

DOI: <https://dx.doi.org/10.18203/2320-1770.ijrcog20210714>

Original Research Article

A comparative study of magnesium sulphate and isoxsuprine as a tocolytic in preterm labour

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Received: 20 September 2020

Revised: 07 February 2021

Accepted: 09 February 2021

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ABSTRACT

Background: Preterm birth is a significant health problem across the world because of associated neonatal mortality and short-and long-term morbidity in later life. The incidence in India is higher than developed countries.

Methods: The present study conducted in the Department of Obstetrics and Gynaecology, MGM Medical College and M. Y. Hospital. Indore, (Madhya Pradesh). The patients selected from labour rooms. 100 antenatal women of gestational age between 28 weeks to 37 weeks presenting with preterm labor, 50 in each group. Group A consisted women receiving magnesium sulphate, group B had women receiving isoxsuprine. Efficacy of the two tocolytics, prolongation of pregnancy and neonatal outcome in preterm labour was assessed.

Results: Intravenous magnesium sulphate was much effective in postponement of preterm labour for at least 48 hours (74%) as compared to isoxsuprine (50%). As a cervical dilatation, effacement increased the success rate of both the drugs came down. Magnesium sulphate side effects were better monitored clinically and tolerated. Also, better neonatal outcome and lesser perinatal mortality were noticed in this group (24%) compared to isoxsuprine (54%).

Conclusions: Prematurity is the one of the major risk factor determining perinatal outcome. There is no ideal tocolytic, short term prolongation till steroid coverage for lung maturity with minimum side effects and to achieve better perinatal outcome recommended. The number of nursery admissions of preterm babies with better perinatal outcome were observed with magnesium sulphate. Also, the number of nursery admissions of preterm babies were less when treated with magnesium sulphate as tocolytic (also found to have neuroprotective effects in various studies), as compared to isoxsuprine.

Keywords: Preterm, Tocolytic

INTRODUCTION

Preterm labour remains one of the challenges in present day obstetrics. Its incidence ranges between 10-15% and 75% of all perinatal deaths occur in preterm infants. The incidence in India varies from 40-150 per 1000 births in comparison to 10-20% in the developed countries.¹

Preterm is defined as babies born alive before 37 weeks of pregnancy. Subcategories based on gestational age. Extremely preterm (<28 weeks). Very preterm (28-32 weeks). Moderate to late preterm (32-37 weeks).²

Preterm labour is defined as regular contractions of uterus resulting in changes in the cervix that start before 37 weeks of pregnancy, changes in the cervix include effacement and dilation.³

Various drugs with different pharmacologic principles are used to suppress preterm labour. The choice is limited by their efficacy, safety and side effects. The main objective of tocolytic therapy is to delay pregnancy long enough to allow time for the administration of antenatal steroids to improve foetal lung maturity and maternal transport to a neonatal intensive care unit.⁴ The secondary purpose of

tocolytic treatment is to delay delivery to reduce the perinatal morbidity and mortality associated with severe prematurity.⁵

METHODS

The present study was conducted in the Department of Obstetrics and Gynaecology, MGM Medical College and M. Y. Hospital, Indore, (Madhya Pradesh) during the period of March 2017 to August 2018. This was prospective type of cohort study. The patients selected from labour rooms.

Sample size

100 antenatal women of gestational age between 28 weeks to 35 weeks presenting with preterm labor, 50 in each group-

Group A: Women receiving magnesium sulphate.

Dosage: Loading dose: 4 gm i.v. in 20 ml NS as i.v. loading dose given over a period of 20 minutes; Maintenance dose: 2gm/hr (10 ampoules of 50% MgSO₄ in 5% dextrose solution at the rate of 25 drops per minute for 24 hours as tolerated after contractions cease.

Group B: women receiving isoxsuprine.

