ORIGINAL ARTICLE

Comparison of Efficacy of Magnesium Sulphate versus Nifedipine for Tocolysis of Preterm Labour

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ABSTRACT

Aim: To compare the efficacy of magnesium sulfate versus nifedipine for tocolysis of preterm labour.
Methods: This randomized controlled trial study was carried out at the department of Obstetrics and Gynecology, Bahawal Victoria Hospital, Bahawalpur from 1st January 2018 to 30 June 2018. 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, history of 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 nominated patients were randomly placed into two groups i.e. Group A (magnesium sulfate) & Group B (oral nifedipine), by using lottery method. Outcome variables like cessation of uterine contractions till 48 hours (efficacy) were noted for successful or unsuccessful outcome.
Results: The average 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 has higher efficacy i.e. 89.1% for acute tocolysis of preterm labour as compared to oral nifedipine and should be used as first line drug to treat preterm labour.
Keywords: Uterine contractions, Tocolytic agents, Preterm birth

INTRODUCTION

Preterm labour is defined by WHO as the start of labour after the age of viability (20-28 weeks) and before 37 completed weeks or 259 days of gestation[1] In developed countries, preterm labour constitutes 5 to 10 % of all deliveries. Many theories describe the mechanism regarding the start of labour, and include progesterone withdrawal, initiation of oxytocin and premature activation of decidua.[2] The most likely pathway is premature decidual activation, and it occurs in occult upper genital tract infection. Early diagnosis of preterm labour results in prevention of premature delivery and possibly progression of pregnancy to term with improved chance of survival of baby.[3] symptoms and signs of onset of labour before term include as many as four or more uterine contractions in one hour with cervical dilatation and effacement and may include leakage of watery vaginal fluid that indicates premature membranes rupture (that are present around the body of fetus). In a few cases, dilatation of cervix occurs without pain, so that the mother is not able to see warning signs until she is in advanced labour. Prematurity is the single most important cause of adverse fetal outcome affecting survival and quality of life[4].

Preterm labour without rupture membrane accounts for approximately one-third of premature births, and account for approximately 70-80% of all neonatal deaths[5]. Prematurity is responsible for significant immediate and long-term morbidity and is associated with sepsis, respiratory distress syndrome, intraventricular hemorrhage, bronchopulmonary dysplasia, retinopathy of prematurity, and necrotizing enterocolitis. The fibronectin test and ultrasonography are useful modalities to diagnose preterm labour so that false positive results can be minimized. The treatments to arrest early labour can prevent premature delivery and enable the mother to be brought to a specialized center for better neonatal resuscitation and glucocorticoid administration[6].

Various drugs are used to arrest preterm labour and include agents beta-agonists, calcium channel blockers, prostaglandin synthetase inhibitors, oxytocin receptor antagonists and nitric oxide donors. Ritodrine hydrochloride, a beta-agonist is mostly used in Europe. The aim to arrest preterm labour is to delay delivery. In such conditions, steroids can be injected to patient and both the incidence and severity of idiopathic respiratory distress syndrome can be minimized and patient can be moved to a specialized center with intensive neonatal care. The role of magnesium sulfate to arrest preterm labour was first described by Steer and Petrie[7] which showed that patient treated with magnesium sulphate had a success rate of 77%, while patient treated with ethanol had a success rate of 45% and 44% success rate in the placebo group. Many observational studies have concluded that magnesium sulphate can be used to treat both preeclampsia and preterm labour in antenatal patients and incidence of cerebral palsy in very low birth weight infants can be reduced by this treatment.[8] Ulmsten et al[9] first reported the role of nifedipine for the treatment of preterm labour. Side effects of nifedipine are dizziness, flushing, light headedness, peripheral edema and headache. These side effects occur in approximately 17% of patients and result in poor compliance in 2–5% of

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patients.[10] So a study was conducted to see which drug is more effective and rapid as acute tocolytic agent in local population.

