

Observational Study

Greater occipital nerve blocks in the treatment of refractory chronic migraine: An observational report of nine cases

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Abstract

AIM

To report the effects of greater occipital nerve (GON) blocks on refractory chronic migraine headache.

METHODS

Nine patients who were receiving the conventionally accepted preventive therapies underwent treatment with repeated GON block to control chronic migraine resistant to other treatments. GON blocking with lidocaine and normal saline mixture was administered by the same physician at hospital once a month (for three times in total). Patients were assessed before the injection and every month thereafter for pain frequency and severity, number of times analgesics were used and any apparent side effects during a 6 mo follow-up.

RESULTS

Eight of nine patients reported a marked decrease in frequency and severity of migraine attacks in comparison to their baseline symptoms; one reported no significant change (not more than 50%) from baseline and did not accept the second injection. GON block resulted in considerable reduction in pain frequency and severity and need to use analgesics up to three months after the injection in the present cases. The patients did not report any adverse effects.

CONCLUSION

Hereby we noticed a remarkable success with refractory chronic migraine patients. We believe that this intervention can result in rapid relief of pain with the effects lasting for perhaps several weeks or even months. Further controlled clinical trials are warranted to evaluate the effect of GON block in the treatment of refractory migraine cases.

Key words: Migraine; Headache; Chronic migraine; Refractory migraine; Greater occipital nerve; Nerve block

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Core tip: In this observational study, we report the results of 9 patients with refractory chronic migraine. The greater occipital nerve block with lidocaine seems to be one of the reliable treatment methods for the transitional treatment of refractory chronic migraine in order to take them back toward non-refractoriness which can be easily solved by the preventive therapies conventionally accepted. We think that this procedure can be effective in refractory migraine cases and should be included in our management plan.

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INTRODUCTION

Migraine is a common problem recently classified as an important cause of morbidity by the Global Burden of Disease 2010 and sometimes its treatment can be difficult^[1]. In some individuals, the migraine is refractory to guideline-based treatment protocols, although there are many substantial advances in migraine therapy^[1,2]. Nowadays, it is believed that knowledge of the scientific basis and techniques for nerve blockade is important in making treatment decisions in these refractory migraine cases, but the mechanisms by which these interventions work are not clear. It is believed that the use of local anesthetics breaks the pain cycle by ameliorating both central and peripheral sensitization^[2-4]. The greater occipital nerve (GON) which is the branch of the second cervical root is the primary sensory nerve of the occipital area of the skull and GON block is the most widely used procedure which is very effective, safe and relatively easy to perform in the examination room^[1-3,5-9]. As a practical estimate, it is a point located approximately two-thirds of the distance on a line drawn from the center of the mastoid to the external occipital protuberance^[1-3]. A small dosage of local anesthetic agent is sufficient to block GON and fairly well accepted indications for aestheticizing GON are occipital neuralgia, cluster headache and cervicogenic headache^[5,8]. Although controlled studies are limited, GON block seems to be particularly effective in migraine cases and even in some patients with refractory chronic migraine too^[6-11]. Occipital area and neck symptoms seen in migraine patients suggest a functional connectivity between nociceptive trigeminal and cervical afferents, although it is unclear how blocking these structures might affect centrally mediated primary neuropathic phenomena^[2,8-12]. GON injections with local anesthetics have been used for the acute and preventive treatment

of migraine for decades^[6,12]. The acute effect of local anesthetics can be explained, but long-term improvement results from anesthesia that lasts some hours is still not clear^[2,11]. Despite reports with pleasing clinical experiences, little support exists for the efficacy of GON block in refractory cases. Here, we noticed a remarkable success in intractable 9 cases with chronic migraine, although it is true that indications for GON blockade in migraine are not yet entirely clear.

MATERIALS AND METHODS

The results of 9 patients with relevant forms of chronic migraine headaches not responding to conventional therapies were evaluated in these observational reports. All patients were suffering from migraine headaches and referred to algology outpatient clinic of Göztepe Teaching hospital in Istanbul in 2015. All patients were suited for the clinical concept of refractoriness defined by The European Headache Federation^[12]. Prophylactic migraine medications (at least 3 different drug regimens) in adequate dosages had been used for at least 3 mo each. All patients had a preventive therapy for at least 1 year. There was no overused medication but 5 of them had histories of drug overuse, which had been treated at the beginning of preventive therapy which started one year ago. All patients had tenderness around GON. None of the patients had injection contraindication, such as infection, open skull defect, known allergies to anesthetic agents, anticoagulant use, and tendency for vasovagal responses to injection. The procedure was explained step-by-step to the patients. During follow-up, all patients continued to use preventive drugs (*i.e.*, beta blockers, flunarizin hidroklorür, topiramate, sodium valproate, amitriptyline, duloxetine) administered previously.

