Clinical Neurology and Neurosurgery 184 (2019) 105417

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Surgical effect and electrophysiological study of patients with hemifacial spasm treated with botulinum toxin or acupuncture before microvascular decompression

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ARTICLE INFO

Keywords:
Hemifacial spasm
Microvascular decompression
Botulinum toxin
Acupuncture
Abnormal muscle response
Compound motor action potential

ABSTRACT

Objective: We investigated patients with hemifacial spasm (HFS) who received a botulinum toxin (BT) injection or acupuncture before receiving microvascular decompression (MVD) to determine whether it affects the success rate of surgery. Abnormal Muscle Response (AMR) and Compound Motor Action Potential (CMAP) are commonly used as electrophysiological monitoring methods in surgery, and we will compare the differences between these patients in this regard.

Patients and methods: A total of 539 patients with HFS underwent MVD treatment in our department between January 2014 and June 2017. Among them, 83 patients had received BT injection before surgery and were recorded as BT group. Eighty-three patients underwent acupuncture before surgery and were recorded as acupuncture group. Five patients received both BT injection and acupuncture before surgery and were recorded as mixed group. A total of 368 patients who had not received any treatment before surgery were recorded as simple MVD group. We calculated the immediate and long-term remission rates after surgery. AMR and CMAP monitoring were routinely performed during surgery.

Results: Immediate remission rate after surgery was 96.4% (80/83) in BT group, 100% (83/83) in acupuncture group, 100% (5/5) in mixed group, and 95.1% (350/368) in simple MVD group, and the immediate remission rate of BT group is significantly higher than that of simple MVD group ($p = 0.04$). Long-term remission rate: the remission rates of the four groups were 94.0% (78/83), 97.6% (81/83), 100.0% (5/5) and 92.7%(341/368), respectively, and there is no statistical difference between them ($p > 0.05$). The amplitude of one branch or several branches of CMAP on the affected side was lower than the healthy side in BT or acupuncture treatment patients.

Conclusions: A preoperative BT injection or acupuncture treatment do not reduce the postoperative remission rate of HFS patients treated with MVD, and the amplitude of CMAP on the affected side was lower than the healthy side.

1. Introduction

Hemifacial spasm (HFS) is a neuromuscular disorder characterized by involuntary, unilateral, and extremely active contractions. Since Jannetta [4] has promoted and improved Microvascular Decompression (MVD), it has become the preferred method for treating HFS. It is widely believed that HFS is caused by vascular compression on root exit zone (REZ) of facial nerve [4,10]. Although the etiology of HFS has been clarified, is caused by vascular compression, but its pathogenesis has not been fully elucidated. Central theory would state that HFS is caused by hyperactivity of facial motor neurons [3] due to demyelination, and the peripheral cause theory suggests that HFS is an ectopic excitation between facial nerve fibers caused by nerve compression [11–13]. Therefore, for the pathogenesis of HFS, a variety of treatment methods have been formed, including medical treatment, MVD (relieve neurovascular conflict), botulinum toxin (BT) injection, acupuncture,

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https://doi.org/10.1016/j.clineuro.2019.105417
Received 4 June 2019; Received in revised form 3 July 2019; Accepted 5 July 2019
Available online 12 July 2019
0303-8467/

etc. Since 1986, BT has been approved by the FDA for the treatment of HFS [2],which is widely accepted because of its almost no wound treatment and high remission rate. Acupuncture is a unique special treatment for HFS in China. In acupuncture, which has a history of thousands of years, needles are penetrated into the patient at a certain angle, and twirling and lifting methods are used to target specific parts of the body to treat disease. In patients with HFS, a considerable number of patients have received BT injection or acupuncture before MVD, the purpose of this paper is to investigate whether these kinds of patients will affect the surgical efficacy, and the difference between the intraoperative Abnormal Muscle Response (AMR) and Compound Motor Action Potential (CMAP).

2. Patient and methods

2.1. Patients and data collection

In all, 539 patients with typical HFS were treated with MVD at the Department of Neurosurgery, Xinhua Hospital Affiliated to Medicine School of Shanghai Jiaotong University, between January 2014 and June 2017. Among them, 83 received BT injection before surgery, 83 received simple acupuncture before surgery, 5 received both BT injection and acupuncture, and 368 did not receive any treatment before surgery. These patients were set as BT group, acupuncture group, mixed group and simple MVD group respectively. The study excluded patients with HFS due to tumor, vascular malformation, or Chiari malformation, and also excluded patients who had received other treatments other than BT injection and acupuncture before surgery.

