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IMPROVING THE QUALITY OF LIFE OF PATIENTS WITH HEADACHE TREATED WITH NEURAL THERAPY

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KEY WORDS

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ABSTRACT

Primary headaches (PHs) are common health complaints with a high impact on health-related quality of life (HRQOL). Treatment is multifactorial, including pharmacological and non-pharmacological strategies. Neural therapy (NT) is a regulatory treatment system that uses local anesthetic injections in chosen points to treat pain. This study aims to evaluate the effect of NT on the HRQOL of patients with PHs. Quasi-experimental prospective study involving 93 patients treated. The impact on HRQOL was evaluated through the SF-36 health, before and after treatment. Seven out of the eight items measured on the SF-36 scale improved after the intervention (p<0.001).

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1. Introduction

Headache is defined as craniofacial pain caused by any structure of the head, neck, or cranial cavity. Primary headache (PH) is defined as a craniofacial pain with no apparent underlying cause with recurrent or persistent head pain, in contrast with secondary headaches that exist in relation to discrete inciting factors. The International Headache Society (IHS), third edition of January 2018 (Headache Classification Committee of the International Headache Society (IHS), 2018), includes as PH disorders: migraine, tension-type headache, trigeminal autonomic cephalalgias, and other primary headache disorders (such as PHs associated with cough, exercise, sexual activity, primary thunderclap headache, cold-stimulus headache or nummular headache, among others).

Among all PHs, migraine and tension-type headaches are the most frequent. Migraine is a debilitating chronic neurologic disorder characterized by recurrent headaches that are moderate to severe and last from 4 hours to 3 days, typically with an episodic presentation that affect one side of the head, pulsating in nature. Associated symptoms may include nausea, vomiting, and sensitivity to light, sound, or smell. The pain usually worsens with physical activity. It can also present itself in a chronic and a refractory form, both of which use recalcitrant to conventional treatments and cause significant disability.

Regarding migraines, it is considered the seventh cause of global disability, causing 3 out of every 100 days of sick leave (Vos, et al., 2012). In the European community, there are data that estimate expenses of 286 million euros related to this condition, which increase to 1,986 million euros when they are associated with painkiller abuse (Olesen, Gustavsson, Svensson, Wittchen, & Jönsson, 2012). In Colombia, the studies of Morillo and Pradilla found a prevalence of people with migraine between 3.2 and 9.8%, which is predominant in women, with a 3 to 1 ratio (Morillo, et al., 2005; Pradilla, Léon, FE, Vesga, & Grupo, 2003).

Patients with a tension-type headaches suffer from episodes of pain that are typically bilateral, pressing or tightening in quality, of mild to moderate intensity, lasting at least 30 minutes and which do not worsen with routine physical activity (IHS, 2018). There is no nausea, but photophobia or phonophobia (fear of bright light or loud sounds) may be present (Chowdhury, 2012).

The etiopathogenic mechanisms of each type of primary headache are different, complex, and extensive. PH diagnosis is based on clinical history and physical examination. A headache diagnosis is based on the diagnostic criteria of the classification proposed by the IHS, third edition of January 2018 (Headache Classification Committee of the International Headache Society (IHS), 2018).

Thus, for a good clinical practice in which therapeutic and therefore prognostic guidelines can be established, the IHS established the classification into 3 divisions: Primary, secondary, and cranial neuropathies, facial pain and other headaches (Headache Classification Committee of the International Headache Society (IHS), 2018).

Therefore, an excellent clinical and life history should be taken, describing anamnesis detailing the age of onset, time of evolution (recurrent or recently progressive), mode of onset (sudden or gradual), frequency, duration, intensity, schedule (morning, evening, specific time, evolving), location, pain characteristics (throbbing, oppressive, stabbing, cramping), aggravating and/or relieving factors, associated symptoms and signs such as fever, nausea, emesis, photophobia, conjunctival injection, tearing, miosis, palpebral ptosis, phosphenes, campimeter blind spots, nasal obstruction and congestion, language alterations, sensation of vertigo, loss of consciousness, weakness, sensory alterations, and to emphasize severity criteria or red flags. It is important to consider the review per system, and the history. The physical examination should be integral with an active search for signs such as: papilledema, optic atrophy, retinal hemorrhage, lesion of the III pair with pupillary alteration, epiphora, rhinorrhea, Horner's syndrome, facial, cranial, cervical sore spots, pain in the temporomandibular joint, or hardening of the temporal artery on palpation, involvement of external and middle ear, limitation in spinal mobility, alteration of the

