

Greater occipital nerve block efficacy in COVID-19 associated headache: a preliminary study

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COVID-19 is an infection caused by the new coronavirus SARS-CoV-2. Headache is one of the most common neurological findings. In the treatment of various chronic headaches, the greater occipital nerve (GON) block is often used as a safe and effective method. The aim of our study was to investigate the effectiveness of the GON block in the treatment of headaches observed in COVID-19 patients. Between March and May 2020, 27 patients (with laboratory-confirmed 2019-nCoV infection by next-generation sequencing confirmation of real-time PCR) that had moderate or severe headache associated with COVID-19 and treated with a single session of GON block were retrospectively analyzed. The visual analogue scale (VAS) values and the number of analgesic usage of patients were recorded before and after the blockade on the 1st and 10th days. Fifteen (55.6%) patients included in the study were male and twelve (44.4%) were female. In terms of VAS values, the difference between pre-treatment and post-treatment values on the 1st and 10th days was found statistically significant. Likewise, the difference between analgesic use before and after the procedure was statistically significant. GON block appears to be an effective pain management method in COVID-19 related headache, and it revealed promising reductions in pain scores and analgesic usage. As well as we know, this is the first study of "COVID-19 associated headache treated with GON blockade". More long term and well-designed prospective studies with more participants are needed to better define this headache and develop effective treatment strategies.

Key words: COVID-19 associated headache, COVID-19, headache, greater occipital nerve, occipital nerve blockade

INTRODUCTION

New coronary virus disease (COVID-19) is a virus identified on January 13, 2020, as a result of research conducted in a group of patients who developed respiratory tract symptoms (fever, cough, shortness of breath) in late December in China. The outbreak was recognized as a global epidemic on March 11, 2020 (Türkan Acar et al., 2020; Mao et al., 2020a).

The new coronavirus disease is caused by the SAR-CoV-2 virus (Türkan Acar et al., 2020; Mao et al.,

2020b; Bolay et al., 2020; Belvis, 2020). There is no long latency period. The incubation period is generally 3–14 days (median 5.1 days), but it has been reported to extend up to 24 days (Guan et al., 2019; Rabaan et al., 2020; Lauer et al., 2020). In asymptomatic or affected cases, it can also be transmitted during the incubation period (Rothe et al., 2020). For the diagnosis; real-time polymerase chain reaction (RT-PCR) is used to evaluate nasal swab, tracheal aspirate or bronchoalveolar lavage samples. Even after remission, positive pharyngeal swab results have been reported, but the virus may not be detected after the 8th day of the disease.

Various neurological symptoms have been reported in more than one-third of patients, including central nervous system (CNS) involvement, peripheral nervous system (PNS) involvement, and skeletal muscle damage (Mao et al., 2020). As symptoms and diseases indicating CNS involvement; dizziness, vertigo, sleep disturbance, headache, loss of consciousness, ataxia, seizure, acute cerebrovascular disease, meningitis and encephalitis have been reported (Mao et al., 2020; Baig, 2020; Poyiadji et al., 2020). Symptoms indicating PNS involvement have been reported as taste and smell disorders, visual impairment and neuralgia (Giacomelli et al., 2020). The most common complaints in patients with PNS symptoms are taste and smell disorders (Mao et al., 2020). Cases of COVID-19 presented with Guillain-Barre syndrome reported from clinics in various countries are also observed in the literature (Alberti et al., 2020; Zhao et al., 2020). Gutierrez-Ortiz et al. (2020) reported two cases of COVID-19 diagnosed as Miller Fisher syndrome and multiple cranial neuropathy. Zhao et al. (2020) described a 66-year-old male with a diagnosis of COVID-19, postinfectious myelitis. Wei et al. (2020) reported a 62-year-old patient with COVID-19 who had oculomotor nerve palsy. Symptoms indicating skeletal muscle damage have been reported as muscle fatigue and pain in the extremities.

