Nifedipine and Magnesium Sulfate: A Comparative Study 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: In this study 100 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. Nifedipine tocolysis 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.

Results: 2 patients (4%) after 24 hours, 5 patients (10%) after 48 hours, 4 patients (8%) after 72 hours and 26 patients (52%) after 7 days had delivery in the nifedipine group and 6 patients (12%) after 24 hours, 6 patients (6%) after 48 hours, 3patients (6%) after 72 hours and 29 patients (58%) after 7 days had delivery in the magnesium sulfate group. This characteristic was not statistically different between the two groups. In this study, 9 patients (18%) in nifedipine group and 6 patient (12%) 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 preterm birth rate continues to in- crease, complicating 12.3% of births in the United States1 and contributing substantially to neo- natal morbidity and mortality, deliveries due to spontaneous preterm birth and preterm premature rupture of the membranes (PROM) have declined among singletons.2 Between 1989 and 2000 spontaneous preterm birth and premature delivery after preterm PROM each declined 0.4% among singletons. The increasing rate of preterm birth has resulted in part from an increase in preterm delivery for medical indications2 and an increase in multiple gestations. Neonatal outcomes have improved at all gestational ages due in part to antenatal steroid administration, which may be enabled by tocolytic agents, and improvements in neonatal care. The cost of preterm birth remains substantial, estimated to be at least $26.2 billion, $51,600 per preterm infant, in the

United States in 2005.3 Tocolytic agents are used to inhibit uterine contractions and delay delivery. Ideally, tocolytics should minimize maternal morbidity while delaying delivery during the administration of antenatal steroids. Magnesium sulfate is the most commonly used first-line tocolytic in North America4,5 although it has not been demonstrated to be superior to saline infusion,6 and its use has been a source of controversy.7 Magnesium sulfate requires intravenous administration, has potential for overmedication8 with serious maternal ad- verse effects7,9 and may be associated with adverse neonatal effects.7,10,11 When compared with betamimetics, magnesium sulfate seems to offer a better maternal safety profile.12 Nifedipine may be more easily tolerated, is administered orally, and appears to have few adverse effects,9 although severe dyspnea, hypoxia, and myocardial infarction have been re- ported among pregnant women,13 as has fetal death.14 When compared with betamimetics, nifedipine has been associated with fewer adverse reactions, prolonged gestation, and better neonatal out- comes.14

Material and methods

This prospective observational study was carried out in the Department of Obstetrics and Gynaecology, 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.

All the patients 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] were included in this study. Patients 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 were excluded from this study.

Methodology

In this study 100 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. Nifedipine tocolysis 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.

Statistical analysis

A statistical analysis program (SPSS version24.0) was used for data analysis.

Results

To evaluate the efficacy and safety of magnesium sulfate and nifedipine (Adalat), a total of 100 women were enrolled; 50 patients were randomly assigned to the nifedipine group and 50 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 diff erences between them. (Table 1 and table 2.). 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. 2 patients (4%) after 24 hours, 5 patients (10%) after 48 hours, 4 patients (8%) after 72 hours and 26 patients (52%) after 7 days had delivery in the nifedipine group and 6 patients (12%) after 24 hours, 6 patients (6%) after 48 hours, 3patients (6%) after 72 hours and 29 patients (58%) after 7 days had delivery in the magnesium sulfate group. This characteristic was not statistically different between the two groups. In this study, 9 patients (18%) in nifedipine group and 6 patient (12%) 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 3).

Table.1 Age distribution

	Nifedipine N (%)=50	**Magnesium sulfate N (%)=50**	**p-value**
Maternal age (years)			
Below 20	4 (8)	2 (4)	0.65
20-35	43 (86)	46 (92)	0.64
Above 35	3 (6)	2 (4)	0.68

Table 2.Gestational age of the patients

Gestational age	**Nifedipine N (%)**	**Magnesium sulfate N (%)**	**p-value**
<34	30 (60)	28 (56)	0.64
>34	20 (40)	22 (44)	0.64

Table. 3 Obstetric parameter

	Nifedipine N (%)	**Magnesium sulfate N (%)**	**p-value**
Delivery			
After 24h	2 (4)	6 (12)	0.48
After 48h	5 (10)	3 (6)	0.51
After 72h	4 (8)	3 (6)	0.54
After 7 days	26 (52)	29 (58)	0.52

Treatment failure	9 (18)	6(12)	0.51
Severe side effect	4 (8)	3 (6)	0.44

Discussion

Based on our search of the PubMed, English-language literature from 1980 to 2007, using the key words "magnesium sulfate," "nifedipine," "preterm labor," and "tocolysis," this is the largest randomized study comparing magnesium sulfate and nifedipine. 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, 10% if patients in nifedipine group and 6% of patients in magnesium sulfate group delivered in the first 48 hours. There was no significant difference between two groups. 52% of patients in the nifedipine group and 58% 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 8% of patients in the nifedipine group and 4% 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 12% 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.

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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