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Özet
Amaç: Bu retrospektif çalışma'da oral karbamazepin ile birlikte % 2 lidokain kullanılarak maksiler ve mandibuler sinir bloğu uygulamanın akut ve uzun dönemde trigeminal nevralji ağrısı tedavisindeki etkilerinin araştırılması amaçlanmıştır.


Sonuç: Trigeminal nevralji hastalarının ağrı atakları oral karbamazepin ve % 2 lidokain ile uygulanan maksiler ve mandibuler sinir blokları ile kontrol altına alınabilmektedir. Bu tedavi yöntemi ile kısa ve uzun dönemde başarılı sonuçlar alınabilmekte ve olguların konforu ve hayat kalitesi yönünden dikkat çeken artışlar gözlenmekte.

Anahtar Kelimeler: Trigeminal nevralji, Karbamazepin, Lidokain, Analjezik sinir bloğu

INTRODUCTION
Trigeminal neuralgia (TN) is a severe unilateral paroxysmal facial pain, often described by patients as the "the world’s worst pain" (1). It is characterized by recurrent episodes of intense, lancinating pain localized to small areas of the face. The attacks are often, but not always, precipitated by mild sensory stimulation of so-called trigger zones, which may be located anywhere within the territory of the affected trigeminal nerve (2).

TN does not respond to primary analgesics; the solution is the use of adjuvant...
analgesics, mainly anticonvulsivants. Several anticonvulsants are known to stabilize plasma membranes of peripheral nerve fibers by inhibiting ectopic discharges in altered membranes (3). Carbamazepine has been the most efficacious (beneficial in 70% of patients) and the most used anticonvulsant in the treatment of TN, and was the only drug to have been evaluated in large placebo-controlled trials (4, 5). Phenytoin, topiramate, lamotrigine, or gabapentin are also used when carbamazepine fails (6, 7).

Carbamazepine is one of the few effective interventions for TN, and is usually the drug of choice (8). With regard to long-term results, in 56% of carbamazepine treated patients it remained effective, often with relatively small doses taken continuously or intermittently for many years (9).

Local anesthetics, which act as Na+ channel blockers, have been used for disrupting the neural firings in certain neuropathic pain conditions (10). Lidocaine is a local anesthetic used for peripheral sensory block for trigeminal nerve block in patients with trigeminal neuralgia (10, 11).

We evaluated the therapeutic efficacy of associating the oral administration of carbamazepine with 2% lidocaine for maxillary and mandibular nerve blocks in acute and long-term pain relief of TN in this retrospective study.

MATERIALS AND METHODS

A total of 13 patients (9 men and 4 women), with TN aged between 34 and 91 years (mean age 53±13.39), and who applied to our Pain Unit between July 2007-July 2009 were included in this study.

Maxillary and mandibular nerve block with 2% lidocaine (Aritmal® 2% amp, Biosel Pharmaceuticals Inc., Istanbul, Turkey) was applied to the patients, in addition to oral carbamazepine treatment (Tegretol® 200 mg tb, Novartis Pharma, Istanbul, Turkey). Pain location on trigeminal branches is shown in the table below (Table 1).

Visual Analog Scale (VAS) scoring was carried out upon patient admission, and the level of the severest pain experienced during each week was recorded. Moderate pain was determined as over 3 and severe pain as over 6 (12). We defined the VAS value of 6 as the threshold for increasing the carbamazepine dose.

In cases where VAS was 6 or more, patients were free to increase their carbamazepine dose by 100 mg/day. If the patient was not using carbamazepine before, a slow titration was started at 200 mg p.o. bid, and the dose was increased by 100 mg increments up to a maximum dosage of 1200 mg/day, based on efficacy. The maximum dose administered for each patient was recorded.

After the patients were informed about the details of the procedure to be applied and gave consent to participate, standard monitoring was exercised in surgery room conditions, and vascular access procedures were performed. The painful side was examined, and it was decided to apply maxillary block to 7 patients with trigeminal nerve V2 branch pain, and mandibular block to 6 patients with trigeminal nerve V3 branch pain. The injections were performed under sterile conditions. In all patients, lidocaine injection was performed as described by Brown, by using a 22-gauge 100 mm nerve stimulator needle with 0.3 mA after stimulus was felt in the jaw (13, 14).

