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Efficacy and Safety of Percutaneous Closure in Patients with Patent Foramen Ovale and Migraine

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Abstract: *Objective:* To analyze the therapeutic effect of percutaneous closure of patent foramen ovale (PFO) and migraine. *Methods:* A total of 150 patients with PFO and migraine who were admitted to the hospital from January 2021 to May 2023 were recruited and divided into groups by random number table, the study group took percutaneous closure and drug treatment, and the control group took conventional drug treatment. The treatment effects between the groups were compared. *Results:* The total effective rate of the study group was higher than that of the control group ($P < 0.05$). Before treatment, there was no difference in migraine quantitative evaluation indicators between the groups ($P > 0.05$). After treatment, the migraine quantitative evaluation indicators in the study group were better than those in the control group ($P < 0.05$). The complication rate of the study group was lower than that of the control group ($P < 0.05$). Followed up for 1 to 3 months, the recurrence rate of the study group was lower than that of the control group ($P < 0.05$). *Conclusion:* Percutaneous closure for patients with PFO and migraine can improve the symptoms of migraine, enhance the curative effect, and have fewer postoperative complications.

Keywords: Patent foramen ovale; Migraine; Percutaneous closure; Efficacy; Safety

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1. Introduction

Patent foramen ovale (PFO) is a common congenital heart abnormality, which refers to the incomplete closure of the foramen ovale of the heart tissue. Some PFO patients have no obvious clinical symptoms, and the rate of missed and misdiagnosed diseases is high. Migraine belongs to neurovascular headache, and its pathogenesis is complex and related to many factors [1,2]. In recent years, studies have found that there is an association between PFO and migraine. Some patients with PFO showed abnormal cerebral blood flow and blood oxygenation, which led to a higher frequency of migraine symptoms. Percutaneous occlusion is an interventional treatment method with a high application rate. It delivers an occluder to the foramen ovale through a skin catheter to seal the foramen ovale and close it. This method has better efficacy in treating PFO and migraine and has fewer postoperative complications [3]. This study selected 150 patients with PFO and migraine to analyze the effect of percutaneous closure and drug treatment.

2. Materials and methods

2.1. General information

A total of 150 patients with PFO and migraine who were admitted to the Fifth Affiliated Hospital of Zhengzhou University from January 2021 to May 2023 were recruited and divided into two groups using the random number table grouping. The study group consisted of 75 cases, 41 males and 34 females, aged from 14 to 65 years with a mean of 52.35 ± 1.75 years, and a course of migraine from 1 to 5 years with a mean of 3.05 ± 0.74 years. There were 75 cases in the control group, 42 males and 33 females, the age ranged from 15 to 62 years with an average of 52.04 ± 1.80 years, and a course of migraine from 2 to 6 years with an average of 3.57 ± 0.55 years. After the data were compared, it was recorded as $P > 0.05$.

2.2. Methods

The control group took conventional drug treatment: flunarizine was taken warmly before going to bed every day, with a dose of 10 mg each time and once daily. Ibuprofen sustained-release capsules were taken with a dose of 0.3 g each time and twice daily. Medications were continuous for 1 to 3 months.

The study group adopted percutaneous closure and drug therapy: D-dimer, blood coagulation function, and other related examinations were carried out for the patients after admission. Ultrasonography was performed on the bilateral femoral and carotid arteries, and a head CT scan was performed concurrently to obtain a dynamic electrocardiogram. After meeting the surgical indications, the patient's femoral vein was punctured, and the right heart catheter was sent to the left upper pulmonary vein and left atrium through the PFO. A hardened guide wire was used to establish a track, and a long sheath was placed along the track to reach the left atrium, the long sheath was used to send the PFO occluder to the foramen ovale to complete the occlusion treatment. Conventional occluders are 18/25 mm and 25/25 mm. If there is a long tubular PFO or bulge, a 30/30 mm occlude was used. Ultrasound was then used to evaluate the actual position of the occlude, and the occlude was released after ensuring that the large blood vessels and heart valves are not affected. Clopidogrel was continued for 3 months postoperatively at a daily dose of 75 mg, and aspirin was taken orally for 6 months at a daily dose of 3 to 5 mg/kg.