Dosage: 10 mg intramuscular 8 hourly for 24 hours followed by tab duvadilon 20 mg BD till contraction ceases. Comparative efficacy of both the drugs were studied

Inclusion criteria

Pregnant women from 28 weeks upto 34 weeks 6 days of gestation presenting with preterm labour. Regular uterine contractions, 2 or more than 2 per 10 minute each lasting for at least 30 seconds. Cervical dilatation not more than 3 cm. Cervical effacement not more than 50%. Membranes intact. Normotensive females

Exclusion criteria

Pregnant females <28 and >35 weeks of gestation. Ruptured membranes. Pregnant females with gestational hypertension, pre-eclampsia, and eclampsia, antepartum haemorrhage, IUFD. Pregnant females with chronic medical ailments (heart disease, diabetes, jaundice, tuberculosis, asthma, glaucoma). Hypersensitivity to MgSO₄ or isoxsuprine. Fetal malformation.

RESULTS

Table 1 shows distribution between gestational age in patient groups which shows 32% and 48% were in the gestational age of 28-32 week while 68% and 52% were in the gestational age of 33-36 week in magnesium sulphate and isoxsuprine groups.

Table 1: Gestational age wise distribution.

Gestational age	Group		Total	
	Magnesium sulphate	Isoxsuprine		
28-32 Week	Count	16	24	40
	%	32.0	48.0	40.0
33-36 Week	Count	34	26	60
	%	68.0	52.0	60.0
Total	Count	50	50	100
	%	100.0	100.0	100.0

Pearson's Chi square =2.667, df =1, P value =0.102 non-significant

The association was found to be non-significant and thus the both groups were comparable.

Table 2: Distribution of patients in study group as per uterine contraction.

Uterine contractions per 10 minute duration	Group		Total	
	Magnesium sulphate	Isoxsuprine		
1	Count	15	11	26
	%	30.0	22.0	26.0
2	Count	23	31	54
	%	46.0	62.0	54.0
3	Count	12	8	20
	%	24.0	16.0	20.0
Total	Count	50	50	100
	%	100.0	100.0	100.0

Pearson's Chi square =2.601, df=2, P value =0.272 not significant

Table 2 shows distribution between uterine contraction and patient groups. Most of the patients had uterine contraction of 2 per 10 minute duration, was 62% and 46% for isoxsuprine group and magnesium sulphate group and which was comparable. The association was statistically not significant.

Table 3: Status of cervical dilatation after 24 hours of tocolysis in patients groups.

Cervical dilatation on 24 hours (in cm)	Group		Total	
	Magnesium sulphate	Isoxsuprine		
<10 cm (undelivered)	Count	39	26	65
	%	78.0	52.0	65.0
10 cm (delivered)	Count	11	24	35
	%	22.0	48.0	35.0
Total	Count	50	50	100
	%	100.0	100.0	100.0

Pearson's Chi square =7.429, df=1, P value =0.006 Significant

Table 3 shows the association between cervical dilatation value after 24 hours of tocolysis and patient groups.

The above association found to be statistically significant ($p < 0.05$) which shows that 78.0% were undelivered in magnesium sulphate group and 52% were undelivered among isoxsuprine group.

Table 4: Association between cervical effacement and patient groups.

Cervical effacement (%)		Group		Total
		Magnesium sulphate	Isoxsuprine	
<20	Count	7	2	9
	%	14.0	4.0	9.0
≥40	Count	11	18	29
	%	22.0	36.0	29.0
20-40	Count	32	30	62
	%	64.0	60.0	62.0
Total	Count	50	50	100
	%	100.0	100.0	100.0

Pearson's Chi square = 4.532, df=2, P value=0.104 not significant

Table 4 shows association between cervical effacement and patient group. The association was not significant. Both groups shows highest effacement under 20-40%. 64% and 60% for magnesium sulphate and isoxsuprine respectively which makes the association comparable.

Table 5: Association between prolongation duration and patient groups.

