Clinical Article

https://doi.org/10.3340/jkns.2024.0004

The Clinical Effects of C2 and C3 Medial Branch Block for Medically Intractable Headache: a Retrospective Study

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Running Title: C2/C3 Medial Branch Block for Headache

• Received : January 7, 2024 • Revised : June 16, 2024 • Accepted : June 19, 2024

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Abstract

Objective: This study aimed to evaluate the clinical effects of medial branch blocks (MBB) C2 and C3 in treating patients with medically intractable headaches.

Methods: The medical records of 81 patients with medically intractable headaches who underwent a C2/3 MBB between January 2019 and March 2022 were retrospectively reviewed. The degrees of pain were evaluated using a visual analogue scale (VAS) score (rating 0–10) on baseline and after procedures. To evaluate patients’ satisfaction for the treatment, self-reporting measurements were examined and were categorized as excellent (>90% pain relief), good (50%–90% pain relief), fair (10%–50% pain relief), and none (<10% pain relief).

Results: The total number of MBB procedure was 107. The average baseline VAS score was 7.4 ±1.5, which improved significantly to 2.6 ±2.3, 3.6 ±2.6, and 4.5 ±3.2 on 1–3 days, 3–7 days, and 3 months after the procedure, respectively (Wilks’ lambda within group test, P <0.001). For the subjective feeling of pain relief, percentages of “excellent” response in the self-reporting measurements were significantly decreased over time (chi-square test; P= 0.001).

Conclusion: This study demonstrates clinical effectiveness of C2/3 MBB in patients with medically intractable headaches, with both early and prolonged benefits.

Key Words: Headache · Spinal nerve · Nerve block · Treatment outcome.

INTRODUCTION

Headache is one of the most common medical problems that inhibits the activities of daily living in the general population.[24] It has been reported that 52.7% of the general population experience
headache in their lives, and 4.5% suffer from headaches for >15 d per month.[24] No laboratory or imaging studies differentiating the headache types exist, and the differential diagnosis of headaches is always based on careful physical examination and collecting the history for each patient.[16] Although our biological and neurological understanding has recently been advanced, the treatment for headaches remains symptomatic.[5,4,20,30,13,7]

Injecting a local anesthetic may be an alternative modality for treating headaches, and the most well-known targets are the greater and lesser occipital nerves.[2,3,14,21] The greater occipital nerve derives from the medial branch of the dorsal ramus of the C2 spinal nerve.[29,23,12] The lesser occipital nerve originates from the branches of the C2 and C3 spinal nerves. Theoretically, sensation in the posterior half of the head and upper neck travels via the C2 and C3 spinal nerves to the brain.

The medial branch block (MBB) is known as a safe interventional procedure for managing chronic lower back or posterior neck pain.[19] Anatomically, the C2 and C3 spinal nerves are responsible for the posterior half of the head; therefore, the MBB of C2 and/or C3 is thought to reduce headaches presented in these areas.[9] For this reason, the authors performed C2/3 MBB in patients with headache in these areas who were refractory to conventional medical treatments. This study focused on the clinical effects of C2/3 MBB performed to relieve medically intractable headaches.

MATERIALS AND METHODS

This study was conducted under the approval of the Institutional Review Board of Soonchunhyang University (IRB no. 2020-05-025-002).

The medical records of the patients were retrospectively reviewed with the approval of the institutional review board of the author’s hospital. The authors defined “medically intractable headache” as a patient complaining of headache-related limitations in their daily life or occupational
activities despite continuous administration of two or more medications. Between January 2019 and March 2022, 81 patients with medically intractable headaches who underwent C2 and/or C3 MBB were identified at our institution. The patient characteristics are summarized in Table 1. All patients experienced no clinical or only partial benefits from medical treatment, and 11 (13.6%) patients received opioids to relieve headache.