Data for headaches associated with COVID-19 are increasing with new studies. Headache is the 5th most frequent COVID-19 symptom after fever, cough, myalgia/fatigue, and dyspnea (Borges do Nascimento et al., 2020). Strategies and practices for treatment are very limited in the studies conducted. There is very little information about headaches. However, according to the data obtained, the rate of COVID-19 related headache was found different among societies. These rates vary between 6–34%. Headaches are often throbbing and tightening. Headache is moderate and severe, and it has been reported to be mostly in the frontal, periorbital and temporoparietal areas. In addition, it was found to be poor in response to analgesics (Bolay et al., 2020). It differs from other headaches due to the presence of some infectious findings, especially fever accompanying the COVID-19-headache, which occurs in temporal relation to COVID-19 infection, and the virus being proven by PCR test.

GON blockade is a treatment that has been used for many years in various types of headaches (Inan et al.,

2015; Karadaş et al., 2017; Cuadrado et al., 2017; Gul et al., 2017). There are studies showing that the frequency and severity of pain is reduced with recurrent GON blocks especially in migraine patients. In recent years, it has also been used in the treatment of different types of headaches. When the conducted studies are examined, the results obtained were found different. Recent and well-designed studies have shown that GON blockade is effective (Inan et al., 2015; Karadaş et al., 2017; Cuadrado et al., 2017; Gul et al., 2017).

Some nonsteroidal anti-inflammatory drugs like ibuprofen used in the acute treatment of COVID-19 associated headaches are thought to pose an increased risk for COVID-19 infection, and may cause serious side effects with drug interactions. In this study, it was aimed to investigate the effectiveness of single session of GON blockade with lidocaine injection in the treatment of COVID-19 associated headache.

METHODS

In this retrospective study, 33 patients who were diagnosed with COVID-19 (laboratory-confirmed 2019-nCoV infection by next-generation sequencing confirmation of real-time PCR) and who had headache during this disease were evaluated between March and May 2020. To avoid the increased risk for COVID-19 infection by using ibuprofen, and side effects due to other prophylactic drug interactions, we generally had preferred to use GON blockade in our patients with headache during the pandemic. Twenty-seven patients who had used at least two analgesics in the last 24 h prior to the procedure and who had one-session of GON blockade for treatment were included in the study and analyzed retrospectively. The localization and characteristics of headache were summarized in Table 1. Patient demographics including age, gender, number of analgesic usage, the visual analogue scale (VAS) values were collected. VAS is sensitive to pharmacological and nonpharmacological procedures that alter the experience of pain and correlate highly with pain measured on verbal and numerical rating scales and is usually presented as a 100 mm horizontal line on which the patient's pain intensity is represented by a point between the extremes of "no pain at all" and "worst pain imaginable."

Table 1. Headache localization of our patients. The pain characteristic of all patients was throbbing and squeezing, and all were bilateral.

Headache localization	Frontal	Occipital	Frontotemporal	Frontoorbital
Number of patients	17 (62.9%)	4 (14.8%)	3 (11.1%)	3 (11.1%)

GON blockade was administered 2 cm lateral and 2 cm inferior to the external occipital protuberance in all patients bilaterally. Each patient sat in a chair and flexed their head on their arms, which were placed on the examination table, during injection to prevent syncope trauma. The site of injection was cleaned and disinfected using a local antiseptic solution. Solutions of 2 mL of 1% lidocaine were administered into the disinfected area subcutaneously using a 26-G 0.45 × 13 mm needle. Local pressure was applied for 2-3 min to spread the solution and prevent bleeding.

We had used the VAS to record the pain severity and the number of analgesic usage in the last 24 h were also recorded to evaluate the response to GON blockade before and after the blockade on the 1st and 10th days.

Approval from the ethics committee of Health Sciences University with the number of 2020-162 and from the Turkish Ministry of Health with the number of 2020-05-04T11_50_57 were taken.