mental sphere, cranial pairs, motor, sensory, coordination, walking involvement and/or meningeal signs, d because the finding of a focal neurological deficit is one of the best predictors of lesions in the central nervous system and therefore, will require supplemental studies (Clinch, 2001; Edlow, Panagos, Godwin, Thomas, & Decker, 2008; Locker, Thompson, Rylance, & Mason, 2006; Strain, et al., 2000; Baraff, et al., 2010).

Additional tests may include a blood test, ocular fundus, lumbar puncture (LP), computed tomography (CT), magnetic resonance imaging (MRI), CT angiography, MRI angiography, and conventional angiography (Clinch, 2001; Edlow, Panagos, Godwin, Thomas, & Decker, 2008; Locker, Thompson, Rylance, & Mason, 2006; Strain, et al., 2000; Baraff, et al., 2010).

Depending on the diagnostic suspicion of whether it is a primary headache or exhibits warning signs –in other words, if the headache is secondary to something serious such as bleeding, a tumor, a neuroinfection, etc.– tests are carried out. The healthcare field also refers to whether the patient is attended in the emergency room, through hospitalization or external consultation, as well as to what specialized services are available, for example, if there is a tomography, or a resonator, or a procedure room to perform a lumbar puncture (Hainer & Matheson, 2013; Mitsikostas, et al., 2015; Do, et al., 2018).

The therapeutic approach includes non-pharmacological and pharmacological strategies. Among the first, oral non-pharmacological treatments for headaches are physical therapy, massages, acupuncture, neural therapy, pericranial nerve blocks (Sabatke, Scola, Paiva, & Kowacs, 2015; Blumenfeld, et al., 2013), stress management techniques, psychotherapy, neurobiofeedback, changes in diet and lifestyle (Tamburin, et al., 2016; Becker, et al., 2015; Institute of Health Economics, 2013).

Pharmacologic management for PHs includes both acute and prophylactic treatment. Treatment for acute episodes includes all pain relievers, such as non-steroidal anti-inflammatory drugs, such as naproxen, ibuprofen, diclofenac, acetylsalicylic acid; derivatives of paracetamol, such as acetaminophen; ergot derivatives, such as ergotamine; triptans; derivatives of opioids, such as codeine, morphine, etc. Non-steroidal anti-inflammatory drugs (NSAIDs) are the ones that best penetrate the central nervous system; however, used chronically they are very toxic to the kidneys, gastric mucosa, colon, and liver. Triptans are very useful, especially in managing migraine pain and trigeminal-autonomic headaches. Derivatives of opioids are the third pain management line, in the context of headaches. Main adverse effects related to painkillers are gastrotoxicity (Harirforoosh, Asghar, & Jamali, 2014; McCrae, Morrison, MacIntyre, Dear, & Webb, 2018; Wongrakpanich, Wongrakpanich, Melhado, & Rangaswami, 2018; Diener, Holle, Dresler, & Gaul, 2018), hepatoxicity (Tittarelli R, et al., 2017; Fokunang, Fokunang, Frederick, Ngameni, & Ngadjui, 2017), and nephrotoxicity (Harirforoosh, Asghar, & Jamali, 2014; McCrae, Morrison, MacIntyre, Dear, & Webb, 2018; Fokunang, Fokunang, Frederick, Ngameni, & Ngadjui, 2017). Pharmacologic chronic use abuse is avoided due to its adverse effects (Lundqvist, Bjørn, Straand, & Kristoffersen, 2019; Fokunang, Fokunang, Frederick, Ngameni, & Ngadjui, 2017; Wongrakpanich, Wongrakpanich, Melhado, & Rangaswami, 2018; Diener, Holle, Dresler, & Gaul, 2018).

