



ORIGINAL ARTICLE

Clinical effectiveness of peripheral nerve blocks with lidocaine and corticosteroid in patients with trigeminal neuralgia

Trigeminal nevralljili hastalarda lidokain ve kortikosteroid kombinasyonu ile yapılan periferik sinir bloklarının klinik etkinliği

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Summary

Objectives: Clinical efficacy of easily applicable peripheral nerve blocks has been in interest except open and closed surgical procedures requiring advanced equipment. We aimed to evaluate the clinical efficacy of triamcinolone and lidocaine injection for peripheral nerve branches in trigeminal neuralgia (TN) in terms of pain severity, pain frequency, and drug doses used.

Methods: This study was a retrospective cohort study. A total of 72 patients with TN, who underwent peripheral trigeminal nerve injection with lidocaine and triamcinolone between 2011 and 2018, were included in the study. Pain severity, pain frequency, changes in carbamazepine (CBZ) equivalent doses, and pregabalin equivalent doses were evaluated. We also evaluated whether there was a correlation between the success of the procedure and independent variables.

Results: There was a statistically significant difference in pain intensity and frequency between baseline and post-procedure at 1, 3, and 6 months ($p=0.000$). There was a statistically significant difference between CBZ equivalent doses at baseline, and 3 and 6 months after the procedure ($p=0.002$ and 0.005 , respectively). Two complications were evaluated, one patient had prolonged painless paresthesia related to the procedure area lasting about 1 week and two patients had ecchymosis at the procedure area.

Conclusion: The injection of lidocaine and corticosteroid combination for peripheral branches of the trigeminal nerve may result in short and mid-term clinical relief. Peripheral nerve blocks may be preferred for short-medium-term pain management with rare complications and simple device requirements also need little experience and skills.

Keywords: Facial pain; local anesthetic injection; peripheral nerve block; trigeminal neuralgia.

Özet

Amaç: Kolay uygulanabilir periferik sinir bloklarının klinik etkinliği, gelişmiş ekipman gerektiren açık ve kapalı cerrahi prosedürler haricinde ilgi konusudur. Trigeminal nevralljide periferik sinir dallarına triamsinolon ve lidokain enjeksiyon uygulamasının klinik etkinliğini ağrı şiddeti, ağrı sıklığı ve kullanılan ilaç dozları açısından değerlendirmeyi amaçladık.

Gereç ve Yöntem: Bu retrospektif kohort çalışmada 2011–2018 yılları arasında lidokain ve triamsinolon ile periferik trigeminal sinir bloğu yapılan trigeminal nevralljili 72 hastanın sonuçları değerlendirildi. Ağrı şiddeti, ağrı sıklığı, karbamazepin ile pregabalin eşdeğer dozlarının işlem öncesine göre işlem sonrası 1, 3 ve 6 aylardaki sonuçları değerlendirildi. Ayrıca işlem başarısı ile bağımsız değişkenler arasında bir korelasyon olup olmadığını değerlendirildi.

Bulgular: İşlem öncesi ağrı şiddeti ve ağrı sıklığı değerleri ile işlem sonrası 1, 3 ve 6 aylar arasında istatistiksel olarak anlamlı bir fark vardı ($p=0.000$). İşlem öncesi karbamazepin eşdeğer dozları ile işlem sonrası 3 ve 6 aydaki değerler arasında istatistiksel olarak anlamlı bir fark vardı (sırasıyla $p=0.002$, 0.005). Retrospektif analizde, bir hastada işlem alanına bağlı olarak yaklaşık bir hafta süren ağrısız parestezi ve iki hastada işlem bölgesinde ekimoz gelişmiş olduğu saptandı.

Sonuç: Trigeminal sinirin periferik dallarına lidokain ve kortikosteroid enjeksiyonu ile kısa ve orta vadede klinik rahatlama sağlanabilir. Periferik sinir blokları, nadir görülen komplikasyonları kısa-orta vadede ağrı tedavisi için tercih edilebilir.

Anahtar sözcükler: Yüz ağrısı; lokal anestezi; periferik sinir blokajı; trigeminal nevrallji

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Introduction

Trigeminal Neuralgia (TN) is characterized by paroxysmal intense, sharp, and electric-shock like pain with recurrent episodes localized at the innervation dermatomes of the trigeminal nerve. The episodes can be triggered with tactile stimulation and facial activities such as chewing, tooth brushing, laughing, and even talking and last for a few seconds to 2 minutes. Furthermore, there may be additional constant background facial pain.^[1] The pain predominantly occurs unilaterally, afflicts more often in the right side, female gender, mandibular, and/or maxillary trigeminal branches.^[2] The estimated lifetime prevalence of TN in a population-based study was 0.3%.^[3] In TN, demyelination often develops as a result of compression of the nerve roots at the pons level. TN may also develop as a result of infiltrative or demyelinating diseases. There is a group of patients whose etiology cannot be elucidated despite all further investigations and evaluations.^[4]