Statistical analysis

SPSS 22.0 package program was used for statistical analysis. In the analysis of descriptive statistical data, mean ± standard deviation for continuous variables, number and % were used for discrete data. For the continuous analysis of the data, it was first analyzed whether the data fit the normal distribution or not. In-

dependent samples test was used for binary group comparison of data suitable for normal distribution. In the dependent groups, the Friedman test was performed in comparison of the triple groups and the Wilcoxon signed rank test was used for the binary groups. The relationship between the variables considered was investigated by Pearson correlation test. For the differences between the groups, the reliability interval was 95% and $p < 0.05$ was considered significant.

RESULTS

In our study, 27 patients who were found to have a positive COVID-19 test and who had GON blockade for the treatment of headache were included. Fifteen (55.6%) of the patients were male and twelve (44.4%) were female. The mean age was 48.07 ± 19.43 (min-max: 20-84) years. The mean number of analgesic use of the patients before the treatment was 3.33 ± 0.92 (2-5) and the pain intensity was 79.81 ± 7.14 according to VAS. No statistically significant difference was found between the number of analgesics used and the VAS scores (Table 2).

VAS scores and the number of analgesics used by the patients before and after the treatment are presented in Table 3.

In 15 (55.6%) patients, there was no need for analgesic use on the first day after GON blockade. On the

Table 2. Age, gender, number of analgesic usage, VAS values.

Comparison		Gender			p*
		Male (n=15)	Female (n=12)	Total (n=27)	
Age	Mean	47.93	48.25	48.07	0.967
	Median	40.00	43.00	40.00	
	Std. D.	20.31	19.18	19.43	
	Min-Max	20-79	25-84	20-84	
Number of analgesic usage	Mean	3.20	3.50	3.33	0.410
	Median	3	4	3	
	Std. D.	0.86	1.00	0.92	
	Min-Max	2-5	2-5	2-5	
VAS	Mean	79.67	80.00	79.81	0.907
	Median	75.00	80.00	7.14	
	Std. D.	8.12	6.03	80	
	Min-Max	70-100	70-90	70-100	

p* Independent samples test, min-max: minimum-maximum

Table 3. Number of analgesic usage and VAS values before and after GON blockade.

Variables	Number of analgesic usage			VAS pain intensity		
		n	%		n	%
Before treatment	2	6	22.2	70	3	11.1
	3	8	29.6	75	9	33.3
	4	11	40.7	80	7	25.9
	5	2	7.4	85	4	14.8
				90	3	11.1
				100	1	3.7
1. day after treatment	0	15	55.6	0	8	29.6
	1	4	14.8	20	3	11.1
	2	5	18.5	25	1	3.7
	3	2	7.4	30	3	11.1
	4	1	3.7	35	2	7.4
				40	1	3.7
				45	1	3.7
				50	3	11.1
				55	1	3.7
				70	1	3.7
				75	1	3.7
				80	1	3.7
10. day after treatment	0	21	77.8	0	12	44.4
	1	3	11.1	10	1	3.7
	2	1	3.7	15	1	3.7
	3	2	7.4	20	4	14.8
				25	1	3.7
				30	4	14.8
				55	1	3.7
				70	1	3.7
				75	1	3.7
				85	1	3.7

10th day, this number increased to 21 people (77.8%). In terms of VAS scores, there was no pain in 8 patients (29.6%) on the first day after treatment, and the number of painless patients on the 10th day increased to 12 people (44.4%). While the median number of analge-

sics used before the treatment was 3, the patients did not use analgesics between the 1st and 10th days after the treatment. While VAS median value was 80 before treatment, it decreased to 30 on day 1 and 15 on day 10 after GON blockade. A statistically significant decrease

Table 4. Comparison of the number of analgesic usage and VAS values before and after GON blockade.

