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Technical Notes & Surgical Techniques

Prophylactic effect of topical diluted papaverine in preventing hearing loss during microvascular decompression for typical trigeminal neuralgia: Case report and technical note

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ABSTRACT

Background and objective: Papaverine hydrochloride is a direct-acting vasodilator used to manage vasospasm during various neurosurgical operations. Transient hearing loss due to vasospasm of Internal auditory artery during Posterior Fossa Microvascular Decompression (MVD) for Typical Trigeminal Neuralgia (TTN) is one of possible complications of this surgical procedure. The aim of this technical note is to underline the potential efficacy of the use of intracisternal diluted papaverine and its proper use.

Materials and methods: BAEP is routinely used to monitoring functionality of vestibulocochlear nerve during MVD for TTN. In one patient recently operated on, during arachnoid dissection BAEP showed a lag of V wave of 1 ms, likely due to vasospasm of Internal Auditory Artery (IAA) probably caused by arachnoid traction. Intracisternal injection of pure papaverine without excipients (60 mg/2 ml) diluted in 20 cm^3 of 0,9% saline solution (0,3%) was used as a direct therapeutic action to manage vasospasm of IAA artery.

Results: Few minutes after the intracisternal injection of diluted papaverine, BAEP's wave V started to get back to normal length and at the end of procedure was the same evoked before starting MVD. After surgery hearing was bilaterally normal.

Conclusions: There is large uncertainty about dose-related efficacy and side effects of intracisternal papaverine (iPPV). Dilution of papaverine in saline is recommended to avoid complications. In our practice, in line with the literature, we use 0,3% diluted pure papaverine to prevent hearing loss during MVD for TTN.

1. Introduction

Topical application of papaverine hydrochloride was first described to treat cerebral vasospasm during neurosurgical operation in the '50s [1]. Despite an uncertain understood mechanism of action, papaverine is still used to treat complications related to vasospasm during several neurosurgical procedures. Several reports suggest that papaverine may cause adverse effects lasting hours to days [2,3].

The purpose of this technical note is to underline the potential efficacy of intracisternal diluted papaverine (iPPV) during a MVD for typical trigeminal neuralgia (TTN) and to describe its proper use, in particular for preventing hearing loss related to possible spasm of Internal Auditory Artery (IAA).

2. Case description

We report the case of a 62 years old man who was referred to our Department with a 6 years history of right TTN (mainly 2nd and 3rd branches), already treated with carbamazepine without success. The cerebral MRI TOF images at level of brainstem showed the neurovascular “conflict” in the cerebello-pontine angle cistern between trigeminal nerve (TN) and a vessel, presumably the superior cerebellar artery (SCA). The patient underwent MVD of right trigeminal nerve by retrosigmoid microneurosurgical approach.

3. MVD surgical procedure and Intraoperative BAEP monitoring

For MVD procedures, we place the patient was in lateral Fukushima position. In all MVD for TTN and hemifacial spasm, brainstem potentials (BAEP) evoked by LS-CE-Chirp® stimulus are always

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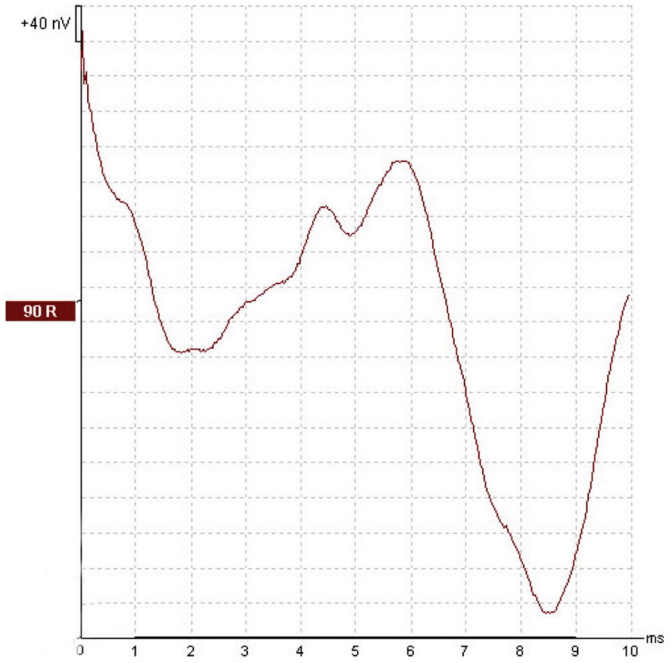

Fig. 1. The graphic shows wave V latency before starting surgery (5.7 ms).

