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Short Communication

Outpatient treatment of migraine headache, can we use a dexamethasone containing regimen?

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Abstract

BACKGROUND: This research is aimed at determining the efficacy of intravenous dexamethasone and metoclopramide for treatment of acute migraine. Dexamethasone is a well-known drug for treatment of long lasting and recurrent migraine headaches. Metoclopramide is also used singularly or as an adjunct to treat the migraine attacks.

METHODS: In a simple randomized study, patients with acute migraine were administered either intravenous dexamethasone and metoclopramide or intramuscular dihydroergotamine. Headache and concurrent symptoms were rated at baseline and 1, 2, 4 and 24 hours post-injection. .

RESULTS: Analysis of headache severities indicated significant alleviation in both groups with time ($p < 0.001$). Side effects and concurrent symptoms did not show any significant difference between the two studied groups.

CONCLUSIONS: In emergency department, intravenous dexamethasone and metoclopramide may be considered as an effective and available treatment with few side effects especially for patients with long-lasing and intractable migraine attacks; however, it must be used limitedly.

KEYWORDS: Dexamethasone, metoclopramide, dihydroergotamine, migraine.

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Migraine is one of the most common diseases in neurological practice.[1] Migraine can be disabling, particularly when the attacks are severe and repetitive.[2,3] Migraine is common and debilitating and because it has significant comorbidities, migraine treatment is important.[4] Drug therapy for migraine can be divided into preventive and acute treatments.[5,6] Simple analgesics are effective in treating many mild to moderate migraine attacks.[3,7] For more severe attacks, migraine-specific agents, such as triptans, dihydroergotamine, and ergotamine are recommended.[3,6] In fact, if there is no contraindications, triptans are the class of choice.[8] But, many patients with migraine are refractory to these drugs.[9] Besides, about a third of the patients taking triptans experience recurrences before 24 hours.[5,10] Triptans are contraindicated in ischemic heart disease, untreated

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hypertension, pregnancy, lactation and in those taking ergot compounds.[9,11] This is why many other drug protocoles are being introduced to treat acute migrane attacks. Phenothiazines, haloperidol, opioids (like meperidine), intravenous valproate and metoclopramide alone or in conjunction with other agents are effective for acute treatment of migraine attacks.[1,9,12-18] However, prescriptions of some of these medications are limited due to their side effects.[10,12,17-22] Despite all the above-mentioned strategies, reliable acute and/or preventive treatments for most headache types are often lacking.[23-25] Therefore, new, more accessible and effective medications with fewer side effects for migraine management are still needed. Clinical use of corticosteroids (especially dexamethasone) in migraine attacks is a matter of debate in some literature. While most authorities limit its effectiveness to cases of long lasting, recurrent and intractable attacks, [10,12,22,26] some others suggest that it can be administered in a more widely fashion.[16,17,21] However, combination of dexamethasone and metoclopramide is used as an outpatient treatment for acute migraine headaches in some medical centers and many patients and physicians seem to be satisfied with the results. To our knowledge, there are few studies evaluating this regimen for this purpose though they are with different doses and the results are sometimes controversial and probably not generalizable.[26]

Methods

In a simple randomized clinical trial, a total of 51 participants aged 15 to 60 years of age were selected from patients of the Emergency Department (ED) of the Shafa Medical Center, Kerman University of Medical Sciences (Iran). Inclusion criteria were International Headache Society (IHS)-defined migraine with or without aura.[27] The duration of the headache was not more than 72 hours in any of the subjects. Exclusion criteria were cardiac problems, hypertension, pregnancy, lactation and finally, history of taking ergot compounds or triptans during the last 12 hours before referring to ED. None of the patients had known allergies to dihydroergotamine (DHE), dexamethasone or metoclopramide. Patients received a neurological examination and measurement of vital signs and if required, lab tests or brain CT scans to rule out underlying causes or comorbidities. Selected patients randomly (by using table of random numbers) received either intravenous combination of "8-mg dexamethasone and 10-mg metoclopramide" (Dexa /MCP) or 1-mg DHE intramuscularly. Headache severity and associated symptoms, i.e., photophobia, phonophobia, nausea, vomiting, flushing, and/or agitation were noted at 1, 2, 4, and 24 hours post-injection (by telephone if patients were discharged). We used a 4-point verbal rating scale (VRS) to score the headache severity. Other concurrent symptoms were recorded only depending on their presence or absence at the recording time. This research was covered by the Kerman University of Medical Sciences Ethics Committee approval number K/85/55.

