

Original Article



Effect of Magnesium Sulfate on Prevention of Preterm Labour and Perinatal Outcome

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Abstract

Background: Preterm labour is a major cause of maternal mortality in our country. Hypomagnesaemia during pregnancy could be an indirect cause of preterm labour. Magnesium has a role on uterine smooth muscle relaxation, which is the basis for the use of magnesium sulphate as a tocolytic agent. **Objective:** This study was done to see the effect of magnesium sulfate to prevent preterm labour and perinatal outcome. **Materials and Methods:** This study was carried out in Comilla Medical College & Hospital, from December 2011 to May 2012. Fifty pregnant women, both primi and multi with preterm labour were selected for the study. **Results:** Study showed labour delayed >24 hours in 86% cases. And the majority of newborn (96%) had Apgar score in 5 minute was 8-10, 4% had Apgar score 7-8. The mode of delivery was vaginal in 70% cases and by c/s in 16% cases; among subject whose labour delayed more than 24 hours. **Conclusion:** Intravenously administration of magnesium sulfate is safe, well tolerated and effective tocolytic agent for prolongation of pregnancy in preterm labour. It produces minimal harmful effects on mother and fetus.

Key words: Magnesium sulphate, Preterm labour, Tocolytic agent.

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Introduction

Preterm labour is defined as one where the labour starts before the 37th completed week (<259 days), counting from the first day of the last menstrual period.¹ The lower limit of gestation is not uniformly defined; whereas in developed countries it has been brought down to 20 weeks, in developing countries it is 28 weeks.¹ The incidence of preterm labour varies between 5-10%.¹ It accounts for 10-15% of all pregnancies. Preterm delivery is the major cause of infant mortality and morbidity.² It is also a major cause of maternal mortality and morbidity. Therefore, any treatment to prevent it would have a profound effect on neonatal outcome in both human and economic term and poses a great challenge to modern obstetrics.³ The cause of preterm labour is not yet completely known; in 50% cases it is

spontaneous and idiopathic. There are some risk factors like premature rupture of membrane, multiple pregnancies, polyhydramnios, hypertensive disorder of pregnancy, infection, cervical incompetence, ante partum hemorrhage, fetal and uterine anomalies, anemia, heavy work, smoking etc. It is also related to socio economic status and geographic location.⁴

Magnesium, one of the trace elements, is an important cation of the body. It is believed that magnesium plays a vital role in the premature onset of labour.⁵ It is a cofactor in more than 300 enzyme reaction. Magnesium activates those enzymes and plays an important role in the mechanism of nerve conduction, uterine contractility and contractile response of other smooth muscle. Magnesium antagonizes the action of calcium.

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It has an action of uterine myometrium causing it to relax by stimulating B2 adrenergic receptor and cyclic AMP (Adenosine Monophosphate). It competes with calcium ion which brings about inhibition of myosine kinase and therefore, a drop in phosphorylated myosine.⁶ Another possible way by which hypomagnesaemia induces uterine irritability by inhibition of adenylyl-cyclase with resultant increase in cytoplasmic calcium level.⁷ Thus hypomagnesaemia during pregnancy decrease the magnesium level in myometrium and low magnesium concentration in pregnant human myometrium could be a cause of preterm labour.⁸ Rising serum magnesium level serves to relax the uterine smooth muscle, thereby proving the basis for the use of magnesium sulphate as a tocolytic agent.⁹

The aim of tocolysis is not only to stop uterine contractions or to prevent preterm delivery but to prevent perinatal morbidity and mortality associated with preterm birth.¹ The commonly used tocolytic drugs are betamimetics, prostaglandin synthetase inhibitor, magnesium sulphate, calcium channel blockers, oxytocin receptor antagonists, nitric oxide and progesterone.¹ Compared with beta-adrenergic agonists, magnesium sulfate is often used as first line therapy for tocolysis. Magnesium sulfate can delay the premature labour for 24-48 hours.¹⁰ Such delay increases the time that may be required for the beneficial effects of adjunctive corticosteroid therapy or for transfer to a tertiary treatment center capable of handling a preterm delivery. It is highly effective and is associated with fewer side effects. Complications associated with use of magnesium sulfate are rare and occurs with toxic level.¹¹ If preterm labour is likely to lead to preterm delivery magnesium sulfate may be used to reduce the risk of cerebral palsy in premature new born.¹²

