

The effect of nonsteroidal anti-inflammatory drugs on eye pain and migraine headache caused by trochleitis

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Abstract:

PURPOSE: Trochleitis has been recognized as one of the causes of eye pain and migraine headaches. This study attempts to investigate the effect of ibuprofen on reducing eye pain and migraine headaches caused by trochleitis.

METHODS: In this before-after clinical trial, out of 1100 clinically examined patients with eye pain and migraine symptoms, 33 patients were diagnosed with having trochleitis and trochleodynia confirmed by orbital magnetic resonance imaging images. Ibuprofen (400 mg/6–8 h) was prescribed to the subjects for 15–30 days. The main outcomes were a reduction in tenderness and pain that were evaluated 2 weeks, a month, and 6 months after the prescription. The data were analyzed by STATA (version 14) and using Wilcoxon and McNemar tests.

RESULTS: The results revealed that 28 of the subjects (84.8%) experienced a significant reduction in tenderness 2 weeks after undergoing the treatment ($P < 0.001$). Standard deviation and average of headache scores before and after the treatment were 7.85 ± 1.75 and 0.64 ± 0.61 based on the visual analog scale. The difference between the pain scores before and after the treatment was statistically significant ($P < 0.001$). Clinical symptoms such as induration ($P < 0.001$), photophobia ($P < 0.001$), upward gaze ($P < 0.001$), and pain after reading ($P < 0.001$) were reduced significantly. Six months after the treatment, none of the mentioned symptoms was reported by the subjects.

CONCLUSION: The findings revealed that noninvasive treatment (ibuprofen) has reduced eye pain, tenderness, and migraine headaches caused by trochleitis. What is important to mention is that trochleitis should be diagnosed properly.

Keywords:

Migraine headache, nonsteroidal anti-inflammatory drugs, trochleitis

INTRODUCTION

The trochlea is a saddle-like cartilaginous structure located in the superomedial orbit, which contains the tendon of the superior oblique muscle. Histologically, the trochlea is surrounded by a synovial membrane analogous to the structure of a joint.^[1] The trochlea is innervated by an ophthalmic nerve branch and is capable of generating pain in the setting of trochleitis, which is most often idiopathic but may develop secondary to autoimmune connective tissue disorders.^[2]

Migraine and tension-type headaches have a significant burden of neurological disease

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globally.^[3] Trochleitis is an inflammation of the trochlea and peritrochlear region, particularly the sheath of superior oblique muscle that is characterized by swelling and tenderness of trochlea.^[4] Swelling may be observed clinically or documented on orbital imaging studies.^[2] Trochleodynia is mostly felt in the forehead. Trochleodynia is commonly produced by trochleitis,^[5,6] a noninflammatory condition or primary trochlear headache.^[2] According to the existing evidence, trochleodynia may be a trigger for migraine headaches.^[6,7]

Trochleitis has been recognized as one of the causes of eye pain and migraine headaches. Although a previous study has shown that local steroid injection of the trochlea may provide a more positive and rapid response compare to

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oral Nonsteroidal anti-inflammatory drugs (NSAIDs),^[8] to our knowledge, there is not sufficient information about trochleitis diagnosis, treatment, and prognosis. In this study, we aimed to investigate the effect of ibuprofen on trochleitis.

METHODS

This prospective before-after clinical trial was performed at a teaching hospital, Kowsar, in Sanandaj, the center of Kurdistan province, northeast of Iran. The Ethics Committee at the Kurdistan University of Medical Sciences evaluated and approved the study protocol which was based on the Helsinki declaration. Among 1100 patients with eye pain and migraine symptoms, who were clinically examined for 6 months, 33 were diagnosed with trochleitis and trochleodynia. We used magnetic resonance imaging (MRI) images findings to confirm the trochleitis and trochleodynia in these patients. Patients who had tenderness and induration in touching had our inclusion criteria and were entered into the study. Complete ophthalmic and neurologic examinations were done to rule out patients suffering from uveitis, scleritis, episcleritis, trigeminal neuralgia, orbital myositis, metastatic diseases, carotid-cavernous fistula, sinusitis, and severe dry eye.

For these 33 patients, we prescribed ibuprofen (400 mg/6–8 h) instead of injection for 15–30 days.^[9] Consequences of the treatment were investigated in terms of reduction in tenderness, induration, and pain severity in 2 weeks, 1 month, and 6 months after the trial.

