

STUDY ON ROLE OF MAGNESIUM SULPHATE AS A TOCOLYTIC AGENT IN PREVENTING PRETERM LABOUR

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Abstract

A prospective study was done to assess the effectiveness of magnesium sulphate therapy given to women in preterm labour with the aim preventing preterm birth and its sequel. The place of study was the Department of Obstetrics & Gynecology, Sir Salimullah Medical College & Mitford Hospital, Dhaka. The study population were all primi and multigravida with preterm labour admitted in the above mentioned hospital, from January to December, 2009. Gestational age, maternal pulse, blood pressure, temperature, urine output, respiratory rate, uterine contractions, cervical effacement, dilatation and amniotic membrane status were elicited. Data were collected by questionnaire and analyzed with SPSS version 12.0. The results showed that magnesium sulphate injection is an effective method for tocolysis and appears to be safe for the mother and fetus and is a promising option for the treatment of preterm labour in a low resourced setting.

Key Words: Magnesium Sulphate, Tocolytic Agent, Preterm Labour.

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Introduction

Preterm labour is one of the commonest clinical events where traditional pregnancy can turn into a high risk situation for the mother as well as the fetus. A diagnosis of preterm labour is made if a patient present at less than 37 weeks of gestation but more than the age of viability with regular painful uterine contractions occurring once in every 10 minutes. This may be associated with cervical dilatation and or effacement. The incidence of preterm labour varies between 5-10%.

Preterm labour with its complications is the leading cause of perinatal mortality and morbidity, specially respiratory distress syndrome, intraventricular hemorrhage, bronchopulmonary dysplasia, necrotizing enterocolitis etc. It is related to socioeconomic status, disease pattern, genetic consultation and geographic location.

Basic biological functions of the body are maintained by various minerals, water, trace

elements. Magnesium, one of the trace elements is an important cation of body. It is believed that Mg appears to inhibit calcium uptake into smooth muscle cells and reduce uterine contractility. Mg is cost effective and found to be well tolerated when given to a patient of preterm labour. Magnesium Sulphate 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 the patient to a center capable of managing the preterm baby. At some intuitions 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 tocolytics, magnesium sulphate is often as a first line therapy as it is highly effective with fewer side effects.

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Materials and Methods

1. Study type: Prospective study
2. Duration: one year, from January 2009-December 2009
3. Study place: Obs and gynae department of Sir Salimullah Medical College and Mitford Hospital.
4. Methods and data collection: The data were collected by directly visiting and examining the patients. Data tools are-History taking (Filling the questionnaire), clinical examinations, close monitoring and record of different parameters of mother and baby after giving MgSO₄
5. Selection criteria: Both primi and multi gravid were included
Gestational age of study population was 28-37 weeks

Cervical dilatation should be less than 4 cm, all preterm PROM were included, and multiple pregnancies were included.

6. Exclusion criteria: Fetal distress, chorioamnionitis in presence of preterm rupture of membrane, fetal demise or fetal anomaly.
7. After admission full history including duration of pregnancy, time and onset of labour pain, past obstetric history were taken. Gestational age was determined from LMP and early USG. Pregnancy of more than 28 weeks and less than 37 completed weeks were included in this study. Maternal pulse, blood pressure, temperature, respiratory rate, deep tendon reflexes, urine output checked. On per abdominal examination fundal height, amniotic fluid volume and fetal conditions are assessed. For confirmation of progress of labour a single sterile per vaginal examination was done to see cervical effacement, dilatation and condition of membrane.

Characteristics of preterm labour pain:

Painful uterine contractions at least once in 10 minutes

Cervical os- less than 4 cm dilatation

After confirmation of preterm labour and gestational age examination and tests were done to rule out any cases of maternal and fetal diseases of disorders in which it would be best to allow labour to continue. Any specific contraindication to magnesium sulphate therapy has been ruled out.