2.3. Observation indicators

Quantitative assessment of migraine included headache symptoms and impact on quality of life. Among them, headache symptoms included headache frequency, duration, and headache degree, and the headache degree is evaluated by the Short Pain Scale, including emotional pain grading index (PPI) with 4 items of exhaustion and distress (12 points), feeling pain rating index (PRI) with 11 items such as throbbing pain (33 points), visual analog scale (VAS) of 10 points with all positive scoring. The impact on the quality of life was evaluated using the headache impact test. There were 6 questions in total, all ranging from 6 to 13 points, giving a total of 78 points. The degree of impact on life is positively scored.

The complication rate of drowsiness, bradykinesia, gastrointestinal symptoms, impaired liver function, infection, bleeding, femoral arteriovenous fistula, and coronary embolism was observed. The patients were followed up for 1 to 3 months, and the recurrence rates of the two groups were counted.

2.4. Efficacy evaluation criteria

Significantly effective means no migraine symptoms and no abnormalities in various laboratory indicators; preliminary effective means that migraine symptoms are relieved and various laboratory indicators are slightly abnormal; no effect means no change in migraine symptoms and various laboratory indicators are serious exceptions.

2.5. Statistical analysis

The data were processed using SPSS 28.0 software, the measured values were tested by *t*-test, and the counted values were tested by χ^2 test. Statistically significant was defined as a *P* value less than 0.05.

3. Results

3.1. Comparison of the total effective rate between the two groups

Table 1 showed that the total effective rate of the study group was significantly higher than that of the control group ($P < 0.05$).

Table 1. Comparison of total effective rate between the two groups [n (%)]

Group	Number of cases	Significantly effective	Preliminary effective	No effect	Total effective rate
Study group	75	38 (50.67)	35 (46.67)	2 (2.67)	97.33 (73/75)
Control group	75	35 (46.67)	30 (40.00)	10 (13.33)	86.67 (65/75)
χ^2	-	-	-	-	5.797
P	-	-	-	-	0.016

3.2. Comparison of migraine quantitative assessment indicators between the two groups

Before treatment, there was no difference in migraine quantitative evaluation indicators between the two groups ($P > 0.05$). After treatment, the quantitative evaluation indexes of the study group were better than those of the control group ($P < 0.05$), as shown in **Table 2**.

Table 2. Comparison of migraine quantitative assessment indicators between the two groups before and after treatment (mean ± SD)

Group	Headache symptoms										Impact on quality of life (points)	
	Headache frequency (times/mth)		Duration (min/time)		Headache degree (points)							
					PPI		PRI		VAS			
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Study group ($n = 75$)	8.81 ± 1.26	1.05 ± 0.33	30.25 ± 3.26	4.26 ± 0.84	6.25 ± 1.71	1.85 ± 0.72	20.35 ± 2.74	8.11 ± 1.53	4.26 ± 1.02	1.15 ± 0.37	40.26 ± 5.31	16.34 ± 1.59
Control group ($n = 75$)	8.82 ± 1.34	1.78 ± 0.37	30.29 ± 3.17	7.49 ± 1.41	6.29 ± 1.65	2.67 ± 0.81	20.13 ± 2.65	12.84 ± 1.65	4.30 ± 1.08	1.62 ± 0.49	40.22 ± 5.19	20.18 ± 1.77
t	0.047	12.752	0.076	17.043	0.146	6.553	0.500	18.204	0.233	6.629	0.047	13.977
P	0.963	0.000	0.939	0.000	0.884	0.000	0.618	0.000	0.816	0.000	0.963	0.000

3.3. Comparison of complication rates between the two groups

Table 3 showed that the complication rate of the study group was lower than that of the control group ($P < 0.05$).

3.4. Comparison of recurrence rates between the two groups

During the follow-up of 1 to 3 months, the recurrence rate of the study group was lower than that of the control group ($P < 0.05$), as shown in **Table 4**.

Table 3. Comparison of complication rates between the two groups [n (%)]

Group	Drowsiness	Bradykinesia	Gastrointestinal symptoms	Impaired liver function	Infection	Bleeding	Femoral arteriovenous fistula	Coronary embolism	Incidence rate
Study group (n = 75)	0	1 (1.33)	0	0	1 (1.33)	1 (1.33)	0	0	4.00 (3/75)
Control group (n = 75)	3 (4.00)	2 (2.67)	4 (5.33)	1 (1.33)	0	0	0	0	13.33 (10/75)
χ^2	-	-	-	-	-	-	-	-	4.127
P	-	-	-	-	-	-	-	-	0.042

Table 4. Comparison of recurrence rates between the two groups [n (%)]

