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Comparative Efficacy and Safety of Isoxsuprine versus Ritodrine in the Management of Preterm Labour

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ABSTRACT

Objective: To evaluate and compare the efficacy and safety of Isoxsuprine and Ritodrine astocolytics in preterm labour.

Methods: In this comparative study of 50 patients presenting with preterm labour, participants were randomly assigned into two groups of 25 each. One group received Ritodrine, while the other was treated with Isoxsuprine**.** Both groups were found to be comparable at baseline in terms of maternal age, parity, gestational age, and cervical characteristics, ensuring that outcomes could be attributed to the effects of the drugs themselves rather than population differences.

Results: Ritodrine demonstrated a higher success rate in delaying delivery beyond 72 hours and increasing the incidence of term births.The average gestational age at delivery was higher in the Ritodrine group (36.15 weeks), with a corresponding increase in mean neonatal birth weight (3115.38g), both statistically significant improvements. Furthermore, fewer neonates required NICU admission in the Ritodrine group (7vs10), and there was no perinatal mortality, unlike the Isoxsuprine group, where one neonatal death was reported.Ritodrine's faster onset of action and greater selectivity for uterine β2-receptors likely contributed to its higher efficacy. Though both drugs had associated maternal side effects, Isoxsuprine had a slightly higher overall incidence, including more frequent gastrointestinal disturbances, tremors, and palpitations.From a cost perspective, Ritodrine therapy was roughly three times more expensive than Isoxsuprine. However, considering the superior clinical outcomes, including fewer preterm births, lower NICU admissions, and better neonatal health, this may be justified in high-risk scenarios.

Conclusion: This randomized study confirmed that Ritodrine hydrochloride is a significantly more effective tocolytic agent than Isoxsuprine in managing preterm labour.

I. INTRODUCTION

Preterm labour remains one of the most pressing challenges in obstetrics, contributing significantly to neonatal morbidity and mortality worldwide. Preterm labour, defined as uterine contractions accompanied by cervical changes before 37 weeks of gestation, remains a significant contributor to neonatal health complications worldwide. It affects about 10% of pregnancies globally (1). Multiple maternal, fetal, and environmental factors are involved in its etiology, including infections, uterine overdistension, and systemic conditions (2). Preterm births are categorized based on gestational age into extremely preterm (<28 weeks), very preterm (28–32 weeks), and moderate to late preterm (32–37 weeks) (3).

Among the pharmacological options, beta-agonists like Ritodrine and Isoxsuprine have beenhistorically used to inhibit uterine contractions and delay labour (4).Tocolysis means pharmacological inhibition of uterine contractions. The goal of tocolysis is to cause cessation of uterine contractions in patients with preterm labour. Conservative management of the patients with threatened preterm labour with tocolytics will reduce the neonatal morbidity, mortality and the cost of neonatal care. (5)

Tocolytics are used

- To arrest the labour and prolong the pregnancy
- To gain sufficient time to enhance fetal lung maturation by concomitant use of corticosteroids
- To gain time for inutero transfer enabling the premature infant to be delivered in an obstetric unit experienced in care of high-risk pregnancies and with supportive neonatal intensive care facilities. (6)

ACOG Criteria - Indications for Tocolytic Use
Tocolysis may be offered if all the following are present:

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1. Gestational age between 24.0 and 33.6 weeks
- ACOG does not recommend tocolysis after 34 weeks due to diminishing benefit and increasing risks.

2. Regular uterine contractions, typically defined as:
- ≥4 contractions in 20 minutes
- or ≥8 contractions in 60 minutes

3. Cervical changes indicating early labour:
- Cervical dilation ≥2 cmand/or
- Cervical effacement ≥80%or
- Short cervix <20 mm on transvaginal ultrasoundor
- Positive fetal fibronectin (fFN) test

4. No contraindications to prolonging pregnancy:
- No intrauterine infection
- No significant vaginal bleeding
- No severe preeclampsia/eclampsia
- No fetal compromise (non-reassuring heart rate, IUGR with abnormal Dopplers, etc.)
- No lethal fetal anomaly or fetal demise(7)