As it was mentioned before, 33 patients (over 18 years old) with trochleitis symptoms, including thirty patients with trochleitis and three patients with trochleodynia, were entered the trial and were examined for 6 months (from June 2017 to January 2018). Migraine headaches were diagnosed according to the diagnostic criteria of migraine.^[10,11] Universal pain assessment tool, visual analog Sscale (VAS) was applied to evaluate the level of pain before and after the treatment.^[12]

Orbital MRI imaging with and without contrast was used to confirm the diagnosis of trochleitis [Figure 1]. Moreover, anti-thyroid peroxidase (TPO), thyroid-stimulating hormone, T4, CRO, erythrocyte sedimentation rate, rheumatoid factor, antinuclear antibody, complete blood count difference, and fasting blood sugar were prescribed for the patients under NSAIDs such as ibuprofen treatment. Ibuprofen is identified as one of the best NSAIDs with the least side effects. Anti-inflammatory dosage of ibuprofen is 1200–3200 mg.^[13,14]

Based on the abovementioned information regarding Ibuprofen dosage, we prescribed oral ibuprofen (400 mg/6–8 h) for 2 weeks. The study participants were examined after 2 weeks to evaluate their pain and tenderness. Those who indicated symptoms of pain and tenderness were advised to continue taking ibuprofen for another 2 weeks. The obtained data were analyzed by STATA (version 14, (STATA Corp, USA)) and by applying Wilcoxon and McNemar tests.

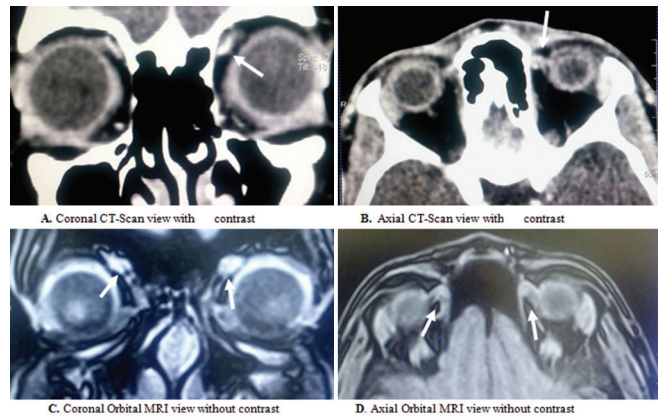


Figure 1: Coronal and axial computed tomography and orbital magnetic resonance imaging of trochleitis. (a and b) Thickening and contrast absorption of the left trochlea. (c and d) Thickening of the bilateral trochlea (left > right)

It should be noted that the subjects were informed properly about the process and goals of the trial, and written informed consent was obtained. Furthermore, this study was approved by the ethics committee at Kurdistan University of Medical Sciences (Code: IR.MUK.REC.1396.385) and Iranian Registry of Clinical Trial, IRCT (IRCT Id: IRCT20180114038350N1).

RESULTS

Thirty-three patients, including 30 patients with trochleitis (90.9%) and three patients with trochlear pain (trochleodynia) (9.1%), were entered into the trial for 8 months. The age of subjects ranged from 20 to 83 years. Mean and Standard deviation of age was 14.44 ± 42.10 years. Thirty-one of the subjects were female (93.9%). The subjects reported that they were suffering from the disease from 6 months to 16 years, and the standard deviation was 5.50 ± 5.19 . Investigating the medical history of the subjects indicated that none of them had been diagnosed with trochleitis and most of them were advised to visit a neurologist or ophthalmologist. Eight subjects (24.2%) reported that they were recommended to take medicine for their migraine headache. Fourteen subjects (42.4%) did not agree to go under migraine treatment, despite being diagnosed with having a migraine. They preferred to tolerate acute migraine headache. Most of the participants who had experienced a sort of treatment for migraine headaches such as sertraline, citalopram, sodium valproate, topiramate, and so on reported no therapeutic responses. None of the subjects were diagnosed with cancer and undergoing a special kind of surgery.

Seven of the participants (21.2%) had bilateral involvement, 14 of them (42.4%) reported that they felt the pain in one side more severely than the other, and 12 of them (36.4%) reported one-sided involvement. Eight of the cases (24.24%) suffered trochleitis due to secondary causes such as lupus (2 cases), rheumatoid Arthritis (3 cases), fibromyalgia (1 case), and polymyalgia rheumatica (2 cases). Three cases of the subjects suffered hypothyroidism and three of them were anti-TPO+.

