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Effect of mecobalamin treatment on the recovery of patients with posterior communicating artery aneurysm inducing oculomotor nerve palsy after operation

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Abstract. – OBJECTIVE: This research aims to evaluate the effect of mecobalamin treatment on the recovery of patients with posterior communicating artery aneurysm inducing oculomotor nerve palsy after embolization.

PATIENTS AND METHODS: A total of 56 patients with oculomotor nerve palsy (ONP) attributed to posterior communicating artery (PcomA), were admitted and treated in the Neurology Department of Hubei College of Medicine affiliated to Xiangyan Hospital from July 2007 to January 2013, and 55 of them were followed up as well. Among them 27 patients were given embolization treatment and 28 received embolization + mecobalamin treatment. The recovery condition of ONP were followed and compared one year after the treatment.

RESULTS: All patients were followed up for more than a year. And 31 patients (56.4%) out of 55 achieved complete recovery, 19 (34.5%) attained partial recovery and 5 (9.1%) had no recovery from ONP. Whereas, 20 patients (71.4%) in the embolization + mecobalamin treatment group achieved complete recovery and 11 (40.7%) in the embolization treatment group achieved partial recovery, and the comparative difference was statistically significant ($p < 0.05$).

CONCLUSIONS: Endovascular is highly efficacious treatment for ONP-inducing PcomA and can promote the recovery of oculomotor nerve palsy after embolism.

Key Words:
Intracranial aneurysm, Oculomotor nerve palsy, Embolization, Prognosis, Mecobalamine.

Introduction

Oculomotor nerve palsy is a common complication which is found in patients with posterior communicating artery aneurysms. Current studies on the recovery of oculomotor nerve palsy after endovascular treatment of posterior communicating artery aneurysms can sometimes be seen in the case analysis of limited samples with relatively large differences among conclusions[1-6]. Clinically, mecobalamin is mainly applied for the treatment of peripheral nervous lesion[7,8]. It takes its effect as a kind of coenzyme during the process of conversion of homocysteine to methionine in order to facilitate the composition of nucleic acids and protein, promote the regeneration of axoplasm flow and neuraxon within the neuraxon, normalize the neuraxon's skeleton protein transportation as well as accelerate the formation of myelin sheath (phospholipids synthesis). A total of 56 patients with ONP attributed to PcomA, who were treated with coils in the Neurology Department of Xiangyang Hospital, an affiliated hospital of Hubei University of Medicine, from July 2007 to January 2013, were enrolled in a randomized, controlled open study, and 55 of these patients were followed up. Embolization treatment was performed in 27 patients while 28 patients received embolization + mecobalamin treatment. The latter showed a better overall curative effect as reported here.

Patients and Methods

Study Subjects

Patients were enrolled in a randomized, controlled open study and were randomly allocated in groups according to the study order. Each group contained four patients and two of them were allocated randomly to accept embolization

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+ mecobalamin treatment or only embolization treatment. There were 6 methods of random permutation and combination, and both treatment groups contained 28 patients. One patient was lost in the follow up case; therefore, 55 patients were included in the study.

Among 55 patients, 16 were male and 39 were female; the age of patients ranged from 35 to 74 years with an average age of 51.87 years. Eleven patients had diabetes mellitus, 21 had arterial hypertension and 38 had subarachnoid hemorrhage. The arterial aneurysm of 35 patients was not bigger than 9 mm in diameter and in 20 patients it was over 9 mm. Patients allergic to mecobalamin, and patients who were engaged in works that required exposure to mercury or its compounds and patients with oculomotor nerve palsy complicated by diabetes were excluded. The diagnostic criteria of oculomotor nerve palsy before operation included: complete paralysis: emergence of diplopia before operation, complete ptosis, external ophthalmoplegia and mydriasis as well as direct or indirect loss of light reflection; partial paralysis: partial ptosis or partial upward gaze, inward gaze, downward gaze inability or partial mydriasis and pupillary reflex reduction before operation. The oculomotor nerve of 34 patients was completely paralyzed and 21 patients were with partial paralysis before operation. Paralysis period was not longer than 10 days in 31 patients and it was longer than 10 days in 24 patients before operation. Twenty five patients received operation within 5 days after being hospitalized; 22 patients received operation during 5 to 10 days after being hospitalized and 9 patients received operation after 10 days of being hospitalized. Treatment method and risks were explained to patients before operation and informed consent was signed by the patients.