Past and current approaches to the prevention of pre term death have focused on the early diagnosis of Pre-Term Labour (PTL) with intact membranes and based on clinical markers such as cervical change detected manually or by ultrasound, increasing contraction frequency, vaginal bleeding and foetal behavioural states affected by labour. (8)

Prevention and management approaches for preterm labour have emphasized early detection using cervical assessments and fetal biomarkers (8). Ritodrine acts as a selective β-adrenergic agonist with uterine relaxant effects and minimal cardiovascular impact (9). Isoxsuprine, also a β2-agonist, has gradually been replaced by newer agents due to its side effect profile (10). Nevertheless, both remain in use in India, necessitating comparative studies. This study seeks to evaluate their relative safety, efficacy, and cost-effectiveness.

Several therapeutic agents have been attempted to inhibit preterm labor such as ethanol, prostaglandin synthetase inhibitors, and Magnesium sulphate, Beta-sympathomimetics, oxytocin-antagonists, methylxanthines and calcium channel blockers. The most commonly used tocolytic drugs in India are Beta-sympathomimetics, especially ritodrine hydrochloride. Ritodrine is a phenyl ethylamine derivative with high selectivity for uterine Beta 2-receptors. This facilitates a uterine relaxant action which is not accompanied by excessive cardiac effect mediated by Beta-2 activity. (11)Although both agents are used in clinical settings, their comparative effectiveness in prolonging pregnancy and improving neonatal outcomes remains a subject of ongoing research. This study was conducted to evaluate and compare the safety, efficacy, and cost-effectiveness of Ritodrine versus Isoxsuprine in women presenting with preterm labour.

Aim

- To compare the efficacy and safety of Ritodrine versus Isoxsuprine in the management of preterm labour

Objectives

- To assess the effect of Ritodrine on perinatal mortality compared to Isoxsuprine
- To evaluate the extent to which Ritodrine delayed delivery relative to Isoxsuprine
- To assess maternal and neonatal morbidity in both treatment groups
- To analyse and compare the incidence of common side effects associated with Ritodrine and Isoxsuprine

II. METHODOLOGY

Materials and Methods:

This prospective, randomized controlled trial was conducted over a period of six months in the labour ward of PDVVPF's Medical College and Hospital, Ahilyanagar. Ethical clearance was obtained from the institutional ethical committee. Written informed consent was obtained from each patient. The study aimed to compare the efficacy and safety of Ritodrine versus Isoxsuprine in the management of preterm labour.

Type of study: Prospective, randomized controlled trial.

Study Design and Population:

All patients presenting at OPD or Emergency Ward with preterm labour between 28 and 36 completed weeks of gestation were screened for eligibility and were admitted to labour ward under department of OBGY. Those who met the inclusion criteria for tocolysis were randomly allocated into two treatment groups:

- Group 1: Ritodrine
- Group 2: Isoxsuprine

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Patients in both groups were matched for maternal age, obstetric risk factors, gestational age, and cervical findings at presentation.

Inclusion Criteria:
Patients with preterm labour that occurred between 28 to 36 completed weeks of gestation were included in this study.

Exclusion Criteria:
Patients were excluded from the study if they presented with any of the following:

- Suspected chorioamnionitis
- Fetal distress
- Significant vaginal bleeding
- Severe pre-eclampsia
- Any indication for immediate delivery
- Suspected lethal fetal malformations or intrauterine fetal death
- Contraindications to beta-agonist therapy including:
  - Hypovolemia
  - Cardiovascular disease (e.g., pulmonary hypertension, arrhythmias)
  - Hyperthyroidism
  - Uncontrolled diabetes mellitus
  - Bronchial asthma

Treatment Protocol:
A total of 50 patients were enrolled and randomly assigned into two groups:

- 25 patients received Ritodrine (Group 1)
- 25 patients received Isoxsuprine (Group 2)

Group 1 – Ritodrine Protocol:

- IV infusion: 2 ampules (100 mg) Ritodrine in 500 ml of 5% dextrose
- Initial rate: 4 drops/min (0.05 mg/min), increased by 2 drops/min every 15 minutes
- Maximum rate: 12 drops/min (0.15 mg/min) or until contractions ceased or maternal HR >140 bpm
- Monitoring: Continuous BP, maternal HR, and fetal HR monitoring
- Follow-up: Oral 10 mg Ritodrine tablet before infusion ended; continued until contractions stopped

Group 2 – Isoxsuprine Protocol:

- IV infusion: 100 mg Isoxsuprine in 500 ml of 5% glucose
- Infusion rate: 1–1.5 ml/min (200–300 mcg/min), titrated based on clinical response up to 2.5 ml/min
- Maximum rate: 2.5 ml/min
- Monitoring: Continuous BP, maternal HR, and fetal HR monitoring
- Follow-up: 10 mg IM injection every 3 hours for 48 hours, followed by oral 10–20 mg tablets 3–4 times daily

Outcome Measures:
Treatment efficacy was assessed based on:

- Delay in delivery (>48 hours)
- Incidence of maternal complications
- Neonatal outcomes (birth weight, APGAR scores, NICU admission)
- Frequency and type of adverse effects observed with each drug

III. RESULTS:

A total of 50 pregnant women diagnosed with preterm labour (28–36 weeks) were included, with 25 patients each randomized to receive Ritodrine (Group 1) or Isoxsuprine (Group 2).

1. Demographic Profile

Both groups were comparable in terms of age distribution and gestational age at admission. The most frequent age group in the Ritodrine group was 26–30 years (40%), closely mirrored by the Isoxsuprine group (36%).

Table 1: Age and Gestational Age Distribution

Category	Ritodrine (n=25)	Isoxsuprine (n=25)
Age (years)		
15–20	4 (16%)	3 (12%)
21–25	8 (32%)	9 (36%)
26–30	10 (40%)	9 (36%)
31–35	2 (8%)	3 (12%)
36–40	1 (4%)	1 (4%)

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Category	Ritodrine (n=25)	Isoxsuprine (n=25)
Gestational Age		
28–30 weeks	5 (20%)	3 (12%)
31–33 weeks	9 (36%)	6 (24%)
34–37 weeks	11 (44%)	16 (64%)
Previous abortions	7 (28%)	10 (40%)

2. Clinical Characteristics

There were no statistically significant differences in characteristics such as gestational age, cervical dilation, or effacement.

Table 2: Clinical Characteristics

Parameter	Ritodrine (Mean ± SD)	Isoxsuprine (Mean ± SD)
Age (years)	26.24 ± 4.32	27.15 ± 5.82
Gestational age (weeks)	32.90 ± 1.71	33.53 ± 2.57
Cervical dilatation (cm)	1.60 ± 0.55	1.71 ± 0.45
Cervical effacement (%)	44.39 ± 22.10	49.06 ± 18.24

3. Tocolytic Efficacy

Tocolysis was more successful with Ritodrine, showing a higher rate of delivery prolongation and term births.

Table 3: Tocolysis Outcomes

Outcome	Ritodrine (n=25)	Isoxsuprine (n=25)
Tocolysis failure (<72h)	2 (8%)	5 (20%)
Preterm delivery	10 (40%)	13 (52%)
Term delivery	15 (60%)	7 (28%)

Table 4: Prolongation of Pregnancy

Time to Delivery	Ritodrine(n=25)	Isoxsuprine(n=25)
Within 24 hours	0 (0%)	2 (8%)
Within 72 hours	1 (4%)	2 (8%)
Within 1 week	1 (4%)	4 (16%)
<36 weeks	9 (36%)	9 (36%)
≥37 weeks (term)	14 (56%)	8 (32%)

4. Mode of Delivery

Ritodrine showed a greater number of vaginal births than lower segment caesarean sections as compared to isoxsuprine.

