

RESEARCH ARTICLE

Preterm Labor with Side Effects: Compare the Effectiveness of Magnesium Sulfate (MgSO₄) with Isoxsuprine

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ABSTRACT

Background: In India, 25% of pregnancies develop preterm labor (PTL), resulting in 10 to 69% cases of preterm birth. Medical intervention to stop labor, reduce infection rate, and avoid infant respiratory distress has been the subject of studies for a long time. PTL patients usually get tocolytics, corticosteroids, antibiotics, and other clinically symptomatic and supportive therapy to accomplish this goal. Studies further showed that these tocolytic drugs lower intracellular calcium bioavailability via biochemical pathways, hindering the interaction of actin-myosin. Due to the poor success rate of labor arrest, researchers concluded from their studies that widespread adoption of medical management for PTL has been hampered. The high rate of major side effects of tocolytic drugs, particularly beta-mimetic ones, exacerbated this. We know of no clinical evidence on PTL management in India.

Objective: The effectiveness and maternal side effects of MgSO₄ and isoxsuprine in PTL arrest.

Methods: In our study, we included a total of 82 pregnant women who had PTL discomfort and were admitted to the labor department. Both groups were randomly assigned patients. "Group 1 patients received isoxsuprine hydrochloride, whereas group 2 patients received MgSO₄". After that, a comprehensive clinical examination included vital signs, general, systemic, external genitalia, and PV (per vaginal) results. Investigations include CBC, BT, CT, urine full examination, ABO, RH group, serum electrolytes, RBS, vaginal swab, and Renal function test (RFT).

Result: Significant difference ($p < 0.05$) indicated that MgSO₄ was more effective.

Conclusion: MgSO₄ can be used as a tocolytic agent in PTL as it shows better tolerance capacity when compared to isoxsuprine.

Keywords: MgSO₄, Isoxsuprine, Preterm labor, Side effects, Tocolytics.

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INTRODUCTION

"According to various past studies, globally accepted definition of preterm labor (PTL), given by the ACOG, states that it is the occurrence of regular contractions accompanied by cervical changes prior to the completion of 37 weeks of gestation".¹ Researchers in their past have concluded that in India, approximately 25% of pregnancies experience PTL, resulting in preterm delivery (PTD) in 10 to 69% cases.² Hence, its prevalence for PTL and PTD had varied factors. Studies revealed that these factors ranged from physical factors like low weight before pregnancy, uterine abnormalities, and time between pregnancies to social factors like low socioeconomic status, mother literacy, racial and ethnic factors, the mother's occupation, and other factors like tobacco smoking, maternal sexual activity, etc.³ Studies have also shown that, even after knowledge of all these risk factors, successful prediction rate is less, even in pregnant women with presence of established

risk factors.⁴ So, studies have been focusing on the "treatment of medical intervention to halt labor, minimize the infection rate, and prevent neonatal respiratory distress for ages. Additionally, tocolytics, corticosteroids, antibiotics, and other clinically symptomatic and supportive care are mostly used in situations of PTL to achieve this goal".⁵ Furthermore, the most commonly employed tocolytic agents, according to various past studies, include "beta-2 agonists such as isoxsuprine hydrochloride, terbutaline sulfate, and ritodrine hydrochloride. Other agents used are calcium channel blockers like nifedipine, oxytocin receptor antagonists such as atosiban, prostaglandin synthetase inhibitors, magnesium sulfate, and nitric oxide donors".⁶ Studies also proved that these tocolytic agents can reduce the intracellular bioavailability of calcium ions through various biochemical pathways which ultimately hinders the interaction between actin and myosin.⁴ Therefore, through their studies, researchers concluded that the wide use

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of medical management for PTL has been obstructed due to low success rate of arrest of labor. This was aggravated due to the high incidence of serious side effects of tocolytic agents, especially beta-mimetic tocolytics. As per our knowledge, there is lack of data available on clinical management of PTL in the Indian population. Hence, in our study our goal was to compare the effectiveness and side effects of magnesium sulfate and isoxsuprine in the arrest of PTL.

Aims

To evaluate and compare the effectiveness and side effects of MgSO₄ and Isoxsuprine in the arrest of PTL.

Inclusion criteria

- Patients with gestational age (GA) of 28 to 37 years .
- All those patients with regular uterine contractions (2 or more than 2 per 10 minute each lasting for 30 sec).
- Patients with 3 cm or less cervical dilatation.
- Patients with CE not more than 50%.
- Patients with an intact membrane.