2.2. Surgical procedures

All surgeries were performed by the same physician to exclude differences in surgical outcomes due to differences in surgical technique. We usually use the standard retromastoid suboccipital craniectomy, after the dura mater is opened, the cerebrospinal fluid is fully released, and then the arachnoid surrounding the facial nerve and auditory nerve are sharply separated from the posterior to the front. Zoom I to IV of the facial nerve were explored to identify all offending vessels. The offending blood vessels are lifted to insert Teflon felt between the vessels and the brainstem or nerve. When AMR did not disappear, we may consider internal conflicts and conduct explorations [5]. When no obvious vascular compression was found in I-IV region, the offending vessel might be located in the internal auditory canal through AMR, Z-L response (ZLR), stim-electromyography (stim-EMG) and magnetic resonance. First, we will not choose to open the internal auditory canal, but will release the arachnoid membranes of the internal auditory canal, suck out the offending vessel with an aspirator, and take advantage of the opportunity to pad the gelatin sponge and Teflon until the AMR disappears. If the responsible vessel is difficult to suck out, we choose to open the internal auditory canal and decompress it carefully according to anatomy [7,14].

2.3. Intraoperative monitoring

AMR can be recorded in the mental muscle, orbicularis oculi and frontal muscle while stimulating the temporal and mandibular branches of facial nerve. AMR with a latency of about 10 ms is usually recorded with a 5–15 mA stimulus, and disappears when the offending vessels are isolated. At this point, the stimulus can be increased to 50 mA, if then AMR still does not appear, it can be considered to have disappeared. The action potentials generated by the motor endplates is called the CMAP in response to motor nerve stimulation. Clinically, the motor nerve conduction function can be evaluated by recording its area, amplitude, latency. When the nerve is damaged, its amplitude will change. We will monitor the patient's left and right facial CMAP and observe the differences between them.

2.4. Postoperative observation and follow-up

The follow-up content mainly included changes in the eyelids and mouth twitches and cranial nerve dysfunction. The surgical results are divided into the following 4 levels [6] : 1)significant(E0, complete remission);2)good(E1, HFS relief ≥ 90%); 3)general(E2, HFS relief ≥ 50%); 4) invalid(E3, HFS relief < 50%, or no remission).We consider E0、E1 as mitigation and E2、E3 as unmitigated.

2.5. Statistical analysis statistical

Statistical analyses were performed using SPSS version 22.0. The differences in the consequent were assessed using $\chi 2$ tests. A p value ≤ 0.05 was considered statistically significant.

3. Results

BT group included 26 male patients and 57 female patients with an average age of 54.7 years and average onset time of 6.8 years. Acupuncture group had 26 males and 57 females at 52.0 and 5.4 years, mixed group had 1 male and 4 females at 59.8 and 4.4 years, and simple MVD group included 112 males and 256 females at 53.7 and 5.1 years. Immediate remission rate after surgery was 96.4% (80/83) in BT group, 100% (83/83) in acupuncture group, 100% (5/5) in mixed group, and 95.1% in simple MVD group (350/368), the remission rate of acupuncture plus MVD patients was significantly higher than that of patients with simple MVD ($p = 0.04$). Long-term remission rate: four groups of remission rates were 94.0% (78/83), 97.6% (81/83), 100.0% (5/5), 92.7% (341/368), respectively, and there is no statistical difference between them. Facial paralysis is the most common complication, there were 10 permanent facial paralysis patients, accounting for 2.4%, 1.2%, 0%, 1.9% in four groups, respectively, and there is no statistical difference between them(Table 1).

Monitoring methods include AMR and CMPA. In our 539 patients, the AMR induction rate reached 94.1%. Among the 507 patients who induced AMR, intraoperative AMR disappeared in 486 patients, a disappearance rate of 95.9%. AMR did not disappear in 21 patients after adequate decompression, we combed the facial nerve and the AMR disappeared. As for CMAP, Waveform changes vary from patient to patient, depending on individual differences and previous treatments. However, compared with the healthy side, the amplitude of the affected side always decreases.

Table 1
Comparison of preoperative and postoperative clinical characteristic.

	A	B	C	D	total
no. of patients (%)	83(100.0)	83(100.0)	5(100.0)	368(100.0)	539(100.0)
female	57(68.7)	57(68.7)	4(80.0)	256(69.6)	374(69.4)
male	26(31.3)	26(31.3)	1(20.0)	112(30.4)	16,530.6
age (years)	54.7	52.0	59.8	53.7	53.6
the average onset time (years)	6.8	5.4	4.4	5.1	5.4
AMR induction (%)	77(92.8)	79(95.2)	5(100.0)	346(94.0)	507(94.1)
AMR disappears (%)	75(97.4)	76(96.2)	5(100)	330(95.4)	486(95.9)
Postoperative remission rate					
immediately (%)	80(96.4)	83(100.0)	5(100)	350(95.1)	518(96.1)
long-term (%)	78(94.0)	81(97.6)	5(100)	341(92.7)	508(94.2)
postoperative facial paralysis (%)	2(2.4)	1(1.2)	0(0.0)	7(1.9)	10(1.9)

Abbreviation: AMR = Abnormal Muscle Response.

