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Original Article

Clinical Trial of Subcutaneous Steroid Injection in Patients with Migraine Disorder

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Abstract

Background: Neurologic literature on therapeutic effect of subcutaneous corticosteroids in patients with migrainous chronic daily headache is scarce. The aim of this research is to assess the therapeutic effects of this management in such patients.

Methods: Consecutive patients with migrainous chronic daily headache enrolled a prospective before-after therapeutic study during 2010-2013. Methylprednisolone 40 mg was divided into four subcutaneous injection doses. Two injections were administered in the right and left suboccipital area (exactly at retromastoid cervicocranial junction) and the other two injections in the lower medial frontal area (exactly at medial right and left eyebrows). A daily headache diary was filled out by the patients before and one month after the intervention. The severity of pain was classified based on a pain intensity instrument using numeric rating scale from 0-10 point scale. Paired t-test and Chi-square test were used for statistical analysis.

Results: 504 patients (378 females, 126 males) with migrainous chronic daily headache were enrolled in the study. Dramatic, significant, moderate, mild, or no improvements respectively constituted 28.6%, 33.3%, 23.8%, and 14.3% of the post treatment courses. Therapeutic effect of intervention on mean pain scores was significant; t=7.38, df=20, P=0.000. Two cases developed subcutaneous fat atrophy in frontal injection site and three cases experienced syncope during injection.

Conclusion: Subcutaneous corticosteroids could be used as an adjunct therapy in patients with migrainous chronic daily headache.

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Keywords ● Subcutaneous injection ● Steroids ● Migraine disorders

What's Known

- In cases of severe migraine, which is refractory to medical therapy, traditional medicine methods have been used successfully.
- These methods include acupuncture, chiropractic, herbal medicine, and subcutaneous botulinum A toxin injection.

What's New

- Therapeutic influence of subcutaneous steroid injection in suboccipital and medial eyebrow regions of patients with severe migraine is for the first time reported in literature, according to the above method.

Introduction

Severe and refractory migraine is a devastating disease. Migraine has been ranked among the top 20 causes of disability and around 12% of the adult population worldwide suffer from migraine.[1] Although migraine represents an important cause of temporary disability, as shown by recent surveys,[1] about 50% of people with migraine, even those with disabling headache, have never consulted a physician for the problem.[1]

Migraine headache occurring more than 15 days per month for more than three months in the absence of medication overuse and not attributed to another disorder is defined as chronic migrainous daily headache.[2] Such migraine is usually

resistant and poorly respond to classical abortive and preventive medical therapies.[3] Since ancient times, traditional herbal medicines (e.g. lavender, acupuncture, chiropractic and acupressure) have been used as abortive and preventive therapy for severe migraine.[4]

Non-pharmacological interventions (e.g. relaxation therapy) is recommended for the management of migraine and a multidisciplinary approach is used for the management of migrainous chronic daily headache.[5] Few unconventional treatments for the prevention of migraine are, namely, applying pressure to the head during headache, applying ice pack, manipulation of the neck, acupuncture, hypnosis, and herbal therapy.[4]

The present research was designed to investigate the abortive and preventive treatment of chronic migrainous daily headache by local subcutaneous steroid injection. Based on our neurologic literature survey, this is the first reported study in this field.

Patients and Methods

Consecutive patients with migrainous chronic daily headache enrolled in a prospective before-after therapeutic study during 2010-2013. Patients with migraine disorder with or without aura, as there is no difference in their management, were included in the study. The presence of cognitive impairment, language barrier, and age less than 12 years were considered as the exclusion criteria. Patients with stressful life events and head trauma during one month before and after the injection were also excluded.

Diagnosis of migraine and chronic migrainous daily headache was made by a headache neurologist according to the second edition of the international headaches society (IHS) criteria[2] that corresponds with the Asian migraine criteria.[6]

All patients were administered with propranolol (40-80 mg), tricyclics (amitriptyline or nortriptyline 25-50 mg), and antiepileptic drugs (valproate, topiramate, or gabapentin) for prophylaxis of migraine attacks based on the opinion of a responsible physician before the intervention.[7] All previous preventive drugs for migraine were administered for 1 month after the injection. A daily headache diary was filled out by the patients before and one month after intervention. Methylprednisolone 40 mg was divided into four subcutaneous injection doses. Two injections were administered in the right and left suboccipital area (exactly at retromastoid cervicocranial junction) and the other two in the lower medial frontal area (exactly at medial right and left eyebrows). Tenderness to palpation or reproduction of headache pain with pressure on the injection sites was not considered as a selection criteria for performing intervention. Dramatic, significant, moderate, mild or no improvements were respectively defined as ≥75%, ≥50, ≥25% and <25% decrease in the number of headache attacks by comparing months after and before the injection. The severity of pain was classified based on a pain intensity instrument using numeric rating scale from 0-10 point scale.[8,9] The patients were requested to allocate a pain scale number (from 0 to 10) for the pain level experienced before and after the treatment.[8,9]

Patients' questionnaire data were entered into the SPSS software version 16 (Chicago, USA) and paired t-test and Chi-square test were used for statistical analysis.