Common drugs for symptomatic treatment:

- Analgesics/NSAIDs: Generally, every 8 hours:
  -Acetylsalicylic acid, dose: 500-1000 mg, orally.
  -Naproxen, dose: 500-1000 mg, orally.
  -Ibuprofen, dose: 400-1200 mg, orally.
  -Diclofenac sodium, dose: 50-100 mg, orally or 75 mg, intramuscular.
  -Paracetamol, 500 mg, orally.

Others:

-Metoclopramide, dose: 10 mg, orally/parenteral.
-Ergotics, Ergotamine tartrate: 1-2 mg, orally.
-Dihydroergotamine, 0.5-1 mg, orally.
-Sumatriptan, 50-100 mg, orally.
-Dexamethasone, 4-20 mg, intramuscular or intravenous.

Prophylactic treatment (Muñoz, et al., 2020) is prescribed for patients with recurrent episodes, chronic headaches, isolated headache episodes that are disabling or very prolonged, poor or no response to painkillers during an acute attack, migraine status, migraine infarction, predictable episodes, such as menstrual cycles, nighttime headaches triggered by exercise and during a specific time of the year, as well as headaches associated with sexual activity. Drugs used for prophylactic treatment are anticonvulsants (Mulleners, McCrory, & Linde, 2015; Silberstein, 2017), beta-blockers, calcium-antagonists (Lai, et al., 2017), tricyclic antidepressants (Xu, Liu, Dong, Zou, & Wei, 2017) and selective serotonin reuptake inhibitors (Ozyalcin, et al., 2005) for a prolonged period of time (at least 3-6 months proven to be effective). The adverse effects associated with the pharmacological treatment are relevant and frequently hinder adherence (Chiang, Schwedt, Wang, & Dodick, 2014; Whyte & Tepper, 2009; Diener, et al., 2002; Jackson, et al., 2019; Yu & Han, 2015).

Common drugs for prophylactic treatment:

- Anticonvulsants:
  -Sodium valproate, dose: 400-1.500 mg, day.
  -Topiramate, dose: 25-100 mg, day.
- Calcium antagonists:
  -Flunarizine, dose: 2.5-5 mg, day.
  -Nimodipine, 30 mg to 90 mg, day.
  -Verapamil, 80 mg to 240 mg, day.
- Beta-blockers:
  - Propranolol, dose: 40 to 160 mg, day.
  - Atenolol, 50 to 200 mg, day.
  - Nadolol, 20 to 120 mg, day.
  - Metoprolol, 100 to 200 mg, day.
- Tricyclic antidepressants:
  - Amitriptyline, dose: 10 to 75 mg, day.
  - Imipramine, dose: 25 to 75 mg, day.
  - Trazodone, dose: 50 to 100 mg, day.
- Selective serotonin reuptake inhibitors (SSRIs):
  - Fluoxetine: dose: 20 to 40 mg, day.

Pharmacological treatments may be combined with other treatments including injections of local anesthetics (LAs), also referred to as neural therapy, peripheral pericranial nerve blocks (Sabatke, Scola, Paiva, & Kowacs, 2015; Blumenfeld, et al., 2013), the application of botulinum toxin type A (Onabotulinum Toxin A-Botox) (Dodick, et al., 2010; Aurora, et al., 2014), acupuncture, physical therapy, and neurofeedback, etc. (Becker, et al., 2015; Institute of Health Economics, 2013; Network Scottish Intercollegiate Guidelines, 2008).

During follow-up, it is important to keep a headache diary to objectively evaluate the result of prophylactic treatment. Improvement is defined as a 50% decrease in the frequency, duration and intensity of headaches (Lundqvist, Bjørn, Straand, & Kristoffersen, 2019; Fokunang, Fokunang, Frederick, Ngameni, & Ngadjui, 2017; Wongrakpanich, Wongrakpanich, Melhado, & Rangaswami, 2018; Diener, Holle, Dresler, & Gaul, 2018).

It is important to educate all patients about their disease, the limitations of the medication and what would happen with the abuse of it. An orientation should be made on the type of diet to be avoided, recommendations on physical activity and sleep hygiene, as well as avoiding perfumes, smells and cigarette smoking. (Chiang, Schwedt, Wang, & Dodick, 2014; Whyte & Tepper, 2009; Diener, et al., 2002; Jackson, et al., 2019; Yu & Han, 2015).

