The effectiveness of percutaneous balloon compression in the treatment of trigeminal neuralgia in patients with multiple sclerosis

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OBJECT Trigeminal neuralgia (TN) is more common in multiple sclerosis (MS) patients than in the general population and among the former has an incidence of approximately 2%. The pathophysiology of TN in MS patients is believed to be caused by a demyelinating plaque at the root entry zone, and therefore procedures that cause direct nerve damage are thought to be the most effective surgical modality. The authors aimed to compare the efficacy of percutaneous balloon compression (PBC) in TN patients with and without MS.

METHODS Retrospectively collected clinical data on 80 consecutive patients who underwent 144 procedures and who received PBC for TN treatment between January 2000 and January 2010 were analyzed. The cohort included 17 MS and 63 non-MS patients.

RESULTS The mean age at first operation was significantly younger in the MS group compared with the non-MS group (59 years vs 72 years, respectively, $p < 0.0001$). After a mean follow-up of 43 months (MS group) and 25 months (non-MS group), the symptom recurrence rate following the first operation was higher in the MS group compared with that in the non-MS group (86% vs 47%, respectively, $p < 0.01$). During long-term follow-up, more than 70% of MS patients required multiple procedures compared with only 44% of non-MS patients. Excellent or satisfactory outcomes were not significantly different between the MS and non-MS cohorts, respectively, at 1 day postoperatively (82% vs 91%, $p = 0.35$), 3 months postoperatively (65% vs 81%, $p = 0.16$), and at last follow-up (65% vs 76%, $p = 0.34$). A similar incidence of postoperative complications was observed in the 2 groups.

CONCLUSIONS PBC is effective in the treatment of trigeminal neuralgia in patients with MS, but, compared with that in non-MS patients, symptom recurrence is higher and requires multiple procedures.

http://thejns.org/doi/abs/10.3171/2014.11.JNS14736

KEY WORDS percutaneous balloon compression; trigeminal neuralgia; multiple sclerosis; pain

TRIGEMINAL neuralgia (TN) is a debilitating pain syndrome that affects people with multiple sclerosis (MS) more often than it does the general population—1 study showed a 20-fold higher risk of TN in MS patients than in the general population and an incidence of around 4.7 per 100,000 per year in the general population. Further, TN is characterized by intense, lancinating facial pain that occurs in attacks that usually last seconds and often occur in bouts that last weeks or months. Such attacks are often precipitated by mild sensory stimuli, including light touch, wind, chewing, washing, shaving, or applying makeup.

Increasing evidence suggests that the pathogenesis of TN is due to a demyelinating process of the root entry zone (REZ) of the trigeminal nerve. This occurs in most cases in the general population (80%–90%), because of compression of the REZ by a loop of artery or vein, which, according to pathology studies, causes focal...
demyelination in this area of the nerve. It has been postulated that the generation of ephaptic transmission along the trigeminal nerve is caused by vascular compression and pulsatile indentation at the REZ.20 This is the basis upon which microvascular decompression (MVD) is carried out, and, at our center, MVD is indeed the operation of choice for treatment of idiopathic TN.

However, pain due to demyelination of the REZ may also be caused by primary demyelination, as is often the case with MS.7,11,14,19,24 Similar areas of demyelination, as outlined previously,15,20 have been demonstrated in patients with MS-related TN. Vascular compression may still contribute to pain in primary demyelinating disorders, and some centers still offer MVD in these circumstances.5,6,23,24

The TN in MS is caused by a primary disease of the nerve, and so ablative procedures are thought to be most effective in pain-relieving treatment. One such well-established procedure is percutaneous balloon compression (PBC), which was first described by Mullan and Lichtor in 1983.27 This procedure involves cannulation of the foramen ovale using standard Hartel’s technique, followed by inflation of a Fogarty balloon in Meckel’s cave under fluoroscopic guidance in order to damage the retrogasserian trigeminal fibers.