Carbamazepine (CBZ) and oxcarbazepine (OXC) are the first-line recommended medications in many clinical guidelines, reduce pain in most patients.^[5] Although these drugs are effective in 80% of patients at the beginning of treatment, there is a need to increase the dose due to autoinduction in half of the patients in the following periods.^[6] The common side effects of these drugs are fatigue, sleep, concentration, cognitive and attention impairment, mood changes, and even calcium metabolism disorder.^[7] Options such as microvascular decompression (MVD), percutaneous radiofrequency rhizotomy, percutaneous glycerol rhizotomy, percutaneous balloon compression, and gamma knife radiosurgery are available for patients who are refractory to pharmacotherapies.

Barker et al.^[8] reviewed 1336 MVD operations and reported transient facial palsy, permanent hearing loss, facial numbness, and cerebrospinal fluid fistula as complications. Carotid artery puncture, trigeminal depressor response, brainstem hematoma, corneal anesthesia, masseter weakness, diplopia, hearing and olfactory disturbances, cranial 3, 4, and 6 palsies, herpes simplex labialis, meningitis, anesthesia dolorosa, dysesthesia, masticatory weakness, cerebrospinal fistula, and intracranial hemorrhage were reported as complications of the percutaneous techniques.^[9]

Clinical efficacy of easily applicable peripheral nerve blocks has been in interest except open and closed surgical procedures requiring advanced equipment.^[5,9] We aimed to evaluate the clinical efficacy of trigeminal nerve peripheral branch injection in terms of pain severity, frequency, and drug doses at 6-month follow-up.

Material and Methods

Patients

After approval of the local ethics committee (Ethics Committee of Clinical Research, Istanbul University School of Istanbul Medicine 2018/352) patients who were referred to our clinic with the diagnosis of TN, who were over 18 years of age, who had a normal neurological examination of trigeminal nerve sensory and motor areas, and who underwent peripheral nerve block with lidocaine and triamcinolone combination between 2011 and 2018 were scanned. Who were unresponsive or could not tolerate the pharmacological treatments evaluated. Those who underwent an interventional procedure for TN for 6 months before the peripheral blocks of trigeminal nerves, patients who have started or increased their dose of carbamazepine, oxcarbazepine, pregabalin, gabapentin, baclofen, antidepressants during the follow-up period, those who were administered and those who had interventional procedures for head and neck pain were excluded from the study.

Interventional Procedure

Patients who were treated with supraorbital nerve for V1, infraorbital nerve for V2, and mental nerve for V3 were evaluated in accordance with the patient's clinical complaints. After foramen areas were identified by palpation, the skin was cleaned with an antiseptic solution and advanced up to the needle periosteum (Gimon, AG, Germany) with 22 GX50 mm (Stimuplex UltraHNS 12 with SENSE®; B Braun) needle 0.3. The procedure was performed ultrasound-guided also confirmed by 0.5 mA stimulation and negative blood aspiration. 0.25 ml of 2% lidocaine and 10 mg triamcinolone with a total volume of 0.5 ml were injected per peripheral nerve.

A 50% or more decrease in pain severity that evaluated with VAS (0–100 mm) from baseline to follow-up periods at 1, 3, and 6 months was considered as clinical improvement. Changes in pain severity, pain

frequency (<1 week, 1–2 times a week, many times a week, 1–2 times a day, and many times a day, continuous classification used in the routine patient follow-up file of our clinic is used), carbamazepine equivalent doses^[10] and pregabalin equivalent doses^[11] were evaluated. In addition, existence of correlation between the success of the procedure at first and third months and independent variables was evaluated.

Statistics

Data analysis was performed using SPSS version 20.0 (IBM corporation, Somers, NY, USA). The Shapiro-Wilk and Kolmogorov-Smirnov tests were used to test the hypothesis of normal distribution. Non-normal distributions were summarized as medians, minimum–maximum values. Categorical data were summarized as numbers and percentages. Kurtosis and skewness values of pain severity, pain frequency, pregabalin equivalent dose, carbamazepine equivalent dose values were not within the range of -1,5- + 1,5.^[12] Kolmogorov-Smirnov and Shapiro-Wilk tests were $p < 0.05$. Statistical analysis of the non-normal data of the patient was performed by nonparametric tests. Variables with non-normal distribution and continuous categorical variables were analyzed with Friedman's analysis. Wilcoxon rank-sum tests were conducted to compare changes pain severity, pain frequency, pregabalin equivalent dose, carbamazepine equivalent dose from baseline to after the intervention 1, 3, and 6. months. Bonferroni correction was used to avoid possible type 1 error. An enter (likelihood ratio) binary logistic regression model for clinical success was constructed using the variables age, duration of disease, pain severity at baseline, and pain frequency at baseline. Univariate logistic regression analysis performed separately for each independent variable with the binary dependent variable was performed.