After ensuring that expectations about treatment regimen were appropriate, the patients were seated on a chair of sufficient height so that the physician could easily perform the injection. A line was drawn from the center of the mastoid to the external occipital protuberance; approximately one-third of the distance from protuberance was accepted as injection target^[2,3,9]. The neck was flexed forward. The plunger of the syringe was pulled back and injection was started only if there was no blood return. A mixture of 2% lidocaine (2 mL) and saline solution (3 mL) was injected subcutaneously into 2 target points around GON bilaterally. The total injected volume was 5 mL. GON infiltration with lidocaine were administered once a month and repeated for 3 consecutive months. The patients were regularly followed up for prognosis and to ensure patient compliance for the next three months. At each visit, the Visual Analog Scale was used to record subjectively experienced pain severity on a 10-point numeric pain rating scale^[13]. MIDAS which is a self-administered questionnaire, including five disability-related questions during the previous 3-mo period was

Table 1 Clinical findings related to migraine during follow-up

Variable (baseline and follow-up results)		Mean	Std. deviation	95%CI for mean		Minimum	Maximum	P value (anova)
				Lower bound	Upper bound			
Attack number per month	Baseline	20.87	4.91	16.76	24.98	10.00	25.00	< 0.001
	1 st month	8.37	3.66	5.31	11.43	4.00	15.00	
	2 nd month	2.87	0.99	2.04	3.70	1.00	4.00	
	3 rd month	2.50	0.75	1.86	3.13	1.00	3.00	
	6 th month	8.00	1.30	6.90	9.09	6.00	10.00	
The number of analgesics used per month	Baseline	24.87	4.64	20.99	28.75	15.00	30.00	< 0.001
	1 st month	9.62	4.98	5.45	13.79	4.00	18.00	
	2 nd month	3.12	0.83	2.42	3.82	2.00	4.00	
	3 rd month	2.25	0.70	1.65	2.84	1.00	3.00	
	6 th month	8.25	1.48	7.00	9.49	6.00	10.00	
Duration of attacks per month (h)	Baseline	16.00	5.39	11.48	20.51	10.00	24.00	< 0.001
	1 st month	12.87	3.22	10.17	15.57	10.00	18.00	
	2 nd month	9.00	2.56	6.85	11.14	7.00	15.00	
	3 rd month	7.62	1.40	6.44	8.8	6.00	10.00	
	6 th month	8.50	1.51	7.23	9.76	6.00	10.00	
Visual analog scale score	Baseline	8.75	0.70	8.15	9.34	8.00	10.00	< 0.001
	1 st month	6.25	1.98	4.59	7.90	2.00	8.00	
	2 nd month	3.12	1.35	1.99	4.25	2.00	6.00	
	3 rd month	2.62	0.51	2.19	3.05	2.00	3.00	
	6 th month	5.62	1.68	4.21	7.03	3.00	7.00	

used to assess disability related to pain at baseline evaluation and at the 6th month visit^[14]. The sum of the scores related to answers of these five questions is the MIDAS score. The patients reported not only the number of lost days due to headache but also the number of additional days with significant limitations of activity (*i.e.*, at least 50% reduced productivity) in any type of work domains. In the present study, analgesic use (triptans, ergot alkaloids and other analgesics) was measured as the number of dosages per month. Changes in attack number, symptom severity and other measured variables were recorded for each visit. The key for success was prevention of attacks at the follow-up periods in the present study.

RESULTS

The mean age of 9 patients (2 males, 7 females) was 38.75 ± 8.23 years. Only 1 patient did not show expected improvement in pain severity and reported no benefit after the first injection. He did not tolerate this invasive procedure because he felt pain; he refused the second injection. Baseline and 6th month MIDAS scores of the eight patients who completed follow-up period were 31.87 ± 3.98 and 6.75 ± 2.76 , respectively ($P = 0.000$). The pain characteristics and follow-up results of the patients are shown in Table 1. The use of GON blocks markedly decreased migraine attack frequency, severity and duration, and analgesics use compared with baseline symptoms in these patients. Comparing these variables between the 3rd month after the injection and previous time points showed that all indices were improved during the first 3 mo and the subsequent 3 mo follow up. Although the results were better compared to the baseline, the number of attacks and attack severity increased in the 6th month. None

of the patients reported paresthesias or prolonged numbness which could indicate mechanical damage to the nerve in the distribution of GON. In addition, no local anesthetic systemic side effects were noticed, including alterations in syncope, consciousness, and rarely, arrhythmias and seizures.

