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**ORIGINAL ARTICLE**

**A COMPARATIVE STUDY ON MAGNESIUM SULPHATE AND ISOXSUPRINE IN THE  
MANAGEMENT OF PRETERM LABOUR**

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**ABSTRACT**

Preterm delivery which accounts for over 75% of all cases of perinatal mortality and morbidity is the most important obstetric problem of world today. Present study was conducted in the Department of Obstetrics and Gynaecology at Rajah Muthiah Medical College and Hospital, Annamalai University, Chidambaram. The objective of this study was to compare the efficacy of isoxsuprine and magnesium sulphate as tocolytic agent. A total of 70 pregnant women were randomly assigned into group I and group II in equal numbers. All the patients were closely monitored and observed for uterine quiescence and side effects. Both isoxsuprine and magnesium sulphate were effective in attaining successful tocolysis in majority of patients. Magnesium sulphate produces significantly lesser maternal side effects.

**Keywords:** Magnesium Sulphate, Isoxsuprine, Preterm Labour, Tocolytic Agents, Hypotension.

**1.INTRODUCTION**

Preterm labour is defined as the onset of regular, painful uterine contractions, at least 4 in 20 minutes or 8 in 60 minutes with cervical effacement of 80% or more, cervical dilatation > 1 cm between 28-37 completed weeks of gestation. According to WHO in 2005, 12.9 million births, or 9.6% of all births worldwide were preterm.

Approximately 11 million (85%) of these preterm birth were concentrated in Africa and Asia, while about 0.5 million occurred in each of Europe & North America & 0.9 million in Latin America and the Caribbean. The highest rates of preterm birth were in Africa, North America (11.9% & 10.6% respectively), and lowest were in Europe (6.2%). The incidence of low birth weight in India is about 30%-40% of which 12%-18% are associated with gestational age less than 37 weeks. It is far more preferable to prevent the initiation of preterm labour than once the cascade of events has already been established (Creasy and Merkatz, 1990). The currently

used method to arrest preterm labour is by inhibiting uterine contractions with tocolytic agents. These drugs delay the delivery and permit the use of glucocorticoids to facilitate the transfer of patient to a unit where intensive neonatal care facilities are available (Kitchen *et al.*, 1992).

**AIMS AND OBJECTIVES**

The objective is to compare the efficacy of magnesium sulphate and Isoxsuprine as tocolytic agent.

The aim is to study the efficacy and maternal side effects of magnesium sulphate and Isoxsuprine in the arrest of preterm labour.

**2.MATERIALS AND METHODS**

This study was conducted in the Department of Obstetrics and Gynaecology, Rajah Muthiah Medical College and Hospital, Annamalai University, Chidambaram.

The study comprised of 70 women with preterm labour admitted in labour room. The cases were divided into two groups: Group I comprised of 35 patients who were put on

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isoxsuprine. Group II comprised of 35 patients who were put on magnesium sulphate.

**TYPE OF STUDY :**

Prospective study

**Selection Criteria**

1. Gestational age 28-37 weeks.
2. Regular uterine contractions, 2 or more than 2 per 10 minutes each lasting for at least 30 seconds.
3. Cervical dilatation not more than 3 cm.
4. Cervical effacement not more than 50%.
5. Membranes intact.

**Exclusion Criteria**

1. Multiple pregnancy
2. Ante-partum haemorrhage
3. Hydramnios
4. Pregnancy with heart disease and diabetes mellitus
5. Fetal malformations.

After selecting the patients, the following details were noted: age of the patient, parity, number of abortions and history of preterm deliveries, exact date of last menstrual period, duration of pregnancy and time of onset of preterm labour. Detailed history and clinical examination of the patients was done which included record of vitals, systemic examination and per-vaginum examination. The investigation which were carried out in all the patients were haemoglobin, bleeding time, clotting time, ABO Rh grouping, urine complete examination, vaginal swab for culture and sensitivity and urine for culture and sensitivity. After selecting the patients the following dosage regime was followed.

**Group I: (Patients Receiving Isoxsuprine)**

4 ampoules (40mg) of isoxsuprine hydrochloride in 500ml of 5% dextrose at 8 drops/min was started, drop rate was increased by 8 drops/min after every half an hour until uterine quiescence was attained or patient develops adverse effect.

The i.v. drip was continued for 24 hrs after uterine quiescence was achieved. Six hours before stoppage of infusion, injection isoxsuprine 10mg i.m. stat was given.

**Group II (Patients Receiving Magnesium Sulphate)**

The patients were given 4g of magnesium sulphate in 20% solution as i.v. loading dose over 20 minutes, after which i.v. infusion of magnesium sulphate was started at a rate of 2gms/1hr (10 ampoules of 50% magnesium sulphate in 5% dextrose at a rate of 25 drops/min).

Drop rate was increased to 37 drops/min if uterine quiescence was not achieved by one hour. The infusion was continued for 12 hours till uterine quiescence was obtained.

