

Original Article

Study on Effect of Magnesium Sulfate as Tocolytic Agent

*Khalil N¹, Halim KS², Ummon IJ³**Abstract**

We face many problems in diagnosis, monitoring and adopting treatment policy. There are very limited studies about preterm labour prevention in our country and few national data are available about the incidence of preterm labour. Acute tocolysis prevents preterm labor for 48 hours, which is the critical period for antenatal steroid administration or maternal transfer to perinatal centers to improve neonatal outcomes. This prospective study was conducted. To determine the effectiveness of magnesium sulfate as tocolytic agent in preterm labour to arrest the premature onset of labour. A total of 90 primigravid and multigravid with preterm labour was included in this study at 250 Beded General Hospital Tangail from January 2012 to December 2015. The mean age of the respondents was 24.13±4.67 year. The mean systolic and diastolic blood pressure were 122.47±12.64 and 71.67±12.67 mm of Hg respectively. Gestational age did not influence on the outcome of treatment with Tocolytic regime. Out of 90 pregnant women, 70% were anemic, 53.3% had vaginal bleeding and 76.7% had abdominal pain. Among 90 respondents only 6 women had premature rupture of membrane and about 40% had inadequate amniotic fluid. The three treatment regime (Antibiotic+ Tocolytic+ steroid) was found indifferent in terms of affectivity. Preterm labour is not a very uncommon pregnancy-related complication. This study evaluates, the effect of magnesium sulphate as tocolytic agent.

Keywords: Magnesium sulfate, tocolytic agent, preterm labour.

INTRODUCTION

Magnesium, one of the trace-element is an important cation of body. It is believed that magnesium sulfate appears to inhibit calcium uptake into smooth muscle cells and reduce uterine contractility. MgSO₄ is cost-effective and found to be well tolerated when given to a patient of preterm labour. Magnesium Sulfate can delay preterm labour at least 24-48 hours. This delay increases the time

that may be required for the maximum beneficial effects of steroids can be achieved or for the transfer of the patient to a center capable of managing the preterm baby. At some institutions, the fetal survival rate approaches 90% at 24-27 weeks of gestation and 98% at 28-31 weeks of gestation. Patient of preterm labour who is treated with tocolytic, magnesium sulphate is often as a first line therapy as it is highly effective with fewer side effects.² The decision to use magnesium sulphate, the dosage to administer, the duration of use, and alternative therapies are physician judgment. These decisions should be made based on a reasonable assessment of the risks of the clinical situation (PTL) and the treatments available versus the benefits of prolonging pregnancy.³

The Magnesium sulphate (MgSO₄) was mostly an acute medication not for prolong period and could not reasonably be expected to be efficacious after the drug was discontinued. Elliott, et al⁴, demonstrated the peril of an inadequate therapeutic level of magnesium by comparing the incidence of successful tocolysis at 48 hours with low dose Mg (4 gm loading dose / 2 gm per hour), medium dose (4 gm loading dose and greater than 2 gm per hour maintenance) and high dose protocols (6 gm loading dose and greater than 2 gm per hour maintenance). Low dose Mg was successful in 69.2% of treated patients. The medium dose was successful in 79.2% and 88.7% of the high dose patients were successfully tocolysed for 48 hours or more.⁴ Preterm labor and delivery continues to be the most common problem in obstetrics today and a major financial burden on the health care system. It has been estimated that this problem costs \$15.5 billion (2002) in neonatal cost alone.¹²

The uses of magnesium sulfate in the context of appropriate clinical obstetric practice include, in particular, prevention and treatment of seizures in women with preeclampsia or eclampsia and fetal neuroprotection before anticipated early preterm (less than 32 weeks of gestation) delivery. Magnesium sulfate also may be used for the short-term prolongation of pregnancy (up to 48 hours) to allow for the administration of antenatal corticosteroids.¹³

