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A comparative study between Nifedipine and magnesium sulfate for treatment of preterm labor

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ABSTRACT

Aim: A comparative study between Nifedipine and magnesium sulfate for treatment of preterm labor.

Methods: Eligible women with preterm labor between 24-37 week gestations were selected for the study. Nulliparous and multiparous pregnancies with intact membranes, showing clinical signs of preterm labor were included in this study. The diagnosis of preterm labor is based on the presence of 4 uterine contractions or more over 30 minutes, each lasting at least 30 seconds, and documented cervical change (dilatation of 0-4 cm and effacement of at least 50%).

Results: 5 patients (5%) after 24 hours, 9 patients (9%) after 48 hours, 7 patients (7%) after 72 hours and 54 patients (54%) after 7 days had delivery in the nifedipine group and 11 patients (11%) after 24 hours, 5 patients (5%) after 48 hours, 5 patients (5%) after 72 hours and 62 patients (62%) after 7 days had delivery in the magnesium sulfate group. This characteristic was not statistically different between the two groups. In this study, 28 patients (28%) in nifedipine group and 14 patient (14%) in magnesium sulfate group had a failure treatment (contractions did not subside) and needed to take other tocolytic medications. This characteristic was also not statistically different between the two groups.

Conclusion: we concluded that the oral nifedipine is a suitable alternative for magnesium sulfate with the same efficacy and side effects in the management of preterm labor.

Keywords: Nifedipine, Magnesium sulfate, preterm labor

Introduction

The incidence of preterm birth is 9% - 13% of births.[1]Tocolytic agents such as beta mimetics, calcium channel blockers, oxytocin receptor antagonists, and magnesium sulfate ($MgSO_4$) are used to suppress preterm labor.[2,3] The first-line tocolytic drug in North America is $MgSO_4$.[4,5] But in European countries, $MgSO_4$ is seldom used for tocolysis.[6]Crowther in a systematic review in 2014 de- clared that $MgSO_4$ administration did not result in a statistical reduction in birth < 48 hours.[7] In addition, $MgSO_4$ may be associated with an increase in maternal and neonatal adverse effects.[8,9] $MgSO_4$ is recommended as a neuroprotective drug for the neonate < 32 weeks.[10-12] Nifedipine as a calcium channel blocker is one of the best drugs for inhibition of preterm labor. Ease of administra- tion, maternal tolerance, low neonatal mortality and respiratory distress syndrome, and low maternal adverse effects are the advantages of nifedipine.[13]Flenady in a systematic review in 2014 claimed that calcium channel blockers reduce the risk of delivery within 48 hours without any serious neonatal morbidity and maternal adverse effects.[1]Nifedipineis vasodilator and it may cause nausea,

flushing, headache, dizziness, palpitations, and transient hypotension.[13] An optimal nifedipine dosing regimen for treat- ment of preterm labor has not been yet established. The American College of Obstetricians and Gynecologists suggests a 30 mg loading dose and then 10 to 20 mg every 4 to 6 hours.[14]

Material and methods

This prospective observational study was carried out after taking the approval of the protocol review committee and institutional ethics committee. Eligible women with preterm labor between 24-37 week gestations were selected for the study.

Inclusion criteria were nulliparous and multiparous pregnancies with intact membranes, showing clinical signs of preterm labor. The diagnosis of preterm labor is based on the presence of 4 uterine contractions or more over 30 minutes, each lasting at least 30 seconds, and documented cervical change (dilatation of 0-4 cm and effacement of at least 50%).[15]

Exclusions criteria were women with clinical intrauterine infection, cervical dilatation >5 cm, medical complications with tocolysis like severe preeclampsia, lethal fetal anomalies, chorioamnionitis, significant antepartum hemorrhage, maternal cardiac or liver diseases ,and evidence of no reassuring fetal status.

Methodology

In this study 200 preterm women between 24-37 week gestations were randomly selected. In the first step all patients were hydrated by 500 ml of Ringer solutions and bed rest. Patients with gestational age lower than 34 weak took dexamethasone for fetal lung maturity. Patients were selected randomly to receive either oral nifedipine or intravenous magnesium sulfate. Nifedipinetocolysis was initiated with a 10 mg capsule which was repeated every 20 min (up to a maximal dose of 30 mg during the first hour of treatment) and then nifedipine maintenance dose was 10 mg every six hours. Tocolysis with magnesium sulfate was initiated with 10g (I.V) and then 5g (I.M) every 4 hours. In all patients, fetal heart rate, blood pressure, pulse rate, and uterine contractions were recorded.

All patients were checked for successful prolongation of pregnancy who had not been delivered at 48 hours (primary tocolytic effects) and at more than 7days (secondary tocolytic effects) after beginning the treatment and side effects of tocolysis. Side effects were assessed with particular emphasis on hypotension, tachycardia, palpitation, flushing, headaches, dizziness, and nausea related to nifedipine side effects; and flushing, nausea, headache, drowsiness, blurred vision and respiratory and motor depression of the neonate related to magnesium sulfate side effects. If contractions did not subside, other tocolytic medication, such as isoxsuprine or indomethacin, was added (treatment failure).

Statistical analysis

A statistical analysis program (SPSS version25.0) was used for data analysis. All characteristics and outcome variables were evaluated with percentage of them. Differences between groups analyzed by using the Mann-Whitney U test, the unpaired t student test.