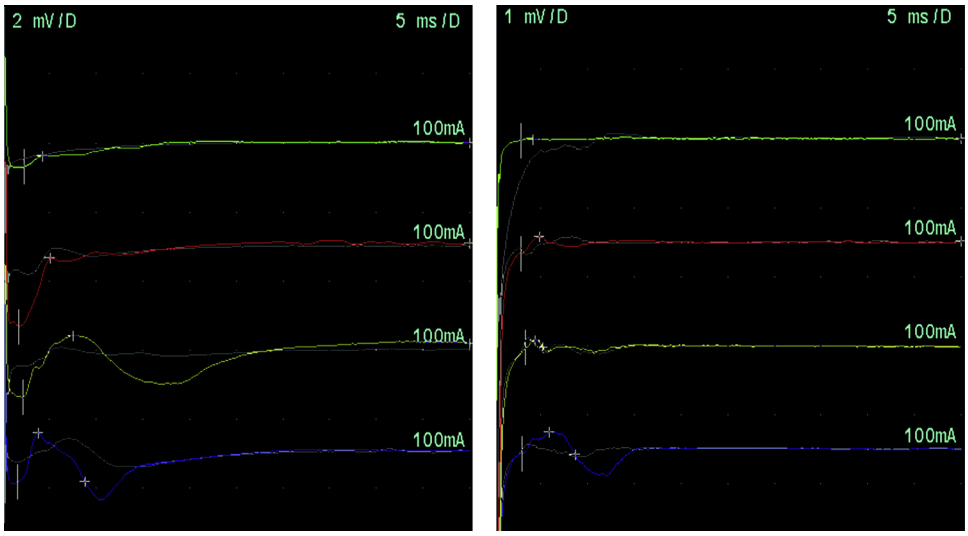

Fig. 1. CMAP waveforms of BT injection and acupuncture patients. Color is the healthy side, white is the affected side, and the frontal muscle, the orbicularis muscle, the orbicularis oculi muscle, and the mentalis are represented from top to bottom. On the left side is the waveform of the patient with botulinum toxin injection. We can see that the amplitude of the orbicularis oculi muscle, the orbicularis oculi muscle and the diaphragm of the patient are lower than the healthy side. On the right side is the waveform of the acupuncture patient. The amplitude of the frontal and temporal muscles of the patient is lower than that of the healthy side.
Abbreviation: CMAP = Compound Motor Action Potential, BT = botulinum toxin.

4. Discussion

BT can inhibit the release of acetylcholine into the synaptic cleft, causing denervation of the muscle, in this case, facial muscles will reduce twitching due to the lack of neurotransmitter transmission. However, BT injection has a time limit, and it is necessary to reinject it to maintain its effect. According to Choe [1], the average number of BT injection sites was 22.6 ± 6.7, the mean BT dosage on the affected side was 28.6 ± 4.9 units, the mean duration of BT efficacy was 28.6 ± 7.7 weeks, and its efficiency has reached 95%. Although BT injection has advantages of minimal invasiveness and considerable effects, the injection is ineffective for a fair number of patients, and the side effects seriously impact quality of life. According to our observation, the most common side effect of BT injection is ptosis, followed by diplopia and severe muscle weakness on the injection side. During the consultation, a considerable number of patients sought surgical treatment because they could not tolerate the facial stiffness after BT injection. Therefore, MVD is a better way to completely solve HFS due to its lower complication rate.

Acupuncture is a unique treatment in China, with a history of thousands of years. Acupuncture treats systemic diseases by conducting meridians and acupoints and applying certain manipulation methods. In different literatures, the effective rate of acupuncture reached 92.5%–98.0% [18,20,21]. The effectiveness of acupuncture is very high, which may be related to the absence of an objective standard, because the majority of acupuncture patients do not achieve complete relief of HFS, and their so-called “alleviation” only refers to the fact that their symptoms after treatment are less than before treatment, regardless of the extent of remission. During our consultations, the vast majority of patients who had undergone acupuncture treatment had their symptoms alleviated, but the degree of relief was generally low, and patients were willing to continue to seek other treatments.