Bangladesh is one of the developing countries of the world, where due to poverty, illiteracy, malnutrition and lack of proper antenatal care infant mortality and morbidity rate is high. New lights being focused on the use of tocolytic agent on preterm labour to minimize infant mortality and morbidity in developed countries but very few studies have been documented in our country. So a need was felt for study on the arrest of preterm labour by using magnesium sulfate as a tocolytic agent and to see the perinatal outcome.

Material & Methods

This Quasi experimental study was carried out in Comilla Medical College & Hospital, from December 2011 to May 2012 (6 months). Total 50 pregnant women, both primi and multi admitted with preterm labour but not in active labour pain were selected in this study. Gestational age determined from LMP (last menstrual period) and from early USG. Pregnancy of more than 28 weeks' duration and less than 37 completed weeks were included in this study. On per abdominal examination fundal height, amniotic volume and fetal conditions are assessed. For confirmation the progress of labour a single sterile per-vaginal examination done to see cervical effacement, dilatation and membrane intact. Painful uterine contraction at least once in 10 minutes is a characteristic of preterm labour pain. On per-vaginal

examination membrane intact and Cervical os less than 4 cm dilatation confirmed preterm labour. Any cases of maternal or fetal diseases or disorders and contraindication to use magnesium sulfate therapy were excluded from this study.

After proper counseling and taking consent from patient, inj. Nalepsin 100 ml containing 4 gm Magnesium sulfate was infused within 30 minutes. Then continuous infusion of magnesium sulfate at 2 gm per hour. This infusion was titrated up by increments of 0.5 gm per hour to a maximum of 4gm per hour until adequate tocolysis is achieved (<4-6 uterine contractions per hour). Infusion was continued until labour subsides or progress to as irreversible stage (cervical dilatation of 5 cm). Treatment progress assessed by observing uterine contraction at 0 hr, 4 hr, 8 hr, 12 hr and at 24 hr. After delivery Apgar score was recorded and all babies' condition were monitored up to discharge. Magnesium sulfate was stopped if urine output is less than 30 ml/hour or patellar reflexes are absent or respiration rate is less than 12/min.

Results

Table I: Distribution of study subjects according to age.

Age	Frequency	Percentage
20 years	15	30.0
21-25 years	21	42.0
26-30 years	9	18.0
>30 years	5	10.0
Total	50	100

Table I shows 42% of patients belongs to age 21-25 years and 30% belongs to age <20 years. The most of our patients were younger than 25 years.

Table II: Distribution of respondents by parity (N=50).

Parity	Frequency	Percentage
Primi	20	40
Multi	30	60
Total	50	100

Table II shows Majority (60%) of the respondents were multipara.

Table III: Distribution of the respondents by gestational age (N=50).

Gestational Age	Frequency	Percentage
28-30 weeks	7	14
31-33 weeks	25	50.0
34-36 weeks	18	36
Total	50	100

Table III shows 50% of the patients is between 31-33 weeks, 36% patients are in 34 to 36 weeks. All of our patients were preterm and the less gestational age carry more complications of neonatal asphyxia, neonatal jaundice, infections, respiratory distress syndrome, PDA, retinopathy of prematurity, cerebral palsy, mental retardation, Intracranial hemorrhage etc.

Table IV: Frequency Distribution of Socioeconomic Status (N=50).

Class	Frequency	Percentage
Poor	35	70
Middle	10	20
Upper	5	10
Total	50	100

[N.B. Socioeconomic status was determined by monthly family income. Poor <6,833tk per month, Lower Middle 6,833-26,900tk per month, Upper middle >26,900-83,167 and upper class >83,167tk. per month] (World Bank atlas method 2012)

Table IV shows Majority of respondents (70%) were from poor socioeconomic status, 20% from middle class and 10% from upper class. Low socioeconomic status is major cause of illiteracy, malnutrition and lack of prenatal and perinatal checkup which leads to more chance of premature baby. It has also effect on maternal and fetal mortality.