Maxillary block application: A 22-gauge, 100-mm needle was inserted through the mandibular notch in a slightly cephalomedial direction. This allows the needle to impinge on the lateral pterygoid plate at a depth of approximately 5 cm. The needle was then withdrawn and redirected in a stepwise manner toward the pterygopalatine fossa. As the needle is walked off the pterygoid plate, a “sense” of walking into the pterygopalatine fossa should be recognized. Once the needle was adequately positioned, 5 mL of 2% lidocaine was injected. Mandibular block application: A 22-gauge, 100-mm needle was inserted in the midpoint of the mandibular notch and then directed to reach the lateral pterygoid plate by taking a slightly cephalomedial angle through the notch. The needle then impinged on the lower pterygoid plate at a depth of approximately 5 cm. The needle was withdrawn and redirected in small steps to “walk off” the posterior border of the lateral pterygoid plate in a horizontal plane. Once the needle tip was appropriately positioned, 5 mL of 2% lidocaine was injected.

There was an immediate decrease in the pain levels of all patients after the injection, and patients were completely pain free in 1-2 minutes. Block was confirmed by performing sensation tests with alcohol. Patients were monitored for 60 minutes and discharged without any problems. Block was repeated 6 times daily for each patient for 7 days, which was the recommended period (15). After the 6th injection, patients were followed up monthly for 12 months in total.

<table>
<thead>
<tr>
<th>Pain Location</th>
<th>Trigeminal Nerve V2 Branch</th>
<th>Trigeminal Nerve V3 Branch</th>
</tr>
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<tbody>
<tr>
<td>Right</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Left</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Bilateral</td>
<td>1</td>
<td>-</td>
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Table 1: Pain Location on Trigeminal Branches
RESULTS
At the end of a 5-week treatment period, pain relapses ceased in all patients. The majority of patients benefited remarkably from the treatment after week three. The mean period of pain of patients included in the evaluation until the start of treatment (Day 0) was at least 1 month and a maximum of 8 years (Mean: 18.69±26 months). Six patients had been using carbamazepine. The other 7 patients began taking oral carbamazepine with a 200 mg/day dose. The maximum carbamazepine dose given to patients was no less than 400 mg/day and no more than 1000 mg/day, with an average dose of 615.38±190.81 mg/day. The mean carbamazepine dose increase in patients was 384.61+-223.03 mg. Over a five-week period, the dates when patients’ attacks stopped were recorded. In the third and fourth weeks, pain attacks stopped in 5 patients in each week. All patients were pain free by the last week (Figure 1).

After the first two injections, pain continued in a 53 years old male patient only in a 2x1 cm area on the upper lip. Infraorbital nerve block was applied for the first time, but it also failed to produce any results. This patient was considered to have insufficient block and his treatment was managed by increasing the dose of carbamazepine. One patient developed ptosis on the same side on the eyelid after maxillary block application. The patient was discharged upon the end of approximately 90 minutes of monitoring. Patients developed dizziness after 5 block applications. Three of these incidents were observed in the same patient. Hypoesthesia developed in the maxillary nerve in one patient, in the left maxillary nerve in two patients and in the left mandibular nerve in one patient after the injection, and disappeared completely in about 2 weeks in all cases (Table 2). During the follow-up, pain attacks started 1 month and 6 months after the discontinuation of injections in 1 patient and 2 patients, respectively. These patients were directed to external centers for radiofrequency ablation. The remaining 10 patients (77% of the total number of patients) did not experience any pain attacks during the 12-month follow-up period.

One of the patients, whose pain started after one month, was a 55 years old male who had been a bilateral TN patient for 8 years. This patient had RF applied 5 years ago and he was pain free until the last 3 months. He was referred to our hospital upon recurrence of his attacks. Since he had more pain on the left side, left maxillary block was applied. His pain was controlled during the period of injections. However, his pain recurred one month after the discontinuation of injections. The patient’s medication was changed to gabapentin.

DISCUSSION
Carbamazepine has been the most widely used drug therapy with significant results obtained in pain relief in large placebo controlled studies (4). Its success in providing pain control in early stages is reported as 70%, but long term results are less successful (9, 16).