DISCUSSION

Migraine is a paroxysmal disorder and increased number of attacks can lead to chronic migraine. Then, migraine becomes less responsive to acute treatment as well as prophylactic medications^[4,15]. It is obvious that all the migraine attacks should be treated in the patients with a reduced efficacy of overused analgesics or migraine medications such as triptans and a lack of responsiveness to the abortive and preventive medications. The anatomic connection between GON and C2 roots supplies the rationale of a central action reducing or minimizing the nociceptive transmission related to pain^[3,4]. Previously, anesthesia of the lesser occipital nerve, the auriculotemporal nerve, the supraorbital and supra-trochlear nerves or the sphenopalatine ganglion were much studied, but efficacy in the treatment of migraine were generally anecdotal or studied in combination with other nerve blocks^[2,3,16,17]. New reports showed that GON blocks may be considered as a new therapeutic opportunity for chronic headaches refractory to conventional medical therapies^[4,6-9,18,19]. In the present observation, we assessed the effect of GON blocking on migraine headaches by evaluating the pain severity, pain frequency, and times to use of analgesics. The results showed that GON block with lidocaine and saline mixture for the treatment of patients with refractory migraine was a safe, simple, and effective technique without any adverse effect. During the period of

monthly injections, decreased prostration and increased productivity, decreased triptan, ergot alkaloids and any other analgesic use, and decreased visits to emergency clinics were recorded. As reported in the results section, our patients had decreased numbers of attacks with low severity, but the effects were temporary, although there was still a significant difference between baseline severity and the 6th month results (Table 1). Afridi *et al*^[11] recommend that tenderness around the GON seems to be predictive of a good response to GON block in the patients. Although evidence is not entirely clear on tenderness over GON, the patients had tenderness and responded very well in the present cases. We think that this might be a selection criteria for evaluation in further studies.

It is well known that local anesthetic agents inhibit neural activity by interfering with voltage-gated sodium channels, so they prevent depolarization resulting in hindered pain transmission by nociceptive C fibers^[2-4]. GON block can produce beneficial effects in migraine type headache involving regions outside of the territory served by these nerves. This result is often explained by the concept of convergence (particularly between trigeminal and upper cervical sensory afferents) in the nociceptive system of the head and neck region^[2-4]. Local anesthetics are easily absorbable and diffuse across nerve membranes and, even low concentrations of local anesthetics block only sensory fibers in mixed nerves without affecting motor function. The ester anesthetics, *e.g.*, procaine and cocaine, were first to be used clinically, but their use was limited due to allergenicity. The amide local anesthetics, *e.g.*, lidocaine, mepivacaine, bupivacaine, and prilocaine, are relatively hypoallergenic, stable, longer acting and well tolerated, hence they are more widely used for blocks in clinical practice. Although bupivacaine has more prolonged action, lidocaine is a more common choice for peripheral nerve blockade^[20,21]. For this reason, we used lidocaine as an easily obtainable agent in the present study. GON block with lidocaine repeated monthly for duration of 3 mo was a simple way of preventing migraine attacks and did not present any particular risk. The tendency in clinical practice is to use bilateral GON block in refractory chronic migraine cases, although this issue has not been clearly defined as yet^[4,22]. Similarly, we used bilateral injections, it was reasonable because the patients had mostly common-type migraine attacks. Lidocaine is metabolized by the hepatic cytochrome enzyme systems and some drugs, *e.g.*, antiarrhythmics, antibiotics, antiepileptics, calcium channel blockers, and antidepressants can inhibit this system^[4]. This can result in adverse effects which are secondary to increased anesthetic levels with only minimal intravascular absorption^[2,14,21,23]. Although most of our patients used drugs which could be interfered with lidocaine, we did not see any adverse effects. Although controlled large trials to study the effectiveness of different local anesthetic procedures are still lacking, lidocaine seems

to be effective.

In fact, the placebo effect on diseases as migraine can be of great relevance and GON block as treatment of refractory chronic migraine can be made only after randomized double blind trials. This represents a main limitation of the findings described in the present paper.

In conclusion, GON blocks with lidocaine seem to be the most reliable path for the transitional treatment of refractory chronic migraine in order to take them back toward non-refractoriness, which can be easily treated by the conventionally-accepted preventive therapies. GON blocking with a lidocaine and normal saline mixture resulted in reduction in pain severity and frequency, and use of analgesics for up to three months after the third injection. We think that this procedure can be effective in refractory migraine cases and should be included in such management plans.