The evolution of PHs is often recurrent, causing suffering and disability, and has an enormous impact on health-related quality of life (HRQOL) worldwide. The chronicity of most PHs makes them an overriding health problem (Burch, Rizzoli, & Loder, 2018). Unlike other chronic diseases, morbidity is largely concentrated in young, middle-aged, otherwise healthy people, especially fertile-aged women (Buse, et al., 2013). The impact of PHs on the national health system is enormous because of its huge economic expense. In North America, nearly 1 in 6 Americans and 1 in 5 women between the ages of 15 and 64 years have experienced a severe headache in the last 3 months, most of them are PHs. Studies conducted in the United States in 2014 show that headaches are the fifth leading cause for seeking medical consultation and accounted for 3% of all emergency room visits.

Health-related quality of life (HRQOL) is an individual's or a group's perceived physical and

mental health over time (Center of Disease Control and Prevention, n.d). It is a multi-dimensional concept that includes spheres related to physical, mental, emotional, and social functioning. It focuses on the impact health status has on quality of life. HRQOL has been used to measure the effects of chronic illness, treatments, and disabilities. SF-36 is a multidimensional concept in which several medical and non-medical factors such as family, friends, religion, work, income level, food, lifestyle, play a role (Organization, World Health, 1994). When evaluating HRQOL, the aim is to measure the impact of a disease and its treatment on the physical, emotional and social functioning of people afflicted with it. In the field of clinical research in PH, HRQOL is an emerging concept of analysis (Abu, et al., 2016).

Within the different scales, it is worth mentioning the HIT-6 scale, a tool used to measure the impact that headaches have on the functionality of people who suffer from it; It was developed by an international group of primary care medicine and neurology headache experts in collaboration with psychologists who participated in the development of the SF-36. Its use is recommended, because different investigations have shown that by determining the degree of affectation of the patient, a more successful response to treatment can be given (Muñoz, et al., 2020).

Want in an investigation conducted in 2001 at a national medical center in Taipei, Taiwan, with 906 patients with headache, to whom they applied the SF-36 instrument, observed a generalized multidimensional decrease in scores, except for the scale of physical functioning. The results suggest that pain improvement in headache patients may produce a general improvement on the SF-36 scale (Wang, Fuh, Lu, Juang, 2001).

On the other hand, Guitera and collaborators in 2002, analyzed the quality of life using the generic SF-36 instrument, in 89 people not selected from an epidemiological study in the general population who met the criteria for chronic daily headache, showing a decrease in the SF-36 scales compared to healthy subjects. The greatest decreases were seen in physical role, body pain, vitality, and social functioning (Guitera, Muñoz, Castillo, Pascual, 2002).

Autret, Roux, Rimbaux-Lepage, an others (2010), published the article, Psychopathology and quality of life burden in chronic daily headache: influence of migraine symptoms, where they compare psychopathology and quality life span of patients with chronic daily headache, migraine and tension headache, finding that scores on the SF-36, except for physical functioning, with respect to those observed in adjusted historical controls, showed a difference of more than 20 points; In addition, the items of physical health, body pain, and mental health were significantly more affected in the migraine group compared to the tension-type headache group. A particular vulnerability to somatic symptoms and a special predisposition to develop negative painful affect was also demonstrated in patients with migraine, compared to the group of patients with tension headache.

In the pilot study where they determined the health-related quality of life (HRQoL) in patients with a history of headache due to excessive use of medications, after performing detoxification, and entering a specific hospital rehabilitation program for headache, measured HRQL, and headache-related disability, using the Short Form SF-36, Hospital Anxiety and Depression Scale, Migraine Disability Score, Coping Strategies Questionnaire, and Symptom Checklist 90 revised, finding that after detoxification and hospital rehabilitation, moderate to high levels of pain and self-reported disability due to headache were observed, while physical function of the SF -36 was not different from the expected level of the norm. Mental health was substantially affected in several dimensions, due to the ability to cope with pain. Patients with excessive use of medications can have high expectations of functionality, low symptoms and well-being (Benz, et al., 2017).