The research was approved by the Ethics Committee of Mashhad University of Medical Sciences and an inform consent was obtained from the patients. Trial registration number, IRCT=13871146254N2.

Results

A total of 558 cases were considered in this study, from which 31 cases were omitted as they refused participation and 23 cases were not available for the follow up and thus excluded due to incomplete data. 504 migrainous chronic daily headache patients (378 females, 126 males) with the mean age of 32.7±7.8 years (female: 30.5±4.1, male: 35.1±2.1) completed the intervention protocol. All patients had been taking preventive agents and abortive treatments for their severe migraine headache. The mean pain scores before and after intervention was 7.38±1.49 and 3.67±2.15, respectively, that showed 49.48±28.27 percent improvement. Among 504 patients, dramatic, significant, moderate and no improvement constituted 28.6%, 33.3%, 23.8%, and 14.3% of the post interventional courses respectively. The frequency of headache attacks increased after infection in 7% of the patients. The influence of gender in the distribution of therapeutic responses after subcutaneous injection of steroid was not significant for the course categories; X^2=0.446, df=1, P=0.931. Table 1 shows the influence of intervention on pain scores in all cases, including gender differentiation. Therapeutic effects of intervention on the mean value of pain score of the patients were highly significant in all patients and in each gender. Among the treated patients, two cases developed subcutaneous fat

Table 1: Influence of intervention on pain scores in 504 cases with gender differentiation

Paired samples statistics	Mean±SD		t	df	P value (2–tailed)
	Pre-treatment pain score	Post-treatment pain score			
Total (504)	7.38±1.49	3.67±2.15	7.38	20	0.000
Females (378)	7.61±2.13	3.12±2.33	7.59	15	0.000
Males (126)	6.77±1.55	3.45±1.62	2.26	4	0.004

atrophy in frontal injection site and three cases experienced syncope during injection.

Discussion

In recent decades, numerous researches have been designed for novel management of severe migraine and refractory headaches. However, neurologic literature review revealed scarcity of investigation resembling our research topic. Consequently, our discussion cannot be supported with an extensive list of referenced articles. On the other hand, this underlines scientific importance of our research in the field of neurology.

A comprehensive online inspection of scientific search engines was performed, which included MEDLINE (Ovid, PubMed), Google, ProQuest, Scopus, Cochrane Library, Elsevier, Thompson, ISI, Index Medicus, Index Copernicus, and ScienceDirect. The following string of keywords entered into the search engines: [Migraine] and [Therapy] and [Corticosteroid] and [Injection], and [Subcutaneous] with the final search date of March 1, 2014. Surprisingly, no article was found about the therapeutic assessment of subcutaneous corticosteroids in patients with migraine and headache.

In patients with chronic migraine and tension headache, a comparison was made between therapeutic effects of acupuncture and medical treatment. Improvement of 50% with acupuncture and marked improvement of 21.9% in patients was reported.[10] Headache patients with local tender muscular points were more likely to have therapeutic response to acupuncture.[10] Occipital nerve block (ONB) with local anesthetics and injectable steroids has therapeutic effects in patients with cluster headache and migraine.[11] The nerve is usually infiltrated with local injection of anesthetic such as lidocaine and sometimes corticosteroid is added in ONB.[12] ONB is reported as an effective management in patients with cervicogenic headache.[13] Occipital tenderness to palpation or reproduction of headache pain with occipital nerve compression has been used as the selection criteria in performing ONB.[13] Therapeutic assessment of local anesthetics with steroid compared with anesthetic alone for migraine, reported slightly worse results with steroids in a blinded randomized controlled trial.[13]

Parenteral corticosteroids are useful in aborting a prolonged migraine attack called status migrainous.[14] Pathophysiological mechanism of corticosteroids in abortion of migraine pain is through trigeminovascular system.[3] However, subcutaneous corticosteroids injection rarely used for the management of migraine disorder as described above. Local injection of botulinum toxin A has been investigated in clinical trials as the preventive therapy for refractory migraine.[15] A few double-blind placebo controlled trials have provided mixed results regarding botulinum toxin type A efficacy as a preventive agent in patients with frequent migraine attacks.[5]

A clinical assessment of self-acupressure was effective in relieving the pain from migraine and tension headaches in 500 patients.[16] Outpatient prescriptions for analgesics, ergotamine preparations, propranolol, and other drugs could be reduced in patients who underwent auto-acupressure.[15] The popularity of some unconventional therapies suggests either a strong placebo effect or true efficacy.[17] Since pain is a subjective variable, bias information is possible in every research on pain management. Despite lack of research in the therapeutic effects of subcutaneous steroids in migraine, this aspect of management requires more attention.[11]

Conclusion

Subcutaneous injection of methylprednisolone has considerable abortive and preventive therapeutic effects in patients with severe refractory migraine. However, double-blind controlled trials are recommended for more investigations.

Conflict of interest: None declared.

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