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Comparison of Efficacy for Tocolysis of Preterm Labour between Magnesium Sulphate and Nifedipine

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ABSTRACT

Aim: To compare efficacy for tocolysis of preterm labour between magnesium sulphate and nifedipine
Methods: A total of 182 patients of preterm labour, 16 to 35 years of age with singleton pregnancy of gestational age between 28 to 36 weeks (assessed on LMP) were included in the study. Patients with severe pre-eclampsia, diabetes mellitus, h/o renal and heart diseases, severe intra-uterine growth retardation (IUGR), fetal distress and antepartum hemorrhage, cervix >4cm dilated, rupture of membranes, congenital fetal malformations, chorioamnionitis and multiple pregnancy were excluded. The selected casesrandomly divided into two groups A and B. Outcome variables like cessation of uterine contractions till 48 hours (efficacy) were noted for successful or unsuccessful outcome.
Results: The mean age of women in group A was 24.66±4.35 and in group B was 23.98±4.05 years ($p<0.05$). The mean gestational age in group A was 32.65±3.71 weeks and in group B was 33.21± 3.31 weeks ($p<0.05$). There was cessation of uterine contractions in 81(89.01%) and no cessation in 10 (10.99%) patients in Group A while in Group B, it was seen in 68 (74.73%) and 23 (25.27%) patients respectively. So, efficacy was 89.01% in group A (magnesium sulfate) and 74.73% in group B (oral nifedipine) with p-value of 0.0124.
Conclusion: Magnesium sulfate is associated with higher efficacy i.e. 89.1% for acute tocolysis of preterm labour as compared to oral nifedipine and should be used as first line tocolytic agent.
Keywords: Tocolytic agents, uterine contractions, preterm birth

INTRODUCTION

Preterm labour is defined by WHO as the onset of labour after the gestation of viability (20 weeks to 28 weeks) and before 259 days or 37 completed weeks of pregnancy[1].The pathogenesis of preterm labor is not well understood, and it is often not clear whether preterm labor represents early idiopathic activation of the normal labor process or results from a pathologic mechanism. Several theories exist regarding the initiation of labor including: oxytocin initiation, progesterone withdrawal and premature decidual activation[2].

The primary purpose of tocolytictreatment are to delay delivery to allow the administration of a complete course of antepartum glucocorticosteroids in order to primarily reduce the incidence and severity of idiopathic respiratory distress syndrome and to arrange in utero transfer to a center with neonatal intensive care unit facilities[3,4]. The secondary purpose of tocolytictreatment is to delay delivery to reduce the perinatal morbidity and mortality associated with severe prematurity.

Petrie and Steer first described the use ofmagnesium sulfate as a tocolytic agent in randomized controlled trial of 71 women with preterm labor[5].This agent readily crosses the placenta, achieving fetal steady-state levels within 1 hour of the start of therapy. No significant alterations in Apgar scores or neurological states have been documented with umbilical cord concentrations of 4 mg/dL or less[6,7].

Nifedipine can be used by oral or sublingual route.Nifedipine readily crosses the placenta, and serum concentrations of the fetus and the mother are comparable[8,9].

As preterm birth is associated with high perinatal morbidity and mortality, so we have conducted a study to see which drug is more effective and rapid as acute tocolytic agent for at least 48 hours or more in preterm labour in local population. Then based on these results, some practical recommendations could be made in our routine practice for preterm labour management and some benefit could be gained from prolongation of pregnancy by enabling corticosteroid administration to accelerate fetal lung maturation which would help us to reduce perinatal mortality and morbidity of both mother and fetus.

MATERIAL AND METHODS

This was a randomized controlled study and conducted at Department of Department of Obstetrics and Gynaecology, AllamaIqbal Medical College / Jinnah Hospital Lahore from December 2014 to June

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2015. Permission was taken from IRC (Institutional Review Committee) before the start of study and written informed consent was taken from every patient.