Comparison of the number of analgesic usage and VAS values		Mean-SD	Median	Min-Max	p*
Number of analgesics used (NA)	Pretreatment	3.33-0.92	3	2-5	<0.001
	1.day after treatment	0.89-1.19	0	0-4	
	10.day after treatment	0.41-0.89	0	0-3	
VAS	Pretreatment	79.81-7.14	80	70-100	<0.001
	1.day after treatment	31.30-26.91	30	0-85	
	10.day after treatment	19.81-25.06	15	0-85	
Pairwise Comparisons					p**
NA 1.day after treatment – NA before treatment					<0.001
NA 10.day after treatment – NA before treatment					<0.001
NA 10.day after treatment – NA 1.day after treatment					0.004

SD; standart deviation, min-max; minimum-maximum; *Friedman test, **Wilcoxon signed rank test

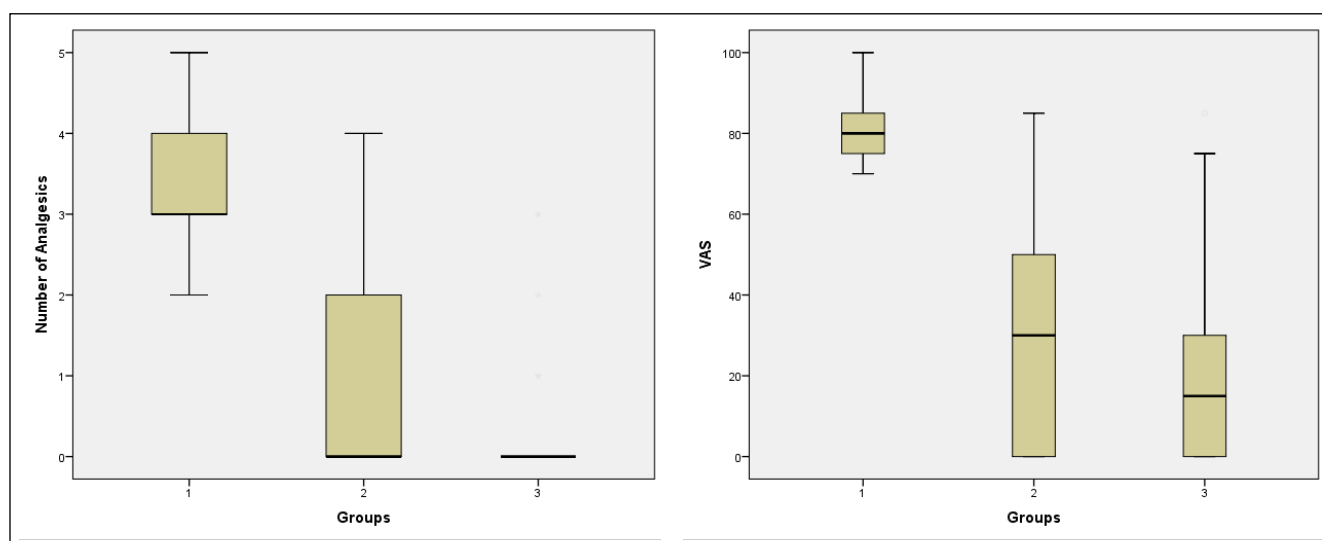


Fig. 1. Comparison of the number of analgesics used before and after treatment and comparison of VAS pain intensities before and after treatment.

was found in both the average number of analgesic use and in the VAS scores on the 1st and 10th days after GON blockage ($p<0.001$) (Table 4, Fig. 1).

The rate of reduction in analgesic use was 75.17% on the first day, and 88.46% on the 10th day after the procedure. The amount of analgesic use decreased by more than 50%, in 70.4% ($n=19$) of the patients on the first day, and 88.9% ($n=24$) on the 10th day after treatment. While the rate of decrease in VAS pain intensity on the first day after treatment was 62.13%, it was 75.96% on the 10th day. The number of patients with more than 50% decrease in VAS scores was 18 (66,7%), people on the first day and 23 (85,2%) people on the 10th day (Table 5).

A positive strong correlation was found between the number of analgesics used and the VAS scores of the patients (Table 6).

