

## Efficacy of intravenous Dexamethasone in treatment of acute migraine headache: A randomized clinical trial running title

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### Abstract

**Introduction:** Migraine is characterized by unilateral and pulsatile headache with or without aura. There are various treatments of migraine attack. One of them is intravenous (IV) Corticosteroids which is used in status migrainous. The aim of this study is comparison of the efficacy of I.V Dexamethasone with intramuscular (I.M) Methadone in improvement of migraine attacks.

**Materials and Methods:** This study was a controlled double- blind randomized clinical trial on all patients whom referred to emergency room with diagnosis of migraine attack. The patients were randomized in four groups. Groups I and II received intravenous 8 mg Dexamethasone, while groups III and IV received intramuscular 10 mg Methadone. Thereafter all of them were evaluated after 2, 4 and 6 hours.

**Results:** One-hundred and eighty one patients were evaluated; 107 patients were treated with IV Dexamethasone and 74 patients with IM Methadone. One-hundred and three of 107 patients (96.2%) had complete or significant improvement whereas 63 of 74 patients (85%) whom received IM Methadone had similar improvement (P= 0.01).

**Conclusion:** Our study showed that treatment of acute migraine headache by using intravenous Dexamethasone is more effective than Methadone.

**Key words:** Dexamethasone, Migraine, Treatment.

### Introduction

Migraine is one of the most common causes of headache. It's prevalence in Caucasians is 4 to 6 percent in men and 13 to 18 percent in women (1). Several drugs such as Ergotamine, Dihydroergotamine, Sumatriptan, sedatives and narcotics are used for subsiding the acute migraine headache.

There are some problems such as high cost, paraesthesia, drug dependence, need for cardiac and blood pressure monitoring, nausea and vomiting in use of these drugs. Ergo derivatives and Triptans are contraindicated in patients with ischemic heart disease, uncontrolled hypertension, and pregnancy (1-3).

One of the therapeutic methods used for resistant migraine attacks (status migrainous) is parenteral corticosteroids (1-5), this drug reduces the sterile Inflammation of extracranial vessels, (extracranial vasodilatation and also strile

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Acceptation date: 86/7/2

Confirmation date: 1386/11/14

inflammation could be most probable factors causing pain in migraine attacks ) Dexamethasone is prescribed for severe migraine attacks without harmful effects even if used as high single dose (3). Dexamethasone is an easily available and cheap drug. There are some evidences that the effects of glucose administration on alleviation of pain are comparable to narcotic drugs in children especially in newborns (6).

This clinical trial is designed for evaluation of the efficacy of IV Dexamethasone with and without Dextrose water serum 5% (DW5%) on recovery of the acute attacks of migraine headache and comparing it with Methadone.

### Materials and Methods

This study was a randomized double-blind clinical trial. We included all of the patients with severe (grade 3,4) migraine headache whom referred to neurologic emergency division of the Ghaem hospital, Mashhad from January 2001 to June 2004. This study was approved by ethic committee of research deputy of Mashhad University of Medical Sciences. The research protocol was explained to patients and their relatives. Patients who did not signed the informed consent were excluded. The diagnosis of migraine headache was made based on criteria developed by International Headache Society (IHS) (7).

The scoring system for evaluation of the severity of headache was defined as (8): Grade 1- Without headache; Grade. 2- Mild and tolerable headache without work dysfunction and sleep disturbance; Grade. 3- Moderate headache with some work dysfunction and sleep disturbance; Grade 4- Severe headache with complete work dysfunction and inability to sleep. Addiction to the narcotics, age less than 14, and pregnancy were considered as exclusion criteria. After obtaining informed consent the demographic data, duration and frequency of previous attacks, the present symptoms, drug history and physical examination were recorded. The patients were randomized in four groups by lotting:

Group 1(D): 8 mg IV dexamethasone with 10 mg IV Metoclopramide (regimen 1). Group 2(DDW): 8 mg IV dexamethasone with 10 mg

IV Metoclopramide with 500 ml D/W 5% (equivalent to 2 cc/kg serum D/W 20%) during 2 hours (regimen 2) (6).

Group 3(MDW): 10 mg IM Methadone with 10 mg IV Metoclopramide with 500 ml D/W 5% during 2 hours (regimen 3).

Group 4(M): 10 mg IM Methadone with 10 mg IV Metoclopramide (regimen 4).

One regimen was selected randomly by lotting for each patient. Therefore during this study, 42 patients were treated with first regime, 65 patients with second, 37 patients with third and 37 patients with fourth regime.

Patients did not know about their therapies. They were regularly visited by another physician every 2 hours who blinded to the treatment regimen. We discharged our patients when the severity of their headache decreased to grade 1 or 2, we regarded it as improvement and if the severity of their headache remained at grade 3 or 4 we regarded it as unimprovement and they were controlled for another 2 hours. We reassessed the patients' complaints after improvement of headache or six hours of admission.

Statistically analysis: We used Chi square test for qualitative variables, for quantitative variables, at first after being normal distribution with Kolmogorov-Smirnov test, we used t-test and one-way ANOVA.

