



Migraine in patients with fibromyalgia and outcomes of greater occipital nerve blockage

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ABSTRACT

Objectives: The aim of this study is to evaluate the efficacy of greater occipital nerve (GON) blockage in patients with migraine and fibromyalgia (FM) comorbidity.

Patients and method: 20 patients who were diagnosed as FM according to 2010 American College of Rheumatology (ACR) diagnostic criteria and migraine according to International Classification of Headache Disorders II criteria and did not receive any medication or GON block for both disorders were included for the study. GON blocks were repeated every week in the first month and repeated monthly for the following 2 months. The frequency and duration of the migraine attacks, pain severity with visual analogue scale (VAS), quality of life (QoL) with revised fibromyalgia impact questionnaire (FIQR) and migraine disability assessment questionnaire (MIDAS) before, 1st month and 3rd months after treatment were recorded and compared.

Results: 95% of 20 patients were female (n = 19) and 5% was male (n = 1). The affected site was left in 60% of the patients (n = 12) and 40% was right (n = 8). There was significant improvement in terms of all evaluation parameters both at 1st month and 3rd months after treatment compared to the baseline. Likely, all parameters were significantly improved at 3rd month compared to the 1st month.

Conclusions: GON blockage reduces pain severity, headache frequency and duration and increases QoL in patients with migraine and FM comorbidity.

1. Introduction

Fibromyalgia (FM) is a widespread pain syndrome characterized by pain, tenderness, fatigue, sleep and mood disorders and is more prevalent in women [1]. Although several mechanisms are hypothesized for pain mechanisms in FM, the most emphasized mechanism is central sensitization [2].

Migraine headache is a pain syndrome associated with poor quality of life (QoL) like FM and affects almost 18% of women [3]. This syndrome is reported to be in comorbidity with several mood, neurological, cardiovascular and other disorders such as musculoskeletal pain syndromes [4]. In a previous study, musculoskeletal pain has found more prevalent in patients with headache compared to those who have not [5]. In another study in patients with migraine headache indicated that headache frequency is a strong predictor for musculoskeletal pain and FM, chronic daily headache and episodic migraine may be parts of the same disorder [6].

Central sensitization is proposed to be the common mechanism which plays a key role both in FM and migraine pathogenesis [7]. In migraine, activation of trigeminovascular system causes a sterile neural inflammation which results in central and peripheral sensitization [8]. Like migraine, central sensitization which occurs due to the chronic modification of the antinociceptive system results in abnormal pain perception like allodynia and hyperalgesia [9].

Prevalence of FM and migraine comorbidity ranges from 18% to 35.6% in previous studies [10]. This comorbidity may complicate diagnosis and common pathophysiological pathways may lead to use one treatment for both diseases. Although different treatment options, requirement for alternative treatment methods increases because of resistant cases and potential medication side effects [11,12].

The association between trigeminal nucleus and greater occipital nerve (GON) which arises from C1 and C2 spinal roots is firstly discovered by Kerr et al [13]. Following studies indicated that blockage of GON results in pain relief in patients with migraine headache [14].