Studies have been carried out with medications, where changes in the SF-36 instrument have been correlated with the change in the most annoying symptoms identified by the patient, in relation to the monthly days of migraine, in subjects with chronic migraine, showing that after the initial intravenous

administration of eptinezumab, there is improvement in SF-36 domains at the end of 12 weeks, supporting the influence of treatment on health-related quality of life (Young, Ailani, Buse, Horblyuk, Hirman, Cady, 2020).

Neural therapy (NT) is a regulatory treatment system commonly used in Central Europe (Weinschenk, Brocker, Hotz, Strowitzki, & Joos, 2013) that stimulates the peripheric and autonomic nervous system (ANS) through local anesthetic agents. The purpose of NT is not to provide local anesthesia, except at diagnosis (Barop, 1996; Fischer, 2001). In contrast to the well-defined and short-time use for analgesia in surgery, the NT approach aims for long-term relief of pain, inflammatory diseases and functional disorders (Weinschenk, 2012) by normalizing a dysfunctional ANS, which is responsible for initiating or propagating chronic pain (Frank, 1999).

NT can be applied as a local therapy (Rey, Muñoz, Catalán, & Vinyes, 2021), for example, infiltration into trigger points and tender areas; as a segmental therapy, for example, injections in or around nerves and ganglia; and in the so-called interference field (irritation zone), which may initiate and/or maintain pain and inflammation, regardless of the involved segment (Barop, 1996; Fischer, 2001; Bahekar, Singh, Saha, Molnar, & Arora, 2007; Cornelissen, Van Kleef, Mekhail, Day, & Van Zundert, 2009).

The high prevalence and impact on HRQOL associated with PH, has led to new therapeutic strategies. Based on the modulating effects of LAs on the neural system and on PH pathogenic mechanisms, we suspected that LAs could play a role in PH treatment. This study aims to evaluate the effect of LA injections in the HRQOL of patients with PH.

2. Materials and methods

A quasi-experimental (before-after) prospective study was conducted between April 2019 and October 2019 in an outpatient clinic and neurology department of a IV-level hospital in the city of Bogotá (Hospital Universitario Clínica San Rafael). Ninety-three (93) patients between the ages 18 and 80 years were chosen, with a diagnosis of primary headache according to the 2018 HIS classification. Exclusion criteria were secondary headache, concomitant treatment with botulinum toxin, pregnancy, sensory deficit, deafness or mutism that prevented completing the questionnaires. Sampling was done for convenience purposes and we included patients who met the eligibility criteria, accepted to participate in the study, and gave their informed consent.

Social and clinical data was registered during the first assessment for all participants. The patients were asked to answer two health questionnaires, SF-36 and HIT-6, before and after treatment. SF-36 is a 36-item instrument to measure HRQOL based on the patient's point of view, which included 8 domains from both the physical and mental spheres.

HIT-6 is a tool used to measure a headache's impact on the ability to function in normal daily life – job, school, home, and social situations.

The intervention consisted of injections of preservative free 1% lidocaine without epinephrine in scalp segmental therapy, which involved 0.2 cc subcutaneous injections several inches apart around the largest diameter of the head, injections in the trigger points of the scalp and neck were intramuscular, Arnold points were infiltered subcutaneously in a fan shape, according to the anatomical distribution of the nerve. Approximately 5 cc of 1% lidocaine without epinephrine is injected per patient in each session.

The first assessment was performed at admission, and the second between one and three months after the intervention.

A univariate analysis with frequency distribution and percentages for qualitative variables was performed. For the quantitative variables, normality tests were conducted using the Shapiro-Wilk test and according to this, the central tendency and dispersion measures were found. An analysis of paired tests between qualitative variables was performed with the McNemar test. In the case of qualitative vs. quantitative variables, a paired student's T or Wilcoxon test was performed, according to normality. Statistically significant difference was considered with values of $p < 0.05$. The information was analyzed using the IBM SPSS Statistics version 26 software.

The research was carried out in accordance with the declaration of Helsinki and was approved prior to its execution by the Research Ethics Committee of the HUCSR. The confidentiality of the information obtained was guaranteed.