Prolongation duration		Group		Total
		Magnesium sulphate	Isoxsuprine	
<1 day	Count	13	25	38
	%	26.0	50.0	38.0
>7 days	Count	8	3	11
	%	16.0	6.0	11.0
1-2 days	Count	20	17	37
	%	40.0	34.0	37.0
2-7 days	Count	9	5	14
	%	18.0	10.0	14.0
Total	Count	50	50	100
	%	100.0	100.0	100.0

Pearson's Chi Square = 7.448, df=3, P value=0.059, not significant

Table 5 shows association between prolongation duration and patient groups. The association was found to be non-significant. The prolongation duration shows comparable values, highest being 40% and 18% for magnesium sulphate and 34% and 10% for isoxsuprine for the duration of 1-2 days and 2-7 days duration. Other durations also shows non-significant differences between two groups.

Table 6 shows comparison of neonatal outcome of patient groups. The comparison was found to be statistically significant ($p < 0.05$). The outcome as healthy or

NICU/nursery admission baby depends on the drug groups given for prolongation.

Table 6: Comparison of neonatal outcome in patient groups.

Outcome		Group		Total
		Magnesium sulphate	Isoxsuprine	
Healthy	Count	38	27	65
	%	76.0	54.0	65.0
Nursery	Count	12	23	35
	%	24.0	46.0	35.0
Total	Count	50	50	100
	%	100.0	100.0	100.0

Pearson's Chi square = 5.319, df=1, P value=0.021, Significant

The outcome of magnesium sulphate shows higher values 76% in healthy category and lesser value in nursery 24% than 54% and 46% in isoxsuprine. This makes a significant difference in both groups.

Table 7: Association of symptoms of vomiting and nausea in patient groups.

Vomiting and nausea		Group		Total
		Magnesium sulphate	Isoxsuprine	
Absent	Count	40	39	79
	%	80.0	78.0	79.0
Present	Count	10	11	21
	%	20.0	22.0	21.0
Total	Count	50	50	100
	%	100.0	100.0	100.0

Pearson's Chi square = 0.060, df=1, P value = 0.806, not significant

Table 7 shows association of symptoms of vomiting, and nausea in patient, which was more with magnesium sulphate group (20%). The association was found to be non-significant ($p > 0.05$).

Table 8: Association between hypotension and patient groups.

Hypotension		Group		Total
		Magnesium sulphate	Isoxsuprine	
Absent	Count	47	37	84
	%	94.0	74.0	84.0
Present	Count	3	13	16
	%	6.0	26.0	16.0
Total	Count	50	50	100
	%	100.0	100.0	100.0

Pearson's Chi square = 7.440, df=1, P value=0.006, significant

Table 8 shows association between hypotension and patient groups. Proportion of 26% in isoxsuprine show

the symptom of hypotension as compared to 6% in group 1 which makes the difference significant ($p < 0.05$).

Table 9: Association between tachycardia in patient groups.

Tachycardia		Group		Total
		Magnesium sulphate	Isoxsuprine	
Absent	Count	42	21	63
	%	84.0	42.0	63.0
Present	Count	8	29	37
	%	16.0	58.0	37.0
Total	Count	50	50	100
	%	100.0	100.0	100.0

Pearson's Chi square =18.919, df=1, P value=0.000, significant

Table 9 shows association between tachycardia and patient groups. The association was found to be significant ($p < 0.05$). Isoxsuprine shows 58% with symptom of tachycardia as compared to 16% in Magnesium sulphate group.

Table 10: Association between lethargy in patient groups.

Lethargy		Group		Total
		Magnesium sulphate	Isoxsuprine	
Absent	Count	36	44	80
	%	72.0	88.0	80.0
Present	Count	14	6	20
	%	28.0	12.0	20.0
Total	Count	50	50	100
	%	100.0	100.0	100.0

Pearson's Chi square =4.000, df=1, P value=0.046, significant

Table 10 shows association between lethargy and patient groups. The association was found to be statistically significant ($p < 0.05$). In magnesium sulphate 28% showed symptom of lethargy as compared to 12% in isoxsuprine which makes the difference in both groups significant.

Table 11: Association between flushing in patient groups.