Protocol: After proper counseling and taking consent from patient and her relatives 4gm (100ml solution) intravenous infusion of magnesium sulphate begin. The rate of infusion slows enough to prevent flushing or vomiting. In this regard inj. Nelepsin 100 ml containing 4 gm of magnesium sulphate infused within 30 minutes. Then continuous infusion of magnesium sulphate at 2 gm per hour i.e. inj. Nelepsin 100 ml solution at a rate of 12-14 drops / min. This solution can titrated up by increments of 0.5 gm per hour to a maximum of 4 gm per hour until adequate tocolysis is achieved (<4-6 uterine contractions per hour). Infusion should be continued until labour subsides to progress to as irreversible stage (Cervical dilatation of 5 cm). Reduce rate of infusion if magnesium toxicity observed. Treatment progress assessed by observing uterine contractions at 0hr, 4hr, 12hr and 24hr.

Precaution: Magnesium sulphate should not be given or must be stopped further infusion when the following monitoring points are seen in the patient: Urine output was less than 30 ml/hours.

Patellar reflexes were absent

Respiratory rate was less than 14/min.

If above mentioned toxicity develops then injection 10 ml of 10% solution of calcium gluconate or chloride was given intravenously over 3 minutes.

8. Ethical consideration: Written informed consent from the patient or guardian of the patients was taken.
9. Data processing and analysis: All data were checked and edited after collection. then data were entered into computer and analyzed with help of SPSS windows version 12 software program.

Results:

Table - I
Age distribution of patients

Age of patient	Number	%
15-20 y	30	21.74
21-25 y	40	28.99
26-30 y	54	39.13
31-35 y	12	8.7
>35	2	1.45

Table - I shows among respondents majority 39.13% patients were in 26-30 years age group and 28.99% are in 21-25 years.

Table - II
Parity distribution of patients:

Parity	No	%
Primi	60	43.48
Multi	78	56.52

Table - II shows 56.52 % patients were mutipara and 43.48% patients were primi.

Table-III
Gestational age group distribution:

Gestational age weeks	No	%
28-30	20	14.49
31-33	68	49.28
34-36	50	36.23

Table - III shows 49.28% patients were in 31-33 weeks of gestation and 36.23% patients were in 34-36 weeks.

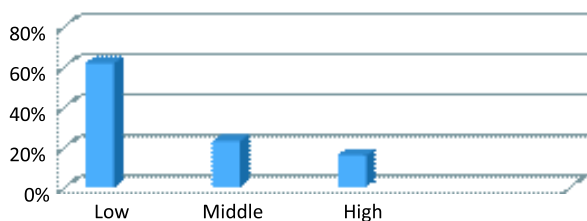


Fig.-I: Socioeconomic group distribution:

Figure - I shows majority (61.60%) of patient came from low socioeconomic group.

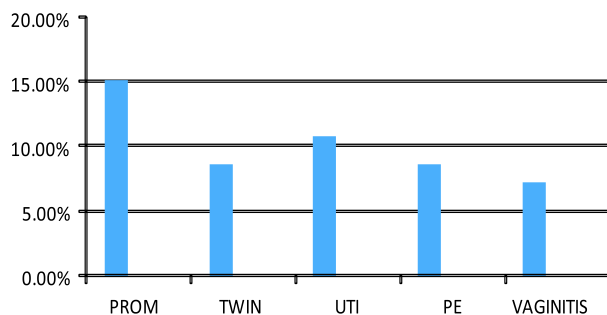


Fig.-2: Preterm labour with associated conditions

Figure - II shows preterm labour associated with 15.22% PROM, 10.87% UTI, 8.7% Twin pregnancy, 8.7% PE and 7.25% vaginitis.

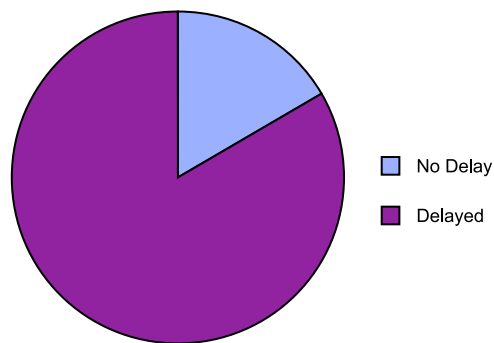


Fig.-3: Preterm labour to be delayed for 24-48 hours:

Figure - III shows preterm labour of 83.33% was delayed for 24-48 hour.