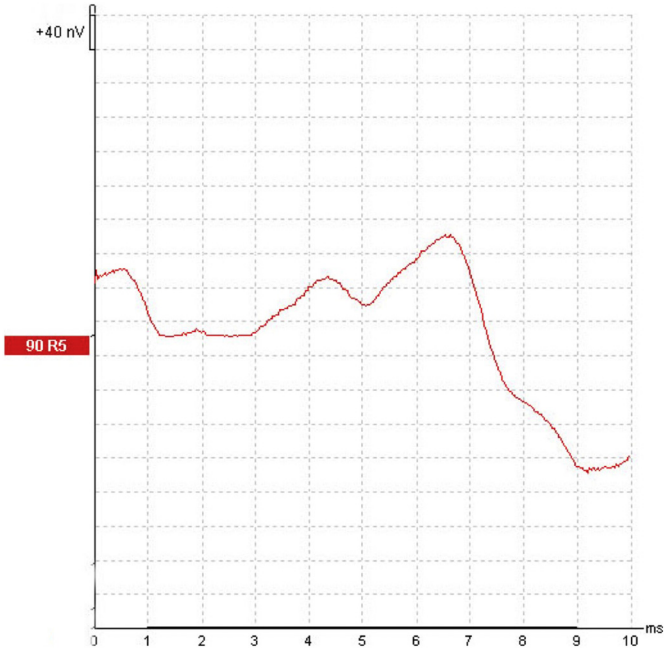

Fig. 2. During arachnoid dissection BAEP showed a lag of V wave of 1 ms, likely due to vasospasm of Internal auditory artery probably caused by arachnoid traction.

intraoperatively used since 2015 [3], in order to continuously monitor the hearing function. LS-CE-Chirp® BAEP provides enhanced neural synchronicity and faster detection of larger amplitude wave V (Fig. 1). Retromastoid skin incision of 5 cm and 3 × 3 craniotomy exposing sigmoid and transverse sinus is performed. Dura and superior lateral cerebellar cistern are opened allowing cerebellar detention and parenchyma gentle retraction until TN and its root entry zone (REZ) are easily exposed.

In the reported case, TN was ventrally compressed by the SCA, confirming the impression coming from MRI images. With microsurgical technique, cutting all arachnoid folds between TN and SCA, this artery was displaced from the nerve, obtaining an optimal decompression. As usual, small pieces of Teflon were placed between TN and SCA and a small piece of gelfoam was inserted at the level of the REZ of the TN (as a “pontine stopper”) to maintain the distance between the two elements, finally covered with fibrin glue.

During arachnoid dissection BAEP showed a temporary lag of V wave (Fig. 2). Intracisternal injection of pure papaverine without excipients (60 mg/2 ml) diluted in 20 cm^3 of 0,9% saline solution (0,3% of iPPV) was applied as a direct therapeutic action, in order to contrast possible vasospasm of IAA artery.

Five minutes after the injection of diluted iPPV, BAEP's wave V started to get back to normal length (Fig. 3) and at the end of procedure wave V was the same evoked at the beginning of the procedure (Fig. 4). After surgery hearing was bilaterally normal.

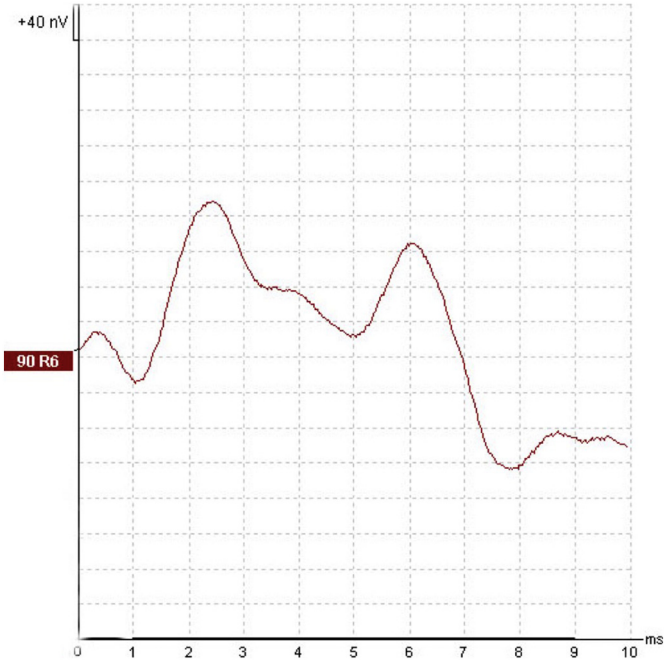

Fig. 3. BAEP's wave V started to get back to normal length from 5 min after the intracisternal injection of 0,3% papaverine.

4. Discussion

Typical trigeminal neuralgia (TTN) is characterized by severe facial pain in the distribution of the TN. It is unilateral, paroxysmal, provokable by touching “trigger points”, in absence of sensory loss [1,2]. The pain typically lasts only few seconds, but is described as one of the most painful conditions in human clinical practices, and is triggered by sensory stimuli [4].