RATIONALE

Magnesium sulfate (MgSO₄) is the agent most commonly used for the treatment of eclampsia and the prevention of eclampsia in patients with severe pre-eclampsia. Another commonly practiced off-label use of this drug is in preventing preterm labor in pregnant women where the duration of the treatment

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might be more than one week. It is usually given either by intramuscular or intravenous route while the survival of infants born preterm has improved, the prevalence of cerebral palsy has risen.^{16,17} The incidence of cerebral palsy decreases significantly with increasing gestational age: 14.6% at 22–27 weeks of gestation, 6.2% at 28–31 weeks, 0.7% at 32–36 weeks and 0.1% in term infants.¹⁸ Twenty-five percent of all cases of cerebral palsy are in infants born at less than 34 weeks of gestation.¹⁹ In children born preterm the proportion whose cerebral palsy is considered to have a perinatal origin (49%) is greater than in those born at term (35%).^{20,21} The harmful effect in the fetus with the shortest duration is not established. In light of the safety information, the drug label for MgSO₄ injection, USP 50% has also been changed, including changing the pregnancy category to D from A and denoting the effect as New teratogenic effects.²² Patient of preterm labour who is treated with tocolytics, magnesium sulphate is often as a first-line therapy as it is highly effective with fewer side effects. With the proper clinical skill, assessment and monitoring of patient and with minimum resources, a definitive plan for the management of preterm labour by MgSO₄ is effective.²³

MATERIAL AND METHODS

This is a prospective study was carried among 90 pregnant women at the department of Obstetrics and Gynaecology in 250-bed general hospital, Tangail. The study was conducted from January 2012 to December 2015 admitted cases in the hospital. Pregnant women both primi and multi with preterm labour were included in this study. After admission full history including duration of pregnancy, time and onset of labour pain were taken, Gestational age was determined from the first day of the last menstrual period (LMP) and early ultrasonography. Pregnancy of more than 28 weeks' duration and less than 37 completed weeks were included in this study. Examination of pulse, blood pressure, fundal height and fetal conditions were assessed for documentation of preterm labour pain, single sterile per vaginal examination done to assess cervical condition. Loading dose: 4-6 gm in Magnesium sulphate (10-20%) solution over 20-30 minutes followed by an infusion of 1-2 gm/hr to continue tocolysis for 12 hours after the contractions have stopped and we patient was monitored to it any evaluate we side effect data were analyzed by SPSS where all calculation rate of less than 0.05 was considered significant.

RESULT

Table I shows Regarding age in years, out of 90 respondents, the majority of the respondents (90%) were below 30 years of age, mean age of the subjects was 24.13±4.67 years ranging from 18 years to 33 years.

Table I: Distribution of Respondents by Age (n=90)

Age (in years)	Frequency	Percentage (%)
≤20	27	30.0
21-25	30	33.3
26-30	24	26.7
>30	09	10.0
Total	90	100.0

Table-II shows, among 90 future mothers, the highest mean systolic blood pressure was found 122.47±12.640 mmHg and that of mean diastolic blood pressure was found 71.67±12.617 mmHg. The table represented that the highest pulse rate was 76.10±19.477 beats per minute.

Table II: Distribution of mothers' by Haemo-dynamics (n=90)

Parameter	Systolic BP (mmHg)	Diastolic BP (mmHg)	Pulse rate (bpm)
Minimum	110	50	24
Maximum	160	100	110
Mean	122.47	71.67	76.10
Std. deviation	12.640	12.617	19.477

Table-III shows, distribution of respondents by parity. Out of 90 respondents, the majority of the respondents (56.7%) were primi. The mean parity of the subjects was 2.1±1.605.