The results in the study were statistically analyzed by means of  $\chi^2$  test, students t test and statistical significance was

defined as a p value of <0.05. A p value of <0.01 indicated highly significant result.

**3.RESULTS AND DISCUSSION**

**Distribution of Gestational Age**

Distribution of gestational age was more between 33 to 35 weeks.

Gestational Age ( weeks)	Isoxsuprine	Magnesium Sulphate
<32	6	8
33-35	23	20
>35	6	7

**Distribution of patients based on Obstetric code**

Among the Patients included in this study, 68.57% were Primi gravida.

Parity	Isoxsuprine	Magnesium Sulphate
Primi gravida	24	24
G2A1	1	2
G2P1L1	7	7
G3A2	-	1
G3P2L2	3	-
G4P1L1A2	-	1

**Distribution of patients with initial uterine contraction:**

In this study, majority of the patients had initial uterine contractions which was lasting for 20 seconds in 10 minutes.

**Cervical dilatation:**

As the cervical dilatation increased, the success rate of both the drugs came down. Successful tocolysis was attained in 91.67 % cases with cervical dilatation of upto 1 cm in group I as compared to 81.81 % cases in group II. In patients with cervical dilatation between 1-2 cm, the success rate was 88.24 % in group I as compared to 72.2 % in group II. The difference was however statistically not significant.

Cervical dilatation (cms)	Tocolytic used						p value
	Isoxsuprine			Magnesium sulphate			
	No of cases	Success-ful cases	%	No of cases	Success-ful cases	%	
0-1	12	11	91.67	11	9	81.81	0.322
1-2	17	15	88.24	18	13	72.22	
More than 2	6	2	33.33	6	3	50.00	

**Cervical effacement**

A decline in the success rate was recorded in group I and group II with increase in cervical effacement. The difference in success rate in two groups was statistically not significant (p > 0.74).

Percentage of Effacement	Isoxsuprine group		Magnesium Sulphate group		P value
	No. of cases	Successful cases	No. of cases	Successful cases	
20% effaced	15	15	14	14	0.742
30% effaced	6	6	4	4	
40% effaced	4	4	3	3	
50% effaced	10	1	14	0	
Total	35	26	35	21	

**Side effects**

The commonest adverse effect experienced by patients in group I was hypotension (30.78 %) and tachycardia (23.08 %) but the commonest side effects experienced by patients in group II was lethargy (26.09%) and nausea (26.09%). Nausea (4%) and headache (4 %) were the other common side effects experienced by the patients in group I and flushing (21.73 %), headache (13.04 %) and hypotension (8.7%) were the other common side effects experienced by patients in group II. Tachycardia and hypotension were significantly more common side effects seen in group I as compared to group II. Lethargy and nausea was significantly more common in group II as compared to group I.

S. No	Side effects	Group I (Isoxsuprine) N=26		Group II (Magnesium Sulphate) N=23	
		No. of Cases	%	No. of cases	%
1.	Tachycardia	6	23.08	1	4.35
2.	Hypotension	8	30.78	2	8.70
3.	Headache	4	15.38	3	13.04
4.	Nausea	4	15.38	6	26.09
5.	Lethargy	3	11.54	6	26.09
6.	Flushing	1	3.84	5	21.73

**CALCULATION OF MEAN AND STATISTICAL SIGNIFICANCE**

Characteristic	Isoxsuprine (mean+standard deviation)	Magnesium Sulphate (mean+standard deviation)	P value
Age (Years)	23.29 + 2.73	24.77 + 3.07	0.036
Gestational age (Days)	235.11 + 11.67	236.00 + 11.10	0.746
Contraction (Seconds)	24.71 + 5.42	24.29 + 7.29	0.781
Effacement (%)	32.57 + 12.91	34.86 + 13.80	0.477

**SUCCESSFUL TOCOLYSIS:**

The delivery was delayed successfully for atleast 2 days in 74.3% cases in the patients receiving isoxsuprine as compared to 60% patients on magnesium sulphate. The difference was however statistically not significant (p<0.20). Furthermore, isoxsuprine was successful in delaying the delivery for 7 days or more in 11 (31.4 %) cases as compared to magnesium sulphate which was successful in 10 (28.6%) cases. This was also statistically not significant (p value <0.79).

Success of tocolysis		Group I Isoxsuprine		Group II Magnesium Sulphate		P value
		No. of cases	%	No. of cases	%	
7 day tocolysis	Success	11/35	31.4	10/35	28.6	0.794
	Failure	24/35	68.6	25/35	71.4	
2 day tocolysis	Success	26/35	74.3	21/35	60.0	
	Failure	9/35	25.7	14/35	40.0	

Prematurity, together with its complications remains the most frequent preventable cause of neonatal loss. In an attempt to prevent the sequel of premature delivery, attention was logically centred on efforts to find safe and effective tocolytic drug. The relative safety of Isoxsuprine and patients acceptance of the drug side effects have been well established from the world wide clinical experiences.