DISCUSSION

Findings from the study suggest that GON block is an effective treatment for patients with moderate or severe headaches associated with COVID-19. In the vast majority of our patients, it was reported that there was a decrease in headache severity and analgesic use after GON block, and the well-being continued in the controls performed 1 and 10 days after the block.

Table 5. Analgesic use rates of patients at the first day and tenth day after GON blockade and reduction rates of VAS pain severity.

		n	%
Reduction rates in the number of analgesics used on the first day after treatment	Group 1	2	7.4
	Group 2	6	22.2
	Group 3	19	70.4
Reduction rates in the number of analgesics used on the tenth day after treatment	Group 1	2	7.4
	Group 2	1	3.7
	Group 3	24	88.9
Reduction rates in VAS pain intensity on the first day after treatment	Group 1	4	14.8
	Group 2	5	18.5
	Group 3	18	66.7
Reduction rates in VAS pain intensity on the tenth day after treatment	Group 1	3	11.1
	Group 2	1	3.7
	Group 3	23	85.2

Group-1: more than 30% decrease; Group-2: decrease between 30%-50%; Group-3: more than 50% decrease

Nonsteroidal anti-inflammatory drugs (NSAIDs) are used in many centers as the first treatment option for headaches. However, there are some conflicting reports about NSAIDs in treatment of COVID-19 patients. NSAIDs, especially ibuprofen, have been reported to increase the expression of angiotensin-converting enzyme-2 (ACE-2), thereby causing the disease to progress more severely (Fang, 2020). As a result, clinicians avoid using NSAIDs due to both poor response and possible negative effects. Therefore, we preferred to apply GON block instead of NSAID usage in our patients with COVID-19 associated headache. Greater occipital nerve blockade applications are common methods. In recent studies, the importance of the greater occipital nerve has been emphasized in many painful conditions such as migraine, primary headaches and medication overuse headache and treatment strategies have been developed for this region.

In the literature, there are many mechanisms proposed for the causes of COVID-19 associated neurological findings and headaches.

Local anesthetics prevent neural depolarization via voltage-gated sodium channels; thereby preventing the transmission of pain by nociceptive C fibers (McEntire et al., 2016). Due to the anatomical and functional proximity of the trigeminal and cervical afferent pathways, modulation of this pathway with occipital nerve blockade provides potential benefit in primary headache disorders (Busch et al., 2006).

Table 6. The correlation between the number of analgesics used before and after treatment and VAS pain intensities.

Correlation	r	p
NA pretreatment – VAS 1. day after treatment	0.801	<0.001
NA 1. day after treatment – VAS 1. day after treatment	0.895	<0.001
NA 1. day after treatment – VAS 10. day after treatment	0.893	<0.001

Peripheral nerve blocks, such as GON block, typically provide a pain-relieving effect that lasts longer than their anesthetic effects. This prolonged analgesia after GON may be due to effects on central pain modulation (Ashkenazi et al., 2010). For these reasons, in our study, we aimed to treat our patients with COVID-19 associated headache by applying GON block.

As a result, COVID-19 associated headache is moderate and severe. In the treatment of this headache, GON blockade application using local lidocaine was determined as an effective treatment method. It was seen that GON blockade application with local one-session lidocaine was sufficient in the treatment. Significant reduction in analgesic use was detected with single-session GON blockade at the end of the study. In addition, no serious side effects were observed during the injection applications, which would lead to termination of the study. This shows the reliability and tolerability of GON blockages with lidocaine in the treatment of COVID-19 related headache.

Studies on the effectiveness of local anesthetic injections for the treatment of different types of headaches have different results. These differences may be caused by factors such as the presence of mixed headache, local anesthetic type, local anesthetic dose, study design, method of application and number of applications. In order to fully demonstrate the effectiveness of GON blockages in the treatment of COVID-19 associated headache, randomized, double-blind, placebo-controlled and long-term studies involving combinations of local anesthetics and steroids as well as repetitive injections are needed.

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