Firstly, pain attacks were rapidly controlled in the treatment of TN by applying maxillary/mandibular nerve block with 2% lidocaine in addition to oral carbamazepine, and the number of patients with pain attacks decreased prominently after the third week. Pain attacks stopped in all patients by week five. Secondly, we observed in long term follow-up that 77% of patients could be pain free for duration of 12 months. Favorable results were obtained in our patients compared to patients receiving carbamazepine treatment alone (9, 16).

We observed that carbamazepine was not effective, despite its application in high doses, and that pain attacks disappeared for longer periods than expected in some patients with the administration of maxillary/mandibular nerve block with 2% lidocaine. Consequently, we decided to apply a lidocaine injection together with oral carbamazepine from the beginning of the treatment.

Although pain relief lasting for days, weeks and months, and the short duration of local anesthetics like lidocaine have been documented, a clear explanation of this effect has not presently been identified (11, 15, 17). Trigeminal nerve block analgesia is a procedure already considered as a trigeminal neuralgia treatment when pharmacological approaches fail (15).

It is possible that the administered lidocaine reduces pain by a systemic effect. There is information available demonstrating the efficacy of intravenous lidocaine injection in neuropathic pain (18). Lemos et al. noted a possible systemic effect in a study where trigger point injection was applied with ropivacaine (19). The same condition may have affected our treatment results.

According to the ignition hypothesis of TN, pain paroxysms begin with discharges in a small set of trigeminal primary afferents resulting from

<table>
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<th>Complaints about blocks</th>
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<tbody>
<tr>
<td>Ptosis on the eye lid</td>
<td>1</td>
</tr>
<tr>
<td>Hypoesthesia</td>
<td>4</td>
</tr>
<tr>
<td>Insufficient block</td>
<td>1</td>
</tr>
<tr>
<td>Dizziness</td>
<td>3</td>
</tr>
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Table 2: Complaints about Nerve Blocks
spontaneous activation, or after cutaneous trigger point activation. Crossed after discharge then excites non-stimulated neighbor fibers through a windup mechanism that self-sustains fiber activity beyond the original focal fiber discharge (20). We are of the opinion that spontaneous activity and dispersion developing over the existing nerve fibers in the painful area of the face may be prevented by peripheral nerve block with 2% lidocaine. Hughes et al. suggested that neural blockade with local anesthetic may also be effective in breaking the cycle of pain when used in combination with antineuralgic medications (21).

Some patients suffering from TN respond to lidocaine injected at the peripheral trigeminal nerve; this has been proven in a double blind controlled study (22). However, in the Stajcic’s study, although short-term efficacy was observed in patients treated with 2% lidocaine injection, only 2 of 8 patients were pain free by week 30. According to our results, rapid analgesia was provided in all 13 patients by the application of lidocaine injection and 10 of the 12 patients were pain free for 12 months. A 2% lidocaine injection together with carbamazepine may produce efficacy by means of similar mechanisms. The mechanisms associated with analgesic action of lidocaine and carbamazepine may be complementary because both drugs act on voltage-gated sodium channels (23). Abnormal ectopic discharge can be suppressed by anticonvulsants and local anesthetics with a sodium channel blocking effect at concentrations in an order of magnitude lower than that needed to block the propagation of action potentials in normal nerves (23).

Although long-term effects were also observed in our treatment, painless periods may last for days and months spontaneously in trigeminal neuralgia (2). We believe that maxillary/mandibular nerve blocks are beneficial in reducing pain rapidly and providing patient comfort during acute periods. Application of maxillary/mandibular nerve blocks should be kept in mind in the beginning of carbamazepine treatment in TN patients. The low number of cases and lack of control group cases may be considered among the limitations of this study. More data should be obtained in randomized double-blind studies to be conducted with more cases, in order to confirm the positive results obtained in our study.

CONCLUSIONS

Pain episodes in TN cases may be controlled by maxillary and mandibular blocks applied with oral carbamazepine and lidocaine. Favorable results are obtained in both the short- and long–term, and notable increases are observed in the comfort and quality of life of patients.

REFERENCES