Table V: Distribution of study subject according to arrest of labour by intravenous MgSO₄.

Injection	Labour delayed >24 hours		Labour occurred < 24 hours		Z	P
	Frequency	Percentage	Frequency	Percentage		
Magnesium sulfate for tocolysis	43	86	7	14	14.67	<0.0001

This table shows after given magnesium sulfate, in 86% cases the labour delayed >24 hours, which is significant (p<0.0001). Most of our health care center and even district hospitals do not have neonatal care unit (NICU). So if we can delay the labour, we can get more time that may be required for the beneficial effects of adjunctive corticosteroid therapy or for transfer to a tertiary treatment center capable of handling a preterm delivery. Thus we can prevent both maternal and fetal mortality and morbidity.

Table VI: Maternal side effects after giving magnesium sulfate.

Maternal side effects	Frequency	Percentage
Flushing	10	20
Nausea	8	16
Headache	2	4
Dry mouth	1	2
No Side Effects	29	58
Total	50	100

This table shows magnesium sulfate implementation gives no side effect in 58% patients. All drugs have some side effect and adverse effect, but if these are within tolerable limit, we can say this is a safe drug. Magnesium toxicity is rare. Toxicity can usually develop after serum concentrations exceed 1.74-2.61 mmol/L. A normal adult can take magnesium oxide up to 350 mg/day orally, and magnesium sulfate up to 40 gm intravenous per day. We usually give 4 g in 250 mL of 5% Dextrose Injection at a rate not exceeding 3 mL per minute.

Table VII: Mode of delivery.

Mode of delivery	Delivered >24 hours		Delivered <24 hours	
	Frequency	Percentage	Frequency	Percentage
Vaginal	35	70	3	6
Cesarean section	8	16	4	8
Total	43	86	7	14

Table VII shows the mode of delivery was vaginal in 70% cases and by c/s in 16% cases; among subject whose labour delayed more than 24 hours. We all knows vaginal delivery is more preferable than cesarean section for both fetal and maternal benefit and also cost effective. If we can delay the labour, our study shows we can avoid the cesarean section and can achieve the goal of healthy mother and healthy baby.

Table VIII: Distribution of new born by Apgar score in 1 and 5 minutes.

Apgar score	In 1 st minute	In 5 th minute
4-6	8(16%)	0
7-8	1(2%)	2(4%)
8-10	41(82%)	48(96%)
Total	50 (100%)	50 (100%)

Apgar score describes the health of a newborn right after birth. It is the measuring tool by which we can say whether the baby is well adapted with environment or not. The Apgar score is determined by evaluating the newborn baby on five simple criteria on a scale from zero to two, then summing up the five values thus obtained. The resulting score ranges from zero to 10. The five criteria are summarized using words chosen to form a backronym (A ppearance, P ulse, G rimace, A ctivity, R espiration).Table VIII shows Majority of newborn (82%) had Apgar score in 1 minute was 8-10, 16% had Apgar score was 4-6. And majority of newborn (96%) had Apgar score in 5 minute was 8-10, 4% had Apgar score 7-8.

Table IX: Fetal effect after giving magnesium sulfate in terms of fetal movement.

Fetal movement	Frequency	Percentage
Good	44	88
Less	6	12
Total	50	100

Fetal movement starts from 16 to 25 weeks of pregnancy.10 movements of any kind in an hour or less is normal. It is a parameter to observe the wellbeing of the fetus.Table IX shows good fetal movement was observed in 88% cases and less fetal movement in 12% cases.

Table X: Fetal effect after giving magnesium sulfate in terms of fetal heart sound.

Fetal heart sound	Frequency	Percentage
110-180 (beat per minute)	46	92
<110 (beat per minute)	4	8
Total	50	100

The fetal heart rate is between 90 and 110bpm in early pregnancy.⁷ It will then rise and peak around the 9th and 10th week, to 170 bpm. Following this, the heartbeat becomes normal and stabilizes between 120 and 160bpm during the second and third trimesters. Table X shows 92% of cases fetal heart sound was between 110-180 beat per minute, 8% cases fetal heart sound was <110 beat per minute.