According to the International Classification of Headache Disorders, 3rd edition, diagnoses of headache were made based on medical history and symptom of patients.[13] Among the 81 patients, 41, 33, and 7 had had primary headaches secondary headaches, and neuropathies, respectively (Table 2). The most common types of primary and secondary headaches were migraine (18 patients) and trauma-related headaches (24 patients), respectively. All patients classified as “the neuropathies & facial pain and other headaches” were diagnosed as having occipital neuralgia.

Regions of pain complained of by patients varied and included the C2 dermatomal distribution (parietal or occipital area), C3 dermatomal distribution (suboccipital or post-auricular area), forehead, eyeball and others. The most common locations of headache complaints were parietal and occipital pain (86.4%), followed by suboccipital and post-auricular pain (46.9%) and periorbital or forehead pain (37.0%).

The patients underwent C2 and/or C3 MBB depending on the location and laterality of the pain, as follows: C2 MBB was performed in patients with headache in the parietal and occipital areas. C3 MBB was performed in patients with suboccipital headache and posterior- or peri-auricular pain. When patients presented without the C2 or C3 area pain, the C2 MBB was performed. Depending on the patient’s symptoms (bilateral or unilateral), the injection was bilaterally or unilaterally performed.

**Procedure of the MBB**

The patient was placed in the prone position and an anteroposterior view was obtained using fluoroscopy, which visualized the upper cervical spine and the suboccipital area of the skull. A caudal
angle degree was required to obtain an appropriate view for an entry route, which was identified by a clear contour of the joint space between the atlas and axis (Figures 1A and D).

For the C2 MBB, a 23–gauge spinal needle was inserted toward the lower one-third of the lateral mass of the axis. The bone was felt at the end of needle insertion. The exact position of the needle tip was determined using the lateral view of the fluoroscope (Figure 1B) and was confirmed by injecting a small amount of radiopaque dye via the spinal needle (Figure 1C). Subsequently, 7.5 mg/2 ml of ropivacaine in saline was injected into the target.

The superior one-third of the lateral mass of C3 was target point of the C3 MBB (Figure 1E). A radiopaque dye was injected when the spinal needle touched the bone to identify whether the needle tip was appropriately located inside the intermuscular fascia rather than in the muscle proper (Figure 1F). Subsequently, the aforementioned solution was injected into the target area.

**Evaluation of procedure outcome**

Baseline and post-procedural pain degrees were evaluated using the visual analogue scale (VAS) score. VAS score was assessed multiple times when the patients visited the outpatient clinic to determine the extent to which the headache had improved. Four time points were adopted to analyze the changes in clinical effects over time after the procedure, i.e., baseline, 1–3 days (3 d), 4–7 d (7 d), and up to 3 months (3 months).

Because pain is a kind of subjective experience by its definition, the purpose of pain treatment should be focused on improving pain-related subjective satisfaction. Therefore, when examining patients after the MBB procedure, the authors asked patients what percentage of headache was relieved after the procedure. The self-reported measure of pain relief was categorized as follows: excellent (> 90% pain relief), good (50%–90% pain relief), fair (10%–50% pain relief), and none (<10% pain relief).
**Statistical analysis**

All statistical analyses were performed using SPSS Statistics, version 19 (IBM Corporation, Armonk, NY, USA). The sequential changes in VAS scores were analyzed using the repeated measure multivariate test with Wilks’ lambda within group test. Because the number of patients diagnosed as occipital neuralgia was too small to conduct statistical analysis, those were grouped into “secondary or other type headache”, which encompassed every type from a secondary headache to the occipital neuralgia. To compare clinical effect of C2/3 MBB between the primary headache and the secondary or other-types headaches and between first block and repeated block, changes of VAS scores were compared using the Wilks’ lambda test between groups. The self-reported clinical improvement after C2/3 MBB was analyzed using paired the chi-square test. The significance level was defined as P < 0.05 unless otherwise specified.