### Results

Four hundred and eighty nine patients with headache were referred to the emergency room during this study period. Two hundred and thirty two out of them had attack of migraine. Fifty-one were excluded; 22 out of patients were under 14 years old; 17 were treated with narcotic drugs before arrival to emergency room; 12 were pregnant. Finally 181 (135 women and 46 men) patients were entered into this study. The mean age was  $35.5 \pm 3.48$  years. One hundred and forty eight out of 181 patients had common type of migraine and the remainders were of classic type. They came to the emergency room with mean time  $22.6 \pm 3.09$  hours after onset of their headache.

Forty two patients were treated with first regimen (D) and 65, 37 and 37 patients were treated with second (DDW), third (MDW) and

fourth (M) regimes respectively. There was no significant difference between four groups as regarded to age, gender, type of migraine, duration of disease (year), number of attacks in a month, duration of attacks (previous) and the

mean time of onset of headache before starting treatment (current), drugs, and also in associated present symptoms and signs including nausea, vomiting, phonophobia, photophobia, vertigo, sweating, hypotension (BP < 90/60 ) (Table 1).

**Table.1:** Comparison of the characteristics and the type of drug consumption of the patients (n=181) at baseline between different groups

Characteristics and drugs	Regimen D (n=42)	Regimen DDW (n=65)	Regimen MDW (n=37)	Regimen M (n=37)	P value
Mean age	36.58 ± 3.48	35.93 ± 2.50	35.47 ± 3.53	34.05 ± 3.13	0.7402
Women/Men	31.11	47.18	31.6	26.11	0.5562
Mean number of attacks in a month	3.06 ± 0.74	3.14 ± 0.73	3.57 ± 0.83	2.52 ± 0.72	0.4000
Mean duration of current attack (hr.)	19.96 ± 5.92	27.3 ± 5.68	19.21 ± 6.52	21.18 ± 6.18	0.1619
Common/ Classic migraine	34.8	52.13	30.7	32.5	0.8687
Non opium sedative consumption	24	41	25	23	0.8183
Ergotamine consumption	3	7	3	2	0.8000
Oral contraceptive consumption	3	9	5	6	0.6412
Anti depressant consumption	10	14	9	5	0.6352

Regimen D: Dexamethasone +Metoclopramide  
Regimen MDW: Methadone + Metoclopramide + Serum D/W5%

Regimen DDW: Dexamethasone +Metoclopramide +Serum D/W5%  
Regimen M: Methadone + Metoclopramide

There was statistically significant difference between regimens consisting of Dexamethasone (i.e. regimens D and DDW) and those consisting of Methadone (i.e. regimens MDW and M) in improving acute attack of migraine headache after first two hours of therapy (p<0.05), and after six hours (p=0.01). Unresponsiveness to the treatment in later groups was two times more than the other groups (regimens D and DDW) after first 2 hours and four times after 6 hours. Patients who treated with Dexamethasone and Metoclopramide

(Regimen D) had better response in comparison to patients who treated with methadone and Metoclopramide (Regimen M) after two and six hours of treatment (p<0.05).

There was no significant difference in rate of remission after 6 hours between group D and group MDW (p>0.05). D/W 5% did not result in statistically significant difference in the rate of improvement of headache after two hours in different groups (Table 2).

**Table-2:** The rate of improvement of headache according to the regimens and the time of evaluation in patients with acute migraine headache

Therapeutic regimen	After 2 hours	After 6 hours
D and DDW (n=107)	94 (87.9%)	103 (96.3%)
MDW and M (n=74)	53 (71.6%)	63 (85.1%)
p value	0.0106	0.0166
D (n=42)	40 (95.2%)	42 (100%)
DDW (n=65)	54 (83.1%)	61 (93.8%)
P value	0.1147	0.2641
D (n=42)	40 (95.2%)	42 (100%)
MDW (n=37)	28 (75.7%)	35 (94.6%)
P value	0.0292	0.4188
D (n=42)	40 (95.2%)	42 (100%)
M (n=37)	25 (67.6%)	28 (75.7%)
P value	0.0035	0.0024
DDW(n=65)	54(83.1%)	61(93.8%)
MDW(n=37)	28(75.7%)	35(94.5%)
p value	1	0.5184

Regimen D: Dexamethasone +Metoclopramide      Regimen DDW: Dexamethasone +Metoclopramide +Serum D/W5%  
Regimen MDW: Methadone + Metoclopramide + Serum D/W5%      Regimen M: Methadone + Metoclopramide

The rate of improvement of headache didn't show significant relation to age, gender, type of migraine, duration of disease, number of attacks in a month, duration of attacks, drugs, and associated presenting signs and symptoms of headache and the rate of improvement of the associated signs and symptoms after improvement of headache had no significant difference in four groups also.

### Discussion

Sixty to seventy percent of patients with migraine have moderate to severe headache and 25 to 35% of them are unable to work adequately after onset of headache and this continues for 1 to 2 days after attack. There are different therapeutic agents advised for management of acute attack (1).