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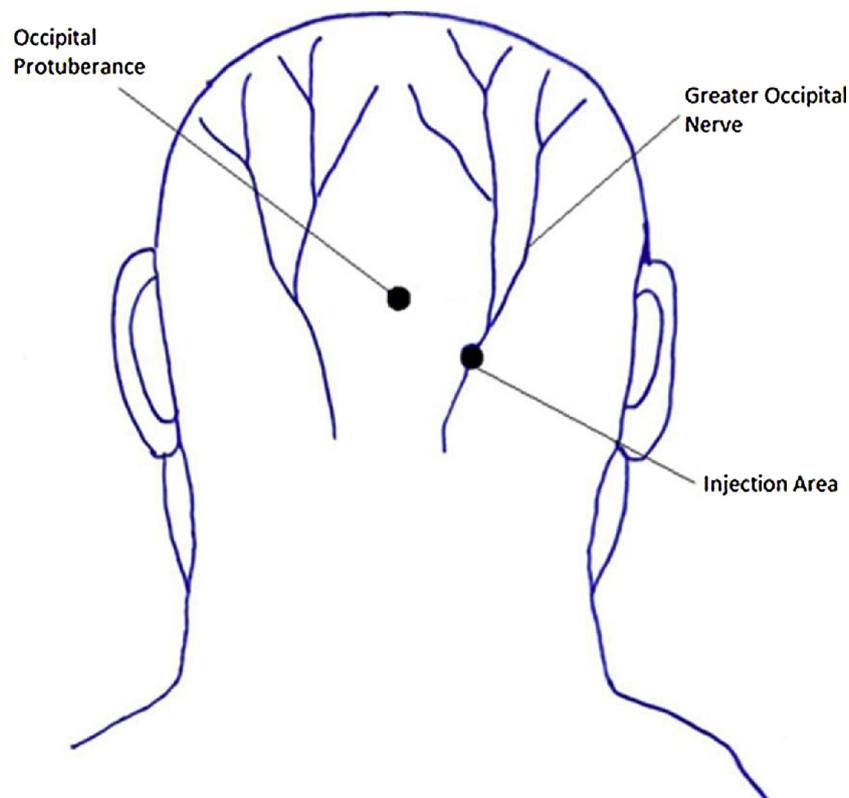


Fig. 1. GON blockage application landmarks.

However, this treatment modality has not been discussed in patients with FM and migraine comorbidity. The aim of this study is to evaluate the outcomes of GON blockage in patients with FM and migraine headache.

2. Material and method

2.1. Study settings

This study was conducted with 20 patients who were diagnosed as FM in our outpatient clinic between January 2016 and February 2017 according to 2010 American College of Rheumatology (ACR) diagnostic criteria [15] and who were also diagnosed as episodic migraine headache without aura according to International Classification of Headache Disorders II criteria by a neurologist [16]. At the beginning of the study, the patients and/or legal caregivers were informed in detail regarding the study and their verbal and written consents to participate were obtained. The study was also approved by the local ethical board and performed in accordance with the principles of the Declaration of Helsinki. The authors confirm that drug/intervention are registered in this trial. The funding source had no role in any stage of the study.

Patients between age 18–65, who had FM symptoms at least one year and did not receive any medication, who had diagnosed as migraine by a neurologist but did not receive any preventive medication previously, who had no sign of infection in injection site, who had no severe bleeding diathesis and no lidocaine hypersensitivity were included for the study. The exclusion criteria were as follows: patients under age 18 or over 65, who had infection in injection site, who had severe bleeding diathesis and hypersensitivity to lidocaine, who had taken a medication for FM in previous year and who had migraine due to medication overuse, previous occipital nerve block or occipital nerve stimulation, a history of occipital region surgery, a history of allergic reaction to the local anesthetic to be applied, pregnancy and breastfeeding, existing active psychiatric disease, uncontrolled hypertension, uncontrolled diabetes mellitus, decompensated congestive heart failure,

chronic renal failure, chronic liver disease, tumor and/or the presence of vascular disease, any existing inflammatory and/or infectious disease, and the use of anticoagulants. We did not allow the patients to receive any medication for FM and any rescue drug for pain which may interfere with the results of the study.

2.2. Demographic and disease characteristics

Demographic characteristics including age, gender, marital status and educational level were recorded. Patients were also wanted to note the number and the duration of headache attacks as hours during the previous month with a headache diary.

2.3. Evaluation parameters

2.3.1. Pain

The worst headache of the patients during a month was questioned and scored by visual analogue scale (VAS). VAS scores pain from 0 (no pain) to 10 (very severe pain).

2.3.2. Functional evaluation

Functional evaluation of the patients were performed by the revised Fibromyalgia Impact Questionnaire (FIQR) [17] and the Migraine Disability Assessment (MIDAS) test [18].

FIQR consists 21 items across 3 domains of function (9 items), overall impact (2 items) and symptoms (10 items). In the severity analysis a total FIQR score < 39 means mild effect, 39–59 points represents moderate effect and > 59 points refers to severe effect.