**RESULTS**

Of the 81 patients, 107 MBB procedures were performed. In total, 58 patients underwent the procedure only once, and 23 patients underwent two or more C2/3 MBBS repeatedly. The baseline mean VAS score was 7.4 ±1.15, which improved significantly to 2.6 ±2.3, 3.6 ±2.6, and 4.5 ±3.2 at 3 d, 7 d, and 3 months after the blocks, respectively (Wilks’ lambda within group test, P <0.001, Table 3). The most obvious reduction in VAS scores was observed on 3 d, which sequentially diminished on 7 d and 3 months. To identify the statistical significance of diminishing clinical effects over time, a post-hoc test was conducted between post-procedural times using Bonferroni correction with modified significance level of “P = 0.017”.

It was found that pain improvements were significant throughout all post-procedural periods. The post-procedural VAS scores of all time periods were significantly different from the baseline (P < 0.001, Figure 2A line with an asterisk). Comparing among the post-procedural VAS scores, a
significant different was found only between 3 d and 3 months (P < 0.001, Figure 2A broken line). VAS scores were not significantly different between 3 d and 7 d, and between 7 d and 3 months (P = 0.033, and 0.073, respectively).

Differences in VAS score did not differ significantly by types of headaches or by first/repeat MBB (Wilks’ lambda between group test, P = 0.58, Table 3 and Figure 2B and C).

For analyses of self-reported measures, an “excellent” response was commonly observed (40.2%) at 3 d, which decreased to 25.2% at 7 d, and 25.3% on 3 months. The degrees of satisfaction were significantly decreased over time (Figure 3 and Table 4, chi-square test; P = 0.001). Regarding both “excellent” and “good” responses as favorable outcomes, favorable outcomes were observed in 63.0%, 58.0%, and 45.7% of patients at 3 d, 7 d, and 3 months, respectively.

When inspecting cases individually, 18 of 25 cases with excellent response by 3 months were patients who showed excellent response at 3 d, and the remaining 7 cases were those whose effects gradually improved over time. (Figure 4) On the other hand, among the 40 cases which reported no pain-relief at 3 months, only 11 were reported also as no pain-relief from the initial evaluation. In the remaining 29 patients, the treatment was initially effective (ranging excellent to fair response), but it disappeared over time.

C2/3 MBB did not cause any permanent adverse events in this cohort. Almost all patients experienced transient numbness of the C2 and/or C3 dermatomes that lasted from several hours to several days. Because the numbness was often accompanied by headache relief, most patients did not report that the numbness was an unpleasant experience. However, four patients (4.9%) reported feeling uncomfortable and/or anxious due to transient numbness on their occipital area.

**DISCUSSION**
This study shows that C2/3 MBB effectively relieved pain in patients with medically intractable headaches. Pain relief was most significant on 1–3 days after the procedure and was maintained throughout the three-month period. This result suggest that C2/3 MBB may be a good complementary modality for treatment of medically intractable headaches.

This clinical effect was comparable to that of other block procedures previously reported. The most popular block procedure reported is the injection of a local anesthetic into the greater occipital nerve.[27] Tobin et al. reported that 71% and 77% of patients with migraine and occipital neuralgia, respectively, benefited from the occipital nerve block.[28] Anthony M. reported headache relief in 88% and 84% of patients with migraine and occipital neuralgia, respectively.[2] These results were comparable to the present study that more than 80% of patients showed headache relief, including excellent, good, and fair responses. Interestingly, persistent headache relief for several days to weeks and even several months after the procedure has been described in several studies.[16,14,27,3,28] Occipital nerve block was effective for treating cervicogenic headache, cluster headache, occipital neuralgia and migraines.[27]

However, few studies have addressed cervical MBB in treating headaches.[9] Inan et al. reported that repeated blocks of the C2/C3 nerve and greater occipital nerve were found to equally have a long-lasting effect in the treatment of cervicogenic headache.[14] However, the detailed method of the C2/3 block has not been described elsewhere, and the number of patients who received the block was relatively small. This study may be the first study describing C2/3 MBB in detail for the treatment of headache disorders.

