Outcome of Medical and Surgical Management in Intractable Idiopathic Trigeminal Neuralgia

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ABSTRACT

Background: The neurovascular conflict in trigeminal neuralgia is considered as annoying and intractable condition for patients and clinicians, so the chance of medical treatment should take reasonable duration. Objectives: This prospective study was designed to assess the outcome of microvascular decompression (MVD) in patients with a more than 3-year history of intractable idiopathic trigeminal neuralgia (TN) and poor drugs response. Methods: Twenty-one patients (8 females/13 males) with intractable idiopathic TN (group-1) were enrolled to MVD and followed up for two years postoperatively. Group-2 (n=15, 6 females/9 males), continued on drug under their will. The outcome responses, pain relief and morbidity, were evaluated using: Ten-cm visual analog scale (VAS), and the Barrow Neurological Institute (BNI) scoring. Results: All patients, who disclosed the inclusion criteria, clinically and MRI brain, got benefits as of MVD surgery. The immediate efficiency in group-1 was 95.2% (n=20) and 90.5% (n=19) pain-freedom during follow-up. Gaze at the morbidity rate in both groups, group-1 had no significant signs of recurrence or surgical complications (P>0.5), although group-2 showed 53.3% (n=8) poor response to medical therapy over the same period of time with experience of drug intolerance (P<0.01). Conclusion: We concluded that MVD should be done early to avoid drug side effects and psychological drawbacks of long term pharmacotherapy and disease comorbidity. (Egypt J. Neurol. Psychiat. Neurosurg., 2009, 46(2): 265-272)

Key words: trigeminal neuralgia, microvascular decompression.

INTRODUCTION

Idiopathic trigeminal neuralgia ‘tic douloureux’ is a painful unilateral (97%) misery of the face, characterized by brief facial lancinating neuropathic pain that is lasting from several seconds to less than two minutes either provoked or spontaneously. It is limited to the distribution of one or more division of the trigeminal nerve, maxillary (17%), mandibular (15%) or both (32%) branches. TN is never spread across the midline and even bilateral (3-4%) pain is never synchronous¹,²,³.

The peak incidence of TN occurs in the fifth to seventh decade, with 90% of cases starting after the age of 40, but it is almost never seen before the third decade unless associated with multiple sclerosis⁴. According to Katusic et al 1990, the incidence of TN is 4.3/100,000, and prevalence is 15.5/100,000 population per year. According to sex, female/male ratio is 1.5/1; there is also familial type of TN where it is presented earlier in each successive generation and behaves as autosomal dominant inheritance with variable penetrance.⁵

It has been suggested that unrelieved vascular compression of the trigeminal nerve at entry zone initiates focal demyelination that causes firing in the trigeminal primary afferents, which is enhanced by impairment of the inhibitory systems in the trigeminal brain-stem complex.⁶,⁷ Anyhow, it is declared that increased bursting of wide dynamic range (WDR) neurons in nucleus caudalis and
hypersensitivity of low threshold mechanoreceptors (LTMs) in nucleus oralis are accountable for paroxysmal trigeminal neuralgia pain to noxious and non-noxious stimuli.  

This prospective study was aiming to assess the long term outcomes of microvascular decompression surgery comparing to pharmacotherapy in idiopathic trigeminal neuralgia cases with poor pain freedom response.

**PATIENTS AND METHODS**

This prospective collaborative study, connecting Mansoura University Hospital in Egypt and Sebea Military Hospital in Libya from June-2005 up to September-2008, twenty one patients (13 males and 8 females, age range was 40 to 70 years, mean±SD= 50.9±7.75 year) with a history of intractable idiopathic trigeminal neuralgia (group-1) were enrolled to MVD and follow up for two years postoperative in favor of each patient. Group-2 included 15 patients (9 males and 6 females, mean age 53.3±8.87 year), continued on drugs under their will (Table 1).

All patients were submitted to history taking, clinical examination and routine laboratory tests (according to inclusion criteria in table 2) included complete blood count, urea, creatinine, fasting blood sugar, potassium, sodium, calcium, phosphorous, liver-function tests, ESR and antinuclear antibody test. Magnetic resonance imaging (MRI) of the brain with stress on brainstem region especially pons was done for both groups and showed no mass lesions that had convincing explanation for the occurrence of pain. First week postoperative follow up MRI brain was done for group-1 to exclude complications and ensure proper surgery.

All patients were followed up after surgery in the outpatient clinic for 2 years according to the date of surgery using the VAS and BNI scales. The presence of residual pain and post operative complications were documented and compared with the preoperative symptoms.

**Evaluation scales:**

We used the Ten-cm visual analog scale (VAS), and the Barrow Neurological Institute (BNI) scoring for all patients pre and postoperative.  