Missing value analysis was evaluated. Since the EM estimates statistics of the missing data were $p < 0.05$, no loss data was assigned. Statistical analysis was performed with the available data.

Results

Patients who underwent peripheral nerve block with lidocaine and triamcinolone combination between 2011–2018 were scanned ($n=114$). Who were unresponsive or could not tolerate the pharmacological treatments evaluated ($n=110$). Those who

Table 1. Pain severity, pregabalin equivalent and carbamazepine equivalent dose at baseline and follow-up periods

	Min.–Max.	Median
Pain severity		
Baseline	70.0–100.0	90.0
1. month	0.0–80.0	0.0
3. months	0.0–100.0	0.0
6. months	0.0–100.0	0.0
Pregabalin equivalent dose		
Baseline	0.0–600.0	150.0
3. months	0.0–600.0	150.0
6. months	0.0–600.0	150.0
Carbamazepine equivalent dose		
Baseline	0.0–1200.0	800.0
3. months	0.0–1200.0	600.0
6. months	0.0–1200.0	600.0

Min.: Minimum; Max.: Maximum.

underwent an interventional procedure for TN for 6 months before the peripheral blocks of trigeminal nerves ($n=2$), patients who have started or increased their dose of carbamazepine, oxcarbazepine, pregabalin, gabapentin, baclofen, antidepressants during the follow-up period ($n=32$), those who were administered ($n=3$) and those who had interventional procedures for head and neck pain ($n=1$) were excluded from the study. 72 patients were included in the study. 58.3% of the patients were female ($n=42$) and 41.7% ($n=30$) were male. V1 nerve, V2 nerve, V3 nerve, combination of V1+V2 nerves, combination of V2+V3 nerves, combination of V1 + V2 + V3 nerves were symptomatic and the percentages of them were 1.4% ($n=1$), 27.8% ($n=20$), 27.8% ($n=20$), 6.9% ($n=5$), 33.3% ($n=24$), 2.8% ($n=2$) respectively. The symptom side was 62.5% ($n=45$) on the right, 36.1% ($n=26$) on the left and 1.4% bilateral ($n=1$). The average of disease duration was 33.3 (3.0–63.0) months.

In this retrospective analysis 66.6% ($n=48$) patients had been followed for 3 months and 37.5% ($n=27$) had been followed for 6 months.

Pain severity values of the patients at baseline, 1, 3, and 6 months after the procedure were showed at Table 1. First, Friedman's analysis was evaluated, there was a statistically significant difference between the

Table 2. Pain frequencies at baseline and follow-up periods

Pain frequency	Percentages (frequencies)							
	Baseline		1. month		3. months		6. months	
	%	n	%	n	%	n	%	n
Continuous	30.6	22	4.2	3	4.2	3	1.4	1
Many times a day	55.6	40	16.7	12	22.2	12	5.6	4
1–2 times a day	9.7	7	18.1	13	4.2	3	8.3	6
Many times a week	2.8	2	4.2	3	1.4	3	21.4	1
1–2 times a week	1.4	1	2.8	2	1.4	2	0.0	0
Less than once a week	0.0	0	0.0	0	0.0	0	0.0	0
1–2 times a month	0.0	0	54.2	39	33.3	39	20.8	15

groups ($p=0.000$) ($R^2=58.084$). Wilcoxon signed-rank test was used to analyze the groups. There was a statistically significant difference between the severity of pain before and after 1 month, before and after 3 months, and before and 6 months (p values= 0.000) and Z values (effect sizes) were -6.801 (0.802), -5.449 (0.642), and -4.295 (0.506).

The numbers and percentages of the pain frequency at baseline, 1, 3, and 6 months are shown in Table 2. Friedman’s analysis was evaluated, there was a statistically significant difference between repetitive measurements ($p=0.000$) ($R^2=57.457$). The pairwise group comparison was evaluated with the Wilcoxon signed-rank test. There was a statistically significant difference between baseline and 1. months, baseline and 3. months, baseline and 6. month values ($p=0.000$, and Z values (effect sizes) were -6.459 (0.761), -4.884 (0.575), -4.045 (0.477), respectively).

The pregabalin equivalent dose mean values at baseline, 3, and 6 months after the procedure are shown in Table 1. There was a statistically significant difference between repeated measures by Friedman’s analysis ($p=0.005$) ($R^2=10.571$). The pairwise group comparison was evaluated with the Wilcoxon signed-rank test. There was a statistically significant difference between pretreatment and 3. months, pretreatment and 6 months after treatment ($p=0.004$, and 0.017 respectively) (Z values (effect sizes) -2.879 (0.339), -2.392 (0.282) respectively).

