	87.78±13.76	171.63±36.24	141.02±11.67	18.50±3.97	412.00±58.03
Second treatment	88.45±10.45	172.94±43.56	100.08±15.54	13.62±2.86	378.6±32.67
Third treatment	89.56±9.67	177.81±47.85	70.25±8.93	11.36±3.56	328±30.65
P Value	<0.05	<0.05	<0.05	<0.05	<0.05

Table 4: **Cardiac catheterization in patients with HD complicated with PAH ($\bar{x}$±s)**

State	Qp/Qs	PVRI	Rp/Rs
Basic state	1.02±0.56	24.86±7.56	1.01±0.34
After treatment	1.34±0.67	19.98±6.45	0.77±0.12

4. Discussion

CHD was a common cardiovascular disease characterized by the congenital cardiovascular anomaly. PAH was a common complication of CHD, the main feature was the progressive increase of pulmonary vascular resistance, which may lead to death in severe cases .(Li X. et al., 2015) (ASNC. et al., 2020) (Pastora G. et al., 2008).

For CHD patients with PAH, early drug treatment can improve the pulmonary vascular abnormalities and other symptoms effectively, thus effectively alleviate the development of PAH. At present, the main drugs for the treatment of CHD complicated with PAH were prostaglandins, phosphodiesterase inhibitors drugs (Donti A. et al., 2007). The patients in this paper mainly use bosentan, vardenafil, tadalafil, sildenafil, and other drugs, most of which belong to phosphodiesterase inhibitors. Some studies have pointed out that after the use of sildenafil, the symptoms of PAH were improved and MPAP decreased (Nazzareno Galiè et al., 2010). However, because some drugs have certain damage to the kidney, the effect of long-term use of these drugs was still controversial (Gilbert C. et al., 2009).

In general, interventional therapy was used to treat the CHD patients complicated with PAH, which was safe and effective, less invasive and short hospital stay, but the promotion was not enough. According to the European and American guidelines for the diagnosis and treatment of PAH, right cardiac catheterization and acute vasodilator testing were recommended for the treatment of PAH (Galiè N. et al., 2015) (Lau EMT. et al., 2015). All the patients in this study were treated with interventional therapy, and the treatment plan was decided after a comprehensive evaluation. Heath and Edwards divided the PAH into six levels, according to different levels to choose different treatment methods, the low grade for reversible pulmonary hypertension, the higher grade for irreversible pulmonary hypertension (Heath D. et al., 1958). Some scholars advocate using the ultrasound combined with a synchronous electrocardiogram to judge the shunt phase of an intracardiac defect in the cardiac cycle, combined with blood gas analysis to determine the response before and after anapetia treatment, so as to select patients who can receive surgical treatment from patients with severe PAH, the effect was good (Carrington M. et al., 2008). It was relatively safe for patients with no cyanosis, SaO2>0.90, P (O2)>60mmHg, QP/Qs≤1, left to right shunt or bilateral shunt close to basic balance after oxygen inhalation. After drug treatment, all the patients achieved good results, the pulmonary artery pressure drop>20mmHg. A total of 175 patients (70.3%) were followed up for 3 months to 5 years, and the prognosis was significantly improved. In 62 cases, the cardiac function was significantly improved above grade Ⅱ, the cardiothoracic ratio decreased in varying degrees, and SPAP and LVEF decreased significantly.

SpO2 and HGB increased significantly after three times of treatment (P<0.05), and the levels of BNP, total bilirubin, and uric acid tended to decrease. The results showed that after treatment, the cardiac structure of the patients with CHD complicated with PAH changed, the shunt was eliminated, and the hemodynamics was improved, which reduced the blood volume of the pulmonary circulation and the pressure of the pulmonary artery.

Cardiac catheterization was the gold standard for the diagnosis of PAH. Another important examination in cardiac catheterization was acute vasodilator testing. Judging the reversibility of pulmonary arterioles was helpful to judge the progress of PAH. Some foreign scholars think that the patients with positive acute vasodilator testing positive and patients with Rp/Rs<0.67, Qp/Qs>1.5 can consider surgical treatment (Therrien J. et al., 2001). Some studies have also pointed out that surgical treatment can be performed if PVRI<6 wood unit/m, and Rp/Rs<0.3 during cardiac catheterization. Surgical treatment was not recommended if the PVRI>10 wood unit/m. For patients with 6<PVRI<9 wood unit/m, 0.3<Rp/Rs<0.5, acute vasodilator testing was recommended to determine whether the patients can be received surgical treatment. After using pulmonary vasodilator, surgical treatment can be performed if PVRI or Rp/Rs decreased by more than 20% (Beghetti M & Tissot C., 2010). The results of this study showed that in the basic state, the values of Qp/Qs, PVRI, and Rp/RS were 1.02±0.56, 24.86±7.56, 1.01±0.34 respectively. After treatment, the three values were 1.34±0.67, 19.98±6.45, and 0.77±0.12 respectively, and there was a significant difference before and after treatment (P<0.05). Both PVRI and Rp/Rs decreased by more than 20%, but PVRI>6 wood unit/m, and Rp/Rs>0.3, indicating that most patients still did not meet the surgical permission. It can be seen that cardiac catheterization can provide a more intuitive basis for the judgment of operability.

5. Conclusion

To sum up, due to technological progress, more and more CHD patients with PAH have been effectively treated, surgical indications can be controlled, surgical feasibility analysis has a certain basis. Therefore, the follow-up evaluation of the prognosis and quality of life of patients needs to be further studied.

Authors' contributions

Hong Gu conceived and designed the experiments; Xiaoyun Fu, Qiangqiang Li and Yan Zhu performed the experiments; Xinyu Zhang analyzed the data and wrote the paper.

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Conflicts of interest

The authors report no conflicts of interest.

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