Results

Patients were randomly allocated, 28 to the Dexa/MCP group and 23 to the DHE group. Table 1 summarizes the demographic data according to the treatment assignment. Each group was similar in distribution with no statistical differences between the groups in terms of age and sex, localization and duration of headache, or baseline headache characteristics.

Table 1. Patient characteristic.

Feature	DHE group (n=23)	Dexa/MCP group (n=28)
Women	17 (74)*	25 (89)
Men	6 (26)	3 (11)
Mean age [range]	33 [22-44]	35 [24-46]

*Values in the parenthesis are percentage in each sex and medication group.
DHE indicates dihydroergotamine; MCP, metoclopramide; Dexa, dexamethasone.

There were also no significant differences (p value ranging 0.20 to 0.34) between the groups in headache severity before treatment and in 1, 2, 4 and 24 hours after intervention. Since the

headache severity was rated by ordinal scale, using Mann Whitney U test, the headache severities in hours 0, 1, 2, 4 and 24 were compared between the two groups. Results of this analysis showed no significant statistical differences in the two groups. Moreover, the above-mentioned headache severities analyzed by Friedman's test indicated that in both groups significant alleviations in headache severities were obtained with time ($p < 0.001$). Treatment side effects and concurrent symptoms including nausea, vomiting, flushing, agitation, photophobia and phonophobia in the specified time did not show any significant differences between the two studied groups.

Discussion

Our results suggested that intravenous combination of dexamethasone and metoclopramide is as effective as intramuscular DHE for acute treatment of migraine headache ($p < 0.001$). In addition, concurrent symptoms, i.e., nausea, vomiting, photophobia and phonophobia were also significantly reduced. Metoclopramide can alleviate migraine attacks when used alone or in combination with other drugs.[1,26] The accompanying nausea and vomiting can also be reduced by metoclopramide. Friedman and colleagues concluded that there is no significant improvement between dexamethasone group and placebo group for treatment of acute migraine headache. They showed that addition of dexamethasone (to metoclopramide) could be useful in patients with migraine lasting longer than 72 hours.[26] These findings suggested that anti-migraine effect of the combination of dexamethasone and metoclopramide is at least partly due to the effect of metoclopramide. Because more evidence is needed to confirm the efficacy of this regimen, the recommendation to withhold routine administration of dexamethasone for migraine attacks seems logical. Our patients who were treated with intravenous combination of dexamethasone and metoclopramide experienced no side effects except for a transient sense of flushing due to intravenous injection of dexamethasone. This could be reduced efficiently by prolonging the administration time (to about one minute). Metoclopramide may cause agitation that can be very discomforting for the patient but it was not frequent among our patients and could be readily treated with a small dose of intravenous diazepam (2-3 mg slowly). Low rate of significant headache after 24 hours in our patients treated with intravenous combination of dexamethasone and metoclopramide (that is comparable with DHE) confirms the premise that dexamethasone decreases the rate of severe recurrent headache due to its anti-inflammatory property. In some areas (e.g., Iran) accessibility to newer drugs for acute migraine attacks, like triptans, is somehow limited in terms of price and availability. However, dexamethasone and metoclopramide are of modest price, and accessible and can be regarded as an option for some cases of long-lasting and intractable migraine attacks on an outpatient basis (though limitedly). Our study did not achieve a good statistical power due to limited sample size.

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