Pain location in 12 cases (36.4%) started from orbital and preorbital areas and had radiation to frontal and temporal areas. In 14 of the cases (42.4%), migraine headache (beating pain in frontal and temporal areas of the involved side) was reported to accompany radiation to preorbital. In 7 cases (21.2%), migraine headache was limited to the preorbit region. Other investigated clinical characteristics and demographic information of the subjects have been summarized in Table 1.

Thirty cases of the subjects (90.9%) indicated inflammation and induration (Trochleitis) and three of them (9.1%) did not indicate inflammation and induration (Trochleodynia).

When the trial started, 27 (81.8%) participants reported severe pain and two of them reported worse pain. The most common accompanying symptoms included photophobia (28 cases), pain in upward eye movements (25 cases), reading pain (7 cases), tearing (5 cases), diplopia in pain attack (4 cases), itchy eyes (3 cases), and Proptosis (1 case). None of the patients

suffered the Brown Syndrome. Two of the patients with severe headache were excluded from the trial to rule out temporal arthritis (GCA) and two other patients underwent examinations to check cerebrovascular diseases.

Average scores (standard deviation) of headaches before and after the treatment were 7.85 ± 1.75 and 0.64 ± 0.61 according to the VAS. There was a significant difference among headache scores before and after the trial ($P < 0.001$). Twenty-eight subjects (84.8%) reported complete relief of tenderness ($P < 0.001$). Only five of the subjects reported slight tenderness remaining after the treatment. Thirty cases of the subjects with symptoms of trochleitis (90.9%) had reported induration before the treatment. Twenty-eight of them reported complete relief of induration after the treatment ($P < 0.001$). Induration remained in only two of the cases (6.1%). The frequency and distribution of the symptoms before and after the trial as well as the significant value of treatment effect have been summarized in Table 2.

Table 1: Baseline characteristics of study subjects

Variables	n (%)
Sex	
Male	2 (6.1)
Female	31 (93.9)
Laterality of trochleitis	
Left	9 (27.3)
Right	3 (9.1)
Right more than left	8 (24.2)
Left more than right	6 (18.2)
Bilateral	7 (21.2)
Acuity of onset	
Acute	25 (75.8)
Chronic	4 (12.1)
Chronic sectional intensity	4 (12.1)
Location	
Frontal and temporal	15 (45.5)
Frontal and temporal and parietal	6 (18.2)
Eyes and periorbital	12 (36.4)
Radiation	
Frontal and temporal	8 (24.2)
Frontal and temporal and parietal	3 (9.1)
Eyes and periorbital	11 (33.3)
Temporal and parietal	1 (3.0)
Periorbital and maxillary	3 (9.1)
No radiation	7 (21.2)
Aura	
Positive	8 (24.2)
Negative	25 (75.8)
Laboratory findings	
Normal	21 (63.6)
Low haemoglobin	2 (6.1)
High anti-TPO	3 (9.1)
FBS >126	1 (3.0)
ANA+	3 (9.1)
High ESR	1 (3.0)
CRP positive	2 (6.1)

FBS=Fasting blood sugar; ANA=Antinuclear antibody; ESR=Erythrocyte sedimentation rate; CRP=C-reactive protein; TPO=Thyroid peroxidase

DISCUSSION

Trochleitis is one of the causes of migraine headache, orbital, and peri-orbital pain, which is usually idiopathic and clinically diagnosable.^[8] Trochleodynia is the pain of the trochlear region that results from trochlear inflammation and trochleitis and can be specified through tenderness, stiffness, and induration in touching.^[6] Indeed, trochleodynia is a pain due to trochleitis with no induration in touching primarily and swelling and induration develop over time.^[15] In our study, patients with tenderness and induration in touching were investigated.

The most common symptoms include orbital and periorbital pain, migraine headache with photophobia, eye pain in upward gaze, pain after reading, tearing, and itchy eyes. Pain and have been reported in all of the patients.^[4] Ophthalmologists and neurologists may pay less attention to trochleitis as a differential diagnosis in such cases. Neurologists may treat migraine headaches induced by trochleitis as migraine, and ophthalmologists also may treat periorbital and orbital pain as ocular surface diseases, whereas patients may still complain from symptoms and unimprovement.

This study is an attempt to investigate the effect of NSAIDs such as ibuprofen on trochleitis. The findings have revealed a significant reduction and relief of symptoms including headache, photophobia, eye pain in upward gaze, and reduction of tenderness, swelling, and stiffness in touching.