A satisfactory pharmacological method for the prevention or treatment of preterm labour is yet to be found. It has been recognised for some time that ionic Magnesium in a sufficiently high concentration can alter myometrial contractility in vivo as well as in vitro.

Hence the present study was undertaken to evaluate the efficiency of Isoxsuprine and Magnesium Sulphate as a tocolytic agent in preterm labour.

**SUCCESSFUL TOCOLYSIS**

In the present study Isoxsuprine was able to attain tocolysis in 74.3 % cases.

Study	Isoxsuprine
Amit mahajan et al	66%
Raghunath et al	84.6%
Singh et al	68%
D kalita et al	64%
Present study	74.3%

The results of this study are consistent with other study (Yogol *et al.*, 2009; Sirohiwal *et al.*, 2001; Bhide *et al.*, 1995.

Study	Magnesium Sulphate
Amit Mahajan et al	82%
Deirdre J Lyell et al	87%
Naagar Jk et al	88%
Begum N et al	83.33%
Holland et al	88%

Magnesium sulphate was successful in attaining tocolysis in 60 % cases. These results are comparable to other studies (Saha, 2002; Larmon *et al.*, 1999). The slight disparity in the success rate in either group could be due to different criteria used for success, varied dosage regime, difference in the number of patients who entered the study with different initial cervical dilatation or cervical effacement, frequency and duration of uterine contractions. In the present study delivery was successfully delayed for 7 days or more in the patients receiving isoxsuprine in 31.4 % cases. These results are similar to results of other studies (Vaja and Goyal, 2014; Singh *et al.*, 1987; Amit Mahajan et al 2014;). In the present study magnesium sulphate was able to maintain tocolysis for 7 days or more in 28.6 % cases. These observations are similar to observation made by other studies (Saha, 2002; Hollander *et al.*, 1987; Amit Mahajan et al 2014;).

**PARITY DISTRIBUTION**

In the present study, among the patients 68.57% were Primi gravida and 31.43% were Multigravida.

**PARITY DISTRIBUTION**

Study	Primi	Multigravida
Begum n et al	43.48%	56.52%
Raghunath MP et al	57.69%	42.31%
Singh et al	45%	55%
Present Study	68.57%	31.43%

**GESTATIONAL AGE DISTRIBUTION:**

In the present study, 65.71% were between 33-36 weeks of gestation in Isoxsuprine group and 62.85% in Magnesium sulphate group.

**Gestational age distribution – Isoxsuprine group**

Gestational age	Nagendrappa Et al	Present study
28-30 weeks	26.66%	14.28%
31-32 weeks	43.34%	20%
33-36 weeks	30%	65.71%

**Gestational age distribution – Magnesium sulphate group**

Gestational age	Begum N Et al	Present study
28-30 weeks	14.49%	17.15%
31-32 weeks	49.28%	20%
33-36 weeks	36.23%	62.85%

**CERVICAL DILATATION:**

In the present study successful tocolysis was obtained in 91.67 % cases with cervical dilatation up to 1 cm in patient of group I as compared to 81.81% in patients of group II. As the cervical dilatation increased the success rate of both the drugs came down. In patients with cervical dilatation between 1-2 cms, the success rate was 88.24 % in group I as compared to 72.22% in group II. The difference is however statistically not significant. These results are comparable to results of other studies (Steer and Petrie, 1977; Singh et al., 1990).

**SIDE EFFECTS:**

In the present study hypotension and tachycardia were the most frequent adverse effects which occurred in 30.78 % and 23.08 % patients in group I. Headache and nausea was reported in 15.38 % each in group I. These results are similar to results of other studies (Singh et al., 1987; Kalita et al., 1998; Sirohiwal et al., 2001).

**SIDE EFFECTS OF ISOXSUPRINE**

Side effects	Rayamajhi et al	Kedar et al	Present study
Tachycardia	26.66%	28%	23.08%
Hypotension	13.33%	36%	30.78%
Headache	3.33%	12%	15.38%
Flushing	-	34%	3.84%
Nausea	3.33%	34%	15.38%

**SIDE EFFECTS OF MAGNESIUM SULPHATE**

Side Effects	Begum N et al	Present Study
Flushing	65.22%	21.73%
Nausea	53.62%	26.09%

Nausea and flushing were the most frequent adverse effects which was noted in Group II. These results are similar to several other studies (Hollander et al., 1987; Larmon et al., 1999; Saha, 2002).

**4.CONCLUSION**

The present study shows that both isoxsuprine and magnesium sulphate are effective tocolytic agents with isoxsuprine having better tocolytic effect than magnesium sulphate. Magnesium sulphate produces lesser maternal side effects like hypotension, tachycardia as compared to isoxsuprine.

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