MATERIALS AND METHODS

This randomized controlled trial study was carried out at Department of Obstetrics and Gynecology, Bahawal Victoria Hospital Bahawalpur, from 1st January 2018 to 30th June 2018.A total of 182 patients with preterm labour were included in study and age range of the patients was between 16 to 35.Lottery method was used for sampling and patients were randomly divided into two groups i.e., group A(magnesium sulphate) and group B (nifedipine). The patients in Group A were treated with magnesium sulphate. The drug was injected intravenously with a loading dose of 4 grams over 15 minutes followed by maintenance dose of 2-3 grams/hr. IV infusion until uterine contractions were inhibited or side effects were became intolerable. While in Group B patients, nifedipine was given as 30 mg tablet stat if uterine contractions were not stopped within 20 minutes, then 30 mg tablet was repeated. If there was no response then after 30 minutes, another 30 mg was given. After this, nifedipine was continued 30 mg twice a day for further 5 days. If after 48 hours of start of treatment, the uterine contractions were remained stopped then the treatment was regarded successful, if contraction observed then it was regarded unsuccessful. All the data was entered and analyzed by using SPSS version 14.0.

RESULTS

The range of age in this study was between 16 to 35 years with average age of 24.24±4.15 years. The average 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 (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 34 to 36 weeks of gestation (Table 2). According to parity in both groups has 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 (Table 4). Stratification of efficacy between two groups in terms of age, parity and gestational age are shown in Table 5.

Table 1: Age distribution for both groups

Age (years)	Group A (n=91)		Group B (n=91)	
	No.	%	No.	%
16-20	27	29.67	28	30.77
21-30	44	48.35	46	50.55
31.35	20	21.98	17	18.68
Mean±SD	24.66±4.35		23.98±4.05	

Table 2: Frequency and percentage of patients according to gestational age in both groups

Gestational age (weeks)	Group A (n=91)		Group B (n=91)	
	No.	%	No.	%
28-30	18	19.78	14	15.38
31-33	36	39.56	35	38.46
34-36	37	40.66	42	46.15
Mean±SD	32.65±3.71		33.21±3.31	

Table 3: Frequency and percentage of patients according to parity in both groups

Parity	Group A (n=91)		Group B (n=91)	
	No.	%	No.	%
Primiparous	49	53.85	44	48.35
Multiparous	42	46.15	47	51.65

Table 4: Comparison of efficacy between both groups (n=182)

Efficacy	Group A (n=91)		Group B (n=91)	
	No.	%	No.	%
Yes	81	89.01	68	74.73
No	10	10.99	23	25.27

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

Variable	Group A (n=91) Efficacy		Group B (n=91) Efficacy		P value
	Yes	No	Yes	No	
Age (years)					
16-20	25 (92.59%)	02 (7.41%)	21 (75.0%)	07 (25.0%)	0.0779
21-30	41(93.18%)	03 (6.82%)	36 (78.26%)	10 (21.74%)	0.0441
31-35	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 (weeks)					
28-30	18 (100.0%)	00 (0.0%)	11(78.57%)	03(21.43%)	0.03
31-33	33 (91.67%)	03(8.33%)	25(71.43%)	10 (28.57%)	0.02
34-36	30 (81.08%)	07 (18.92%)	32 (76.19%)	10 (23.81%)	0.59