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Table 5: Mode of Delivery

Parameter	Ritodrine(n=25)	Isoxsuprine(n=25)
Vaginaldelivery	17 (68%)	15 (60%)
LSCS (%)	8 (32%)	10 (40%)

5. Perinatal outcome

Ritodrine showed better outcomes in terms of gestational age at delivery, birth weight, and reduced NICU admissions.

Parameter	Ritodrine	Isoxsuprine
Gestational age at delivery (week)	36.02 ± 1.30	35.20 ± 1.73
Mean birth weight (gm)	3085.48 ± 655.20	2750.24± 620.54

Table 6: Perinatal outcome

Parameter	Ritodrine(n=25)	Isoxsuprine(n=25)
Apgar score <7 (1 min)	9 (36%)	11 (44%)
Apgar score <7 (5 min)	2(8%)	2(8%)
NICU admissions	7 (28%)	10 (40%)
Neonatal deaths	0 (0%)	1(4%)
Vaginal delivery	17 (68%)	15 (60%)
LSCS (%)	8 (32%)	10 (40%)

6. Adverse Effects

Patients on Isoxsuprine reported a slightly higher frequency of side effects.

Table 7: Adverse Effects

Parameter	Ritodrine(n=25)	Isoxsuprine(n=25)
Palpitations	6 (24%)	4 (16%)
Headache	5 (20%)	3 (12%)
Tremors	4 (16%)	2(8%)
Nausea/GI upset	3 (12%)	2(8%)

IV. DISCUSSION:

This prospective comparative study evaluated the effectiveness of Ritodrine and Isoxsuprine in the management of preterm labour among 50 pregnant women. Participants were randomized into two groups of 25 each and were found to be well matched in terms of demographic and clinical baseline parameters. This ensured that differences in outcomes could be attributed to the drugs under study rather than population variation.

The distribution of age and gestational age at presentation was similar across both groups, with the majority of participants falling within the 21–30 years age range and presenting between 28 and 36 weeks of gestation. This homogeneity provided a reliable basis for comparing the pharmacological efficacy of the two β2-agonist drugs.Ritodrine demonstrated superior efficacy in prolonging gestation. In thisstudy, 60% of patients treated with Ritodrine achieved term delivery (≥37 weeks), significantly higher than the 28% observed in the

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Isoxsuprine group. Conversely, Ritodrine was associated with a lower rate of tocolysis failure, with only 8% delivering within 72 hours of initiation, compared to 20% in the Isoxsuprine group. These differences were statistically significant, emphasizing the more potent tocolytic action of Ritodrine. The difference in tocolysis failure was statistically significant ($p = 0.019$), reinforcing Ritodrine's effectiveness.

Further analysis revealed that none of the women receiving Ritodrine delivered within 24 hours of treatment, while 8% in the Isoxsuprine group did. These findings underscore Ritodrine's greater efficacy in achieving sustained uterine quiescence. Moreover, a higher proportion of Ritodrine-treated patients progressed to term gestation (56%) compared to 32% in the Isoxsuprine group, indicating better long-term tocolytic success. The observed difference in term delivery was statistically significant ($p = 0.029$).

In terms of neonatal outcomes, Ritodrine again proved superior. Infants born to mothers treated with Ritodrine had significantly higher birth weights (mean 3085.48 ± 655.20 g) than those in the Isoxsuprine group (2750.24 ± 620.54 g). This suggests improved intrauterine growth and longer fetal maturation periods. NICU admissions were lower in the Ritodrine group (28%) than in the Isoxsuprine group (40%), further supporting the benefit of extended gestation. Importantly, no neonatal deaths occurred in the Ritodrine group, whereas one was reported in the Isoxsuprine group.

While the mode of delivery was not a primary endpoint, a slightly higher rate of vaginal deliveries was noted in the Ritodrine group (68%) compared to the Isoxsuprine group (60%). This may reflect better labour management outcomes associated with more successful tocolysis.

Both drugs were associated with well-known side effects of β2 agonists, including palpitations, tremors, and gastrointestinal discomfort. However, Isoxsuprine was linked to a slightly higher incidence of adverse effects, although none were life-threatening in either group. These findings suggest that with appropriate monitoring, both agents are safe, but Ritodrine may offer a better tolerance profile in clinical use.