Flushing		Group		Total
		Magnesium sulphate	Isoxsuprine	
Absent	Count	27	44	71
	%	54.0	88.0	71.0
Present	Count	23	6	29
	%	46.0	12.0	29.0
Total	Count	50	50	100
	%	100.0	100.0	100.0

Pearson's Chi Square =4.000, df=1, P value=0.046, significant

Table 11 shows association between flushing and patient groups. The association was found to be significant ($p < 0.05$). The difference was significant as 12% in isoxsuprine showed the symptom of flushing as compared to 46% in magnesium sulphate

DISCUSSION

The study was done to compare the efficacy of tocolytics (magnesium sulphate and isoxsuprine), prolongation of pregnancy to term and to assess neonatal outcome in preterm labour.

In the study 26% patients were primigravida and 74% were multigravida, 52% in isoxsuprine group. In magnesium sulphate group 78% were undelivered whereas in isoxsuprine group 52% were undelivered after 24 hours of tocolysis.

The commonest side effect experienced by patients in magnesium sulphate group was flushing 46% and lethargy 28% but the commonest side effect of isoxsuprine group was tachycardia 58%, hypotension 26% and nausea and vomiting 22%.

The association of prolongation of gestation to term/preterm was found to be not significant ($p > 0.05$). In magnesium sulphate group 94% and isoxsuprine group 100% delivered in preterm gestation i.e. < 37 weeks. Maximum prolongation of gestation was 34 days with magnesium sulphate tocolysis.

The comparison of final perinatal outcome was found to be statistically significant ($p < 0.05$). 65% babies were handed over as healthy after delivery and 35% were admitted in nursery/NICU and cause of admission in most babies were low birth weight followed by respiratory distress. Out of which 10 babies were certified. Perinatal mortality were more with isoxsuprine group. Final outcome shows a higher value of healthy perinatal outcome 72.2% with magnesium sulphate.

In a study by Elliott et al- low dose magnesium sulphate (4 gm loading dose/2 gm per hour) were successfully tocolysed for 48 hours in 69.2% treated patients.⁶

Nasser et al reported 78 cases were carried out for more than 48 hours, compared to 77 who received for less than 48 hours and mean duration of treatment range was 2.5-80 days.⁷ 2 mothers have osteopenia postpartum with normal calcium levels.

Schanier et al showed similar findings with abnormal bone mineral content noted by ultrasound which disappeared shortly after birth.⁸

Risk to mother was much lower (2%) for serious side effects, careful monitoring recommended. In babies bone demineralization seen which was reversible.⁹

Mahajan et al showed successful tocolysis in 82% cases and 66% cases with magnesium sulphate and isoxsuprine respectively. Magnesium sulphate was able to maintain successful tocolysis for 7 days in 74% cases as compared to 50% in patients receiving isoxsuprine. Lethargy (20%) and nausea (14%) were most frequent side effects with magnesium sulphate while fetal tachycardia and maternal hypotension were with isoxsuprine.

There are some limitations. Careful monitoring of the tocolytics required for better maternal and fetal outcome. Maintenance of therapeutic drug levels required, hence effective as short term tocolytic.

CONCLUSION

Preterm labour remains one of the challenges in present day obstetrics despite the use of wide range of tocolytics used to arrest the preterm labour. Newborn death accounts for 40% of all death among children under 5 years of age.¹¹ The choice for the ideal tocolytic method to be used is controversial. Preterm labour before 34 weeks gestation needs to be arrested for at least 48 hours so that lung maturity could be attained with steroid coverage and neonatal outcome could be improved with the help of proper intensive care facilities.

In the present study tocolysis with magnesium sulphate was found to be better than isoxsuprine as it prolonged the pregnancy for more than 48 hours. Also, the number of nursery admissions of preterm babies were less when treated with magnesium sulphate. It has also found to have neuroprotective effects in various studies.

ACKNOWLEDGMENTS

Authors would like to thank Dr. Gayatri Mathuriya (Associate professor Department of Obstetrics and Gynecology, Indore).

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Mathuriya G, Tarware R. A comparative study of magnesium sulphate and isoxsuprine as a tocolytic in preterm labour. *Int J Reprod Contracept Obstet Gynecol* 2021;10:950-4.