In this study, we aimed to compare the efficacy of PBC in patients with TN with or without MS.

Methods

Retrospective analyses of prospectively collected data were carried out on 80 consecutive patients who underwent 144 procedures and who received PBC for TN between January 2000 and January 2010 in a large neurosurgical center. Ethics committee approval was not required. Results of meticulous examinations of facial sensation and pain relief were recorded at 1 day postoperatively, 3 months postoperatively, and at last follow-up. For patients who underwent multiple operations, each patient was considered independently and was censored at repeat surgery. In cases that involved operative complications, all procedures were included.

Under general anesthesia, the patients were placed in the supine position with 30° of head flexion, and a portable C-arm image intensifier was positioned for a lateral view of the skull. Standard Hartel’s landmarks were used. A 1.9-mm-diameter blunt-tipped Menghini biopsy needle was guided to the foramen ovale, and, once it was engaged, a short track for the balloon was made and the stylet was removed. A No. 4 Fogarty catheter was introduced, and contrast medium, usually 0.5–1.0 ml, was then injected to inflate the balloon to a pear shape to fill Meckel’s cave. The balloon was inflated for 3–4 minutes. The technique was identical regardless of the etiology of TN.

Data were analyzed using a commercially available statistical software program (Microsoft Excel). Results are expressed as proportions (%), mean values ± SD, or median, as appropriate. Chi-square and t-tests were used to compare categorical and numerical variables between MS and non-MS cohorts, respectively. All p values of < 0.05 were considered to be statistically significant.

Results

Cohort Details

During a 10-year period, 144 PBC procedures were carried out on 80 patients with TN following failed medical treatment. Of these, 17 patients had MS (43 operations), and 63 did not (101 operations). Patients with MS undergoing their first PBC procedure were significantly younger than those who did not have MS (58.5 ± 10.7 years vs 71.6 ± 10.3 years, respectively, p < 0.0001). Sex distribution was similar between the MS and non-MS groups (male/female 4:13 vs 24:39, respectively, p = 0.26).

The duration of symptoms prior to the patient’s first operation was longer for the MS cohort, which had a mean of 5.3 ± 3.4 years (range 1.5–10 years) of symptoms before initial operation compared to 7.8 ± 5.1 years for the non-MS group (range 0.5–26 years). This difference was, however, not statistically significant.

MS patients were followed up for longer, on average, than those who did not have MS: 43.1 ± 34.3 months versus 24.5 ± 25.5 months, respectively, p = 0.015.

Outcomes

Outcomes were defined as excellent (pain free, off medication); satisfactory (occasional pain that was controlled with or without medication); poor (moderate/severe dysesthesia); failure (no postsurgical pain relief); or recurrence (return of symptoms after an initial period of positive outcome). Outcomes further were stratified as positive or negative: Positive was defined as excellent or satisfactory, and negative was defined as poor, failure, or recurrence (outcome scale adopted from Abdennebi et al.1).

Outcome was assessed at 3 time points—immediately postoperatively, at 3 months postoperatively, and at last follow-up (Fig. 1). All patients had a postoperative examination at 3 months, and, for those subsequently lost to follow-up or discharged at 3 months, last follow-up was defined as 3 months.

Positive outcomes were not significantly different between the MS and non-MS groups at any of the 3 assessed time points. Acute postoperative pain relief was achieved in 82% of MS and 91% of non-MS patients (p = 0.35). At 3-month follow-up, 65% of MS and 81% of non-MS pa-
Patients had a positive outcome (p = 0.16). At the last follow-up, 65% of MS and 76% non-MS patients had a positive outcome (p = 0.34).

Recurrence
Recurrence of symptoms was more common following successful first PBC (i.e., acute pain relief) in the MS cohort than it was in patients without MS (86% vs 44%, respectively, p < 0.001, Fig. 2). The median number of procedures undertaken was higher in the MS group than in the non-MS group (2 ± 1.5 [range 1–5, mode 2] vs 1 ± 0.85 [range 1–4, mode 1], p < 0.001).

