Role of Magnesium Sulphate in Suppression of Preterm Labour

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Summary

The efficiency of magnesium sulphate was evaluated in 75 patients for suppressing pre-term labour. In the age group 22 to 35 years. Delivery was deferred for more than 72 hours in 90.7% cases. The tocolytic effect started within 30min after administration. There were neither serious hypotensive, nor major side effects like urinary suppression, respiratory failure and loss of patellar reflexes. Minor side effects occurred without any harmful effects or Apgar score of babies. Overall success in achieving the target with live babies were 89.3%. Deferment of preterm labour provided sufficient time for corticosteroid therapy to reduce the incidence of RDS in the newborn. Proper selection of the cases, judicious use and monitoring the effects of the drug is a key to success.

Introduction

Pre-term delivery which accounts for over 75% of all cases of perinatal morbidity and mortality remains the most important obstetric problem of the world today. (Anderson 1977). The incidence of low birth-weight in India is about 30% to 40% of which 12% to 18% is associated with gestational age less than 37 weeks (Krishna Menon et al, 1982).

Incidence of RDS (Respiratory Distress Syndrome) is 15% to 20% in 32-36 weeks (Beherman & Vaughan, 1983). Foetuses between 28 to 32 weeks of gestational age need glucocorticoids to enhance lung maturity. This can be achieved if delivery is possible by 24-72 hours. Infants weighing more than 700 to 1500 gms have an overall survival rate approximately 50%. Inhibition of uterine contractibility for at least 3 days or more than 7 to 15 days may be regarded as an optional action of any tocolytic agent to reduce perinatal mortality.

A satisfactory pharmacological method for the prevention or treatment of preterm labour is yet to be found. It has been recognized for sometime that ionic magnesium in a sufficiently high concentration can alter myometrial contractility in vivo as well as in vitro. Kurzel (1991) reported that patients going to preterm labour were shown to have sufficiently lower serum magnesium level. Its role is that of a calcium antagonist. Hence magnesium sulphate has been chosen as one such drug to study its effect on preterm labour.

Materials and Methods

This longitudinal study was conducted at North-Bengal Medical College, Department of Obstetrics & Gynaecology at Susrut Nagar, Darjeeling, West Bengal in 75 cases of Singleton pregnancy of gestational age 28-37 weeks from 1st January 2000 to 30th June 2000. Selection of cases was based on the criteria of at least 2 uterine contraction in 15 minute lasting for atleast 30 seconds, intact foetal membranes, cervical effacement

80% and cervical dilatation not more than 4 cm. Any maternal disorder like PIH, heart disease, APH, uncontrolled diabetes mellitus and foetal disorders like IUFD, foetal distress, IUGR and polyhydramnios were excluded from the study.

On admission meticulous history and informed consent were taken and in the 30 minute observation period foetal heart rate, uterine activity and maternal blood pressure were recorded.

An initial loading dose of 4gms magnesium sulphate (four ampoules of 50% magnesium sulphate equivalent to 4gms of the drug were dissolved in 20cc of 5% dextrose solution) was given intravenously slowly over 5 to 10mins. This loading dose was followed by 2gm/hour continuous infusion with 5% dextrose solution. If contraction persisted after 1 hour, the infusion rate was increased to 3gm/hour and usually contractions subsided. Intravenous drip was maintained for another 4 hours at the rate of 2gm per hour after the contractions subsided. Treatment was declared successful if contractions were abolished and pregnancy prolonged for 72 hours from the beginning of the therapy.

If contactions reappear after 48 hours the doses may be repeated as stated above. Efficacy of the drug was monitored by observing subsidence of uterine contraction, F.H.S., respiration rate of the mother of at least 14 per minute. Urine output more than 30 ml per hour, presence of deep reflexes, knee jerk, and diastolic blood pressure less than 100 mm of Hg.

Results and Analysis

Age and parity distribution of the cases were as follows

18 (24%) were below 25 years of age

54 (72%) were between 25-35 years of age

3 (4%) were above 35 years

52 (69.3%) were primiparas

19 (25.3%) were 2nd to 5th gravidas and 4 (5.3%) were multiparas.