Table III: Distribution of respondents by parity (n=90)

Parity	Frequency	Percentage
<2	51	56.7
2-3	24	26.7
>3	15	16.6
Total	90	100.0

Table IV shows According to table 4, out of 90 respondents 36.7% were of 28-30 weeks of gestation, 26.7% were of 31-32 weeks of gestation and 36.7% were of 33-35 weeks of pregnancy

Table IV: Distribution of the respondents by gestational age (n=90)

Gestational age	Frequency	Percentage
28-30 wk	33	36.7
31-32 wk	24	26.7
33-35 wk	33	36.6
Total	90	100.0

Table V shows, distribution of respondents by anemia, vaginal bleeding and abdominal pain. Out of 90 women, 70% were anemic, 53.3% had vaginal bleeding and 76.7% had abdominal pain.

Table V: Distribution of the respondents by anemia, vaginal bleeding & abdominal pain (n=90)

Parameter	Frequency	Percentage
Anemia		
Present	63	70.0
Absent	27	30.0
Total	90	100
Vaginal bleeding		
Present	48	53.3
Absent	42	46.7
Total	90	100
Abdominal pain		
Present	69	76.7
Absent	21	23.3
Total	90	100

According to figure 1 out of 90 respondents in 93.3% membrane was intact. The membrane was ruptured in 6 women.

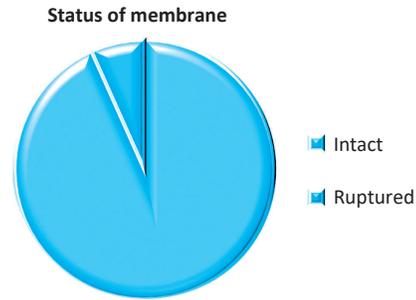


Figure 1 : Distribution of status of the membrane (n=90)

Table-VII shows, distribution of the respondents by body build and effectivity. Following the Chi-square test effectivity of treatment is found to be independent of body build or nutritional status ($p>0.05$). The Gestational age doesn't seem to have an influence on the outcome of treatment with the Tocolytic regime ($p>0.05$). In case of effectivity of Tocolytic treatment with pattern of antenatal visit, Antenatal care doesn't have statistically significant impact on pregnancy outcome ($p>0.05$) And the Fetal presentation which didn't have statistically significant impact on pregnancy outcome ($p>0.05$). But among 90 respondents, inadequate amniotic fluid almost 40% ineffective favorable outcome of their current ailment ($p>0.001$).

Table VII: Distribution of the respondents by the effectivity and body build, gestational age, antenatal care, presentation of fetus and volume of amniotic fluid (n=90)

Body built/Nutrition	Effectivity		Test statistics
	Effective	Ineffective	
Poor	15 (100%)	Nil	Chi sq=3.945
Average	63 (95.5%)	3 (4.5%)	df=2
Good	6 (66.7)	3 (33.3%)	p=0.139
Gestational age (wks)			
28-30	30 (90.9%)	3 (9.1%)	Chi sq=0.779
31-32	24 (100.0%)	Nil	df=2
33-35	30 (90.9%)	3 (6.7%)	p=0.677
Antenatal care			
No	12 (80.0%)	3 (20.0%)	Chi sq=2.143
Irregular	30 (100%)	Nil	df=2
Regular	42 (3)	3 (6.7%)	p=0.343
Presentation			
Cephalic	69 (95.8%)	3 (4.2%)	Chi sq=2.545
Breach	9 (75.0%)	3 (25.0%)	df=2
Others	6 (100%)	Nil	p=0.280
Volume of amniotic fluid			
Adequate	75 (100%)	Nil	Chi sq=10.71
In adequate	9 (60%)	6 (40%)	df=1
			p=0.001

Table-VIII shows statistical association was sought between different regime used and the outcome of treatment. The three treatment regime was found indifferent in terms of affectivity ($p>0.05$).