DISCUSSION

Preterm labour is defined as the presence of uterine contractions of such a frequency and intensity that leads to progressive effacement and dilation of the cervix before 37 completed weeks of gestation. Occurring at 20-37 weeks' gestation, almost half of preterm births are preceded by preterm labour. In the United States, prematurity is a leading cause of neonatal death.[11] The exact mechanisms of preterm labour are still not known, but mechanical factors such as uterine over distension resulting from multiple gestation or polyhydramnios are significant contributor. Other include cervical incompetence, uterine distortion, cervical inflammation, maternal inflammation/fever, decidual hemorrhage i.e., abruption, uteroplacental insufficiency and hormonal changes. Preterm labour is a very serious complication of pregnancy. Early diagnosis results in prevention of preterm birth and progression of pregnancy to term which results in improved survival rate. In suspected case of preterm labour, obtaining a vaginal fetal fibronectin (FFN) sample before pelvic examination may provide information regarding possible diagnosis. The FFN specimen should be sent for laboratory analysis even if the diagnosis is not confirmed after the examination. The fibronectin test and ultrasonography are useful modalities in making diagnosis of preterm labour and reduces the false positive result. Currently no treatment is absolutely effective to prevent preterm birth, however if early diagnosis is made, it allows the use of interventions that may delay delivery for 48 hours or more[12]. Tocolytics are drugs given to stop uterine contractions. Acute tocolysis is used to decrease or stop uterine contractions and slows cervical change during preterm labour. Maintenance tocolysis refers to medication administered after acute tocolysis, to prevent a recurrence of preterm labour in women in whom preterm labour is arrested.[13] Criteria that indicate administration of drug to arrest preterm labour include more than 6 contractions in one hour leading to significant cervical dilatation and effacement or presumed prior cervical change (transvaginal cervical length <25 mm, >50% cervical effacement, or cervical dilation ≥20 mm). If contractions occur without cervical change, then patient can be managed by continued observation or by offering therapeutic sleep (e.g. bymorphine sulphate 10-15 mg subcutaneous).[14] The most common tocolytic agents used to treat preterm labour includes the following:

Magnesium sulfate ($MgSO_4$) is widely used as the basic drug to treat preterm labour, and is as efficient as terbutaline (one of the previous agents of choice),and is better tolerated by patients. Indomethacin is another drug that is considered appropriate as first-line therapy especially for prevention of early preterm labour (<30 wk).It is also a drug of choice in cases where preterm labour is associated with polyhydramnios. Despite its unlabeled status, several randomized studies favour nifedipine a potent drug to prolong pregnancy and has higher success rate as compared to other tocolytics. In this study, we have compared the magnesium sulfate with oral nifedipine in acute tocolysis for at least 48 hours or more in preterm labour patients. The mean age of patients in our study was 24.66±4.35 years in group A and 23.98±4.05 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[15] study that had a mean age of 26 years for both groups. In our study, majority of patients were primigravida i.e., 51.1%. Taherianet al[15] has also shown 50.05% primigravida in his study. So, according to results of our study, younger primigravida females have greater risk of preterm labour .Study conducted by Lyell et al[8] and Glock et al[10] have also shown that preterm labour usually develops in younger females and 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 Taherianet al[15] had found mean gestational age for magnesium sulfate group as 32.06 weeks and for oral nifedipine group as 32.23 weeks. In developed countries,6-7% of births are preterm, hence become a major cause of perinatal morbidity and mortality.[16] Many tocolytic agents are used for a long time. There are many Cochrane reviews that have compared individual tocolytic drugs with placebo or other tocolytics.[17] Regarding side effects, no significance difference exist in between two groups. Nifedipine must be taken by the oral route, in comparison with magnesium which must be used by only the parenteral route. Patients taking magnesium sulfate should be monitored for adverse side effects which include respiratory depression or even cardiac arrest (occurring at super-therapeutic levels). Common maternal side effects include flushing, drowsiness nausea, headache, and blurred vision. Respiratory and motor depression in the neonate may occur due to transplacental passage of magnesium sulphate[18] On the other hand, some studies have shown that calcium channel blockers have minimal side effects and may be more effective than magnesium and beta sympathomimetics and should be considered as the first line drug to arrest preterm labour[19]. A recent prospective cohort study is conducted in the Netherlands and Belgium. The study reported that among 542 women(that were treated with nifedipine) 5 women (0.9%) had a serious adverse side effect while 6 women (1.1%) had a mild adverse side effect[20]. So, this study concluded that magnesium sulfate was associated with higher efficacy for acute tocolysis of preterm labour as compared to oral nifedipine and gives some benefit 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.

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 agent to treat preterm labour.

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