The MBB performed in the cervical spine was derived from the lumbar MBB used to relieve lower back pain.[19,17] From the information retrieved from multiple cadaver studies involving the structures of the cervical nerves, the conventional cervical MBB procedure is thought to target the dorsal ramus of the cervical spinal nerve rather than its medial branch.[22,12]
The dorsal rami of the C2 and C3 branches of the greater occipital nerve and the third occipital nerve deliver sensory signals from the posterior half of the head. The primary sensory neuron is responsible for conducting of sensory signals from the scalp to the spinal cord. Its soma resides in the dorsal root ganglion and its proximal axons enter the spinal cord and synapse at the dorsal horn (Figure 5). Meanwhile, nociceptive input from the trigeminal nerve travels caudally toward the caudal portion of the spinal trigeminal nucleus. The caudal spinal trigeminal nucleus in the medulla oblongata is a continuous structure of the dorsal horn at the higher cervical spinal cord. This is the region of convergence between nociceptive information from C2-3 nerves and the trigeminal nerve, so called the trigeminocervical complex. Several studies reported headaches in the frontotemporal region could accompanied by occipital pain because of this crucial anatomical feature.

Injection of local anesthetics near the primary sensory neuron could spread throughout the axon of C2/3 nerves. Therefore, injecting local anesthetics with steroids at C2 and C3 would spread via the dorsal root entry zone and reach the dorsal horn of the spinal cord. This might affect the resting membrane potential around these structures, which reduces the excitability of secondary sensory neurons in the trigeminocervical complex.

The original purpose behind performing MBB for medically intractable headache was to determine whether headache was related to cervical spinal nerve or not. Long-term improvement in headache was an unintended outcome in patients enrolled early in the study period. It could be argued that C2/3 MBB is not practically useful because occipital nerve blocking is easier to perform and equivocally effective. However, there is an important advantage of the C2/3 MBB over the occipital nerve block in treating headaches, namely, the presence of constant anatomical landmarks for target localization. A standard procedure for occipital nerve block could not be determined because significant variations exist in the passage of the greater and lesser occipital nerves. Moreover, the C2/3 MBB could be useful for the diagnostic purpose of differentiating causes of
headaches. A significant improvement after the procedure suggests that the pathology of the headache may be related to occipito-cervical structures.[23,21,12]

This study has several limitations. First, objective measurements to examine the degree of pain are lacking. Other complementary scales, such as the quality of life, activities of daily life and neuropsychiatric evaluation, may be helpful in objectively determining the effect of the treatment. While this paper primarily focuses on discussing the therapeutic effects of the procedure, there is a noticeable lack of discussion concerning treatment-related complications. Moreover, the inclusion of multiple headache types in this study limited the interpretation of the results. Furthermore, a larger number of patients should be included in future studies to reduce selection bias. A prospective study with a randomized controlled design and a longer follow-up period should be conducted to overcome these limitations.

CONCLUSION

This study showed significant early and prolonged clinical benefits of C2/3 MBB in patients with medically intractable headaches. Future studies are required to elucidate the exact role of injecting local anesthetics in treating headaches, which could be related to unknown pathology of headache disorders.

AUTHORS' DECLARATION

Conflicts of interest

No potential conflict of interest relevant to this article was reported.
Informed consent

This type of study does not require informed consent.

Data sharing

None

Preprint

None

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• Acknowledgements

This work was supported by the Soonchunhyang University Research Fund.

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4610.2009.01549.x

Table 1. Patients characteristics

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>81</td>
</tr>
<tr>
<td>Sex (male : female)</td>
<td>26 : 55</td>
</tr>
<tr>
<td>Age (mean ±SD)</td>
<td>52.5 ± 13.5</td>
</tr>
<tr>
<td>Duration of headache (median, range)*</td>
<td>12, 1–120 months</td>
</tr>
<tr>
<td>No. of patients with headache ≥12 mos.†</td>
<td>36</td>
</tr>
<tr>
<td>Baseline VAS score (mean ±SD)</td>
<td>7.2 ±1.5</td>
</tr>
</tbody>
</table>

VAS: visual analog scale; MBB: medial branch block

*Headache duration was considerably different between patients and was nonparametrically distributed. The duration was 120 months for patients who answered that they had experienced headaches for more than 10 years.

