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Original Article

Comparison of the Controlling Effect of Uterine Contractions of "Isoxsuprine and Oral Magnesium Fort" With "Isoxsuprine" in Preterm Labor Prevention

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Abstract

Background and Objective: Preterm labor is a significant challenge in obstetrics and gynecology. Various pharmacological agents have been explored for their ability to delay delivery and improve neonatal outcomes. This study aimed to compare the effectiveness of isoxsuprine alone versus a combination of oral magnesium fort and isoxsuprine in controlling uterine contractions and preventing preterm labor.

Materials and Methods: In this clinical trial, 100 pregnant women between 24 and 34 weeks of gestation with a history of uterine contractions were enrolled. Participants were randomly assigned to two groups: the intervention group received oral magnesium fort combined with isoxsuprine, while the control group received isoxsuprine alone. The treatment continued until 37 weeks of gestation. The primary outcome was the interval from contraction control to delivery, and the secondary outcome was the frequency of uterine contractions.

Results: Overall, women in the intervention group had a significantly more extended latency period from contraction control to delivery and experienced fewer uterine contractions compared to the control group ($P < 0.05$). In a subgroup analysis of women in their second pregnancy, the mean gestational age at delivery was 243.79 ± 13.90 days in the control group versus 256.17 ± 8.60 days in the intervention group, with a statistically significant difference ($P = 0.004$).

Conclusions: Combining oral magnesium fort with isoxsuprine appears to be more effective than isoxsuprine alone in prolonging gestation and reducing uterine contractions. Further studies with larger sample sizes are warranted to confirm these findings.

Keywords: Isoxsuprine, Oral magnesium fort, Preterm labor, Uterine contractions

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Introduction

Preterm labor is a significant concern in obstetrics and gynecology because the care and treatment of complications in premature infants impose a significant economic burden and may also cause long-term psychological distress for families [1, 2]. Preterm birth accounts for approximately 12% of all deliveries, and approximately 65% of neonatal and infant deaths are attributed to prematurity [3]. The risk of recurrence in subsequent pregnancies is estimated to be 6%–8% [4]. According to the World Health Organization and the American College of Obstetricians and Gynecologists, preterm birth refers to delivery before 37 weeks of gestation. It remains a leading cause of neonatal mortality within the first 28 days of life [1, 5]. Despite decades of research, the incidence of preterm birth has not significantly declined, underscoring the need for more effective preventive strategies [6].

Various interventions have been investigated to postpone preterm labor, including bed rest, hydration, beta-adrenergic receptor agonists, indomethacin, calcium channel blockers, and magnesium-based agents. Each approach has certain advantages and limitations, and no single therapy has proven universally effective [7, 8]. Among these, **isoproterenol**, a beta-adrenergic agonist, has been widely used since 1961 to relax uterine smooth muscle and remains one of the most prescribed medications for the prevention of preterm labor. However, its effectiveness and safety profile remain debated [5–7]. Reported maternal side effects include hypotension, tachycardia, chest discomfort, nausea, vomiting, and dizziness [8, 9].

Magnesium-based therapies have also been used as tocolytic agents. While intravenous magnesium sulfate has long been administered during acute uterine contractions, its efficacy as a maintenance therapy is controversial [10-12]. However, oral magnesium supplementation has been proposed as a means to reduce uterine contractions with fewer systemic side effects than parenteral magnesium sulfate [13, 14]. Nevertheless, clinical evidence regarding its effectiveness remains limited.

Given the continued use of isoxsuprine in many clinical settings and the potential role of oral magnesium fort, this study was designed to compare the effectiveness of isoxsuprine alone versus the combination of isoxsuprine and oral magnesium fort in controlling uterine contractions and preventing preterm labor.

Participants and Methods

Study Design

This clinical trial was conducted on women aged 25-35 years with preterm labor who were referred to Hajar Hospital in Shahrekord, Iran. This study aimed to compare the effectiveness of isoxsuprine alone versus a combination of oral magnesium fort and isoxsuprine in controlling uterine contractions and preventing preterm labor. The study was conducted from October 2019 to July 2020. The research protocol was approved by the Ethics Committee of Shahrekord University of Medical Sciences, Shahrekord, Iran (approval code: IR.SKUMS.REC.1395.31).

Participants

Inclusion and Exclusion Criteria

Pregnant women aged 25–35 years with singleton pregnancies between 24–34 weeks' gestation, presenting with uterine contractions and progressive cervical changes with a reactive NST, were included. Women with multiple pregnancies, active infection, placental abnormalities, lethal fetal anomalies, severe uncontrolled maternal disease, contraindications for treatment, or indications for immediate delivery were excluded.