MIDAS questionnaire was developed to measure the effect of headaches to patient's daily functionality. This test takes into account the past 3 months and is composed of 5 questions. The total score is calculated by counting all number of the days in total. Total score of 0–5 points means little or no disability (grade 1), 6–10 points represents mild disability (grade 2), 11–20 points refers to moderate disability (grade 3) and > 20 points means severe disability (grade 4).

2.4. Injection procedure

GON blocks were repeated every week in the first month and repeated monthly for the following 2 months to only effected side. There are different applications of GON block procedure in the literature. We performed the procedure like Catav et al. in which they included 28 patients with migraine headache without FM [14]. The injections were performed radially at 2 cm lateral and 2 cm inferior to protuberantia occipitalis externa (Fig. 1). Each patient is placed in sitting position and the injection site was cleaned with 10% polyvinylpyrrolidone (PVP) iodine solution and covered with a disposable patch prior to injection. No pre-medication or sedative drug was administered before the procedure. Following, a 26 G 0.45 × 13 G needle was inserted in the injection site and a gentle aspiration was performed. Then a total of 2 mL of 0.25% bupivacaine was delivered to both injection sites. The injection site was cleaned with same PVP iodine solution after injection.

2.5. Comparisons

The frequency and duration of the migraine attacks, VAS, FIQR and MIDAS scores of the patients before, 1st month and 3rd months after treatment were recorded and compared.

2.6. Statistical analysis

Statistical Package for the Social Sciences (SPSS 22.0 for Windows) software package programme was used for data analysis. The continuous variables were evaluated with Shapiro Wilk test as to whether or not they were different from normal distribution. In descriptive statistics, data were expressed as median, mean ± standart deviation (SD) for continuous variables, and as frequencies and percentages (%) for nominal variables. Possible statistical significant differences between repetitive measurements were evaluated with Wilcoxon Sign test. Bonferroni correction was used to avoid possible type 1 errors and $p > 0.017$ values were expected as statistically significant.

3. Results

95% of 20 patients were female ($n = 19$) and 5% was male ($n = 1$). The affected site was left in 60% of the patients ($n = 12$) and 40% was right ($n = 8$). Demographic and disease characteristics are given in Table 1.

Median FIQR score of the patients before GON block was 52.00 which indicates a moderate impact of FM on QoL and median MIDAS score was 24.00 which is associated with severe disability.

The distribution and comparison of the evaluation parameters at 1st

Table 1
Demographic and disease characteristics of the patients before treatment.

	n = 20 mean ± SD, n%
Age (year)	48.45 ± 9.89
Gender	
Male	1 (5)
Female	19 (95)
Marital status	
Married	20 (100)
Single	0
Divorced	0
Education duration (year)	8.50 ± 3.88
Headache duration (month)	6.12 ± 1.74
VAS (0-10 cm)	6.85 ± 1.03
FIQR	53.65 ± 8.08
MIDAS	23.35 ± 5.55
Headache frequency (times/month)	9.65 ± 3.06
Headache duration (hours)	21.90 ± 8.45

VAS: visual analogue scale, FIQR: fibromyalgia impact scale revised, MIDAS: migraine disability assessment questionnaire.

Table 2

The distribution and comparison of the evaluation parameters at 1st month 3rd months after treatment.

	Before Treatment mean ± SD	1st month mean ± SD	3th month mean ± SD
VAS (0–10 cm)	6.85 ± 1.03	3.50 ± 1.05	1.90 ± 0.85
FIQR	53.65 ± 8.08	43.80 ± 7.33	35.90 ± 7.48
MIDAS	23.35 ± 5.55	13.25 ± 4.66	5.45 ± 3.47
Headache frequency (times/month)	9.65 ± 3.06	5.10 ± 1.99	2.10 ± 1.16
Headache duration (hours)	21.90 ± 8.45	11.65 ± 6.93	6.20 ± 4.56

SD: standard deviation, VAS: visual analogue scale, FIQR: Fibromyalgia Impact Questionnaire Revised, MIDAS: Migraine Disability Assessment Questionnaire.

month and 3rd months after treatment are given in Tables 2 and 3.