Treatment Methods

Embolization + mecobalamin treatment was performed on 28 patients: patients with oculomotor nerve palsy upon admission to the hospital were given mecobalamin injections o.5 mg per day 3 days after admission (patients without oculomotor nerve palsy upon admission were given injections 3 days after the emergence of oculomotor nerve palsy). Fifteen days later, mecobalamin injections were changed to oral mecobalamin tablets, 0.5 mg 3 times a day. Patients who met the following conditions stopped taking mecobalamin: (1) the oculomotor nerve palsy was completely recovered for half a month; (2) the oculomotor nerve palsy did not continue to improve or did not improve for 3 months; (3) the course of mecobalamin treatment had reached 4 months.

Endovascular embolization treatment: Puncture was implemented through arteria femoralis to myelin sheath, an electrolytic or mechanical detachable coil was then imbedded in the posterior communicating artery aneurysms through catheter under X-ray. Among all patients, 7 of them were with wide-necked aneurysm and were given stent implantation combined with the previously mentioned treatment. Whereas, other 27 patients were treated with embolization treatment only and additional treatment was basically the same.

Observation Target

The condition of oculomotor nerve palsy before operation and 1 year after operation were observed and follow-ups were stopped six months after a complete recovery of oculomotor nerve palsy. The recovery standards for oculomotor nerve palsy after operation include; complete recovery: no diplopia appears when gazing whichever direction or photophobia; no ptosis: normal upward, inward and downward eye movement range, and partial or complete recovery of pupil response[9]. Recovery condition which clinically cannot be defined as complete recovery with improvement compared to the condition before treatment is clinically defined as a partial recovery. The condition which is not changed compared with the condition before treatment is defined as no recovery.

Statistical Analysis

SPSS 17.0 statistical software (SPSS Inc., Chicago, IL, USA) was applied in the analysis; the measurement data are represented as mean ± standard deviation (`x±s) of mean, and the comparison method adopted was *t*-test. The enumeration data are represented with percentage; the comparison method adopted was t-test, and the results only had statistical significance when the difference was $p < 0.05$.

Results

Comparison Between the Baseline Information of Patients in 2 Treatment Groups

No significant difference was observed for the age, gender composition, the percentage of complicated diabetes mellitus, hypertension, sub-

Table I. The basic information of patients in two groups.

Group	Age (years)	Gender (male/female)	Diabetes (cases)	Hypertension (cases)	Subarachnoid hemorrhage (cases)	Preoperative oculomotor palsy (cases)	Arterial aneurysm size (mm)	Time of preoperative oculomotor palsy (d)
Embolization +mecobalamin treatment group	51.180 ± 9.133	10/18	4	9	20	18	8.700 ± 2.750	11.040 ± 5.330
Embolization treatment group	52.59 ± 9.943	6/21	7	13	18	16	8.963 ± 2.464	10.87 ± 4.636
t/x^2 value	0.413	1.213	1.164	1.467	0.146	0.147	0.066	0.197
p-value	0.585	0.271	0.281	0.226	0.702	0.701	0.711	0.903

arachnoid hemorrhage and complete oculomotor nerve palsy before operation, the size of arterial aneurysm and the duration of oculomotor nerve palsy before operation between the patients in embolization + mecobalamin and only embolization treatment groups ($p > 0.05$), which indicates that the 2 groups are comparable (Table I). 2. Comparison of complete recovery rate of oculomotor nerve palsy between patients in two treatment groups

Fifty-two patients had complete embolizing arterial aneurysm and 3 patients had residual aneurysm. No increase in the residual aneurysm, relapse of arterial aneurysm and significant stricture in the position where stents were implanted was found when following up CTA three months after operation. No soft neurological signs, aggravation of oculomotor nerve palsy or death occurred after the embolism.

All patients were followed for up to a year and 31 out of 55 patients were completely recovered from oculomotor nerve palsy (56.4%), and among them 20 were from embolization + mecobalamin treatment group (71.4%) and 11 were from embolization treatment group (40.7%). The comparative difference between the two treatment groups had statistical significance ($X^2 = 5.263$, $p = 0.022$). Also 19 patients (34.5%) had partially recovered, and five patients (9.1%) had no recovery. The effective rate was 90.9%. Four patients showed a slight loss of appetite, and no other apparent side effects were found.