The incidence of TTN is reported to be approximately 4 per 100,000 population and gradually increases with age [5,6]. Though the condition has been well-studied, it is still debated its pathophysiology. Most experts agree that the etiology is segmental demyelination of trigeminal sensory nerves in the nerve root or brainstem, and the demyelination is due to chronic compression of the nerve root where it comes out from the pons [4,6,7]. This chronic compression brings to an ephaptic transmission occurred at micro-injury site of TN fibers compressed by a vessel, which may also result in hyperexcitability of trigeminal nucleus [8]. Mostly the nerve is compressed by the superior cerebellar artery (SCA) [10,11].

Most theories, however, consider compression from an artery and/or vein at TN exit point as the main cause of typical TTN [12]. As regards possible treatments, at first patients would take medications, usually antiepileptic drugs like carbamazepine; other choices are

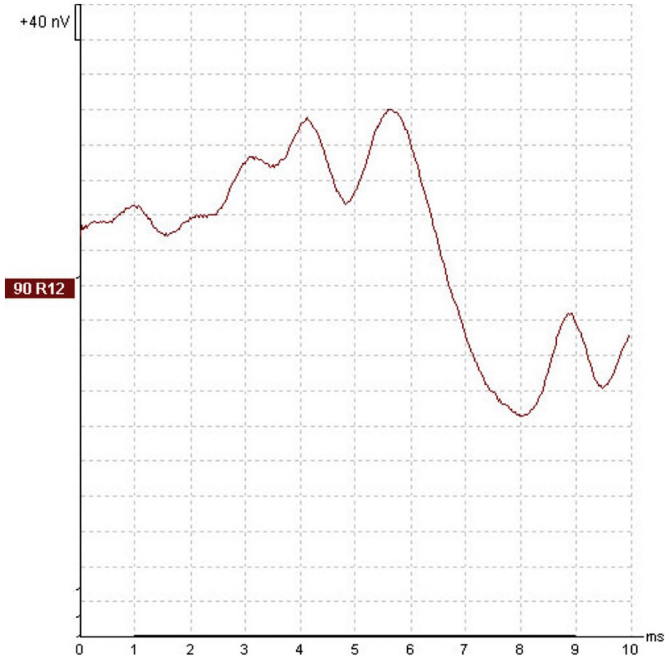

Fig. 4. Wave V latency at the end of surgery came back to starting length (5.6 ms).

ablative procedures, such as glycerol injections, radio-surgery, radio-frequency rhizotomy [13]. According with the international literature [11], MVD performed by RS approach is the most effective treatment for patients affected by TTN. An immediate postoperative pain free condition can be achieved by expert neurosurgeons with good knowledge of cerebello-pontine anatomy in about 90% of cases [11]. The procedure is performed via a RS craniotomy, and the REZ of TN is explored for searching possible vascular compressions, which are then relieved by microdissection, cutting of arachnoidal bridges, and mobilization of the offending vessel. Small pieces of teflon, with the adjunct of small pieces of hemostatics and drops of fibrin glue are placed for maintaining the distance between TN and offending vessel.

The most common vessels identified as causing compression are the SCA, anterior inferior cerebellar artery, and/or veins [9,10,14–16]. Xia et al. [11] analyzed MVD side effects and found transient complications that included incisional infection [1.3%], cerebrospinal fluid leak [1.6%], facial palsy [2.9%], facial numbness [9.1%], and hearing deficits in 1.9%. The mortality of all the patients studied was 0.1%.

According Tomasello et al. [17], some key surgical steps appear essential to avoid complications, such as: 1. appropriate skin incision avoiding damage to Greater Occipital Nerve, Lesser Occipital Nerve, or Greater Auricular Nerve, minimizing post-operative pain and sensory disturbances; 2. muscles dissection, without using monopolar cautery (preserving the vascularization of the neck muscle), in order to prevent the postoperative muscle atrophy; 3. water-tight dural closure, avoiding postoperative CSF fistula, using also bone wax, closing the mastoid cells for preventing rhinoliquorrhea; 4. Cerebello pontine angle exposure without retractors, opening the arachnoid and wait for sufficient CSF outflow; 5. superior petrosal vein (SPV) preservation; 6. careful handling of VIII cranial nerve and its vascularization.