Five patients (6.7%) had gestation below 30 weeks, 57 (76%) between 31 to 33 weeks and 13 (17.3%) between 34 to 37 weeks (Table-I).

Dilatation of the cervix when treatment was initiated and onset of action interval is shown in Table II. Out of 75 patients 30 (40%) had cervical dilatation 2-3.5cm and 29 (38.6%) had cervical dilatation 4cm. Inhibition of uterine contraction started in 28 (37.3%) cases within 2-4 hours of onset of treatment and in 17

Table I

Distribution of cases according to Age (a) Parity (b) and period of Gestation (c):

Age in years	a No. of Cases 75	Percentage %	Parity	b No. of cases	Percentage %	Period of gestation in weeks	c No. of cases	Percentage %
Less than 25	18	24	P -P	52	69.3	28-30	5	6.7
25-35	54	72	P_2-P_5	19	25.3	31-33	57	76
Above 35	3	4	Above P_5	4	5.4	34-37	13	17.3

Table II

Distribution of cases according to dilatation of cervix when treatment was initiated (a) and time for set of action (b)

Dilatation of Cervix in cm	a No. of Cases (75)	Percentage %	Inhibition of contraction started within	b No. of cases (75)	Percentage %
			½ hr.	10	13.4
0-1.5	16	21.4			
			1-2 hr.	17	22.7
2-3.5	30	40	2-4 hr.	28	37.3
			Greater than	13	17.3
4	29	38.6	4hr		
			No. effect	7	9.3

(22.7%) cases within 1 to 2 hours of treatment while there was no effect in 7 (9.3%) cases. In 13 (17.3%) cases contraction was inhibited after 4 hours and only in 10 (13.4%) cases contraction disappeared within ½ hour of therapy and labour was inhibited in 68 (90.7%) cases.

The time interval between putting the patient on therapy and delivery is shown in table-III. Overall success rate was 89.3% and 67 babies survived. Out of 75 patients 73 had live born babies and 2 had still born. 8 babies had poor apgar score and died in perinatal period from RDS, asphyxia, infection and jaundice (Table IV).

Out of these 6 cases 4 cases were primiparas aged 25 years and 2 were 2nd gravida aged 33 years had period of gestation 29 weeks and 31 weeks respectively. On admission 2 to 3 uterine contractions each of 30 seconds duration was observed within 15 minutes and had cervical dilatation of 3.5cm and 4cm respectively.

On administration of magnesium sulphate as per regime inhibition of uterine contractions started within 2 to 4 hours and postponement of labor was for 36 hours and 24 hours respectively, and all the cases ended in spontaneous vaginal delivery. The subsequent perinatal outcome is as observed in Table IV.

Of these successful cases 62 patients had normal delivery, 3 required forceps for maternal distress and 5 needed L.S.C.S. for prolonged second stage with foetal distress (Table III). Postponment of delivery for more than 3 weeks was seen in 48 patients while 3 delivered within 3-7 days of therapy. Transient side effects noted during the study are shown in table-V

Table III
Time interval between drug action and delivery

Time from drug administration to delivery (No. of days taken)	No. of Cases (75)	Percentage %
Below 3 days	9	12
Between 3-7 days	3	4
7-14 days	7	9.33
15-21 days	8	10.67
Above 21 days	48	64

Table IV
Causes of Perinatal death (a) and Apgar score at delivery in successful cases (b)

a			b		
Causes of death	No. of cases (8)	Percentage	Apgar score	No. of cases (18)	Percentage
RDS	2	25	Less than 3	4	5.48
Asphyxia	2	25	3 to 5	2	2.74
Infection	1	12.5	5 to 7	6	8.21
Jaundice	1	12.5	Greater than 7	6	8.37
Stillbirth	2	25			

Table V
Transient side effects during Trial

Side effects	No. of cases examined	Percentage %
Depression	30	40
Palpitation	7	9.33
Dizziness	5	6.66
Headache	7	6.66
Flushing	15	20
Dyspnea	6	8
Tremor	10	13.33

Discussion

In our country where sophisticated neo-natal intensive care units are not commonly available by reducing the incidence of pre-term labour, neo-natal morbidity and mortality can be reduced.