Table - IV
Side effects of MgSO4:

Side effects	Number	%
Hot flush	90	65.22
Nausea/vomiting	74	53.62
others	5	3.62

Table shows that 65.22% patient experienced hot flush and 53.62% patient had nausea and/or vomiting.

Table - V
Discontinue for side effects:

Number	%
5	3.61

Table shows due to side effects 3.62% patients had to discontinue infusion of MgSO₄.

Table - VI
Time bought for administration of inj. Dexamethason:

Dose completed	%	Dose not completed	%
105	76.09	23	16.67

Table shows 76.09% patients had bought time for administration of injection Dexamethason for fetal lung maturity.

Table - VII
Fetal outcome:

	Delayed > 24 hours		Not delayed > 24 hours	
Good	15	74.95	4	16
asphyxiated	4	21.05	19	84

Table shows babies delivered after 24 hours of giving Dexamethason have good apgar score (78.95).

Table - VIII
Mode of delivery:

	Delivered		Undelivered
	vaginal	C/S	
No	32	10	96
%	23.19	7.25	69.56

Table shows majority (69.56) patients were discharged undelivered. Among rest of them 23.19% patients delivered per vaginally and 7.25% delivered by caesarean section.

Discussion

Total 138 patients were observed in this study. All of them were admitted with symptoms and signs of preterm labour. All patients were tried to delay delivery for at least 24-48 hours with MgSO₄ infusion and inj. corticosteroid was also given for fetal lung maturity.

Of the total subjects majority were in 26-30 years (39.13%) Table-1. 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.

Among the study population majority were multigravidas (56.52%). A retrospective cohort study (Lumley, 1998)² found an incidence of preterm birth in primigravida women was 5.9%. Majority of preterm labour was found in between 31-33 weeks of gestation (table-III). A study by Goldenberg RL (2008)³, 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). This is the sample structure shows that majority of patients were from low socioeconomic group (61-60%) Figure 1. In a recent investigation (Mercer et al 1996)⁴ close to 300 women were prospectively evaluated by univariate analysis and multivariate logistic regression and it was found that socioeconomic status was associated with preterm labour in primipara but not in multipara but in my study both multi and primi were from low socioeconomic status.

In this study preterm labour was associated 15.22% with PROM (figure 11), 8.7% with twin pregnancy, 8.7% with PE, 10.87% with UTI and 7.25% with vaginitis. A recent study by SOGC⁵, published on 1st September 2010 notifies these as risk factors for developing preterm labour. The mach of Dimes Multi center premonitory and prevention study found preterm labour is 54% in twin pregnancy and that is 9.6% in singletone birth and 20-30% after PROM.

After giving MgSO₄ preterm birth delayed for 24-48 hours in 83-33% patients. A study on MgSO₄ in preventing preterm labour (2007)⁶ found preterm labour to be delayed for 24-48 hours was also 83-33%. But the side effects that noticed were hot flush (65.22%), nausea & vomiting (57.79)%, which were not good experience for arrest preterm labour. MgSO₄ is more likely than another common treatment to cause mild to serious side effects in pregnant women according to a study from researcher at Lucile Packard children's hospital and Stamford University School of medicine. In my study MgSO₄ infusion was to be discontinued in 3.62% cases due to intolerance of patients.

Among the study population labour delayed more than 24-28 hours and discharged

undelivered about 69.56% and delayed was conducted in rest of cases. Among them 23.19% delivered vaginally and 7.25% patients needed caesarean section due to fetal distress. The patients delivered after 24 hours have babies of good apgar score 78.95% that is only 16 % in patients delivered before 24 hours.