Ten-cm visual analog scale (VAS) was classified into excellent if no pain, failure if worst pain and good if there is improvement of pain.  

The Barrow Neurological Institute (BNI) scoring system was used to label the degree of pain relief as follows; Grade I, no pain and no medication required; Grade II, occasional pain and no medication required, Grade IIIa; no pain and continued use of medications required; Grade IIIb, some pain which was adequately controlled on medication; Grade IV, pain improved but not adequately controlled on medication; and Grade V, no pain relief whatsoever. After surgery, if pain came back to the grade IV or V we regarded it as poor response, patients with grade III pain relief, we considered them as good response, and grade I is considered as excellent response.

Clinical outcome, according to the results of both scores, was plotted as “excellent” if total absence of symptoms had happened, “good” if an improvement of the symptoms was observed, and as “failure” if the preoperative clinical status has been unaffected or became poorer.

**Surgical procedure:**

The surgical approaches were individualized for every patient consistent with the anatomic and pathological interactions that were based on the preoperative imaging. After induction of general anesthesia, the patient may be positioned in the prone, lateral decubitus, setting or supine position depending on the surgeon’s preference. A retromastoid suboccipital craniotomy is then performed. The trigeminal nerve was examined microsurgically for vascular compression at or near its entry zone into the brain stem. Complete decompression of the trigeminal nerve is achieved with Teflon, autologous muscle tissue, or a tentorial sling.

**Statistical analysis:**

All demographic, clinical, and technical data were collected using the “Data Collection Form” and entered into a computerized database. Data obtained from all patients were statistically analyzed. Continuous variables were compared using analysis of variance for repeated measures. P-value < 0.05 was considered statistically significant. All data were expressed as mean ± standard deviation (mean±SD) or number (%) as appropriate.
Table 1. Demographic and clinical data of enrolled groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Age (year)</th>
<th>Sex M/F</th>
<th>D-D (year)</th>
<th>Right TN %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>21</td>
<td>50.9±7.75</td>
<td>13/8</td>
<td>3.6±0.87</td>
<td>71.4%</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>53.3±8.87</td>
<td>9/6</td>
<td>3.23±1.15</td>
<td>66.6%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>V1</th>
<th>V2</th>
<th>V3</th>
<th>V2+3</th>
<th>V1-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>1</td>
<td>5</td>
<td>7</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Group 2</td>
<td>0</td>
<td>3</td>
<td>6</td>
<td>5</td>
<td>1</td>
</tr>
</tbody>
</table>

V1= Ophthalmic division, V2= Maxillary division, V3= Mandibular division M= male F= female n= number, DD= disease duration.

Table 2. The inclusion and exclusion criteria for MVD patients.

1- Age: between 40 and 70 years old.
2- Unilateral facial pain due to idiopathic TN with no other neurological disorders.
3- Disease duration was less than 5 years
4- Patients who had poor response to multiple drug trials for at least 2 years prior to the surgery had been included.
5- Dull aching interictal continuous pain; patients with this history were excluded.
6- Multiple risk factor patients not fit for surgery had been excluded.
7- Patients who refused any surgery for their own reasons were also excluded

RESULTS

90.5% of our patients with TN documented their disease severe according to the pain scores. Both groups had a marked limitation in daily activities as well as they were not satisfied by drug therapy results.

In eighteen patients, the pain disappeared on the first postoperative day, and the pain is gradually disappeared within four days after surgery in the enduring patients. There was no recurrence during 2-year follow up except one patient with no definite aberrant vessels who developed mild to moderate recurrent facial pain after one year of surgery and also achieved improvement on low dose of carbamazepine (400 mg per day).

Although TN completely disappeared in all patients, six of them developed facial numbness after surgery, which required no treatment. Our final surgical results include 17 patients described as “Excellent” , 4 classified as “good” and no poor outcome or major complications recorded apart from 2 patients who developed postoperative surgical wound infection which had been improved under intensive course of antibiotics without any consequences.

In our series, the compressing arteries that had been identified during surgery were the superior cerebellar artery in 61.9% (n=13), the AICA in 9.5% (n=2) and the existed offending veins were transverse pontine vein in 19.1% (n=4) and no definite cause in 9.5% (n=2). The Teflon had been used in 17 patients; muscle in 3 cases and tentorial slings in one patient.

Preoperative MRI scans were performed and correlated with the intraoperative findings in all patients (Fig. 1). In 2 out of 21 patients (9.5%) with confirmed MVD consent showed no evidence of vascular compression, nevertheless the Teflon was used intraoperatively.