Results

To evaluate the efficacy and safety of magnesium sulfate and nifedipine (Adalat), a total of 200 women were enrolled; 100 patients were randomly assigned to the nifedipine group and 100 were randomly assigned to the magnesium sulfate group. The baseline characteristics such as maternal age, parous, gestation age, prior preterm birth, abortion, twin gestations, urinary infection and hemoglobin were checked in both groups. There were no statistically

significant differences between them. (Table 1). On the other hand, the main outcome variables such as days gain in utero, success rate and side effects were examined in the two groups. 5 patients (5%) after 24 hours, 9 patients (9%) after 48 hours, 7 patients (7%) after 72 hours and 54 patients (54%) after 7 days had delivery in the nifedipine group and 11 patients (11%) after 24 hours, 5 patients (5%) after 48 hours, 5 patients (5%) after 72 hours and 62 patients (62%) after 7 days had delivery in the magnesium sulfate group. This characteristic was not statistically different between the two groups. In this study, 28 patients (28%) in nifedipine group and 14 patient (14%) in magnesium sulfate group had a failure treatment (contractions did not subside) and needed to take other tocolytic medications. This characteristic was also not statistically different between the two groups (Table II).
7 patients (7%) in the nifedipine group had severe hypotension and 3 patient (3%) in the magnesium sulphate group had severe flushing. These side effects caused drug discontinuation. Patients in the nifedipine group and magnesium sulfate group had the general side effects: 7 cases (7%) of headache and 3 case (3%) of flushing, respectively. All of obstetric characteristics were also not statistically different (Table II).

Table.1 Maternal and preterm labor characteristics

	Nifedipine N (%)	**Magnesium sulfate N (%)**	**p-value**
Maternal age (years)			
<18	4 (9)	2 (5)	0.53
18-40	43 (84)	46 (90)	0.52
>40	3 (7)	2 (5)	0.56
Primiparous	27 (53)	24 (49)	0.52
Multiparous	23 (47)	26 (51)	0.52
Gestational age			
<34	31 (61)	29 (57)	0.52
>34	19 (39)	21 (43)	0.52
Prior preterm birth	5 (5)	3 (3)	0.56
Abortion	9 (9)	13 (13)	0.53
Twin gestations	5 (5)	3 (3)	0.59
UTI	15 (15)	11 (11)	0.51
Hb			
<10 mg/dl	9 (9)	7 (7)	0.55
<11mg/dl	13 (13)	11 (11)	0.54

Table. 2 Obstetric characteristics

	Nifedipine N (%)	**Magnesium sulfate N (%)**	**p-value**
Delivery			
After 24h	5 (5)	11 (11)	0.47
After 48h	9 (9)	5 (5)	0.50
After 72h	7 (7)	5 (5)	0.53
After 7 days	54 (54)	62 (62)	0.51
Treatment failure	18 (18)	14(14)	0.50
Severe side effect	7 (7)	3 (3)	0.43

Discussion

Preterm labor is a common obstetric problem that in it delivery occurs between 24 and 37 weeks before completed gestation. Prevention and treatment of preterm labor are important by reducing adverse events for the neonate. A wide range of tocolytics have been tried, but obstetricians still do not have an ideal drug available. However magnesium sulfate is the most widely used tocolytic, an effective role of it has never been established. Nifedipine is an effective and rather safe alternative tocolytic agent for management of preterm labor. We undertook this study to compare the efficacy and safety of magnesium sulfate and nifedipine in the management of preterm labor.

In this study, 9% if patients in nifedipine group and 5% of patients in magnesium sulfate group delivered in the first 48 hours. There was no significant difference between two groups. 54% of patients in the nifedipine group and 62% of patients in the magnesium sulfate group delivery for more than 7 days. This characteristic was also not statistically different between two groups. These results have been shown by other studies. In a randomized study, one hundred ninety-two patients were enrolled. This study showed there were no differences in delivery within 48 hours in two groups.[16]Another study showed two groups postponed delivery for more than 48 hours.[17] In our study, in 7% of patients in the nifedipine group and 3% of patients in the magnesium sulfate group, therapy was discontinued because of severe side effects like hypotension and flushing. These obstetric characteristics were not statistically different. On the other hand, 18% and 14% patients in the nifedipine and magnesium sulfate group had a failure treatment because contractions did not subside and needed to take other tocolytic medications. This characteristic was also not statistically different between two groups. The same results were also obtained from the other study.[17]In a study, nifedipine compared with magnesium sulfate and ritodrine hydrochloride in the management of preterm labor. They concluded that side effects were much more in the magnesium sulfate and ritodrine group than the nifedipine group and nifedipine is an effective, safe, and well-tolerated tocolytic agent.[18]In another study, Larmon and colleagues compared oral nicardipine (closely related to nifedipine) and magnesium sulfate in acute therapy for preterm labor. They showed there was a significant decrease in the time to uterine quiescence in the nicardipine group. Patients in the magnesium sulfate group had more side-effects in the form of nausea and vomiting and they were more likely to have another tocolytic agent.[19] Several investigators demonstrated that nifedipine treatment did not influence either fetal or uteroplacental circulation.[20,21] It is generally considered to be safe for both mother and fetus and it reduces respiratory distress syndrome, necrotizing enter colitis and intraventricular hemorrhages. The direct maternal adverse effects are related to the vasodilatation caused by nifedipine and are primarily headache and facial flushes. Generally, these complaints disappear within 24 hours.

On the other hand, other factors that have contributed to the growing interest in nifedipine as a tocolytic are the availability of a wide range of immediately acting and extended-release preparations for oral use and the fact that it is very cheap. Magnesium must be used by only the infusion route and requires special monitoring and close observation. Patients taking magnesium sulfate should be monitored for toxic side effects such as respiratory depression or even cardiac arrest. Magnesium crosses the placenta and can cause respiratory and motor depression of the neonate. Moreover, Grimes and colleagues showed that the risk of total pediatric mortality was significantly higher for infants exposed to magnesium sulfate and it should not be used for tocolysis.

Conclusion

We concluded that the oral nifedipine is a suitable alternative for magnesium sulfate with the same efficacy and side effects in the management of preterm labor.

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