Exclusion criteria

- Patients with multiple pregnancies .
- Those with ante-partum haemorrhage in past or present.
- Patients with polyhydraminos
- Pregnant patient with DM presence.
- Patient with foetal malformation.
- Patient with any kind of heart disease, COPD, bronchial asthma.

MATERIALS AND METHOD

Study Setting

Our study was conducted in Tertiary Care Hospital, Karad, Maharashtra.

Type of Study

Our study was a randomly comparative prospective interventional type of study.

Study Population

Our study was conducted on a sample of pregnant women who presented to the Department of Obstetrics and Gynecology with a gestational age from 28 to 37 weeks and were experiencing preterm labor.

Methodology

The study, which obtained in-depth patient histories, included all of the cases that the department received. This included information such as the “patient’s age, parity, previous history of abortions, past history of PTD, LMP, gestational age, and time of onset of PTL. After which, a full clinical examination included a recording of vital signs, general examination, systemic examination, examination of the external genitalia, and PV (per vaginal) examination”. The investigation includes CBC, BT, CT, urine complete examination, ABO, RH group, serum electrolyte, random blood sugar level, vaginal swab and renal function test. In our study, 82 pregnant females were included with chief complaints of PTL pain and admitted in

labor room. Here, patients were divided randomly in both groups. Group 1 received isoxsuprine hydrochloride, whereas group 2 patients received MgSO₄.

Group 1: The patient got “4 mg Isoxsuprine in 500 mL 5% dextrose at 8 drops/minute (0.04 mg/minute)”. The intravenous drip lasts 24 hours after uterine quiescence. First 24 hours, inject 10 mg isoxsuprine intramuscularly 6th hourly. Take “40 mg of isoxsuprine twice a day for 7 days”.

Group 2: The patients received a loading dose of 4 grams of MgSO₄ in 12 mL of normal saline intravenously over a period of 20 minutes. Following this, an intravenous infusion at 2 g per hour initiated by” “10 ampoules of 50% magnesium sulfate in 5% dextrose”, with a “flow rate of 25 drops per minute”. “The drop rate would be increased to 38 drops if uterine quiescence, defined as less than four contractions per hour, is not achieved within one hour. If uterine quiescence is achieved within 2 hours, the intravenous infusion will be continued for a total of 12 hours”. The patient’s vital signs, including pulse and blood pressure, were monitored every 30 minutes. The deep tendon reflexes, urine output, and respiratory rate were monitored at four-hour intervals. The infusion will be terminated if uterine quiescence is not achieved within 2 hours or if the patient experiences any adverse effects.

Statistical Analysis

Data was collected using Excel and analyzed using Epi Info™ for Windows 7.2. All qualitative data were presented by frequency and age percentage. The study and control groups’ initial profiles were compared. Next was a head-to-head outcome variable comparison between study groups. When a qualitative variable, chi-square test was performed to establish statistical significance and the variable was examined using an unpaired t test.

RESULT

The study was conducted among 82 women having preterm labor. Group 1 was given isoxsuprine and group 2 received MgSO₄ to arrest PTL.

In our study we have found that, the mean age in group 1 was 25.43 years, with a standard deviation of 5.7 and in group 2 was 26.03 years, with a standard deviation of 7.01. Hence, no statistically difference was seen. ($p > 0.05$) (Table 1).

In our study we have found that, average weight in group 1 was 63.17 kg, with a standard deviation of 8.84 and for group 2 was 59.51 kg. Hence, no statistically difference in mean was seen. ($p > 0.05$)(Table 2).

In our research, we found that , in group 1, 8 out of 41 (19.51%) had a GA of less than 32 weeks, whereas in group 2, 7

Table 1: Comparison in age group for females

Age (year)	Group 1-Isoxsuprine (n=41)	Group 2-MgSO ₄ (n=41)
<20	3	3
20–25	13	12
25–30	18	17
>30	7	9
Total	41	41

Table 2: Comparison of weight of female.

