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## Is Dexamethasone a Suitable Alternative for Dihydroergotamine on Migraine Attacks?

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**Abstract:** This study was conducted to compare the effect of dexamethasone with dihydroergotamine on migraine attacks. A clinical study was carried out on 72 migraineurs, aged 15 to 55 years old. Patients who met the diagnostic criteria for migraine, as defined by the International Headache Society (HIS) were selected from the ones referred to emergency department. Patients received 1 mg dihydroergotamine (DHE) or 4 mg dexamethasone intravenously. Headache intensity was scored based on McGill method on a 1-15 point scale. Data were collected by questionnaires, which were filled on entry, 10 and 30 min after drug injections. The average frequency of migraine attacks was 2.2 per month and the duration of attacks was 12.2 h. The average score of headache intensity in start of study was 12.86. The intensity of headache 10 min after drug injection was less in both DHE and dexamethasone groups compared to the intensity of headache before drug injection ( $p < 0.01$ ). It was the same in both groups 30 min after injection of drugs compared to the intensity, 10 min after injection ( $p < 0.01$ ). There was no difference for intensity of headaches between two groups, 10 or 30 min after injection of DHE or dexamethasone. Twenty patients in DHE groups showed side effects, however, side effects was not seen in dexamethasone group. Therefore, dexamethasone seems to be a suitable alternative for ergot alkaloids in emergency migraine headaches.

**Key words:** Dexamethasone, dihydroergotamine, headache, migraine

### INTRODUCTION

Migraine is a chronic condition with recurrent acute attacks with a wide variety of neurologic and non-neurologic manifestations. It affects 18% of women and 6.5% of men in the United States<sup>[1]</sup>.

Effective long-term management of patients with migraine is challenging because of the complexity of the condition. Experts suggest several goals for successful treatment of acute attacks of migraine. These include treating attacks rapidly and constantly to avoid headache recurrence, to restore the patient's ability to function and to minimize the use of backup and rescue medications<sup>[2]</sup>.

There are no general rules to say how to treat these patients. However, if patients have severe attacks and respond to common analgesics, only abortive therapy is required. On the contrary, frequent, severe and long-lasting attacks demand prophylactic management<sup>[3]</sup>. Commonly used drugs for preventive treatment of migraine are tricyclic antidepressants, beta-blockers, calcium blockers, 5-HT antagonists and some antiepileptics. Commonly used medications for acute treatment of migraine include NSAIDs, opioids, ergot alkaloids, 5-HT<sub>1B/ID</sub> agonists and calcium antagonists<sup>[3,4]</sup>.

It is very tempting for clinicians to use corticosteroids in migraine attacks, despite there being no evidence of any benefit resulting from this type of management. One open retrospective study evaluated the effect of dexamethasone in intractable migraine, but the study had major methodological flaws and its data was not subjected to statistical analysis<sup>[5]</sup>. Two other studies have evaluated the effects of dexamethasone on migraine recurrence, when added to other antimigraine medications<sup>[6,7]</sup>. This study was conducted to compare the effect of dexamethasone with dihydroergotamine on migraine attacks.

### MATERIALS AND METHODS

A clinical study was carried out on 72 migraineurs aged 15 to 55 years old. Patients were selected from the ones having headache, referred to the emergency section of neurology department of Kashani Hospital in Shahrekord.

To be eligible, patients had to meet diagnostic criteria for migraine as defined by the International Headache Society (HIS), i.e. at least 5 headache attacks lasting for 2 to 72 h with at least two of following symptoms: lateralized

headache, pulsing pain of moderate to high intensity, exacerbation by effortful physical activity, nausea or vomiting in addition to photo and phonophobia<sup>[8]</sup>.

Patients with secondary headache and also those with a neurological disorder were excluded. The minimal duration of the disorder had to be one year with at least two attacks having taken place during the last month. Exclusion criteria included last two months trials of medication for migraine prophylaxis, sever medical or psychiatric illness, use of contraceptive pills, analgesic usage and presence of alcohol or drug abuse. Pregnant women and patients having cardiovascular disease were also excluded.

Patients allocated randomly to one of two groups. Group one received 1 mg dihydroergotamine (DHE) and group two 8 mg dexamethasone intravenously (IV). Headache intensity was scored on a 1-15 point scale, with 1 reflecting the less intensity and 15 reflecting the most intensity. Data were collected by questionnaires, which were filled on entry, 10 and 30 min after drug injections, to record the intensity of headaches base on the short form of McGill pain questionnaire<sup>[9]</sup>. The patients or the investigator who was collecting the data were blinded to the injected drugs. Data were analyzed using SPSS package by Mann-Whitney method.  $p < 0.05$  was considered as significant.