On the basis of anatomic study, the transverse pontine vein is hypothesizing to be the frequent aberrant vein. This vein, which drains into Meckel’s cave from the medial side, is usually close to the superior or inferior surface of the trigeminal nerve just facing Meckel’s cave. So, missing the venous compression site might lead to surgical disappointment. A meticulous understanding of the venous anatomy around the trigeminal nerve and Meckel’s cave may help surgeons to recognize in charge veins or arteries accurately.
In two cases, there was no definite vascular compression instituted, this may be explained by position of patient’s head during operative procedure which may separate the vessel from the nerve; anyhow Teflon was used as a protection to the nerve against artery.

Regular follow up was done using aforementioned scales every 3 months and disclosed no recurrence among patients who had excellent or good response postoperative. All patients after 12 months addressed excellent response with no pain apart from one patient (p>0.05) who received carbamazepine (400 mg/day) for additional 17-22 months and mentioned no more pain by this low dose of carbamazepine. In this study no major complications from MVD were recorded apart from temporary hearing loss in 3 patients who got back their hearing after 4-6 months (p>0.5).

Regarding the morbidity rate, in this clinical study, the group-2 showed 46.7% good response to medical therapy over the same period of time with experience of drug intolerance.

**Fig. (1):** 76 yo male patient has a 7 years history of right trigeminal neuralgia and no response to regular medical treatment, above image is T2 weighted MRI that showed no significant changes Apart from high suspension of right vascular loop artifacts around trigeminal nerve entry zone. (A) and (B) pictures during surgery of the same patient: picture (A) there is a compression of the right trigeminal nerve by superior cerebellar artery, picture (B) showed separation of the artery and nerve with a piece of Teflon.
**DISCUSSION**

MVD for compression syndromes in the posterior fossa is performed with high safety and a low down morbidity rate. In this study, we valued the vascular loop compression as the commonest cause of TN at the root entry zone that initiated focal annoyance, demyelination, and consequent devastating pain.

90.5% (n=19) of our patients who experienced MVD have documented vessel compression of the trigeminal nerve either before surgery or intra-operative apart from 2 cases who have been suspected to be idiopathic TN clinically and also admitted to surgery and experienced good response postoperatively.

We avoided the recommendation of repeat surgical exploration that carries 30% complications of hearing loss and facial weakness, so the patient who recurred pain after one year, we retried medications and showed excellent recovery.

There were short-term hearing loss in 3 cases who regained their hearing after 4-6 months (p>0.05). The short duration of hearing loss of conductive type secondary to fluid in the mastoid air cells (as detected by postoperative MRI) after surgery and not direct trauma to the nerve as a result of cerebellar retraction avoidance during surgery that is in comparison to other studies that showed death in 1% of patients (cerebellar hemorrhage and infarction), intracranial hemorrhage 2%, permanent hearing loss 3-8%, temporary hearing loss in 21% and sensory loss in 5-31%.

The difference between our results and previous studies may be referred to the high selective criteria; meticulous preparation and long term follow up. The high selective principles of inclusion and exclusion criteria (table 2) in this study excluded the patients who were clinically or radiologically had a suspicion of postoperative bad outcome. Our study in line with Hamlyn and King 1992 results who instituted that 90% of patients who experienced MVD had vessel compression compared to just 13% of age and gender-matched non-trigeminal neuralgia cadaver patients (Table 3).

Anyhow patients with demonstrable abnormal vascular loop around trigeminal nerve at the root entry zone as seen by MRI/MRA will get befit from microvascular decompression surgery as the “gold standard” surgical procedure, and it offers the best long term cure rates. Outcome also varies with the case load of operating surgeons.

Even other therapy modalities have hazards such as, acupuncture is effective with 44% recurrence of TN attacks; extracranial peripheral denervation has high pain relief percentage (50-100%), nevertheless it has short term pain relief which is suitable for medically unfit or short life expectancy patients.

<table>
<thead>
<tr>
<th>Aberrant vessel</th>
<th>Patient (n=21)</th>
<th>Primary outcome</th>
<th>Secondary outcome</th>
<th>Follow up duration (Mean±SD)(m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sup. Cerebellar A</td>
<td>Eleven</td>
<td>Pain freedom</td>
<td>Excellent–Good</td>
<td>28.5±3.6</td>
</tr>
<tr>
<td>AIKA</td>
<td>Three</td>
<td>Pain freedom</td>
<td>Excellent</td>
<td>29±4.1</td>
</tr>
<tr>
<td>Trans. Pon. V</td>
<td>Two</td>
<td>Pain freedom</td>
<td>Excellent</td>
<td>28±3.5</td>
</tr>
<tr>
<td>Pon. Trigeminal V</td>
<td>One</td>
<td>Pain freedom</td>
<td>Excellent</td>
<td>27</td>
</tr>
<tr>
<td>No Definite cause</td>
<td>Two</td>
<td>Pain freedom</td>
<td>Good</td>
<td>31.5±2.9</td>
</tr>
<tr>
<td>Multiple type of contact</td>
<td>Two</td>
<td>Pain freedom</td>
<td>Excellent</td>
<td>26±2.8</td>
</tr>
</tbody>
</table>