Study groups	Weight of women in kg	Standard deviation
Group 1 - Isoxsuprine (n = 41)	63.17	8.84
Group 2 - MgSO ₄ (n = 41)	59.51	10.10
<i>p-value</i>	0.084 (t test) (Not significant)	

Table 3: Comparison of GA of female

Gestational Age (week)	Group 1 - Isoxsuprine (n = 41)		Group 2 - MgSO ₄ (n = 41)	
<32	8	19.51	7	17.07
33–35	21	51.22	18	43.90
35–37	12	29.27	16	39.02
Total	41	100	41	100

Table 4: Comparison of gravidity of female

Gravidity	Group 1 - Isoxsuprine (n = 41)		Group 2 - MgSO ₄ (n = 41)	
Primigravida	26	63.41	25	60.98
Multi gravida	15	36.59	16	39.02
Total	41	100	41	100

Table 5: Comparison of past history of abortion (AB)

History of Abortion	Group 1 - Isoxsuprine (n = 41)		Group 2 - MgSO ₄ (n = 41)	
Yes	4	9.76	3	7.32
No	37	90.24	38	92.68
Total	41	100	41	100

Table 6: Comparison of cervical dilatation (CD)

Cervical dilatation (cms)	Group 1 - Isoxsuprine (n = 41)		Group 2 - MgSO ₄ (n = 41)	
0–1	14	34.15	15	36.59
1–2	19	46.34	19	46.34
>2	8	19.51	7	17.07
Total	41	100	41	100

Table 7: Comparison of successful tocolysis according to CD.

Cervical dilatation (cm)	Group 1 - Isoxsuprine (n = 41)		Group 2 - MgSO ₄ (n = 41)		<i>p-value</i> (Z test of proportion)
	Total cases	Successful Tocolysis (%)	Total cases	Successful Tocolysis (%)	
0–1	14	13 (92.9%)	15	15 (100.0%)	<0.0001
1–2	19	12 (63.2%)	19	16 (84.2%)	0.1415
>2	8	2 (25.0%)	7	4 (57.1%)	0.2055
Total	41	27	41	35	

out of 41 women (17.07%) had less than 32 weeks. In group 1, there were 21 women (51.22%) with a gestational age of 33 to 35 weeks. In group 2, 18 women (43.9%) were in the same range. In group 1, there were 12 women (29.27%) aged 35 to 37 weeks; in group 2, there were 16 women (39.02%) with the same age range. Hence, no statistically difference. ($p > 0.05$) (Table 3).

In our study we have found that, among the participants in group 1, a total of 26 women (63.41%) were identified as primigravida. In group 2, 25 women (60.98%) were classified as primigravida. In group 1, there were 15 women with multigravidity, accounting for 36.59% of the total. In group 2, there were 16 women with multigravidity, representing 39.02% of the total. Thus, no difference seen ($p > 0.05$) (Table 4).

Our study found that, in group 1, 4 (9.76%) had a past history of AB, whereas 3 (7.32%) in group 2. Hence no statistically significant difference seen ($p > 0.05$) (Table 5).

In our study, we found that, out of 41 women in group 1, 14 (34.15%) had CD less than 1 cm, while 15 (36.59%) had CD less than 1 cm in group 2. Group 1 and Group 2 each had 19 women with 1–2 cm of CD. Group 1 and Group 2 each had 8 (19.51%) and 7 (17.07%) women with more than 2 cm of CD. Hence, the distribution was statistically non-significant ($p > 0.05$) (Table 6).

In our study we have found that, successful tocolysis was seen in 92.9% of cases of group 1 and 100% of cases of group 2 in women with less than 1 cm of cervical dilatation. A statistically significant difference was seen ($P < 0.01$), suggesting that MgSO₄ was more effective. The success rate of tocolysis in group 2 was similarly greater in 1 to 2 cm more than group 1, although we know that difference was not significant ($p > 0.05$) (Table 7).

Our research found that, among the 41 participants in group 1, a total of 24 women (58.54%) exhibited a percentage of CE less than 25%. In group 2, 26 participants (63.41%) demonstrated a percentage of CE less than 25%. In group 1, 17 women (41.46%) had 25 to 50% effacement. In group 2, there were 15 women (36.59%) with 25 to 50% CE. Thus, no difference was seen. ($p > 0.05$) (Table 8).

Table 8: Comparison of percentage of CE between 2 study groups.

Percentage of Effacement	Group 1 - Isoxsuprine (n = 41)		Group 2 - MgSO ₄ (n = 41)	
<25%	24	58.54	26	63.41
25–50%	17	41.46	15	36.59
Total	41	100	41	100

Table 9: Comparison of successful tocolysis according to percentage.