The durability of the PBC procedure (i.e., the time to reoperation) in those patients who required reoperation following a successful first procedure was slightly shorter for patients with MS, but this difference was not statistically significant (15.5 ± 7.0 months for MS patients vs 22.0 ± 15.8 months for non-MS patients, p = 0.12, Fig. 2).

Complications
Overall postoperative complication rates (for all operations) were similar between the groups (20.9% for MS patients vs 17.8% for non-MS patients, p = 0.88, Table 1).

For MS patients, 9 out of 43 operations resulted in complications: 1 case of meningitis, 1 case of concurrent meningoencephalitis and dysesthesia, 3 cases of cheek hematoma, 2 cases of masseter weakness, 1 case of dysesthesia, and 1 case of concurrent masseter weakness and dysesthesia. All were transient other than 1 case of masseter weakness.

For non-MS patients, 18 of 101 operations resulted in complications: 4 cases of cheek hematoma, 5 cases of masseter weakness, 5 cases of dysesthesia, 3 cases of concurrent masseter weakness and dysesthesia, and 1 case of concurrent transient abducens nerve palsy and dysesthesia. Four cases of masseter weakness were permanent.

Discussion
We found that PBC is an effective surgical treatment of TN both in patients with and without MS. However, symptom recurrence was higher in patients with MS, and they were more likely to have repeated procedures. The treatment of TN in patients who have MS remains challenging, both for physicians and surgeons, because of an incomplete understanding of the pathogenesis of pain in these patients.

The number of articles in the literature on the use of PBC for TN in MS is small. There is one systematic review encompassing 2 series with 21 MS patients undergoing PBC. The overall postoperative pain relief rate was 94.0 ± 8.4%. Again, this was made up of 2 series, one of 17 patients with rate of 88% (15 of 17), and another of 4 patients with a 100% immediate pain relief rate. Two recent papers showed a 65% acute postoperative pain relief rate in 69 patients, the other 21 patients and an 81% pain relief rate for MS-related TN undergoing PBC.

The AAN-EFNS (American Academy of Neurology and the European Federation of Neurological Societies) guidelines suggest that “There is insufficient evidence to support or refute the effectiveness of the surgical management of TN in patients with MS.” They recommend, therefore, that due to uncertainty about surgical outcomes, patients with MS should have compelling evidence of drug-resistant TN before they are considered for surgical treatment.

Few case series specifically address the efficacy of surgical treatment for TN in the context of MS, and they generally report lesser efficacy in this population compared with treatment of TN in the general population. Most authors recommend the use of ablative procedures in MS patients unless there is clear evidence of REZ vascular compression, and, even then, MVD in patients with MS is less efficacious than in non-MS patients.

In the study reported here, acute pain relief, defined as an excellent or good outcome immediately postoperatively was achieved in the majority of patients (86.5% overall, 82% in MS patients, and 88% in non-MS patients) and is comparable to the rates reported in the published literature, which suggested an immediate postoperative pain relief rate in MS patients of 65%–100%. About 70% of patients with MS remained pain free both at 3 months and at last follow-up, although it should be noted that they required more procedures to achieve this rate of success. Mallory et al. reported a comparable 3-month pain-free rate of 58%.