There was significant improvement in terms of all evaluation parameters both at 1st month and 3rd months after treatment compared to the baseline. Likely, all parameters were significantly improved at 3rd month compared to the 1st month.

4. Discussion

FM prevalence is age and sex related and varies between countries [19]. The prevalence of FM in our country is reported to be 3.6% in general population, however the prevalence among episodic migraine patients is 31.4% [20,21]. The impact of these disorders on functionality and life quality increases when they are presented together. In our study the patient group has represented a moderate impact of FM to life quality but severe disability because of migraine headache before treatment. We found significant decrease in FIQR and MIDAS scores at 1st month evaluation compared to baseline and this recovery has continued significantly at 3rd month. These findings suggest a common pathway for both disorders.

Central sensitization secondary to the imbalance of neuromediators which play a role in pain transmission and antinociception in central nervous system (CNS) is crucial for FM [22]. Clinical evidence of this sensitization appears as generalized decrease of pain thresholds against different types of stimuli in somatic level [23]. However increased pain sensitivity as a result of central sensitization is also responsible mechanism for migraine headache. Clinical observations also report that migraine headache is associated with exacerbation of typical FM symptoms as well as musculoskeletal pain plays a triggering role for headache [24]. This finding is also the initial point of our hypothesis that GON blockade may be effective on both migraine and fibromyalgia symptomatology.

Efficacy of GON blockade has been demonstrated in several studies previously [25]. Pain relief with GON blockage may include the changes in brain nociceptive pathways and diffuse noxious inhibitory control mechanisms. The sensory nerve fibers of upper cervical spinal cord is in association with trigeminal nucleus caudatus (TNC) complex. Therefore, sensory input from both trigeminal and cervical spinal nerves are transmitted to this complex. GON blockade causes a “winding down” in central pain mechanisms which results in the interruption of the input to dorsal horn of spinal cord and TNC neurons. At least clinical result would be the relief of migraine headache pain as well as the relief of generalized pain due to chronic pain syndromes such as FM [26,27]. In our study, we found significant improvement in VAS, FIQR and MIDAS scores of patients in accordance with this data. The frequency and the duration of the migraine attacks were significantly decreased in our patient group both in 1st month and 3rd months evaluation compared to baseline.

The impact of migraine and FM comorbidity on QoL had been studied several times previously and most of these studies had indicated poor QoL and increased symptom severity regarding to common pain

Table 3

The comparison of the variations of evaluation parameters at baseline, 1st month and 3rd months after treatment.

	Before-1st month mean \pm SD	p	Before-3th month mean \pm SD	p	1stmonth-3th month mean \pm SD	p
VAS (0–10 cm)	–3.35 \pm 0.67	0.001	4.95 \pm 0.88	0.001	1.60 \pm 0.88	0.001
FIQR	–9.85 \pm 3.16	0.001	–17.75 \pm 5.32	0.001	–7.80 \pm 3.33	0.001
MIDAS	–10.10 \pm 3.43	0.001	–17.90 \pm 5.21	0.001	–7.80 \pm 3.75	0.001
Headache Frequency (times/hours)	–4.55 \pm 2.03	0.001	–7.55 \pm 2.91	0.001	–3.03 \pm 1.83	0.001
Headache Duration (hour)	–10.25 \pm 4.12	0.001	–15.70 \pm 5.25	0.001	–5.45 \pm 3.99	0.001

SD: standard deviation, VAS: visual analogue scale, FIQR: Fibromyalgia Impact Questionnaire Revised, MIDAS: Migraine Disability Assessment Questionnaire.