3. Results

3.1. Demographic data and medical condition of patients

Of the 93 patients, 79 (84.9%) were women and 14 (15.1%) were men, age oscillated between 18 to 71 years with a mean of 40 (ST+/-14.10) (Table 1).

Table 1. Demographic characteristics of the study's population

Gender	**n**	**%**	**Age (years)**		
			Mean	Median	Range
Female	79	84.9	40.9	41	18-71
Male	14	15.1	40.3	40	18-64
Total	93	100	40.6	40.5	18-71

Source: own elaboration

Two patients (2.2%) were diagnosed with chronic daily headache, 21 (22.6%) with tension headache, 57 (61.3%) with migraine with aura, and 13 (14%) with migraine without aura (Table 2).

Table 2. Clinical diagnosis ICD-10

	n = 93	**Percentage**
Daily chronic headache	2	2.2%
Tension headache	21	22.6%
Migraine with aura	57	61.3%
Migraine without aura	13	14%

Source: own elaboration

Table 3 summarizes clinical characteristics of primary headache in the study's population.

Table 3. Clinical characteristics of primary headache in the study's population

VARIABLES	**n = 93**	**%**
Time of Evolution		
<1 year	24	25.8
1-3 years	23	24.7
4-6 years	13	14.0
>7 years	31	33.3
Not registered	2	2.2
Symptom severity		
Mild	1	1.1
Moderate	30	32.3
Severe	62	66.7
Treatment time before intervention		
< 1 month	9	9.7
1-12 months	23	24.7
>1 – 5 years	17	18.3
>5 years	8	8.6
Treatment on demand	21	22.6
Not recorded	15	16.1
Chronic diseases		
None	28	30.1
Medical	60	64.5
Surgical	5	5.4

Source: own elaboration

At admission, 36 (38.7%) patients reported medication abuse, all of them due to analgesic abuse.

At first assessment, all patients who entered the study had a normal neurological physical examination, four (4.3%) had an altered axial tomography, and two (2.2%) had an abnormal nuclear magnetic resonance, incidental imaging findings, which were not related to the headache.

3.2. Outcomes

The clinical characteristics of patients with PH were compared before and after receiving LA treatment. A statistically significant difference was evident in symptom frequency and duration (p = 0.013 and p = 0.035), medication requirement (p = <0.001), response to treatment (p = <0.001), and analgesic requirement (p = <0.001) (Table 4).

Regarding the frequency of symptoms, 10 patients (10.8%) after treatment reported they did not have a headache and 33 patients (35.5%) reported significant improvement.

Table 4. Clinical characteristics in patients with PH before and after receiving treatment with local anesthetics.

Variables	Before treatment n (%)	After treatment n (%)	*p* value
Symptom Frequency			
None or < once a week	7 (7.5)	24 (25.8)	
1-3 times a week	42 (45.2)	46 (49.5)	0.013
Daily	38 (40.9)	23 (24.7)	
Not recorded	6 (6.5)	0 (0)	
Symptom Duration			
Occasional or not present	7 (7.5)	18 (19.4)	
< 24 hours	39 (41.9)	34 (36.6)	
1-3 days	21 (22.6)	21 (22.6)	0.035
Permanent	24 (25.8)	20 (21.5)	
Not recorded	2 (2.2)	0 (0)	
Pharmacological treatment			
Analgesics	76 (81.7)	38 (40.9)	
None	6 (65)	47 (50.5)	<0.001
Others	4 (4.3)	3 (3.2)	
Prophylactic treatment	7 (7.5)	5 (5.4)	
Response to treatment			
Good	12 (12.9)	24 (25.8)	
Regular	9 (9.7)	13	
Bad	66 (71.0)	(14.0)	<0.001
Not applicable	2 (2.2)	11 (11.8)	
Not recorded	4 (4.3)	43 (46.2)	
		2 (2.2)	

Source: McNemar test

There was a significant difference in the impact of headaches on the functional scale, according to the HIT-6 questionnaire, before and after receiving treatment with local anesthetics (p <0.001) (Table 5).

Table 5. HIT-6 in patients with PH before and after receiving treatment with local anesthetics.