P value in comparison to non surgical group <0.001
Postoperative hospital stay 4.8±0.7 days
Percutaneous denervation of the gasserian ganglion and retrogasserian rootlets are done with either radiofrequency or thermocoagulation with 65% pain recurrence rate, corneal sensory loss in 20%, 50% temporary weakness of mastication muscles and severe dysesthesias in 10%, or glycerol trigeminal rhizotomy with 50% recurrence by 2 years follow up and 28% recurrence within 6 months in balloon compression. As a final point, Gamma knife radiosurgery, induced pain free effect in 75% of medical and surgical nonresponders.25 As well, the intraoperative documentations revealed that 80.8% of loops compression are arterial and arise out of the superior cerebellar artery and about 19.1% of patients were caused by venous compression.22,23

The morbidity rate in group-2 had 46.7% good response to drug therapy over the same period of time with familiarity of drug adverse effects that harmonized with Taylor et al., 1981 results in TN patients who used Carbamazepine for 16 years and they found that Carbamazepine was effective in 56% and 19% experienced CBZ- intolerance, Phenytoin’s effectiveness decreases with time, with less than 30% of patients responding after 2 years.26 Baclofen is adjuvant therapy and 10% of patients can not tolerate it, Clonazepam is effective in 65% but Valproic acid induces 30% pain free. Anyhow, pimozone is highly effective in intractable cases but it has severe adverse effects in 83% of patients. Topiramate, Oxcarbazepine, Levetiracetam, Gabapentin, Lamotrigine, analgesics, tricyclic antidepressant, and anxiolytics drugs have variable effectiveness.27,28

In Conclusion, although TN could be managed both medically and surgically: little is known about the decision process in handling of idiopathic TN "tic douloureux". The available treatments of TN, either membrane-stabilizing drugs or surgical procedures, carry threats of recurrence, adverse effects and comorbidity.

REFERENCES

16. Tomaseillo F, Alafaci C, Angileri FF, Calisto A, Salpietro FM. Clinical presentation of trigeminal


الملخص العربي

نتائج العلاج الدوائي والجراحي في حالات الاعتلال الذاتي للعصب الجمجمي الخامس

يتم الاعتلال الذاتي للعصب الجمجمي الخامس من الأمراض المزمنة والتي تستجيب للعلاج الدوائي لفترات قصيرة و بصورة غير شفافة. يهدف هذا البحث إلى تقييم دور جراحة عزل تلامس العصب الجمجمي الخامس بالأوعية الدموية المجاورة به باستخدام الجراحة الدقيقة بالميزكروسكوب الجراحي مقارنة باستخدام أنواع متعددة من الأدوية لفترات طويلة حتى ينثني لـ نتائج الخروج بتوجيه مدى أعباء العلاج الجراحي مقارنة بالعلاج الدوائي.

وقد أجريت الدراسة على مجموعتين من المرضى، المجموعة الأولى تحتوي على واحد وعشرين مريضاً (13 ذكور و 8 إناث) وتتم تجربة العلاج الدوائي لمدة أكثر من 3 سنوات ولم يستجيبوا بصورة مرضية والمجموعة الثانية تحتوي على خمسة عشر مريضاً (9 ذكور و 6 إناث) واستمرنا على العلاج الدوائي بأنواع مختلفة من الأدوية وجرعات أيضاً مختلفة وذلك بإشرافهم الشخصي. وتم فحص المرضى كلينيكياً وقياسهم باستخدام مقياس العناصر سنتيمترات البصري لألمن و مقياس معيد بارو للأعصاب وقد وجدنا أن نسبة 95.2% من المرضى في المجموعة الأولى استجابوا بسرعة ممتازة. أيضاً مع المتابعة لفترة طويلة لم نلت نسبة الشفاء إحصائيا بصورة مؤنثة حيث كانت 90.5% مقارنتا بالمجموعة الثانية التي أظهرت عدم تحسن في الدواء ذلك بنسبة 53.3% مع ظهور آثار جانبية للدواء وآثار نفسية ناتجة عن أن المرض مزمن.

نستنتج من هذا البحث أن نتائج التجربة للعلاج الدوائي مع المرضى المصابين بالاعتلال العصب الخامس المخى لفترة مناسبة وإذا لم تتم الاستجابة يجب طرح العلاج الجراحي للمرضى حتى يتم تفادي الآثار الجانبية والنفسية الناتجة عن استعمال الدواء لفترة طويلة.