pathways [28]. However none of these studied the efficacy of GON blockage particularly in FM previously. To our best knowledge this is the first study which evaluates the efficacy of GON blockage in patients with migraine comorbid FM. The major limitation of the present study is the limited number of patients. One of the reasons for the limited number of patients is that the difficulty to find individuals who did not receive any medication both for migraine and FM previously. Further studies in large patient groups may indicate different results. Nonetheless, our results of GON blockage in this patient group is significant and this treatment modality has beneficial effects on symptom severity and QoL in patients with migraine comorbid FM. The injection technique we have performed for this study is similar to Catav et al [14]. In their study with 28 patients with pure migraine headache they have performed 4 injections weekly during a month. Differently we have applied 2 more injections monthly to demonstrate the decrease of FIQR scores and relief of FM symptoms. We did not include any control group in the study. This may give an impression of a bias but we aimed to evaluate the efficacy of GON blockage on treatment prognosis of FM in patients with migraine comorbid FM. Any control group with FM but not with migraine would not require GON block treatment, so this situation can be ignored. On the other hand, FM has psychological determinants and placebo effect of the GON block could not be excluded with a pure FM control group. In our study, we evaluated the patients with FIQR which also includes psychological determinants to exclude the placebo effect.

5. Conclusion

There are different levels of central sensitization in patients with migraine, FM or both conditions and these common pathophysiological pathway results in a bidirectional relationship between these disorders. GON blockade reduces pain severity, headache frequency and duration and increases QoL in patients with migraine and FM comorbidity.

Compliance with ethical standards

There is no financial disclosure for the study. All procedures performed in the study are in accordance with the ethical standards of the institutional and/ national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Conflict of interests

There is no funding resources.
There is no conflict of interest.