Table VIII: Distribution of the respondents by the efficacy with treatment paradigm (n=90)

Treatment paradigm	Effectively		Test statistics
	Effective	Ineffective	
Antibiotic+Tocolytic	2 (100%)	Nil	Chi sq=0.917, df=2, p=0.632
Tocolytic+steroid	7 (100%)	Nil	
Antibiotic+Tocolytic+steroid	19 (90.5%)	2 (9.5%)	

DISCUSSION

In the current study, it is shown that regarding age in years, the majority of the respondents (90%) were below 30 years of age, mean age of the subjects was 24.13 ± 4.67 years ranging from 18 years to 33 years. Lipi et al.² study observed the majority of 39.13% of patients were in the 26-30 years' age group and 28.99% are in 21-25 years. This study was consistent with the findings of the study of Block et al (1977)¹. According to his study, the age group was 22-35 years. In the present study, it is revealed that the majority of the respondents (56.7%) were primi-para. Compared to the study of Lipiet al.² 56.52 % of patients were multi-para and 43.48% patients were primi. A retrospective cohort study Lumley⁵ found the incidence of preterm birth in primi-gravida women was 5.9%. In the present study, it is shown that out of 30 subjects 36.7% were of 28-30 weeks of gestation, 26.7% were of 31-32 weeks of gestation and 36.7% were of 33-35 weeks of pregnancy. A study by Goldenberg RL⁶, by gestational age 5% of preterm birth occur at less than 28 weeks (extreme prematurity), 15% at 28 – 31 weeks (severe prematurity), 20% at 32-33 weeks (moderate prematurity), and 60-70% at 34-36 weeks (late preterm). Lipi et al.² observed 49.28% of patients were in 31- 33 weeks of gestation and 36.23% of patients were in 34-36 weeks. In this study, it was observed that anemia was found in 21(70.0%) patients, vaginal bleeding 16(53.3%) and abdominal pain 23(76.7%). After commencement of treatment, patients were kept under meticulous follow-up. The frequency of contractions was counted as a tangible measurement of the efficacy of treatment. The outcome was coded as adverse in case of rupture of membrane. The

membrane of 93.3% of subjects was left unbroken. The membrane of only six women was ruptured. Elliott et al.³ study showed that 274 patients (77%) had a singleton pregnancy with intact membranes, 38 (11%) had a singleton pregnancy with ruptured membranes, 35(10%) had a multiple gestation with intact membranes and eight (2%) had multiple gestations with ruptured membranes. Treatment was defined as effective if uterine contractions were reduced by more than 30% in frequency compared to those occurring during the last 2 hours before magnesium sulfate infusion. Treatment was defined as ineffective if uterine contractions were not reduced by 30%, labor progressed with apparent changes in cervical findings, or the attending physician resumed ritodrine in the magnesium-alone group due to insufficient tocolytic efficacy. For the intention-to-treat analysis, women who needed to deliver before 48 hours of observation due to some complications other than preterm labor were also classified as ineffective. The statistical association was sought between different regimes used and the outcome of treatment. In this study found that 100% effective to used combination therapy and the three treatment regime was found indifferent in terms of affectivity ($p>0.05$). Similar results were found in Kawagoe et al study they showed after magnesium sulfate infusion, 90% prolonged their pregnancy for >48 hours. Combination therapy was effective in 95% (18/19), which was significantly higher than 50% (7/14) for magnesium alone. It is logical to speculate that there may be some additive effects that inhibit uterine contractions since both agents have different mechanisms of action. Historically, the combination therapy may^{7,8,9,10} or may not¹¹ improve tocolytic efficacy. Kawagoe et al.¹ results agreed that combination treatment is superior to magnesium alone in prolonging pregnancy, even in the stage of desensitization during ritodrine treatment. This study showed that association was sought between different regimes used and the outcome of treatment. The three treatment regime was found indifferent in terms of effectivity ($p>0.05$). Kawagoe et al.¹ after magnesium sulfate infusion, 90% prolonged their pregnancy for >48 hours. Combination therapy was effective in 95% (18/19), which was significantly higher than 50% (7/14) for magnesium alone.

CONCLUSION

Labour is the process of coordinated uterine contraction leading to progressive cervical effacement and dilatation by which the fetus and placenta are expelled out. If there is no contraindication Magnesium sulfate is effective tocolytic agent to prevent premature labour.

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