In this study labour was delayed in 68 (90.3%) cases for 3 or more days with magnesium-sulphate therapy. This could allow sufficient time for cortico-steroid therapy to exert a favourable effect for reducing the incidence of RDS in the newborn (Higgin & Howie 1972 and Block et al 1977).

The tocolytic effect starts instantly after the administration of magnesium sulphate. The concentration of magnesium in plasma rises slowly after intramuscular injection requiring 90 to 120 mins. While by intravenous administration optimum level of serum magnesium contraction was achieved within 30 mins. Oral magnesium salts are an alternative to adrenergic agents for the prophylactic treatment of pre-term contractions (Martin et al 1987). According to Petric et al (1976) intravenous administration of 3 gm of magnesium sulphate to woman in labour has been found to decrease uterine activity by approximately 10%. Steer and Petrie (1977) concluded that intravenously in administered magnesium-sulphate, 4gm as a loading dose, followed by continuous infusion of 2gm/hour. will usually arrest labour. Elliot (1983) in a retrospective study found tocolysis with magnesium sulphate to be successful, inexpensive and relatively non-toxic and reported 87% success rate when the cervix was 2cm or less dilated, but the period of inhibited labour was as short as 48 hours. However Cox and associates (1990) found no benefit from such therapy and this method of tocolysis was abandoned at Parkland hospital.

Magnesium administered to the mother promptly crosses the placenta to achieve equilibrium in foetal serum and less so in amniotic fluid (Hallak et al 1993). Gray et al (1994) reported that therapeutic magnesiumsulphate for tocolysis did not alter the bio-physical profile in 25 foetuses studied. The neonate may be depressed only if severe hypermagnesemia exists at delivery. They have not observed neonatal compromise with intramascular therapy with magnesium sulphate. Therefore, women given high doses of magnesium sulphate must be monitored very closely for hypermagnesemia that might prove toxic to them and the foetus. Somjen et al (1966) induced in themselves by intravenous infusion marked hypermagnesemia, achieving plasma level upto 15m.Eq/l, respiratory depression developed that necessitated mechanical ventilation, but depression of the sensorium was not dramatic as long as hypoxia was prevented. More recently, Nelson and Grether (1995) described a possible protective effect of magnesium against cerebral palsy in very low birth weight infants.

Transient side effects during treatment like depression, palpitation, dizziness, headache and dyspnoea were noted within two hours of treatment.

It is significant that side effects of magnesiumsulphate therapy are easily reversible with intravenous administration of 1 gm calcium gluconate and withholding of magnesium sulphate.

Block et al (1977) demonstrated that in foetuses between 28 to 33 weeks of gestation, glucocorticoid is to be given to the mother to accelerate foetal pulmonary maturity it is appropriate and necessary that delivery be delayed for at least 24-72 hours which is the desired target of any tocolytic therapy. The present study suggests this aim can be safely attained by magnesiumsulphate therapy.

Conclusion

Success of such therapy depends on proper selection of cases, judicious administration and monitoring the effect of the drug. Pre treatment serum magnesium level is within 2 to 5m. eq. lit and the desired level of serum-magnesium should be within 5 to 7m.eq lit and should not exceed 10m.eq/lit, when loss of patellar reflexes begins and never beyond 12m.eq lit when respiratory arrest may occur.

Doses should be adjusted according to the frequency of uterine contraction. Higher doses may be required if there is increased tonicity and lower doses with poor G.F.R (Glomular Filteration Rate), higher serum level resulting from poor excretion of magnesium. So doses should be regulated and controlled by infusion pump. There are very few studies on tocolytic effect of magnesiumsulphate. Hence meticulous study is desired to evaluate optimum outcome.

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