Initial Management and Randomization

Baseline serum magnesium levels were measured at enrollment. Samples from both groups, matched for vaginal examination findings and gestational age, were evaluated for latent phase duration, cervical dilation, and uterine contraction frequency after contraction control was achieved until delivery.

All patients received intravenous magnesium sulfate as tocolytic therapy under continuous supervision in the obstetrics emergency department and intensive care unit until uterine contractions were effectively suppressed. Subsequently, patients were transferred to the midwifery ward, where treatment was continued for an additional 24 hours.

Forty-eight hours after discontinuation of intravenous magnesium sulfate, participants were randomly allocated into two groups of 50 each using

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(specify randomization method or software). Both groups were matched for gestational age and cervical status at the time of study entry.

Intervention

Experimental Group: Isoxsuprine 10 mg orally every 8 hours plus oral magnesium fort 150 mg (Haden Camp, Germany, Sun Life Company)

Control Group: Isoxsuprine 10 mg orally every 8 hours

Patients were monitored for 24 hours for complications or recurrence of preterm labor. The treatment continued until 37 weeks of gestation. Follow-up was conducted via hospital visits or telephone calls.

Outcome Measures

Primary Outcome: Duration of the latent phase from contraction control until delivery

Secondary Outcomes: Cervical dilation, frequency of uterine contractions, and serum magnesium levels at delivery

Statistical Analysis

Data were entered into Excel 2010 and analyzed using SPSS software (version 20). Descriptive statistics were used to summarize the demographic and clinical characteristics. Independent t-tests were used to compare continuous variables between groups. A *P*-value ≤ 0.05 was considered statistically significant.

Results

Participant Characteristics

The mean age of the 100 pregnant women studied was 31.25 ± 4.37 years (range, 25–35 years). The mean gestational age at the estimated date of confinement visit was 29.63 ± 1.23 weeks. Blood magnesium levels did not change significantly before and after drug administration.

Gestational age and cervical dilation at the time of study enrollment did not differ significantly between the control and experimental groups (Table 1).

Table 1. Gestational Age and Cervical Dilatation Before Intervention in "Isoxsuprine Group" and "Magnesium Fort and Isoxsuprine Group"

Group / Variables Before Intervention	Isoxsuprine Group	Magnesium Fort and Isoxsuprine Group	P-Value
Gestational age (week ± day)	28.43 ± 4.54	29.49 ± 5.67	0.69
Cervical dilatation (cm)	2.00	1.50	0.08

* The difference between the two groups is significant ($P < 0.05$).

Delivery Time and Uterine Contractions by Parity

Analysis of delivery time and uterine contraction frequency across parities showed no statistically significant differences between groups for the first, third, and fourth parities. However, in the second parity, co-administration of magnesium fort and isoxsuprine resulted in a significantly longer gestational age at delivery and a considerably lower uterine contraction frequency ($P < 0.05$) (Tables 2 and 3).

Table 2. Mean and Standard Deviation of Gestational Age at Delivery Time in "Isoxsuprine Group" and "Magnesium Fort and Isoxsuprine Group"

Group Variables		Gestational Age of the Isoxsuprine Group (Week ± Day)	Gestational Age of Magnesium Fort and Isoxsuprine Group (Week ± Day)	*P*-Value
Delivery frequency	First parity	257.28 ± 15.18	258.76 ± 9.05	0.70
	Second parity	243.79 ± 13.90	256.17 ± 8.60	0.004 *
	Third parity	255.57 ± 10.83	259.80 ± 14.34	0.57
	Fourth parity	248.40 ± 7.83	250.25 ± 5.68	0.70
	Total	252.47 ± 14.68	257.19 ± 9.36	0.06

* The difference between the two groups is significant ($P < 0.05$).

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Table 3. Mean and Standard Deviation of Uterine Contraction Frequency at Delivery Time in "Isoxsuprine Group" and "Magnesium Fort and Isoxsuprine Group"

Variables / Group		Gestational Age of Isoxsuprine Group (Week ± Day)	Gestational Age of Magnesium Fort and Isoxsuprine Group (Week ± Day)	*P*-Value
Uterine contraction frequency (in minutes)	First parity	2.45 ± 0.66	2.42 ± 0.45	0.09
	Second parity	2.48 ± 0.75	1.78 ± 0.66	0.03 *
	Third parity	1.95 ± 0.45	2.12 ± 0.54	0.65
	Fourth parity	2.35 ± 0.75	2.33 ± 0.44	0.70
	Total	2.15 ± 0.65	2.25 ± 0.52	0.36

* The difference between the two groups is significant ($P < 0.05$).