### RESULTS

Seventy two patients whose their migraine was diagnosed by HIS criteria completed the study. 26 (74.21%) female and 10 (27.8%) male patients were allocated in each group. The average of frequency of migraine attacks was 12.2 h.

The average score of migraine headache in start of study was 12.86. In DHE group 10 patients had aura and 26 patients had not aura. In dexamethasone group, 10 patients had aura and 27 patients had not aura.

The headache of 42 patients (58.3%) was lateral and of 30 patients (41.7%) bilateral. There were no differences for frequency, duration or intensity of attacks in two groups at the start of the study.

The intensity of headache 10 min after drug injection was less in both DHE and dexamethasone groups compared to the intensity of headache before drug injection (Mann-Whitney test,  $p < 0.01$ ). It was the same in both groups 30 min after injection of drug, compare to the intensity of headache 10 min after injection ( $p < 0.01$ ).

There was no difference for intensity of headaches between two groups 10 or 30 min after injection of DHE or dexamethasone (Table 1).

Table 1: Average of headache scores at different times (t=0, 10 or 30 min) following drug injection

Drugs	Drug injection time (min)		
	0	10	30
Dexamethasone	12.7±1.9	8.6±2.2	4.3±2.6
Dihydroergotamine	12.9±1.6	7.6±2.6	3.3±1.9

$p > 0.05$  between two drug groups (at t=0, 10 or 30)  $p < 0.01$  when the headache scores at t=10 were compared with the scores at t=0 or t=30

26 patients (72.3%) in DHE group showed side effects including chest tightness, hypertension, claudication and vomiting. Side effect was not seen in dexamethasone group.

### DISCUSSION

This study was carried out to compare the acute effects of dexamethasone and dihydroergotamine. Both drugs were effective in aborting migraine attacks. The pathogenesis of migraine or the mechanism involved in antimigraine medications is not clearly understood. An antimigraine drug could raise the threshold to activation of the migraine process either centrally or peripherally. Antimigraine medications could decrease activation of the migraine generators, enhance central antinociception, raise the threshold for spreading depression, or stabilize sensitive migrainous nervous system by changing serotonergic or sympathetic tone<sup>[10]</sup>.

Some have suggested that down regulating the 5-HT<sub>2</sub> receptors or modulating the discharge of serotonergic neurons may be involved in the mechanism action of antimigraine drugs<sup>[11,12]</sup>. Dihydroergotamine is ergot alkaloid. Ergot alkaloids act on several types of receptors. Their effects include agonist, partial agonist and antagonist actions at alpha adrenoreceptors and serotonin receptors and agonist action at central nervous system dopamine receptors. These agents have agonistic activities at 5HT<sub>2</sub> receptors<sup>[13]</sup>.

Ergotamine and related compounds constrict most human blood vessels in a predictable, prolonged and potent manner. While much of the vasoconstriction elicited by ergot alkaloids can be ascribed to partial agonist effects at alpha adrenoreceptors, some may be the result of effects at 5HT receptors. The remarkably specific antimigraine action of the ergot derivatives is thought to be related to their actions on neuronal or vascular serotonin receptors<sup>[14]</sup>.

Some of the above mentioned actions of dihydroergotamine are not related to acute actions of this drug. For example vasoconstriction elicited by dihydroergotamine is responsible for abortion of acute attacks. However, modulating the discharge of

serotonergic neurons and down regulating the 5HT<sub>2</sub> receptor, may be involved in prophylactic activity of this drug<sup>[13]</sup>.

The abortive antimigraine mechanism of dexamethasone remains to elute. Inflammation is a critical factor in migraine genesis<sup>[11]</sup> and dexamethasone is a powerful anti-inflammatory agent. However, it does not seem the abortive effect of dexamethasone to be due to anti-inflammatory action of this drug. Because dexamethasone reduced migraine headache in 10 min, however its anti-inflammatory action does not appear during this time.

It is not known whether immunosuppressive activity of dexamethasone play any role in antimigraine activity of this medication or not. Some immunosuppressive agents such as cyclosporine, tacrolimus and muromonab-CD3 are known to precipitate headache<sup>[15]</sup>. Therefore, antimigraine activity of dexamethasone should not be due to immunosuppressive activity of this agent.

As it was mentioned dexamethasone demonstrated antimigraine activity the same as dihydroergotamine in acute migraine headache. Dihydroergotamine is contraindicated in pregnancy, peripheral vascular disease, hepatic or renal impairment, coronary artery disease, sepsis and uncontrolled hypertension. This study, showed some adverse effects, but no adverse effect was seen in dexamethasone group. Therefore, dexamethasone seems to be a suitable alternative for ergot alkaloids in emergency migraine headaches.

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