References

- G. Ifergane, D. Buskila, N. Simishvly, K. Zeev, H. Cohen, Prevalence of fibromyalgia syndrome in migraine patients, *Cephalalgia* 26 (2006) 451–456.
- M. De Tommaso, Prevalence, clinical features and potential therapies for fibromyalgia in primary headaches, *Expert Rev. Neurother.* 12 (2012) 287–295.
- Stovner Lj, K. Hagen, R. Jensen, Z. Katsarava, R. Lipton, A. Scher, T. Steiner, J.A. Zwart, The global burden of headache: a documentation of headache prevalence and disability worldwide, *Cephalalgia* 27 (2007) 193–210.
- A.I. Scher, M.E. Bigal, R.B. Lipton, Comorbidity of migraine, *Curr. Opin. Neurol.* 18 (2005) 305–310.
- K. Hagen, C. Einarsen, J.A. Zwart, S. Svebak, G. Bovim, The co-occurrence of headache and musculoskeletal symptoms amongst 51050 adults in Norway, *Eur. J. Neurol.* 9 (2002) 527–533.
- V. Centonze, A. Bassi, M.A. Cassiano, I. Munno, L. Dalfino, V. Causarano, Migraine, daily chronic headache and fibromyalgia in the same patient: an evolutive “continuum” of non organic chronic pain? About 100 clinical cases, *Neurol. Sci.* 25 (2004) 291–292.
- A. Vgontzas, R. Burch, Episodic migraine with and without aura: key differences and implications for pathophysiology, management, and assessing risks, *Curr. Pain Headache Rep.* 22 (October (12)) (2018) 78.
- M. De Tommaso, V. Sciruicchio, Migraine and central sensitization: clinical features, main comorbidities and therapeutic perspectives, *Curr. Rheumatol. Rev.* 12 (2) (2016) 113–126.
- M.A. Giamberardino, G. Affaitati, P. Martelletti, C. Tana, A. Negro, D. Lapenna, M. Curto, C. Schiavone, L. Stellin, F. Cipollone, R. Costantini, Impact of migraine on fibromyalgia symptoms, *J. Headache Pain* 17–28 (2015).
- M. De Tommaso, A. Federici, C. Serpino, E. Vecchio, G. Franco, M. Sardaro, P. Livrea, Clinical features of headache patients with fibromyalgia comorbidity, *J. Headache Pain* 12 (2011) 629–638.
- F.M. Cutrer, A. Charles, The neurogenic basis of migraine, *Headache* 48 (9) (2008) 1411–1414.
- N.E. Kelley, D.E. Tepper, Rescue therapy for acute migraine, part 3: opioids, NSAIDs, steroids, and post-discharge medications, *Headache* 52 (3) (2012) 467–482.
- F.W. Kerr, R.A. Olafson, Trigeminal and cervical volleys. Convergence on single units in the spinal gray at C-1 and C-2, *Arch. Neurol.* 5 (1961) 171–178.
- S. Catav, F.A. Solmaz, P. Kirdemir, The results of greater occipital nerve block applied for migraine headache, *Agri* 29 (1) (2017) 33–37.
- F. Wolfe, D.J. Clauw, M.A. Fitzcharles, D.L. Goldenberg, R.S. Katz, P. Mease, A.S. Russell, L.J. Russell, J.B. Winfield, M.B. Yunus, The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity, *Arthritis Care Res (Holboken)* 62 (May 5) (2010) 600–610.
- Headache Classification Committee of the International Headache Society, The international classification of headache disorders. 2nd edition, *Cephalalgia* 24 (2004) 1–160.
- L. Ediz, O. Hiz, M. Toprak, I. Tekeoglu, S. Ercan, The validity and reliability of the Turkish version of the revised fibromyalgia impact questionnaire, *Clin. Rheumatol.* 30 (March 3) (2011) 339–346.
- U. Gedikoglu, O. Coskun, L.E. Inan, S. Ucler, T. Tunc, U. Emre, Validity and reliability of Turkish translation of migraine disability assessment (MIDAS) questionnaire in patients with migraine, *Cephalalgia* 25 (June 6) (2005) 452–456.
- J.C. Branco, B. Bannwarth, I. Faillde, J. Abello Carbonell, F. Blotman, M. Spaeth, F. Saraiva, F. Nacci, E. Thomas, J.P. Caubere, K. Le Lay, C. Taieb, M. Matucci-Cerinic, Prevalence of fibromyalgia: a survey in five European countries, *Semin. Arthritis Rheum.* 39 (2010) 448–453.
- M. Topbas, H. Cakirbay, H. Gulec, E. Akgol, I. Ak, G. Can, The prevalence of fibromyalgia in women aged 20–64 in Turkey, *Scand. J. Rheumatol.* 34 (140) (2005) 144.
- S. Kucukşen, E. Genc, H. Yilmaz, A. Salli, İ.A. Gezer, A.Y. Karahan, E. Salbaş, H.T. Cingoz, O. Nas, H. Uğurlu, The prevalence of fibromyalgia and its relation with headache characteristics in episodic migraine, *Clin. Rheumatol.* 32 (2013) 983–990.
- J.N. Ablin, D. Buskila, Update on the genetics of the fibromyalgia syndrome, *Best Pract. Res. Clin. Rheumatol.* 29 (2015) 20–28.
- L. Vecchiet, M.A. Giamberardino, P. de Bigontina, Dragani I comparative sensory evaluation of parietal tissues in painful and nonpainful areas in fibromyalgia and myofascial pain syndrome, in: G.F. Gebhart, D.L. Hansmond, T.S. Jensen (Eds.), *Proceedings of the 7th World Congress on Pain, Progress in Pain Research and Management* 2 (1994).
- G. Affaitati, R. Costantini, A. Fabrizio, D. Lapenna, E. Tafuri, Giamberardino MA Effects of treatment of peripheral pain generators in fibromyalgia patients, *Eur. J. Pain* 15 (2011) 61–69.
- S. Weibelt, D. Andress-Rothrock, W. King, J. Rothrock, Suboccipital nerve blocks for suppression of chronic migraine: safety, efficacy, and predictors of outcome, *Headache* 50 (2010) 1041–1044.
- A. Ashkenazi, M. Levin, Greater occipital nerve block for migraine and other headaches: is it useful? *Curr. Pain Headache Rep.* 11 (2007) 231–235.
- M.H. Seleklir, Greater occipital nerve blockade: trigeminocervical system and clinical applications in primary headaches, *Agri* 20 (2008) 6–13.
- M. Whealy, N. Sanjeev, A. Vincent, J. Mandrekar, F.M. Cutrer, Fibromyalgia in migraine: a retrospective cohort study, *J. Headache Pain* 19 (61) (2018).