COMMENTS

Case characteristics

Nine consecutive migraine patients with refractory to the most accepted treatment protocols.

Clinical diagnosis

The authors used European Headache Federation proposed criteria for refractory chronic migraine diagnosis (chronic migraine, no medication overuse, prophylactic migraine medications in adequate dosages used for at least 3 mo each, contraindications or no effect of the following preventive medication with at least 3 drugs, adequate treatment of psychiatric or other comorbidities by multidisciplinary team).

Imagings for differential diagnosis

All patients had cranial computed tomography or magnetic resonance imaging to exclude organic pathologies.

Laboratory diagnosis

All labs were within normal limits.

Treatment

A mixture of 2% lidocaine (2 mL) and saline solution (3 mL) was injected subcutaneously into 2 target points around greater occipital nerve (GON) bilaterally.

Related reports

GON injections have been used for the acute and preventive treatment of migraine for decades. The acute effect of local anesthetics can be explained easily, but long-term good results continuing for months from anesthesia is still not clear.

Term explanation

A mixture of lidocaine and saline solution was injected subcutaneously into 2 target points (one-third of the distance from occipital protuberance to mastoid) around GON bilaterally.

Experiences and lessons

GON injection can be dramatically effective in refractory migraine cases and should be included in the practitioner's management plan.

Peer-review

This manuscript describes the effect of GON blocks in the treatment of refractory

chronic migraine. It is an interesting pivotal report.