†Several patients who had headaches for long periods >1 year could not remember when their headache had begun.
Table 2. Classification of headache of enrolled patients

<table>
<thead>
<tr>
<th>ICHD-3 classification*</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary headache</td>
<td></td>
</tr>
<tr>
<td>Migraine</td>
<td>18</td>
</tr>
<tr>
<td>Migraine without aura</td>
<td>3</td>
</tr>
<tr>
<td>Chronic migraine</td>
<td>15</td>
</tr>
<tr>
<td>Tension-type headache</td>
<td>11</td>
</tr>
<tr>
<td>Frequent episodic tension-type headache</td>
<td>1</td>
</tr>
<tr>
<td>Chronic tension-type headache</td>
<td>10</td>
</tr>
<tr>
<td>Trigeminal autonomic cephalalgia</td>
<td>4</td>
</tr>
<tr>
<td>Short-lasting unilateral neuralgiform headache attacks</td>
<td>4</td>
</tr>
<tr>
<td>Other primary headache disorders</td>
<td>8</td>
</tr>
<tr>
<td>Primary thunderclap headache</td>
<td>1</td>
</tr>
<tr>
<td>New daily persistent headache</td>
<td>7</td>
</tr>
<tr>
<td>Secondary headache</td>
<td>33</td>
</tr>
<tr>
<td>Headache attributed to trauma or injury to the head and/or neck</td>
<td>24</td>
</tr>
<tr>
<td>Headache attributed to cranial or cervical vascular disorder</td>
<td>2</td>
</tr>
<tr>
<td>Headache or facial pain attributed to disorder of the cranium … or cervical structure</td>
<td>3</td>
</tr>
<tr>
<td>Headache attributed to psychiatric disorder</td>
<td>4</td>
</tr>
<tr>
<td>Neuropathies &amp; facial pain and other headaches</td>
<td>7</td>
</tr>
<tr>
<td>Painful lesion of the cranial nerves and other facial pain</td>
<td>7</td>
</tr>
<tr>
<td>Occipital neuralgia</td>
<td>7</td>
</tr>
</tbody>
</table>

*Types of headache were classified according to The International Classification of Headache Disorders (ICHD) 3rd edition
Table 3. Sequential changes in the VAS score

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>Baseline</th>
<th>3 days</th>
<th>3–7 days</th>
<th>3 months</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All procedures</td>
<td>107</td>
<td>7.4 ±1.5</td>
<td>2.6 ±2.3</td>
<td>3.6 ±2.6</td>
<td>4.5 ±3.2</td>
<td>&lt; 0.001†</td>
</tr>
<tr>
<td>Type of Headache</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary headache</td>
<td>50</td>
<td>7.5 ±1.4</td>
<td>2.6 ±2.7</td>
<td>3.6 ±2.6</td>
<td>4.0 ±3.3</td>
<td></td>
</tr>
<tr>
<td>Secondary or other</td>
<td>57</td>
<td>7.2 ±1.6</td>
<td>2.6 ±2.4</td>
<td>3.6 ±2.7</td>
<td>4.9 ±3.1</td>
<td>0.58‡</td>
</tr>
<tr>
<td>headache</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First or Repeated</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First Block</td>
<td>81</td>
<td>7.2 ±1.5</td>
<td>2.5 ±2.5</td>
<td>3.5 ±2.5</td>
<td>4.1 ±3.1</td>
<td></td>
</tr>
<tr>
<td>Repeated Block</td>
<td>26</td>
<td>7.8 ±1.4</td>
<td>2.9 ±2.8</td>
<td>3.9 ±2.9</td>
<td>5.5 ±3.4</td>
<td>0.58‡</td>
</tr>
</tbody>
</table>

*Repeated measure multivariate analysis with Wilks’ lambda within group test, †Repeated measure multivariate analysis with Wilks’ lambda between groups test
**Table 4. Clinical effect over time of all procedures**