CBZ equivalent dose values at baseline, 3, and 6 months after the procedure are shown in Table 1.

There was a statistically significant difference between repeated measures by Friedman’s analysis ($p=0.005$) ($R^2=15.273$). The pairwise group comparison was evaluated with the Wilcoxon signed-rank test. There was a statistically significant difference between pretreatment and 3. months, pretreatment, and 6. months ($p=0.002$ and 0.005 respectively) and Z values (effect sizes) -3.072 (0.362) and -2.840 (0.334) respectively.

In the present study, the effect size values were large for the decrease in pain severity at 1 month, moderate for a decrease in pain severity at 3 and 6 months, moderate for pain frequency at 1 and 6 months, decrease in pain frequency at 3 months and small for a decrease in carbamazepine equivalent and pregabalin equivalent doses at 3 and 6 months.

When the success of the procedure was considered as a 50% or more reduction in pain severity, 79.2% ($n=57$), 33.3% ($n=24$), 24.6% ($n=19$) of the procedures were successful at 1, 3 and 6 months respectively.

The relationships between the success of the procedure at 1. month and the dependent variables which that age, disease duration, baseline pain intensity, baseline pain frequency was evaluated by binary logistic regression analysis ($p=0.750$, 0.900 , 0.142 , 0.991 respectively) (odds ratio= 1.007 , 1.018 , 0.965 , 1.000 respectively).

The relationships between the success of the procedure at 3. month and the dependent variables which that age, disease duration, baseline pain intensity,

baseline pain frequency was evaluated by binary logistic regression analysis ($p=0.780, 0.804, 0.741, 0.920$ respectively) (odds ratio= $1.004, 1.001, 1.007, 1.000$ respectively).

The relationships between the success of the procedure at 6. month and the dependent variables which that age, disease duration, baseline pain intensity, baseline pain frequency were evaluated by binary logistic regression analysis ($p=0.824, 0.389, 0.459, 0.995$ respectively) (odds ratio= $1.007, 1.008, 1.027, 0.000$ respectively).

Complications were evaluated, 1 patient had prolonged painless paresthesia related to the procedure area lasting about 1 week and 2 patients had ecchymosis at the procedure area.

Discussion

In this study peripheral trigeminal nerve blocks were found to be effective in relieving pain severity, and frequency for short and intermediate periods. Also, peripheral nerve blocks have a dose-reducing effect on carbamazepine, oxcarbazepine, and gabapentins for up to 6 months after the procedure in patients with TN. Peripheral nerve blocks were found to be safe when evaluated in terms of complications and side effects. Similar results have been shown in the case series in which peripheral nerve blocks were evaluated in 3–9 patients with TN, consistent with the clinical efficacy that may extend up to 6 month.^[13–15] Stani et al.^[16] demonstrated that the combination of lidocaine injection for the peripheral branches of the trigeminal nerve with pharmacological therapy was superior to pharmacological therapy in the short term follow-up. Bainton et al.^[17] showed a prolonged clinical response of peripheral nerve blocks was associated with neurotoxicity of local anesthetics. Neurotoxicity was explained by increased perineurial permeability, and endoneurial fluid pressure, by axonal injury. Bainton et al.^[17] showed the neurotoxicity of local anesthetics in their electrophysiological study by compound action potential reduction and long-term conduction block.

In the present study, the combination of local anesthetic with corticosteroid was evaluated. Eker et al.^[18] demonstrated that corticosteroid addition to local anesthetic in short-term follow-up in patients

with TN provides superiority in clinical efficacy. It has been shown that corticosteroids may be effective on pain by inhibiting proinflammatory cytokine synthesis^[19] and that corticosteroid addition provides more effective and long-lasting clinical efficacy in blocks and infusions.^[20]

In the present study, there was no correlation between clinical efficacy and age, disease duration, baseline pain intensity, baseline pain frequency. Han et al.^[21] showed that a short duration of disease was positively correlated with treatment efficacy for trigeminal nerve block in patients with TN. Consistent with the literature, our study also showed that peripheral nerve injections were safe in terms of side effects and complications.^[13–16]

One of the limitations of our study is its retrospective design. Prospective randomized controlled studies with long-term follow-up may clarify the clinical efficacy of peripheral nerve blocks in TN and help to identify the factors related with clinical success.

Peripheral nerve blocks help pain relief in patients with TN who were unresponsive or could not tolerate to the pharmacological treatments. Furthermore, peripheral nerve blocks requiring less experience and skills with rare complications, and simple devices requirement.

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