Discussion

In this study intravenous administration of magnesium sulfate has been studied as tocolytic agent for prolongation of pregnancy in preterm labour. Potential advantage of magnesium sulfate as tocolytic agent is that, it provides sufficient time for the action of corticosteroid in premature lung of baby or transfer the mother to a tertiary center capable of handling preterm baby.

In this study 50 women were enrolled. All of them came with sign and symptoms of preterm labour. They were treated with intravenous magnesium sulfate for tocolysis and its fetomaternal outcome are summarized in different table.

Maternal age at pregnancy is increasing worldwide as well as preterm birth. However, the association between prematurity and advanced maternal age remains controversial. Study shows mothers younger than 24 years and older than 35 years, preterm birth was significantly more frequent compared to the reference group (30-34 years).¹³

Among the patients 42% were in 21-25 years. This finding is consistent with the findings of the study Block et al,¹⁴ According to his study the age group was 22-35 years.

Among the study population majority were multigravida (60%) and (40%) were primi. Majority of preterm labour was found between 31-33 weeks of gestational.

In our country multiparity is the many cause of dense population which leads to malnutrition, lack of maternal health care and more fetomaternal complication. Increased maternal age, multiple pregnancies and medical complications are significantly associated with the risk of preterm birth.¹⁵

In Goldenberg RL study, gestational ages were 34-36 weeks in 60-70% cases.¹⁶ A Study by Mahajan A majority of cases gestational age was 33-34 weeks.¹⁷

In this study among the study subjects 70% were from low socioeconomic status. This finding is similar with study by Lipi LB.¹⁸ In her study majority patient (61.60%) were from low socioeconomic group.

Royal College of obstetricians and gynaecologist rules out the justification of use of tocolytic agent in their October¹⁹ issue of clinical guideline 1(B) due to clear possible evidence of

their effectivity. In this study after giving magnesium sulfate preterm birth delayed for more than 24 hours in 86% patients, so tocolysis was achieved in 86% patients. The study is comparable to other studies, Mahajan A, Marwah P.¹⁷ In his study magnesium sulfate was successful in attaining tocolysis in 82% cases. This finding is similar with study by Sudarshan Saha.²⁰ In this study tocolytic was effective in 90.3% cases in delaying labour.

In this study flushing (20%), Nausea (16%) was the commonest side effects. These side effects were not so significant in comparison to other tocolytic agents. Few patients reported headache (4%), dry mouth (2%). This finding is similar to other study by Mahajan A, Marwah P (2015).¹⁷ Among the study population whose labour delayed more than 24 hours, 70% patients delivered vaginally and 16% patients needed caesarean section due to fetal distress.

Newborn with good Apgar score was found 82% cases 8-10 and 16% cases 4-6 and 2% cases with Apgar score was 7-8 at 1 minute. In 96% cases Apgar score was 8-10 and 4% cases 7-8 at 5 minute.

In this study less fetal movement was found 12% cases. Fetal heart sound below 110 beat sounds was found in 8% cases.

The present descriptive study has shown that intravenously administered magnesium sulfate is an effective tocolytic agent in preterm labour and has comparatively better fetomaternal outcome than other tocolytic agent.

The result of this study is suggestive but not conclusive that magnesium sulfate may prolong pregnancy in preterm labour. One important thing in this study is that after commencement of treatment with magnesium sulfate, the patients were kept under meticulous follow up. Frequency of uterine contraction was counted as a tangible measurement of effective treatment. The patient was also observed for signs and symptoms of magnesium sulfate toxicity.

Further studies are needed to assess the use of magnesium sulfate in preterm labour in rural settings. There are some controversies to give treatment with magnesium sulfate in preterm labour in our country. Moreover, sample size is not enough to avoid all bias. Very few studies have been documented on tocolytic effect of magnesium sulfate in our country. Hence detailed study is necessary with appropriate design and adequate sample size.

Conclusion

Magnesium sulfate is effective, safe and well tolerated tocolytic agent for prolongation of preterm labour. It produces lesser maternal and fetal side effects. So we recommend Magnesium sulfate should be used to prevent preterm labour for better maternal and fetal outcome. A large scale study can bring out more effective results.

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