<table>
<thead>
<tr>
<th></th>
<th>1–3 days</th>
<th>4–7 days</th>
<th>Up to 3 mos</th>
<th>Total</th>
<th>P-value*</th>
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</thead>
<tbody>
<tr>
<td>Excellent (&gt;90%)</td>
<td>43 (40.2%)</td>
<td>27 (25.2%)</td>
<td>25 (25.3%)</td>
<td>95 (30.4%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Good (50–90%)</td>
<td>33 (30.8%)</td>
<td>34 (31.8%)</td>
<td>22 (22.2%)</td>
<td>89 (28.4%)</td>
<td></td>
</tr>
<tr>
<td>Fair (10–50%)</td>
<td>10 (9.3%)</td>
<td>22 (20.6%)</td>
<td>12 (12.1%)</td>
<td>44 (14.1%)</td>
<td></td>
</tr>
<tr>
<td>None (&lt;10%)</td>
<td>21 (19.6%)</td>
<td>24 (22.4%)</td>
<td>40 (40.4%)</td>
<td>85 (27.2%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>107</td>
<td>107</td>
<td>99</td>
<td></td>
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</tbody>
</table>

*Chi-square test
**Fig. 1.** Procedure of C2/3 medial branch block. The C2 and C3 medial branches were targeted using fluoroscopy. For the C2 medial branch block (MBB), a spinal needle was inserted toward the lower one-third of the lateral mass of the axis (A). The exact position of the needle tip was confirmed using the lateral view (B). Dye injection revealed that the needle tip was placed in the fascial space (C). The target point of the C3 MBB was the superior one-third of the lateral mass of C3 (D). The proper location of the spinal needle was identified using the lateral view (E), and the final location was confirmed by dye injection (F).
Fig. 2. Changes of pain intensity over time. Changes in visual analogue scale (VAS) score over time are illustrated. Baseline VAS score was significantly improved from 1–3 days up to 3 months after C2/3 MBB, which is indicated by an asterisk (A). The most prominent improvement was observed on 1–3 days, and effectiveness was diminished over time. Even though VAS score on 3 months was significantly different from those of 3 days (indicated by broken line), it was still significantly better than the baseline. Improvement in VAS score was compared between headache types (B), and between sessions of C2/3 MBB (C). There were no significant differences in headache improvements between primary and secondary/other types of headaches, and between first and repeat MBB sessions.
Fig. 3. Distribution of patients’ self-report for headache relief. Patients’ satisfaction for headache relief was most prominent on 0–3 days after the procedure. The ratio of satisfaction was sequentially reduced over time. (chi-squared test; P=0.001).
Fig. 4. Changes of self-reported measures between 3 d and 3 months. Changes of self-reported measures between 3 d and 3 months are illustrated using Sankey diagram. Numbers depicted on flow lines indicate number of cases belonging to both groups of different time periods. For instance, number ‘12’ written on a flow line between excellent at 3 d and none at 3 months indicates 12 cases showed excellent response at 3 d and none response at 3 months of follow-up.
Fig. 5. Anatomical structures where nociceptive information converges. The trigeminal nerve conducts sensory information from the face, forehead, and meninges, of which soma resides in the Gasserian ganglion (depicted by blue color). Interestingly, primary sensory neurons conducting nociceptive perception from the trigeminal nerve travels caudally toward the caudal spinal trigeminal nucleus and to the dorsal horns of the upper cervical cord. Meanwhile, spinal nerves C2 and C3 relay sensory signals of posterior half of the head (depicted by red color). It travels upward, and synapses with the secondary sensory neuron in the dorsal horn of upper cervical cord and continuously in the caudal spinal trigeminal nucleus. Therefore, nociceptive information from the trigeminal nerve and from the C2/3 nerves was converged between the caudal spinal trigeminal nucleus and the dorsal horn of the upper cervical cord, so called the trigeminocervical complex (depicted by purple color).