Group	Number of cases	Follow-up for 1 month	Follow-up for 2 months	Follow up for 3 months
Study group	75	0	0	1 (1.33)
Control group	75	4 (5.33)	5 (6.67)	7 (9.33)
χ^2	-	4.110	5.172	4.754
P	-	0.043	0.023	0.029

4. Discussion

The pathogenesis of PFO with migraine is not completely clear, and it may be related to the following factors: (1) Abnormal circulatory system: PFO can easily lead to poor blood flow between the left and right atrium, making the blood contain more platelets and coagulation factors, thereby increasing blood clotting, leading to migraine symptoms [4,5]; (2) Abnormal blood oxygenation: PFO will cause arterial blood to mix with venous blood, thereby reducing arterial blood oxygen saturation. Insufficient blood oxygenation will affect the oxygen supply state of the brain, triggering migraine [6]; (3) Vasodilation and contraction: PFO can induce abnormal expansion and contraction of cerebral blood vessels, which in turn affects cerebral blood flow and blood perfusion pressure, and eventually triggers migraine attacks; (4) Inflammatory response: PFO can change brain blood flow and blood components, trigger an inflammatory response, activate inflammatory mediators, and then affect the excitability and sensitivity of neurons, thereby inducing migraine [7-9]; and (5) Abnormal neuro-regulation: PFO can affect the neuro-regulation mechanism of the brain, including vasoconstriction and dilation regulation, which can lead to migraine.

Drug therapy is a common treatment for this disease, which can regulate nerve function and blood vessel activity, and reduce the intensity and frequency of headaches, which then reduce the pain of migraine attacks [10]. Among them, flunarizine belongs to the tricyclic antidepressant drugs, which can regulate the level of neurotransmitters, inhibit cerebral vasoconstriction, and thus relieve migraine symptoms. Ibuprofen has an anti-inflammatory effect that can block the synthesis process of prostaglandins and inhibit the excessive release of inflammatory mediators, as well as has an analgesic effect that can reduce peripheral sensitivity of blood vessels and avoid massive aggregation of platelets, which then reduces the actual release of vascular endothelin to relieve migraine manifestations [11]. However, drug treatment needs to be maintained for a long time, and after stopping the drug, the risk of recurrence of migraine symptoms is high. There are many adverse reactions to drugs, such as gastrointestinal symptoms and drowsiness, which affect the quality of life of patients. Long-

term use of certain drugs may also lead to tolerance of the drug, the efficacy of the drug gradually weakening, leading to the need of increasing the dose or replacing the drug, thereby increasing the difficulty of treatment [12].

Percutaneous closure can effectively close the foramen ovale and restore normal cardiac blood flow, thereby improving cerebral blood flow and blood oxygen supply, reducing the frequency of migraine attacks, and reducing the intensity of headaches. After blocking the foramen ovale, it can prevent the mixing of platelets and coagulation factors, thereby reducing the risk of blood clot formation, and can prevent cerebrovascular accidents [13]. This procedure improves blood circulation and oxygenation, reduces inflammation in the brain, and relieves migraine symptoms. This operation is an interventional therapy, and the patient's femoral vein is punctured for closure without open surgery, therefore, the surgical trauma is small, and the postoperative recovery is faster, which can shorten the rehabilitation period of patients and reduce their treatment burden [14]. For percutaneous occlusion, the appropriate occlusion device specifications can be selected according to the specific conditions of the patient to adapt to different sizes and types of PFOs, so as to achieve individualized treatment effects.

The results showed that the total effective rate of the study group was higher than that of the control group; after treatment, the migraine quantitative evaluation index of the study group was better than that of the control group; the complication rate of the study group was lower than that of the control group; the recurrence rate of the study group was lower ($P < 0.05$). The reason is that percutaneous closure can close the foramen ovale, avoid backflow of blood when passing through the heart, and block larger blood clots and other substances from entering the circulation of the brain through the foramen ovale, thereby reducing migraine headaches. This operation also reduces the possibility of thrombosis, thereby reducing related complications [15]. In addition, percutaneous closure can adjust abnormal hemodynamics of the cardiovascular system, such as right ventricular overload, improve heart and blood vessel function, and further relieve migraine symptoms.

In summary, percutaneous closure for PFO patients with migraine can improve the curative effect, improve migraine symptoms, reduce the impact of migraine on quality of life, has high treatment safety, and a low recurrence rate.

Disclosure statement

The authors declare no conflicts of interest.

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