Percentage of Effacement	Group 1 - Isoxsuprine (n = 41)		Group 2 - MgSO ₄ (n = 41)		<i>p-value</i> (Z test of proportion)
	Total cases	Successful (%)	Total cases	Successful (%)	
<25%	24	23 (95.8%)	26	26 (100.0%)	<0.0001
25–50%	17	4 (23.5%)	15	9 (60.0%)	0.0359
Total	41	27	41	35	

Table 10: Comparison of side effect between two study groups

Side effects	Group 1 - Isoxsuprine (n = 41)		Group 2 - MgSO ₄ (n = 41)	
Tachycardia	7	17.07	1	2.44
Hypotension	9	21.95	2	4.88
Headache	5	12.20	4	9.76
Flushing	5	12.20	5	12.20
Lethargy	6	14.63	5	12.20
Nausea vomiting	2	4.88	7	17.07

Table 11: Comparison of success rate between 2 study groups.

Success of tocolysis after 2nd day	Group 1 - Isoxsuprine (n = 41)		Group 2 - MgSO ₄ (n = 41)	
Successful	27	65.85	35	85.37
Failure	14	34.15	6	14.63
Total	41	100	41	100

In our study we found that, women with less than 25% effacement had a successful tocolysis rate of 95.8% in group 1 and 100% in group 2. A statistically significant difference was seen ($p < 0.01$). This suggests that in cases where effacement is less than 25%, MgSO₄ is significantly more effective than isoxsuprine for tocolysis. In group 2 (MgSO₄), the rate of successful tocolysis was higher (60%) in cases with 25 to 50% effacement compared to group 1 (Isoxsuprine) (23.5%). Thus this difference was found to be statistically significant ($p < 0.05$) (Table 9).

In our study we found that, higher incidence of tachycardia and hypotension was observed in group 1 compared to group 2, with rates of 17.0 and 21.95%, respectively in group 1, while these side effects were observed in 2.44 and 4.88% of cases respectively in group 2. A higher incidence of nausea and vomiting was observed in group 2 (17.07%) in comparison to group 1 (4.88%). Hence, in group 1, a prevalence of 12.2% was observed for headache, flushing, and lethargy, respectively. In group 2, the prevalence of these symptoms was 9.76, 12.2, and 12.2% respectively (Table 10).

Our study found that, in group 1, out of 41, in 27 (65.85%) women labor was “successfully arrested till the end of 2 days and 35 (85.37%) for group 2” showed a significant difference ($p < 0.05$) (Table 11).

DISCUSSION

In the current study, the average age for group 1 was 25.43 years, with a standard deviation of 5.7 and group 2 was 26.03 years, with a standard deviation of 7.01, which showed no difference. Another study concluded that the “researchers found that the mean age of women in the Isoxsuprine group was 25.43 years, with a standard deviation of 5.7. Conversely, in the magnesium sulphate group, the mean age of women was 26.03 years, with a standard deviation of 7.01. The observed difference did not reach statistical significance, as shown by a *p-value* of 0.70”.⁷ Group 1 women in the current study had a mean weight of 63.17 kg (88.4lb), with a standard deviation of

8.84lb. The standard deviation was 10.1%, while group 2 was 59.51 kg. This showed no significant difference in mean weight ($p > 0.05$) for two groups. In a different study, “the mean weight of the women in the isoxsuprine group was 63.17 kg with a standard deviation of 6.84, while the mean weight of the women in the magnesium sulfate group was 59.6 kg with a standard deviation of 10.1. The *p-value* for the difference between the two groups was 0.09. The majority of women (62.11 percent) were overweight or obese (BMI 25 kg/m2)”.⁷

In the current study, a total of 41 participants were assigned to group 1 (Isoxsuprine). Among these participants, 8 women (19.51%) had less than 32 weeks GA. In group 2 (MgSO₄), seven participants (17.07%) had a GA of less than 32 weeks. In group 1 (Isoxsuprine), 21 women (51.22%) had a GA of 33 to 35 weeks. In group 2 (MgSO₄), 18 women (43.9%) had the same GA. In group 1 (Isoxsuprine), 12 women (29.27%) had a GA of 35 to 37 weeks. In group 2 (MgSO₄), 16 women (39.02%) had the same GA. The distribution of cases based on pregnancy duration was found to be statistically similar between the two groups, with a *p-value* greater than 0.05. Another study found that the majority of the highest cases (57 cases) had a gestational age ranging from 33 to 35 weeks. This was observed in both the Isoxsuprine group (65.7%) and the MgSO₄ group (57.14%).⁸

