Original Research Article

The Effect of Nifedipine versus Magnesium Sulfate in preterm labor: A randomized clinical trial

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Abstract

Aim: The aim of this study to evaluate the effect of Nifedipine versus Magnesium Sulfate in preterm labor. **Methods:** 120 women with preterm labor between 24-37 week gestations were include in this study. 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. **Results:** Total of 120 women were included ; 60 patients were randomly assigned to the nifedipine group and 60 were randomly assigned to the magnesium sulfate group. 3 patients (5%) after 24 hours, 5 patients (8.33%) after 48 hours, 4 patients (6.67%) after 72 hours and 33patients (55%) after 7 days had delivery in the nifedipine group and 6 patients (10%) after 24 hours, 3 patients (5%) after 48 hours, 3 patients (5%) after 72 hours and 37 patients (61.67%) after 7 days had delivery in the magnesium sulfate group. This characteristic was not statistically different between the two groups. In this study, 11 patients (23.33%) in nifedipine group and 9patient (15%) 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.4 patients (6.67%) in the nifedipine group had severe hypotension and 2 patient (3.33%) 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: 5 cases (8.33%) of headache and 2 case (3.33%) of flushing, respectively. All of obstetric characteristics were also not statistically different. **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: Labour,preterm,contractions

Introduction

Preterm labour is defined as regular contractions of the uterus resulting in changes in the cervix that start before 37 weeks of pregnancy. Changes in the cervix include effacement and dilatation. When birth occurs between 20 weeks of pregnancy and 37 weeks of pregnancy it is called preterm birth[1]. Factors that increase the risk of preterm birth include the following: a previous preterm birth, short cervix, short interval between pregnancies, previous surgery on the cervix or the uterus, pregnancy complications such as multiple pregnancy and vaginal bleeding, low pregnancy weight, smoking during pregnancy and drug abuse during pregnancy[1].The risk of neonatal mortality and morbidity is low after 34 weeks of gestation; although a trial of acute tocolysis may be initiated; aggressive tocolytic therapy is generally not recommended beyond 34 weeks, due to potential maternal complications[2]. Between 24 and 33 weeks' gestation, benefits of tocolytic therapy are generally accepted to outweigh the risk of maternal and/or fetal complications and these agents should be initiated provided no contraindications exist. The administration of steroids is recommended in the absence of clinical infection whenever the gestational age is between 24 and 34 weeks. An attempt should be made to delay delivery for a minimum of 12 hours to obtain the maximum benefits of antenatal steroids. However, a randomized clinical trial by Porto *et al.* showed that treatment with corticosteroids at 34 - 36 weeks of pregnancy does not reduce the incidence of respiratory disorders in newborn infants[3].

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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 America[4,5] although it has not been demonstrated to be superior to saline infusion and its use has been a source of controversy[6,7]. Magnesium sulfate requires intravenous administration, has potential for overmedication[8] with serious maternal adverse effects7,9 and may be associated with adverse neonatal effects[7]. When compared with betamimetics, magnesium sulfate seems to offer a better maternal safety profile. Nifedipine may be more easily tolerated, is administered orally, and appears to have few adverse effects, although severe dyspnea, hypoxia, and myocardial infarction have been reported among pregnant women, as has fetal death. When compared with betamimetics, nifedipine has been associated with fewer adverse reactions, prolonged gestation, and better neonatal outcomes[9,10]. The aim of this study is to compare the effectiveness of magnesium sulfate and nifedipine in the management of patients admitted with the diagnosis of preterm labor.

Material and methods

The randomized clinical trial study was conducted in the Department of Gynaecology from June 2020 to May 2021, after taking the approval of the protocol review committee and institutional ethics committee. 120 women with preterm labor between 24-37 week gestations were include in this study.

Inclusion criteria

- Nulliparous and multiparous pregnancies with intact membranes
- Women showing clinical signs of preterm labor

Exclusion criteria

- 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

In this study 120 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. If contractions did not subside, other tocolytic medication, such as isoxsuprine or indomethacin, was added (treatment failure).

Statistical analysis

A statistical analysis program (SPSS version21.0) 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 ,Total of 120 women were included ; 60 patients were randomly assigned to the nifedipine group and 60 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.

Table 1. Maternal and preterm labor characteristics

	Nifedipine N (%)	%	Magnesium sulfate N (%)	%	p-value
Maternal age (years)					
<18	6	10	3	5	0.57
18-40	50	83.33	54	90	0.52
>40	4	6.67	3	5	0.56
Primiparous	33	55	28	46.67	0.52
Multiparous	27	45	32	53.33	0.52
Gestational age					
<34	38	63.33	35	58.33	0.50
>34	22	36.67	25	41.67	0.53
Prior preterm birth	3	5	2	3.33	0.57
Abortion	5	8.33	6	10	0.52
Twin gestations	3	5	2	3.33	0.59
UTI	9	15	7	11.67	0.53
Hb					
<10 mg/dl	6	10	4	6.67	0.55
<11mg/dl	7	11.67	6	10	0.54

UTI: urinary tube infection., Hb: hemoglobin.

3 patients (5%) after 24 hours, 5 patients (8.33%) after 48 hours, 4 patients (6.67%) after 72 hours and 33patients (55%) after 7 days had delivery in the nifedipine group and 6 patients (10%) after 24 hours, 3 patients (5%) after 48 hours, 3 patients (5%) after 72 hours and 37 patients (61.67%) after 7 days had delivery in the magnesium sulfate group. This characteristic was not statistically different between the two groups. In this study, 11 patients (23.33%) in nifedipine group and 9patient (15%) 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 2).4 patients (6.67%) in the nifedipine group had severe hypotension and 2 patient (3.33%) 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: 5 cases (8.33%) of headache and 2 case (3.33%) of flushing, respectively. All of obstetric characteristics were also not statistically different (Table 2)

Table 2:Obstetric characteristics

	Nifedipine N	%	Magnesium sulfate N	%	p-value
Delivery					
After 24h	3	5	6	10	0.45
After 48h	5	8.33	3	5	0.55
After 72h	4	6.67	3	5	0.59
After 7 days	33	55	37	61.67	0.52
Treatment failure	11	23.33	9	15	0.52
Severe side effect	4	6.67	2	3.33	0.47

Discussion

Spontaneous preterm labor (SPTL) and preterm birth (PTB), defined as birth before 37 completed weeks, is the single most important cause of perinatal mortality and morbidity in high-income countries. All the pharmacological agents used to inhibit preterm uterine contractions act by affecting intracellular calcium concentration in the myometrial cells. Some of these agents promote the extrusion of calcium from the cell (be- ta-adrenergic agents and indomethacin), some displace calcium (magnesium sulphate) and some block the entrance of calcium into the myometrial cells (calcium channel blockers)[11].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, 8.33% 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. 55% of patients in the nifedipine group and 61.67% 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[12]. Another study showed two groups postponed delivery for more than 48 hours.[13] In our study, in 6.67% of patients in the nifedipine group and 3.33% 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, 23.33% and 15% 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[13]. 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 [14]. 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[15]. Several investigators demonstrated that nifedipine treatment did not influence either fetal or uteroplacental circulation[16]. 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[7].

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. However, other workers have advocated that before nifedipine is introduced into clinical practice, the effectiveness should be assessed in a placebo-controlled trial and nifedipine may not be effective for all patients.

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