REFERENCES

- 1 **Steiner TJ**, Birbeck GL, Jensen RH, Katsarava Z, Stovner LJ, Martelletti P. Headache disorders are third cause of disability worldwide. *J Headache Pain* 2015; **16**: 58 [PMID: 26109437 DOI: 10.1186/s10194-015-0544-2]
- 2 **Lionetto L**, Negro A, Palmisani S, Gentile G, Del Fiore MR, Mercieri M, Simmaco M, Smith T, Al-Kaisy A, Arcioni R, Martelletti P. Emerging treatment for chronic migraine and refractory chronic migraine. *Expert Opin Emerg Drugs* 2012; **17**: 393-406 [PMID: 22862686 DOI: 10.1517/14728214.2012.709846]
- 3 **Busch V**, Jakob W, Juergens T, Schulte-Mattler W, Kaube H, May A. Functional connectivity between trigeminal and occipital nerves revealed by occipital nerve blockade and nociceptive blink reflexes. *Cephalalgia* 2006; **26**: 50-55 [PMID: 16396666 DOI: 10.1111/j.1468-2982.2005.00992.x]
- 4 **Martelletti P**, Giamberardino MA, Mitsikostas DD. Greater occipital nerve as target for refractory chronic headaches: from corticosteroid block to invasive neurostimulation and back. *Expert Rev Neurother* 2016; **24**: 1-2 [PMID: 26959293 DOI: 10.1586/14737175.2016.1164599]
- 5 **Bovim G**, Sand T. Cervicogenic headache, migraine without aura and tension-type headache. Diagnostic blockade of greater occipital and supra-orbital nerves. *Pain* 1992; **51**: 43-48 [PMID: 1454403 DOI: 10.1016/0304-3959(92)90007-X]
- 6 **Kashipazha D**, Nakhoshtin-Mortazavi A, Mohammadianinejad SE, Bahadoram M, Zandifar S, Tarahomi S. Preventive effect of greater occipital nerve block on severity and frequency of migraine headache. *Glob J Health Sci* 2014; **6**: 209-213 [PMID: 25363127 DOI: 10.5539/gjhs.v6n6p209]
- 7 **Saracco MG**, Valfrè W, Cavallini M, Aguggia M. Greater occipital nerve block in chronic migraine. *Neurol Sci* 2010; **31** Suppl 1: S179-S180 [PMID: 20464617 DOI: 10.1007/s10072-010-0320-7]
- 8 **Cuadrado ML**, Aledo-Serrano Á, Navarro P, López-Ruiz P, Fernández-de-Las-Pe-as C, González-Suárez I, Orviz A, Fernández-Pérez C. Short-term effects of greater occipital nerve blocks in chronic migraine: A double-blind, randomised, placebo-controlled clinical trial. *Cephalalgia* 2016; Epub ahead of print [PMID: 27296456 DOI: 10.1177/0333102416655159]
- 9 **Ashkenazi A**, Levin M. Greater occipital nerve block for migraine and other headaches: is it useful? *Curr Pain Headache Rep* 2007; **11**: 231-235 [PMID: 17504651 DOI: 10.1007/s11916-007-0195-3]
- 10 **Sjaastad O**, Bakkeiteig LS. Migraine without aura: comparison with cervicogenic headache. Vågå study of headache epidemiology. *Acta Neurol Scand* 2008; **117**: 377-383 [PMID: 18031560 DOI: 10.1111/j.1600-0404.2007.00966.x]
- 11 **Afridi SK**, Shields KG, Bhola R, Goadsby PJ. Greater occipital nerve injection in primary headache syndromes--prolonged effects from a single injection. *Pain* 2006; **122**: 126-129 [PMID: 16527404 DOI: 10.1016/j.pain.2006.01.016]
- 12 **Martelletti P**, Katsarava Z, Lampl C, Magis D, Bendtsen L, Negro A, Russell MB, Mitsikostas DD, Jensen RH. Refractory chronic migraine: a consensus statement on clinical definition from the European Headache Federation. *J Headache Pain* 2014; **15**: 47 [PMID: 25169882 DOI: 10.1186/1129-2377-15-47]
- 13 **McCormack HM**, Horne DJ, Sheather S. Clinical applications of visual analogue scales: a critical review. *Psychol Med* 1988; **18**: 1007-1019 [PMID: 3078045 DOI: 10.1017/S0033291700009934]
- 14 **Ertas M**, Siva A, Dalkara T, Uzuner N, Dora B, Inan L, Idiman F, Sarica Y, Selçuki D, Sirin H, Oğuzhanoglu A, Irkeç C, Ozmenoglu M, Ozbenli T, Oztürk M, Saip S, Neyal M, Zarifoğlu M. Validity and reliability of the Turkish Migraine Disability Assessment (MIDAS) questionnaire. *Headache* 2004; **44**: 786-793 [PMID: 15330825 DOI: 10.1111/j.1526-4610.2004.04146.x]
- 15 **Negro A**, Rocchietti-March M, Fiorillo M, Martelletti P. Chronic migraine: current concepts and ongoing treatments. *Eur Rev Med Pharmacol Sci* 2011; **15**: 1401-1420 [PMID: 22288302]
- 16 **Speciali JG**, Gonçalves DA. Auriculotemporal neuralgia. *Curr Pain Headache Rep* 2005; **9**: 277-280 [PMID: 16004845 DOI: 10.1007/s11916-005-0037-0]
- 17 **Govindappagari S**, Grossman TB, Dayal AK, Grosberg BM, Vollbracht S, Robbins MS. Peripheral nerve blocks in the treatment of migraine in pregnancy. *Obstet Gynecol* 2014; **124**: 1169-1174 [PMID: 25415168 DOI: 10.1097/AOG.0000000000000555]
- 18 **Inan LE**, Inan N, Karadaş Ö, Gül HL, Erdemoglu AK, Tükel Y, Akyol A. Greater occipital nerve blockade for the treatment of chronic migraine: a randomized, multicenter, double-blind, and placebo-controlled study. *Acta Neurol Scand* 2015; **132**: 270-277 [PMID: 25765043 DOI: 10.1111/ane.12393]
- 19 **Takmaz SA**, Inan N, Uçler S, Yazar MA, Inan L, Başar H. Greater occipital nerve block in migraine headache: preliminary results of 10 patients. *Agri* 2008; **20**: 47-50 [PMID: 18338279]
- 20 **Barash P**, Cullen BF, Stoelting RK. Handbook of Clinical Anesthesia. 5th ed. Ch 17. Local anesthetics. Lippincott Williams and Wilkins, 2006: 269
- 21 **Arbona FL**, Khabiri B, Norton JA. Ultrasound-Guided Regional Anesthesia: A practical Approach to Peripheral Nerve Blocks and Perineural Catheters. Chapter 1: Pharmacology: local anesthetics and additives. Cambridge University Press, 2010: 1-9
- 22 **Lambru G**, Abu Bakar N, Stahlhut L, McCulloch S, Miller S, Shanahan P, Matharu MS. Greater occipital nerve blocks in chronic cluster headache: a prospective open-label study. *Eur J Neurol* 2014; **21**: 338-343 [PMID: 24313966 DOI: 10.1111/ene.12321]
- 23 **Imaoka S**, Enomoto K, Oda Y, Asada A, Fujimori M, Shimada T, Fujita S, Guengerich FP, Funae Y. Lidocaine metabolism by human cytochrome P-450s purified from hepatic microsomes: comparison of those with rat hepatic cytochrome P-450s. *J Pharmacol Exp Ther* 1990; **255**: 1385-1391 [PMID: 2262908]

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