In the current study, tocolysis succeeded in 92.9% of cases in group 1 (Isoxsuprine) and 100% in group 2 (MgSO₄) among women with less than 1 cm of CD. This difference was statistically significant ($P < 0.01$), indicating that MgSO₄ is substantially more efficacious than isoxsuprine for tocolysis in cases of 1 cm CD. In group 2 (MgSO₄), the tocolysis success rate was also higher for 1 to 2 cm and greater than 2 cm dilatation than in group 1 (Isoxsuprine), but the difference was not significant.” The effectiveness rate of MgSO₄ and Isoxsuprine decreased as the cervical dilatation was adversely affected by many studies. In the magnesium sulfate group, tocolysis was successful in 94.11% of cases with cervical dilatation of up to 1-cm, compared to 80% in the isoxsuprine group. There is no statistically significant difference.”⁹ Another study showed that isoxsuprine was successful as a treatment in several randomized controlled trials. In cases of preterm labor and abortion risk, these trials also include them. When administered orally, intramuscularly, or intravenously, isoxsuprine has an excellent safety profile.^{9,10}

CONCLUSION

The PTL causes one-third of preterm babies and significant prenatal mortality and morbidity. Pharmacotherapy aimed at stopping labor, reducing infection rates, and preventing neonatal respiratory distress became more popular due to the lack of an effective approach to detect and prevent preterm labor. Our study found that MgSO₄ had a greater tocolytic effect than isoxsuprine. Therefore, it causes less maternal and fetal side effects than isoxsuprine. Hence, MgSO₄ is suggested for use as a tocolytic agent in PTL since it is better tolerated than isoxsuprine.

REFERENCES

1. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin. Assessment of risk factors for preterm birth. Clinical management guidelines for obstetrician-gynecologists. Number 31, October 2001.(Replaces Technical Bulletin number 206, June 1995; Committee Opinion number 172, May 1996; Committee Opinion number 187, September 1997; Committee Opinion number 198, February 1998; and Committee Opinion number 251, January 2001). *Obstetrics and Gynecology*. 2001 Oct;98(4):709-16. Available from PMID: 11592272
2. Sukladas S, Prasad US. A Prospective Study to Assess the Neonatal Mortality and Morbidity Associated with Preterm labor and Delivery in a Tertiary Care Hospital. 2016. Available from <https://imsear.searo.who.int/handle/123456789/177661>
3. Egbe TO, Nana Njamen T, Halle Ekane G, Tsingaing JK, Tchente CN, Beyiha G, Barla E, Nyemb E. outcome of late second trimester emergency cerclage in patients with advanced cervical dilatation with bulging amniotic membranes: A report of six cases managed at the Douala General Hospital, Cameroon. *International Scholarly Research Notices*. 2013;2013. Available from <http://dx.doi.org/10.1155/2013/843158>
4. Chandraharan E, Arulkumaran S. Recent advances in management of preterm labor. *J Obstet Gynecol India*. 2005 Mar;55(2):118-24. Available from <https://api.semanticscholar.org/CorpusID:202123195>
5. Schleußner E. The prevention, diagnosis and treatment of premature labor. *Deutsches Ärzteblatt International*. 2013 Mar; 110(13):227. Available from <https://doi.org/10.3238%2Farztebl.2013.0227>
6. Singh N, Dubey P, Gupta N, Dwivedi S, Balyan R, Chandanan A. Comparative study of various tocolytics in preterm labor. *Int J Reprod Contracept Obstet Gynecol*. 2015 Apr 1;4:334-7. Available from doi: 10.5455/2320-1770.ijrcog20150409
7. Alavi A, Rajae M, Amirian M, Mahboobi H, Jahanshahi KA, Faghihi A. Effect of maintenance therapy with isoxsuprine in the prevention of preterm labor: randomized controlled trial. *Electronic physician*. 2015 Aug;7(4):1144. Available from <https://doi.org/10.14661%2F2015.1144-1149>
8. Jaju PB, Sood A, Chavan V, Devgarha G, Jain S, Kundapur V, Hegde R. Practice patterns in the management of preterm labor in India: a multicentric, retrospective study. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2017 Dec 1;6(12):5306-13. Available from <https://doi.org/10.18203/2320-1770.ijrcog20175233>
9. Mahajan A, Marwah P. Arrest of preterm labour: A comparative study between magnesium sulphate and isoxsuprine. *International Journal of Basic and Applied Medical Sciences*. 2014;4(3):19-25. Available from <https://api.semanticscholar.org/CorpusID:36454705>
10. Giorgino FL, Egan CG. Use of isoxsuprine hydrochloride as a tocolytic agent in the treatment of preterm labour: a systematic review of previous literature. *Arzneimittelforschung*. 2010 Jul;60(07):415-20. Available from doi: 10.1055/s-0031-1296305