Eliot (1983)⁷ in a retrospective study found tocolysis with MgSO₄ to be successful inexpensive and relatively nontoxic and reported 87% success rate but period of inhibited labour was as short as 48 hours. Cox and associates (1990)⁸ found no benefit from such therapy and this method of tocolysis abandoned at Parkland hospital.

MgSO₄ is the most widely used tocolytic at the American University of Beirut medical center inspite the fact that an effective tocolytic, role of MgSO₄ never been established.

In this study, cases in which time bought for Dexamethason administration was 76.09%. In another study antibiotics and steroids along with tocolytics were given in 70% of patients. According to Opin (2004)⁹ there appears to be a place for short term tocolysis to gain time so that cortisosteroid can be transfer the patient to a center with neonatal intensive care.

After commencement of treatment patient were kept under meticulous follow up. Frequency of contractions was counted as a tangible measurement of efficacy of treatment. There are a score of factors which have the potential capacity of confounding or ever intervening the finding of correct study. Appropriate measures are indispensable for controlling the effect of the variables. To address the relevant issues cross tabulation was done for all possible factors.

Over all, the treatment option with tocolytics to arrest preterm laour was found to be effective in 83.33% cases. Royal college of obstetrecians and gynaecologists rules out the justification of use of tocolytic agent in their October 2002¹⁰ issue of clinical guideline 1(B) due to clear possible evidence of their effectivity. However the finding of current study is identical to that of shudarshan (2002)¹¹. In this study tocolytic was effective in 90.3% cases in delaying labour.

There are opinions of both for and against the study findings. Moreover sample size is not enough to avoid all possible bias. Very few contemporary studies have been documented on tocolytic effect of MgSO₄. Hence detailed study is necessary with appropriate design and adequate sample size including all possible parameters and issues like dose response, fetal safety to be addressed accordingly.

Conclusion

As a single tocolytic agent intravenous injection of magnesium sulphate is effective method for tocolysis still now and appears to be safe for the mother and fetus and is a promising option for the treatment of preterm labour. This study also found inj MgSO₄ as an effective tocolytic agent with various side effects. With proper clinical skill, assessment and monitoring of patient and with minimum resources, a definitive plan for management of preterm labour by MgSO₄ is effective. But our reseachrch should be continued for a better tocolytic with specific uterine action and with less side effects so that patients will be more beneficial.

Limitation of the Study

1. Gestational age has to be ascertained mainly from the history and clinical examination and USG record findings which may not be found in all cases
2. Certain information has to be recorded as per statement of the patients such as aga, income of the family may not be accurate in some cases.
3. The study period is short and less number of study populations is another limitation.

References:

1. Block MF, Klintg OR and Corsby WM. Preterm labour. *Obstetrics & Gynaecology* 1977;50:186
2. Lumley J, The association between prior spontaneous abortion, prior induced abortion and preterm birth in first singleton birth. *prenat neonatal med*, 1998,3:21-24.
3. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth, *The Lancet*, 2008;271:75-84.
4. Mercer BM, Goldenberg RL, Das A et al, The preterm prediction study-a clinical assessment system, *Am J Obstet Gynaecol*, 1996;Jun;174(6).

5. The society of Obstetrician and Gynaecologists of Canada, Risk factor for developing preterm labour. 1st September, 2010.
6. Dr. Farzana begum, Study on role of MgSO₄ as tocolytic agent in preventing preterm labour, 2007.
7. Elliot F. Preterm labour. *Am J Obstet Gynaecology*, 1983; 142:277.
8. Cox SM, Serinan ML, Leveno KS, Preterm labour. *Am J Obstet Gynaecology*, 1977; 50:186.
9. Expert Opin pharmacother, Recent Pharmacological advances in the treatment of preterm membrane rupture, labour and delivery. Doggrell SA. 2004.
10. Royal College of Obstetrician and Gynaecologist. Tocolytic drugs for women in preterm labour. Clinical Guideline no, 1(B); 2002: 216-230.
11. Sudarshan Saha. Role of magnesium sulphate in suppression of preterm labour. *J Obstet Gynaecol ind*, 2002; 52:53-57.