Due to the strong side effects of BT injections and the unsatisfactory effects of acupuncture, MVD has become the choice for further treatment of these patients. According to reports, the remission rate of MVD in the treatment of HFS was 50%–98%, and the 10-year remission rate was 84% [9,16]. The immediate remission rate of our 539 patients was 96.1% (518/539) and the long-term remission rate was 94.2% (508/539). Among the 539 patients, the immediate remission rate was 96.4% in BT group, 100% in acupuncture group, 100% in mixed group and 95.1% in simple MVD group; As for the long-term remission rate, 94.0% in BT group, 97.6% in acupuncture group, 100% in mixed group and 92.7% in simple MVD group. The postoperative remission rate did not decrease regardless of the BT injection or acupuncture compared to patients who received simple MVD. Among them, the immediate remission rate of acupuncture patients was significantly higher than that of patients who underwent simple MVD ($p = 0.04$). Therefore, we can conclude that the short-term prognosis of patients with acupuncture plus MVD is better than that of patients with simple MVD, and there is no difference in long-term remission rate. But this does not mean that this is the case. According to Thirumala [17], 15 of the 16 patients who relapsed after surgery had BT injection treatment before. Thus, more long-term follow-up is needed.

Although the incidence of postoperative complications of MVD is lower than that of BT injection, it cannot be ignored. Complications of MVD for HFS include permanent and temporary complications, and temporary complications may gradually improve over time. Seung-Jae [15] reported that 12.1% of patients had complications after operation, including facial paralysis, hearing impairment, cerebrospinal fluid leak, cerebellar infarction and hemorrhage, the proportion of facial paralysis, hearing impairment was 8.0% and 3.7%, which accounted for the top two. Of the 539 patients, 10 had permanent facial paralysis (2, 1, 0, and 7 patients in four groups, respectively, and there was no statistical difference between them). The number of facial paralysis in patients treated with BT injection was significantly higher before surgery than that in other groups, similar to the survey conducted by Wang [19]. However, when BT was metabolized, the number of patients with facial paralysis was not higher than that of other patients after MVD.

AMR is an important monitoring method in our surgery. AMR can assist tremendously with MVD surgery [8], it can help surgeons reduce unnecessary operations during surgery, particularly when the intraoperative situation is complex, or the risk for surgery is high, as the disappearance of the AMR allows the physician to end the surgery with confidence. Thirumala [17] found that 259 of the 293 patients detected AMR, accounting for 87.7% of all patients. However, of our 539 patients, only 32 patients had no AMR induced, and the induction rate was 94.1%. AMR disappeared in most patients, but there are still 21 patients whose AMR persisted during the operation, for these patients, we will use nerve combing technology until AMR disappeared. Although AMR monitoring is widely used in MVD surgery, few papers have reported AMR waveforms after acupuncture or botulinum toxin treatment. The Pittsburgh Medical Center found that patients treated with BT injection had higher baseline amplitudes compared to normal patients, which may be related to muscle re-innervation after use of the BT [2].

BT injection or acupuncture treatment may cause damage to nerves and cause changes in AMR amplitude. Each patient's own AMR amplitude is not the same for individual reasons, so the amplitude of BT injection or acupuncture patients cannot be directly compared with the amplitude of simple MVD patients. For this reason, we additionally

monitored the CMAP. So far, we have not found any reports of CMAP in patients who have undergone BT treatment or acupuncture. CMAP includes waveform results of the frontal muscle, the orbicularis muscle, the orbicularis oculi muscle, and the mentalis. Its amplitude is related to the number of activated nerve fibers, the synchronization of nerve impulses, and the surface area of the recording electrodes. Abnormal amplitude attenuation can occur in motor nerve block and chronic denervation nerve regeneration. We compared the CMAP between the healthy side and the affected side of the BT injection patients and acupuncture patients, and found that the amplitude of one branch or several branches of CMAP on the affected side was lower than the healthy side. The degree or number of branches of decline may be related to the number of treatments (degree of nerve injury) or the location of the treatment. In general, the more treatments, the more the amplitude of the decline(Fig.1).

5. Conclusion

Although BT injection and acupuncture are good treatments for HFS, MVD remains the better choice. Administering a BT injection or acupuncture before MVD does not reduce the success rate of surgery. Electrophysiological monitoring is an important part of MVD treatment for HFS, AMR is helpful for the surgical procedure, and CMAP amplitude of patients who receive a BT injection and acupuncture treatment will decrease because they have a more or less damaged facial nerve.

Disclosure

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgments

The authors acknowledge the collaboration of all of the staff and technical members at Department of Neurosurgery, Xinhua Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China.

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