Discussion

Pressure of posterior communicating aneurysm on oculomotor nerve was considered the primary mechanism of nervous lesion and surgical clipping was once regarded as the preferred treatment[10,11]. Since the spring coil could enlarge the space occupied by arterial aneurysm, which could affect the recovery of oculomotor nerve palsy, embolization was used conservatively for the treatment of ONP attributed to PcomA.

In 1999, Birchall et al[12] reported for the first time 3 cases of complete recovery of ONP attributed to PcomA. In 2001 Ma et al[13] reported 5 cases of ONP attributed to intracranial aneurysm, among which 3 of them were PcomA, and all 5 cases were treated with embolization and recovered from ONP within 3 months after operation. In 2013, Chalouhi reported that 14 of 37 cases (37.8%) were recovered completely, 19 (51.4%)

recovered partially and 4 (10.8%) did not recover. Chalouhi et al[1] also enumerated 13 foreign reports with a total of 132 cases, and a total recovery rate was between 0-100%. Combining the 37 cases of his medical center, he reported that the average complete recovery rate was 43.2%, partial recovery rate was 43.2% and no recovery rate was 13.6% among a total of 169 patients.

In the current report, 31 cases out of 55 recovered completely (56.4%), 19 recovered partially (34.5%) and 5 (9.1%) did not recover. Fifty cases were valid (90.9%). The recovery rate in current study is better compared to the average complete recovery rate of 43.2% as reported by Chalouhi et al. Considering the result might have correlation with the mecobalamin treatment given to some patients, this study indicates that the embolization + mecobalamin treatment can affect the prognosis of patients observably for the complete recovery rate of ONP of the 2 groups at 71.4% and 40.7%, and the difference is statistically significant ($p < 0.05$).

Sun et al[14] summarized the results of 7 randomized controlled trials from 1954 to July 2004, concerning vitamin B12 or mecobalamin applied for the diabetic neuropathy treatment, and found that the vitamin B12 or mecobalamin could alleviate pain, paresthesia and other somatic manifestations. Li et al[15] applied mecobalamin for the treatment of external ophthalmoplegia and ONP, which enhanced the clinical effect. Dai and Zhang[16] applied mecobalaminfor the treatment of ONP and the result manifested that the mecobalamin can accelerate the process of neural restoration and growth.

Yaqub et al[17] and Li et al[18] both observed therapeutic effect of mecobalaminin the diabetic peripheral neuropathy through a double-blind randomized clinical trial and the course of treatment with mecobalamin were 16 and 12 weeks respectively. The results revealed that the mecobalamin was effective; had no side effects and was well tolerated by patients. In this study, the longest course of mecobalamin treatment was 4 months, and the difference in ONP recovery rate between 2 groups of patients after 1 year of operation had statistical significance ($p < 0.05$), which shows that the mecobalamin treatment could promote the recovery of ONP after embolization.

Li et al[19] found through animal experiments that after oculomotor nerve injury, motor neurons within the oculomotor nucleus reduced in number and distribution range. Tanaka[20] summarized the results of a study on the effects of mecobalamin on neurons (including *in vitro* and *in vivo* studies as well as results of clinical use) before 2013 and considered that the mecobalamin could accelerate the process of synapse's growth and restrain the apoptosis of nerve cells. He presumed that the high dose of mecobalamin treatment had great potential for the treatment of nervous system diseases. It was believed at that moment that the pulsatile hammering effect was not simply a space occupying effect but was the pathophysiological basis of ONP[21-23]. The author speculated that the mechanism which mecobalamin + embolization treatment takes effect in recovering ONP may alleviate or eliminate the arterial aneurysm's pulsatile hammering effect after operation, which further reduces injury to the oculomotor nerve. Mecobalamin can accelerate the growth process of myelin sheath and synapse, restrain the apoptosis of nerve cells and enhance the recovery effect[24-27].

Besides, no apparent side effects were observed except that 4 patients showed slight loss of appetite otherwise mecobalaminwas well tolerated by all 55 patients.

Conclusions

The posterior communicating aneurysm embolization can effectively alleviate ONP attributed to PcomA, and mecobalamin + embolization treatment can promote the recovery of ONP. Considering the low occurrence rate of ONP attributed to PcomA, the sample size of this study is relatively small and the influence of mecobalaminor other medications on the recovery of ONP is waiting to be further evaluated through multicenter randomized controlled trials.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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