Total 182 patients with preterm labour were selected for this study. Preterm labor is a labor (regular painful uterine contractions, 3 in 10 minutes and cervical dilatation < 4cm with intact membrane) before 37 weeks of pregnancy. Patients having age from 16-35 years and having gestational age between 28-36weeks assessed on LMP, single normal fetus with cephalic presentation and regular painful uterine contractions about 3 in 10 minutes and cervical dilatation < 4cm with intact membranes were included in this study. Patients having age <16 and >35 years, gestational age <28 and >36 weeks, patients with history of diabetes mellitus, pre-eclampsia, cardiac disease and hepatic dysfunction, patients who have severe intra-uterine growth retardation (IUGR), fetal distress and antepartum hemorrhage, cervix >4cm dilated, rupture of membranes, congenital fetal malformations, chorioamnionitis and multiple pregnancy, contraindication to nifedipine (allergy to nifedipine, maternal cardiac disease, hypotension <90/50 mmHg), and contraindications to Salbutamol (cardiac disease, hypertension were excluded from this study.

All the selected patients were randomly divided into two groups A and B. In the Group A, magnesium sulfate was given intravenously in a loading dose of 4 grams over 15 minutes, then a maintenance dose of 2-3 grams/hr IV infusion until uterine contractions were inhibited or side effects were became intolerable. While inGroup B patients, nifedipine was given as 30 mg tabletstat if uterine contractions were not stopped within 20 minutes, then 30mg tablet was repeated. If there was no response then after 30 minutes, another 30 mg was given. After this, nifedipine was continued 30mg twice a day for further 5 days.

All cases in both groups (A and B) were evaluated by the senior gynecologist for prolongation of gestation at 48 hours after the start of therapy. In each group, if uterine contractions were remained stopped till 48 hours after the start of treatment, the treatment was regarded successful otherwise it was labeled as unsuccessful. Efficacy was measured in terms of cessation of uterine contractions in preterm labor. If uterine contraction were ceased till 48 hours after the start of treatment, it was regarded successful otherwise labeled as unsuccessful. All the findings was noted in pre-designed proforma along with demographic data of all the patients.

All the data entered in SPSS version 18 and analyzed. Numerical data was presented as mean and SD and categorical data was presented as frequencies and percentages.Chi-square test was used to detect the difference between the efficacy of both groups and p-value ≤0.05 was taken as significant.

RESULTS

Age range in this study was from 16 to 35 years with mean age of 24.24±4.15 years.The mean age of women in group A was 24.66 ± 4.35 and in group B was 23.98±4.05 years. Majority of the patients 90(49.45%) were between 21 to 30 years of age as shown in Table 1.

Gestational age was from 28 to 36 weeks with mean age of 32.82±3.35 weeks. The mean gestational age in group A was 32.65 ± 3.71 weeks and in group B was 33.21±3.31 weeks. Majority of the patients 79(43.41%) were between 33 to 36 weeks of gestation as shown in Table 2. %age of patients according to parity in both groups shown in Table 3.

There was cessation of uterine contractions in 81 (89.01%) and no cessation in 10 (10.99%) patients in Group A while in Group B, it was seen in 68 (74.73%) and 23(25.27%) patients respectively. So, efficacy was 89.01% in group A (magnesium sulfate) and 74.73% in group B (oral nifedipine) with p-value of 0.0124 as shown in Table 4. Stratification of efficacy between two groups in terms of age, parity and gestational age has shown in Table 5.

Table 1: Age distribution for both groups.

Age (yrs)	Group A Frequency	Group B Frequency	Total Frequency
16-20	27(29.67%)	28(30.77%)	55(30.22%)
21-30	44(48.35%)	46(50.55%)	90(49.45%)
30-35	20(21.98%)	17(18.68%)	37(20.33%)
Mean±SD	24.66±4.35	23.98±4.05	24.24±4.15

Table 2: Distribution for Gestational age

Gestational Age (yrs)	Group A Frequency	Group B Frequency	Total Frequency
28-30	18(19.78%)	14(15.38%)	32(17.58%)
31-33	36(39.56%)	35(38.46%)	71(39.01%)
34-36	37(40.66%)	42(46.15%)	79(43.41%)
Mean ± SD	32.65 ± 3.71	33.21±3.31	32.82± 3.35

Table 3: Distribution according to parity

Parity	Group A Frequency	Group B Frequency	Total Frequency
Primiparous	49(53.85%)	44(48.35%)	93(51.1%)
Multiparous	42(46.15%)	47(51.65%)	89(48.9%)

Table 4: Comparison of Efficacy between both Groups

Efficacy	Group A (Frequency)	Group B (Frequency)
Yes	81(89.01%)	68(74.73%)
No	10(10.99%)	23(25.27%)

P value is 0.0124 which is statistically significant.

Table 5: Stratification of efficacy of both groups according to age, parity and gestational age.