The rate of symptom recurrence is high in MS patients: 86% of patients with MS who underwent PBC had symptom recurrence and generally required further procedures, compared with 46%–74% in the published literature who required additional interventions. This difference may be

<table>
<thead>
<tr>
<th>Complication</th>
<th>Non-MS Patients</th>
<th>MS Patients</th>
<th>Total</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysesthesia</td>
<td>9 (8.9)</td>
<td>3 (9.3)</td>
<td>12 (8.3)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Cheek hematoma</td>
<td>4 (4.0)</td>
<td>3 (9.3)</td>
<td>7 (4.9)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Masseter weakness</td>
<td>7 (6.9)</td>
<td>3 (9.0)</td>
<td>10 (6.9)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Abducens palsy</td>
<td>1 (0.9)</td>
<td>0 (0.0)</td>
<td>1 (0.7)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Meningitis</td>
<td>0 (0.0)</td>
<td>2 (4.7)</td>
<td>2 (1.4)</td>
<td>0.03</td>
</tr>
<tr>
<td>Overall*</td>
<td>18 (17.8)</td>
<td>9 (20.9)</td>
<td>27 (18.8)</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

* Expressed as number of operations that resulted in a complication; some operations resulted in more than 1 concurrent complication.

FIG. 2. Rate of symptom recurrence and rate of patients requiring multiple procedures.
explained by the shorter periods of follow-up reported for the groups with lower rates of recurrence. Patients with MS required a repeat procedure sooner than did non-MS patients (16 months for MS patients vs 22 months for non-MS patients, p = 0.12). Table 2 shows a comparison of the published data for various outcomes of PBC in the context of MS.

An important distinction should be made between good pain relief outcome at different time points and recurrence. Recurrence refers to the status in a given patient who, at a previous time point, had a positive outcome but upon subsequent examination exhibited such pain that the outcome became negative. Such distinctions and analyses were made to facilitate identification of those patients who experienced transient pain relief without censoring all of them as negative outcomes.

Although we have noted that there is insufficient evidence to support or refute surgical management of MS-related TN, there is relatively little agreement in the literature regarding the most effective surgical treatment. Montano et al. presented a literature review in an attempt to answer this question. In comparison with our acute pain relief rate of 81% (74% overall in the literature on PBC, Table 2), no surgical technique appeared to be statistically superior: Montano et al. included MVD (91%), percutaneous retro-gasserian glycerol rhizotomy (86%), Gamma Knife surgery (85%), and percutaneous radiofrequency rhizotomy (96%). Furthermore, overall complication rates were reported to be 20.7%, which is concordant with our study’s complication rate of 21%.

Nearly all of the complications we saw were transient or mild. The overall rate was approximately 20% for both groups, and no particular complication occurred with significantly higher frequency in the context of MS. This is comparable to the series published by Mallory et al., 21 who report an overall complication rate of 17.4% for MS-related TN. Kouzounias et al. reported a complication rate of 0%, but this was likely to reflect only serious or permanent complications.

There are limitations to our study comparing PBC treatment of TN patients with and without MS. Prospective data collection was performed, but we did not have detailed information about the severity of MS for our patients. The relatively small sample size is another consideration, but our small series significantly contributes to the limited current world literature on this topic.

Conclusions

The treatment of TN in the context of MS remains challenging, both for physicians and surgeons, because of the incomplete understanding of the pathogenesis of pain in these patients. We have shown that PBC is an effective surgical treatment of TN both in patients with and without MS. However, symptom recurrence is higher in patients with MS, and they are more likely to undergo multiple procedures.

Taken together with findings reported in the literature, our data support the conclusion that PBC is a reasonable choice of first-line operative treatment for MS-related TN, especially because it is readily repeatable. It has an acceptable rate of efficacy and a low rate of significant complications.

References


Author Contributions
Conception and design: all authors. Acquisition of data: Teo. Analysis and interpretation of data: Martin, Teo. Drafting the article: Martin. Critically revising the article: all authors. Reviewed submitted version of manuscript: Martin. Statistical analysis: Martin. Study supervision: Suttner.

Supplemental Information
Previous Presentation
Portions of this work were presented as proceedings at the World Federation of Neurosurgical Societies XV World Congress of Neurosurgery, Seoul, South Korea, September 2013, and at the Spring Meeting of the Society of British Neurological Surgeons, Sheffield, United Kingdom, March 2013.

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