In 2002 Jason and Germy (8) found that IV Dexamethasone is more effective than Pethidine for controlling acute migraine headache. They used Pethidine plus Promethazine and Dexamethasone for acute migraine attack and studied the effect of IV Dexamethasone versus Pethidine in the treatment of acute migraine. In this research some important points did not considered, including: the patients characteristics such as sex, age, psychological character, and finally methods of using for therapeutic agents. We used 10 mg of intramuscular Methadone, because it is more available than Pethidine. Our standards for diagnosis and severity of migraine were similar to Jason's standard but we considered age, sex, drug consumption and other mentioned characteristics. Acute migraine will disappear in 90% of patient treated with injection of Dihydroergotamine and in 70-75% of patients with oral ergo derivatives only if it is administered early in the course of headache (1,2,9). Triptans can be effective even after beginning of severe migraine although their effect is less and it is better to use them early in acute attack (9, 10). Therapeutic response to Sumatriptan is 70% when administered very soon (3). We found that the rate of response to Dexamethasone is comparable to the therapeutic effects of many drugs that are commonly used

for treatment of severe migraine headache. Headache alleviated in 96.2% of our patients whom treated with Dexamethasone.

99 percent of them had remission in the first 2 hours of admission. With consideration of the mean time of starting treatment after onset of headache ( $22.6 \pm 20.8$  hours), it seems that Dexamethasone is effective even after several hours of attack, while triptans and ergot alkaloids are effective only if they are administered in early phase of acute migraine headache. IV Dexamethasone is a cheap and available drug without side effects in single dose and can be used with high rate of success. In this study Dexamethasone was more effective than Methadone because there was significant difference between regimens D and M. The Metoclopramide was common between two regimens so this demonstrates the obvious difference between therapeutic effects of Dexamethasone and Methadone in relieving of migraine attack.

There are some evidences that the effects of glucose administration on alleviation of pain are comparable to the narcotic drugs (6). As noted in table 2, it seems that adding D/W5% to the Dexamethasone or Methadone has no important role in relief of acute migraine headache. With improvement of headache, associated presenting symptoms and signs including nausea, vomiting, vertigo, phonophobia, photophobia, sweating, hypotension (BP < 90/60), were relieved in almost all patients. In 5 patients of regimes MDW and M whom headache did not alleviate even after 6 hours we tried IV Dexamethasone for them and headache was alleviated during 2 hours. After 6 hours, we had 7 patients of regime DDW who did not show any improvement of headache, after administration of methadone 6 of them unimproved. Thus it seems if no other drug could alleviate acute attack of migraine, Dexamethasone can be used for treatment.

### Conclusion

This clinical trial showed that Dexamethasone is more effective than Methadone for treatment of acute attack of migraine and efficacy of this treatment is comparable to the other form of migraine managements and also it is an effective drug even if patients are treated lately.

### Acknowledgement

This research was supported by Research Committee of Mashhad University of Medical Sciences. We thank all of the staffs in emergency department of Ghaem particularly.

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### خلاصه

## مطالعه بالینی اثرات دگزامتازون وریدی در درمان حملات سردرد میگرنی

دکتر محسن فروغی پور، دکتر پیمان پدرامفر، دکتر مرتضی سعیدی، دکتر محمد علی اکبرنژاد، دکتر سعید ابراهیم زاده

**مقدمه:** میگرن با سردردهای یک طرفه ضرباندار با یا بدون aura مشخص می شود. روش های درمانی متعددی برای حملات حاد میگرنی وجود دارد، که یکی از آن ها استفاده از کورتیکواستروئید های وریدی است که در درمان حملات مداوم میگرن استفاده می شود. هدف از این مطالعه، بررسی و مقایسه اثرات دگزامتازون وریدی با متادون داخل عضلانی در بهبود حملات سردرد میگرنی است.

**روش کار:** این بررسی یک مطالعه تصادفی دوسویه کور، بر روی بیمارانی بوده است که با تشخیص حمله میگرنی حاد به بخش اورژانس اعصاب مراجعه می نمودند. بیماران به صورت تصادفی در ۴ گروه قرار می گرفتند. بیماران گروه های ۱ و ۲ به میزان ۸ میلی گرم دگزامتازون وریدی دریافت می کردند و به بیماران گروه های ۳ و ۴ به میزان ۱۰ میلی گرم متادون عضلانی تزریق می شد و سپس همه بیماران ۲ و ۴ و ۶ ساعت بعد از تزریق مورد بررسی قرار می گرفتند.

**نتایج:** در مجموع ۱۸۱ بیمار مورد بررسی قرار گرفتند. ۱۰۷ نفر آن ها با دگزامتازون وریدی درمان شده و به ۷۴ نفر متادون عضلانی تزریق شد. از گروه اول ۱۰۳ نفر (۹۶/۲٪) بهبودی کامل و یا قابل توجه داشته اند در حالی که از گروه دوم ۶۳ نفر (۸۵٪) به میزان مشابهی بهبودی را نشان داده اند (p=۰/۰۱).

**نتیجه گیری:** این مطالعه نشان می دهد که در درمان حملات حاد میگرنی استفاده از دگزامتازون وریدی از متادون موثرتر است.

**واژه های کلیدی:** دگزامتازون، میگرن، درمان