Age of patients	Group A		Group B		p-value
	Efficacy		Efficacy		
	Yes	No	Yes	No	
16-20 years	25 (92.59%)	02 (7.41%)	21 (75.0%)	07 (25.0%)	0.0779
21-30 years	41(93.18%)	03 (6.82%)	36 (78.26%)	10 (21.74%)	0.0441
31-35 years	15 (75.0%)	05 (25.0%)	11 (64.71%)	06 (35.29%)	0.4948
Parity					
Primiparous	47 (95.92%)	02 (4.08%)	34 (77.27%)	10 (22.73%)	0.007
Multiparous	34 (80.95%)	08 (19.05%)	34 (72.34%)	13 (27.66%)	0.33
Gestational Age					
28-30 weeks	18 (100.0%)	00 (0.0%)	11(78.57%)	03(21.43%)	0.03
31-33 weeks	33 (91.67%)	03(8.33%)	25(71.43%)	10 (28.57%)	0.02
34-36 weeks	30 (81.08%)	07 (18.92%)	32 (76.19%)	10 (23.81%)	0.59

DISCUSSION

Preterm labor is defined as the presence of uterine contractions of sufficient frequency and intensity to effect progressive effacement and dilation of the cervix prior to term gestation[10,11].

Magnesium sulfate (MgSO4) is the most common agent used for the treatment of preterm labor. It is used as primary tocolytic agent due to similar efficacy to terbutaline[12].

In this study, we have compared the magnesium sulfate with oral nifedipine in acute tocolysis for at least 48 hours or more in preterm labor patients. The mean age of patients in our study was 24.66 ± 4.35 years in group A and 23.98 ± 4.05 years in group B. Majority of the patients 90 (49.45%) were between 21 to 30 years of age in both groups. These results were very much comparable with Taherianet al[13] In our study, majority of patients were primigravida i.e. 51.1%. Taherianet al[13]has also shown 50.05% primigravida in his study. So, the results of our study had shown the increase risk of preterm labor in younger primigravida females. Study conducted by Lyell et al[7] and Glock et al[9] have also reported that preterm labor usually develops in younger females & this may be associated with primiparity. Mean gestational age in group A was 32.65 ± 3.71 weeks and in group B was 33.21 ± 3.31 weeks, in this study while Taherian et al[13]had found mean gestational age for magnesium sulfate group as 32.06 weeks and for oral nifedipine group as 32.23 weeks.

In this study, there was cessation of uterine contractions in 89.01% after magnesium sulfate therapy while oral nifedipine has shown this in 74.73% patients. In a study by Naz et al[14] showed that the efficacy of oral nifedipine as a tocolytic agents in stopping uterine contractions at 48 hours was 74.1% while Kawagoe et al[15] showed that after magnesium sulfate infusion, 90% patients prolonged their pregnancy for >48 hours. In addition, one trial[22] reported that severe maternal adverse effects were significantly less frequent among women receiving nifedipine than among women receiving magnesium sulfate (10.0% vs 21.7%). There were no significant differences between the groups in the risk of major adverse neonatal outcomes, although a significant reduction was seen in the risk of admission to NICU (37.3% vs 51.9%) and NICU length of stay in the nifedipine group compared with the magnesium sulfate group.

Lyell et al[7] in his randomized trial has shown opposite results as compared to this study i.e. 38.6.8% patients in nifedipine group and 49.2% patients in magnesium sulfate group delivered before discharge in the first 48 hours (primary tocolytic effect). Forty eight percent patients in the nifedipine group and 38% patients in the magnesium sulfate group postponed delivery for more than 48 hours (secondary tocolytic effect). Glock et al[9]in his comparative trial had found that both these drugs were equally effective in arresting labor and delaying delivery > 48 hours, 92% versus 93%. Both study groups had a similar incidence of side effects, although four (10%) of magnesium sulfate-treated patients required drug discontinuation because of severe symptoms.

CONCLUSION:

This study concluded that magnesium sulfate is associated with higher efficacy i.e. 89.1% for acute tocolysis of preterm labor as compared to oral nifedipine. Moreover, magnesium sulfate have also shown better efficacy for younger primigravida females. We recommend that magnesium sulfate should be used as a first line tocolytic agent in cessation of preterm labor, so that some benefit could be achieved from prolongation of pregnancy by enabling corticosteroid administration to accelerate fetal lung maturation which would help to reduce perinatal mortality and morbidity of both mother and fetus.

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