As mentioned above, a relevant complication of posterior fossa MVD is hearing loss (HL). Conductive HL is usually transient and caused by middle ear impairment secondary to fluid entering the mastoid air cells during craniotomy. Potential causes of permanent sensorineural HL include stretching of cochlear nerve while retracting the cerebellum, direct trauma to it, manipulation of labyrinthine artery or of anteroinferior cerebellar artery, “neocompression” of the nerve by the spacer material, and acoustic trauma from drill noise or warming [18–20]. According to Bartindale et al. [21], the distinction between conductive and sensorineural HL is critical when the audiogram is performed shortly after surgery. This is because new-onset of conductive HL after posterior fossa surgery is almost uniformly transient [20]. Therefore, timing of the audiogram becomes important because an observation period of 2 to 3 months will allow for middle ear and mastoid fluid to resolve and conductive hearing to normalize in most patients.

Sensorineural HL, on the other hand, is more likely permanent and can result from a number of factors. A first step toward better controlling the rate of HP would be to clearly identify the harmful intraoperative events that cause hearing loss. In particular stretching of coclea nerve due to cerebellar retraction and vasospasm of the labyrinthine artery or the IAA seems to be the two main causes of hearing loss during MVD.

Among several existing monitoring methods, intraoperative BAEP is useful and reliable for HP in patients undergoing MVD, as suggested by many Authors. The American Clinical Neurophysiology Society (ACNS) and American Society of Neurophysiological Monitoring recommend alerting the surgeon when significant changes (SCs) in BAEP occur during surgery. SCs happen when wave V latency increases ≥ 1.0 ms and/or amplitude decreases $\geq 50\%$ [22].

In a recent meta-analysis regarding > 18.000 cases, Bartindale et al. [21] estimated that the true prevalence of HL in patients who underwent posterior MVD for TTN and hemifacial spasm was 5.58%.

Lee et al. [19] made a retrospective study evaluating the length of cerebellar retraction and the changes of intraoperative BAEP during MVD: they highlighted the distance from the cerebellar surface of the petrous temporal bone to the neurovascular compression point as the main cause of HL-group of patients during MVD. BAEP changed immediately after cerebellar retraction in 7 out of 12 postoperative deaf patients, suggesting the role of retraction on hearing outcomes.

Spasm of IAA and labirinthine artery is thought to be a relevant cause of postoperative sensory HL during MVD. Morawski et al. [23] demonstrate how the use of topical diluted papaverine, a nonspecific vasodilator, can influence successfully the “distortion product otoacoustic emissions” after inducing mechanically vasospasm of IAA in animal model.

Possible adverse effects of topical papaverine during intracranial surgery are well known. Proposed mechanism of action includes direct vasodilation and cAMP-mediated effect. Known transient side effect of iPPV includes cranial nerve palsy, brainstem dysfunction, and hemodynamic changes [24]. Topical papaverine seems to have relatively moderate effects compared to intraarterial and intracisternal infusions that may lead to more severe reactions [25], although diluted iPPV shows better results in treatment of vasospasm compared to topical one, with acceptable risks. Chadwick et al. reported a rapid BAEP's worsening in 11 MVD cases (6 TN and 5 HFS), using papaverine of 3% with excipients [25].

There is large uncertainty about iPVV dose-related efficacy and side effects. Reported concentrations vary from 0.4% to 3.0%. Safe iPPV concentrations might be < 0.2 while concentrations $> 0.8\%$ may readily cross the blood brain barrier and become toxic. Although definitive data is not available, 0.3% iPPV solution without excipients likely represents an effective dose for vasospasm while decreasing the risk of cranial neuropathies. According to Zhou et al. [24], concentrated solutions ($> 0.3\%$), and other potential culprits such as excipients, should be avoided. In our experience, in line with the literature, we use iPPV 60 mg/2 ml diluted in 20 cm^3 of 0,9% saline solution (0,3%) is well tolerated and, in the case reported, very effective.

In our department we use LS-CE-Chirp® BAEP [3]: LS-CE-Chirp® is a new acoustic stimulus used in newborn hearing testing, designed to provide enhanced neural synchronicity and faster detection of larger amplitude wave V, especially with low-intensity stimuli, and represents a safe and effective method in neuromonitoring functionality of cochlear nerve during surgery. Using CE-Chirp® BAEP, a series of about

600 stimuli is sufficient to evoke clear V-waves. This means that neuromonitoring can be performed up faster than classical BAEP, because they need a reduced numbers of stimulations at the double frequency [3].

5. Conclusion

Papaverine hydrochloride is an efficient direct-acting vasodilator used to manage vasospasm of IAA during MVD for TTN. Dilution of papaverine in saline prior to application is recommended. Although definitive data is not available, a 0.3% iPPV represents an effective and safe dose for vasospasm. In our daily practice, in accordance with the literature, we use intracisternal injection of pure papaverine without excipients, 60 mg/2 ml diluted in 20 cm^3 of 0,9% saline solution (0,3%) to prevent HL during MVD. These findings have clinical implications for several CPA surgical procedures.

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