HIT-6.	Before treatment n (%)	After treatment n (%)	P value
Low or null impact	4 (4.3)	29 (31.2)	
Some impact	6 (6.5)	14 (15.1)	<0.001
Significant impact			

	8 (8.6)	17 (18.3)
Very severe impact		
	75 (80.6)	33 (35.5)

Source: McNemar test

When evaluating the quality of life with the SF-36 scale, before and after receiving treatment, there was a significant difference in the physical and emotional role, social function, mental health, vitality, general health, and body pain. No difference was found in the physical function (Table 6).

Table 6. Health-related quality of life (HRQOL) measured by SF-36 scale in patients with PH before and after receiving treatment with local anesthetics.

SF- 36 scale	Before n (%)	After n (%)	p value
Physical function*			
Mean (SD)	72.9 (25.85)	76.4 (25.07)	0.127
**Physical role ** **			
Mean (SD)	32.2 (40.47)	64.2 (42.89)	< 0.001
Emotional role**			
Mean (SD)	57.7 (45.61)	69.5 (41.04)	0.013
Social function*			
Mean (SD)	63.9 (25.50)	58.4 (19.50)	0.037
Mental health*			
Mean (SD)	60.5 (19.75)	65.0 (19.21)	0.018
Vitality*			
Mean (SD)	46.8 (18.92)	58.6 (20.35)	< 0.001
General health*			
Mean (SD)	40.8 (9.71)	54.0 (18.98)	< 0.001
Body pain*			
Mean (SD)	41.7 (22.63)	57.1 (25.02)	< 0.001

Source: SD: Standard deviation *Paired T- test **Wilcoxon test

3.3. Adverse effects

Injections with lidocaine 1% were overall well-tolerated. Occasional local pain, ecchymosis and hematomas were the only adverse effects observed, and they tend to be mild, predictable, and temporary.

4. Discussion

4.1. Findings and interpretation

Comparing data before and after intervention, statistically significant differences were found in seven out of the eight items on the SF-36 scale (physical, emotional role, social function, mental health, vitality, general health, and body pain), in the impact of headaches on functionality and in medication consumption. Pain intensity (Table 3) and duration of episodes decreased. No adverse effects were recorded.

Lidocaine local injections in defined points are an effective and safe treatment for this study's population.

No statistical difference was found in the physical role on the SF-36 scale, likely due to the fact that physical aspects in patients with PH (such as self-care, walking, climbing stairs, bending over, picking up, or carrying weights) are less affected than other items (such as social and emotional aspects).

We opted for injections with therapeutic LAs (neural Therapy, NT) subcutaneously around the largest diameter of the head, Arnold points, and scalp and neck trigger points. The primarily purpose of this technique is not to function as local anesthesia. The therapeutic effect of LAs in usual medical practice has mainly been related to their nerve blocking properties, secondary to their interaction with Na^{2+} channels. In recent decades, a wide range of attributes, in addition to nerve-blocking and membrane-stabilizing effects, have been related to LAs, likely due to their action on K^{+} and Ca^{2+}channels (Scholz, 2002), inhibitory actions on G protein coupled receptors (Cassuto, Sinclair, & Bonderovic, 2006) and inhibitory action on *N*-methyl-D-aspartate (NMDA) receptors (Hahnenkamp, et al., 2006; Sugimoto, Uchida, & Mashimo, 2003). LAs also appear to have a profound anti-inflammatory effect through polymorphonuclear neutrophil mediators and free radical release (Hollmann, et al., 2004). Kevin Tracey reported that LAs can interrupt the release of proinflammatory substances at the neuron end plate (Tracey, 2002).

NT utilizes the nervous system' regulatory mechanisms and plastic properties. LA modulating effects on the neural system have been previously described in medical literature (Hollmann, et al., 2004; Cassuto, Sinclair, & Bonderovic, 2006). LAs may interrupt the vicious circle of nociceptors acting on different pathogenic mechanisms involved in pain perception, such as sympathetic excitation, vascular alteration, neurogenic inflammation, and muscle contraction. (Egli, et al., 2015; Cassuto, Sinclair, & Bonderovic, 2006). Thus, LAs used in NT are believed to reduce pathological nociceptive activity and eliminate the pathological memory of the sympathetic nervous system; thus, providing long-term pain relief (Egli, et al., 2015).