NSAIDs such as ibuprofen are usually prescribed to treat rheumatoid arthritis (400–800 mg) three to four times per day, and it takes few days to indicate optimal therapeutic response, which can continue for 1 month in order to complete the treatment.^[14] Given that the trochlea is a saddle-like cartilaginous structure and is surrounded by a synovial membrane analogous to the structure of a joint,^[9] we used ibuprofen in our experiment.

Table 2: Difference between frequency of symptoms before and after the treatment

	Before, n (%)	After, n (%)	P*
Tenderness			
Yes	33 (100.0)	5 (15.2)	<0.001
No	0	28 (84.8)	
Induration			
Yes	30 (90.9)	2 (6.1)	<0.001
No	3 (9.1)	31 (93.9)	
Photophobia			
Yes	28 (84.8)	4 (12.1)	<0.001
No	5 (15.2)	29 (87.9)	
Supraduction gaze			
Yes	25 (75.8)	3 (9.1)	<0.001
No	8 (24.2)	30 (90.9)	
Reading pain			
Yes	7 (21.2)	0	0.01
No	26 (78.8)	33 (100)	
Itching			
Yes	3 (9.1)	0	0.2
No	30 (90.9)	33 (100)	
Tearing			
Yes	5 (15.2)	0	0.06
No	28 (84.8)	33 (100)	
Diplopia			
Yes	4 (12.1)	0	0.1
No	29 (87.9)	33 (100)	

*Mc Nemar test

In general, both orbital MRI and orbital computed tomography scans with the trochlea protocol are considered as the most efficient methods to diagnose trochleitis and rule out other possible causes.^[6] Regarding the fact that MRI images are better to investigate contrast absorption and inflammation, orbital MRI with and without contrast clearly illustrates thickening and absorption in both axial and coronal views clearly, although in some cases the axial view was obvious and in the other cases the coronal view. It is not required to do MRI with contrast injection because thickening is visible in the trochlea through MRI without injection. One of the diseases that can indicate similar symptoms is called frontal and ethmoid sinusitis. In such cases, treating sinusitis suffices. After checking the tests for diagnosing autoimmune diseases, treating the diagnosed disease should be considered, too. It seems that trochleitis is more likely to emerge in patients suffering from rheumatic diseases, but it is less likely to be diagnosed because of the effects of NSAIDs and corticosteroids.

Regarding the related studies, intratrochlear corticosteroids injection has been considered as the first step in treating trochleitis. Due to the fact that trochlea is close to supratrochlear artery (one of the ending branches of ophthalmic artery), hematoma is more likely to happen as the side effect of injection in Trochlea. As a result, the researcher decided to investigate a noninvasive method to treat it. Considering that trochleitis is the inflammation of trochlear tendon, NSAIDs treatment can effectively cure arthritis. Optimal anti-inflammatory effects of NSAIDs emerge within 2 weeks. Ibuprofen has the least

side effects and the most anti-inflammatory effects. Due to these facts, we prescribed ibuprofen (400 mg) for 2 weeks in our trial. The participants were advised to continue taking ibuprofen for another 2 weeks if they had tenderness and pain. Ninety percent of the cases reported complete relief of pain and tenderness, and in none of the cases intratrochlear injection was required. None of the participants reported migraine headache and periorbital pain within 6 months after the trial. Taking ibuprofen for 2 weeks can be repeated if migraine headache relapses. Diseases such as hypertension, anemia, pathology of cervical vertebra, and ophthalmic migraine can cause headaches. The most important responses in patients are reduction in pain and tenderness.

In this study, some of the patients complained about headaches which did not relate to trochlear migraine. In further investigations and examinations, the researcher found that, in two of the cases, the patients suffered some problems related to their cervical vertebra, and in three and two of the cases, headaches resulted from anemia and hypertension, respectively. Thus, it is required to do further investigations to rule out pathology of cervical vertebra, anemia, hypertension, allergic rhinitis, and ophthalmic migraine.

CONCLUSION

Our results revealed that NSAIDs are an efficient treatment for trochleitis, and our experiments and clinical examinations of trochlea showed that trochleitis is diagnosable. We recommend all ophthalmologists and neurologists to consider trochleitis as one cause of migraine headache and orbital/periorbital pain in these patients and regard clinical examination of trochlea essential in order to rule out trochleitis.

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Conflicts of interest

There are no conflicts of interest.

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