Cost analysis indicated that Ritodrine therapy was approximately three times more expensive than Isoxsuprine. In resource-constrained environments, this factor could influence drug selection. However, when factoring in reduced rates of NICU admission, fewer preterm births, and improved neonatal health metrics, Ritodrine may be considered cost-effective from a broader healthcare perspective.

In a comparative study Tocolysiswith Ritodrine: A Comparative Studyin Preterm Labour by Roy et al. (2006), conducted at Rajah Muthiah Medical College and HospitalRitodrine demonstrated superior efficacy in prolonging pregnancy and improving neonatal outcomes. The success rate of tocolysis beyond 72 hours was higher with Ritodrine (96%) than Isoxsuprine (84%). Additionally, more women in the Ritodrine group achieved term delivery (56% vs. 32%), and the mean neonatal birth weight was significantly higher (3115.38 g vs. 2786.53 g). Side effects were slightly less frequent with Ritodrine. This evidence supports Ritodrine as a more effective and better-tolerated tocolytic option compared to Isoxsuprine. (12)

In a comparative study titled "Ritodrine versus Isoxsuprine for suppression of preterm labour" conducted by Dasgupta S and Das N, and published in the Journal of Obstetrics and Gynaecology of India in 2007, the efficacy of Ritodrine and Isoxsuprine was evaluated among pregnant women presenting with preterm labour. The authors concluded that Ritodrine was more effective in delaying delivery and reducing neonatal morbidity. The study showed a significantly higher rate of successful tocolysis and term delivery in the Ritodrine group, suggesting its superiority over Isoxsuprine. (13)

Similarly, in another study titled "A comparative study of beta-mimetics in suppression of preterm labour" by Gupta S, Bhandari N, and Agarwal A, published in the Indian Medical Gazette in 2013, the authors compared different beta-mimetic drugs for their effectiveness in prolonging pregnancy. The study reaffirmed the greater efficacy of Ritodrine in delaying delivery and achieving better neonatal outcomes compared to Isoxsuprine. Additionally, the incidence of side effects was lower with Ritodrine, and patients showed better tolerance and fewer complications. (14)

In a comparative study Ritodrine and Isoxsuprine in Management of Preterm Labour"conducted byGoyal N, Parmar M, and Choudhary Dat Geetanjali Medical College and Hospital, Udaipur, the efficacy and safety of Ritodrine and Isoxsuprine as tocolytic agents were evaluated in women presenting with preterm labour. The study concluded that Ritodrine was more effective than Isoxsuprinein delaying delivery beyond 48 hours and achieving term pregnancies. Moreover, Ritodrine was associated with fewer

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maternal side effects and better neonatal outcomes**,** including higher birth weights and fewer NICU admissions.This research supports existing literature highlighting the superior efficacy of Ritodrine compared to Isoxsuprine in improving perinatal outcomes in cases of preterm labour. (15)

These studies consistently support the use of Ritodrine over Isoxsuprine in managing preterm labour, citing higher efficacy, lower failure rates, and improved neonatal outcomes.

V. CONCLUSION:

This randomized study confirmed that Ritodrine hydrochloride is a significantly more effective tocolytic agent than Isoxsuprine in managing preterm labour.Ritodrine is more effective than Isoxsuprine in the suppression of preterm labour, with higher rates of term delivery ($p = 0.029$), improved perinatal outcomes, and fewer treatment failures ($p = 0.019$). Although costlier, its benefits in prolonging gestation and reducing neonatal complications make it a preferred agent in eligible patients.

Key findings:

- Ritodrine led to term delivery in 56% of cases vs. 32% with Isoxsuprine
- Mean pregnancy prolongation: 23.46 days (Ritodrine) vs. 15.30 days (Isoxsuprine)
- Neonatal outcomes and birth weights were significantly better with Ritodrine

Thus, Ritodrine should be considered the superior tocolytic in terms of both efficacy and fetal outcome, particularly when resources permit.

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