For these reasons, LAs (NT) may be useful in treating PHs.

The reduction of perceived pain after the first session is a common observation of NT; it is considered a beneficial diagnostic sign and if necessary, more additional sessions can be performed (Egli, et al., 2015). In this study, we conducted a single session.

4.2. Strengths and weakness

The study's main limitation is the absence of a control group and the convenience sampling.

The absence of systemic side effects, low cost, and the simplicity of the intervention were the treatment's main milestones.

4.3. Similarities and differences versus other studies

Sabatke et al. described improvement of headaches in women suffering from fibromyalgia after injecting the trigger point in the temporalis muscles. In this study, we failed to find statistical differences between LA injections and a physiological serum, although the results were better in the group that received the LAs (Mermod, Fischer, Staub, & Busato, 2008; Sabatke, Scola, Paiva, & Kowacs, 2015)

Local lidocaine injections in chosen head points proved to be an effective and safe treatment for this study' population. Pain intensity and duration decreased, HRQOL and HIT-6 improved, and medication consumption was decreased post-intervention.

Seven out of the eight items measured on the SF-36 scale (physical and emotional role, social function, mental health, vitality, general health, and body pain) improved.

Further randomized controlled trials could determine the use of local anesthetic injections in PH treatments.

5. Conclusions

- Neural therapy is a therapeutic alternative for people with a diagnosis of primary headache, which showed improvement in the HIT-6 scale that measures the impact of headache on functionality, as well as on the physical, emotional, social function, mental health, vitality, general health and body pain, seven of the eight items of the SF-36 scale that measures quality of life.
- Neural therapy proved to be a well-tolerated treatment, with few systemic side effects, and low cost, in patients with a diagnosis of primary headache.
- Further research should be done to elucidate the role of local anesthetic injections for PHs.
- In future studies, it is considered relevant to include a control group, in order to reduce biases and give greater statistical relevance.

Learning points

- Headaches may have a typical or atypical presentation, the diagnosis is clinical, its differential diagnosis is important, its prognosis depend on the cause.
- It is important to apply the diagnostic criteria of the current headache classification in order to differentiate primary from secondary headaches.
- The early identification of warning signs in headache patients is relevant because these cases require complementary studies to rule out causes that put the patient's life at risk.
- The treatment of headaches in multifactorial, it is important to identify the triggers of pain, in order to avoid them, as well as to seek the best therapeutic option for each patient, and to emphasize the importance of avoiding the abuse of analgesics, given the degree of toxicity presented by over-abuse, as well as the perpetuation cycle of pain.
- Headache treatments must be well tolerated, improve functionality and quality of life for patients.

Patient's perspective

"The truth is that throughout my life, I have faced medical situations that have pushed me to the limit, and I have questioned my faith. I see that the medical practice is a daily challenge that is growing and that although I received the best care and management according to my pathology, the changes in my functionality have not varied. However, I want this testimony to be published for the knowledge of other people, who, like me, have suffered chronic headaches, which have impacted my quality of life and functionality, have led me to take a variety of drugs without substantial improvement; Recognizing that many drugs seek to do good, they can generate adverse events depending on the susceptibility of each individual. Thank you for considering my illness real, because the truth is that I was going around for a long time to help me relieve my headaches, and I have found neural therapy as my best therapeutic option, after a long journey".

List of abbreviations

LA: Local anesthetics
CT: Computed tomography
HRQOL: Health-related quality of life
NT: Neural Therapy
PH: Primary headaches

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Availability of data and materials

All data generated or analyzed during this study will be made available by the corresponding author upon reasonable request.

Consent for publication

Written informed consent was obtained from all participants before any study procedures took place. A copy of the written consent is available for review by the editor of this magazine.

Ethical approval and consent to participate

The protocol was developed in accordance with the Declaration of Helsinki, as well as its

subsequent approval by the ethics committee of the Hospital Universitario Clínica San Rafael. Written informed consent was obtained from all participants before any study procedures took place.

Conflict of interests

The authors declare that they have no conflicts of interest.

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