Discussion

The present study evaluated whether the addition of oral magnesium sulfate to standard isoxsuprine therapy could prolong gestational age and reduce uterine contractions in women with preterm labor according to parity. Preterm labor remains one of the leading causes of neonatal morbidity and mortality worldwide, and effective interventions to delay delivery are essential for improving neonatal outcomes and reducing healthcare costs. Our findings demonstrated that the combination of magnesium sulfate and isoxsuprine significantly prolonged gestational age and reduced uterine contractions among second-parity women. However, no significant benefits were observed among first-, third-, or fourth-parity women, suggesting that the effectiveness of this combined regimen may be influenced by parity.

Our findings are consistent with previous studies supporting the role of magnesium-based therapies in the management of preterm labor. Toghroli et al. (2020) reported that both magnesium sulfate and indomethacin effectively prolonged pregnancy, although no significant difference was observed between the two treatments [15]. Similarly, Faraji et al. (2013) demonstrated that nifedipine was more effective than magnesium sulfate in delaying delivery for more than 48 hours; however, both agents showed clinically relevant tocolytic effects, supporting the role of magnesium-containing regimens in prolonging pregnancy [16]. Furthermore, Sariri et al. (2006) found no significant difference between magnesium sulfate and celecoxib in suppressing uterine contractions, suggesting comparable efficacy among different tocolytic agents [17]. Collectively, these studies support the therapeutic value of magnesium-based interventions and provide indirect support for the beneficial effects observed with magnesium fort supplementation in our study.

In addition to tocolytic therapies, preventive strategies for preterm birth have also demonstrated promising results. Zethelius et al. (2026), in a systematic review and meta-analysis, concluded that universal cervical length screening followed by vaginal progesterone administration in women with a short cervix reduced the risk of preterm birth [18]. Their findings emphasize the importance of identifying high-risk pregnancies and implementing timely interventions. Although our study focused on treatment rather than prevention, both investigations highlight the potential benefits of targeted approaches in reducing adverse outcomes associated with preterm labor.

However, the literature presents conflicting evidence regarding the superiority of specific tocolytic agents. Salari et al. (2012) compared vaginal progesterone with oral isoxsuprine and found no significant differences in gestational age at delivery, recurrence of preterm labor, neonatal outcomes, or maternal complications between treatment groups [19]. Similarly, Seehusen et al. (2012) reported comparable efficacy between human chorionic gonadotropin and magnesium sulfate in suppressing

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uterine contractions, suggesting that magnesium sulfate may not provide superior outcomes in all patient populations [20]. Lotfalizadeh et al. (2010) also observed no significant difference between nifedipine and magnesium sulfate in delaying delivery, although nifedipine was associated with fewer maternal adverse effects [21]. Moreover, Yogol et al. (2009) reported that ritodrine was more effective than isoxsuprine in controlling preterm labor and promoting fetal maturation [22]. Likewise, Flenady et al. (2014) concluded that calcium channel blockers were generally more effective than other tocolytic agents in prolonging pregnancy while minimizing maternal and neonatal adverse effects [23]. These discrepancies suggest that treatment response may be influenced by several factors, including parity, cervical status, gestational age, underlying etiology of preterm labor, and individual patient characteristics.

The parity-specific effects observed in the present study warrant particular attention. The significant benefits detected among second-parity women may reflect physiological differences in uterine responsiveness, cervical remodeling, or hormonal regulation compared with women of other parity groups. Alternatively, the absence of significant findings among first-, third-, and fourth-parity women may be related to limited sample size and insufficient statistical power to detect modest treatment effects. Further investigation is needed to clarify the biological mechanisms underlying these parity-related differences.

Strengths and Limitations of the Study:

A key limitation of this study is the inability to isolate the independent effect of magnesium because the comparison was between combination therapy (isoxsuprine + magnesium fort) and isoxsuprine monotherapy. Ethical constraints and resource limitations precluded the inclusion of a placebo-controlled magnesium group.

One limitation of the present study is the lack of control for all confounding variables, including a history of early delivery and prior analgesic use, which is essential in future research.

Conclusion

Since the use of combined tocolysis has better effects in delaying preterm labor as well as the side effects of imitating beta drugs, especially isoxsuprine, in the fetus were confirmed, and considering the obtained results, it can be said that the use of magnesium and isoxsuprine compounds to prevent preterm delivery is more effective than applying isoxsuprine alone. Based on the results, it is recommended that this study be conducted using field methods and with a larger sample size. Moreover, other factors, such as cervical epiphenomenal and uterine contraction intervals, are also measured.

Ethics Approval

The manuscript is taken from the thesis of Dr. Tahereh Nazari Dehkordi, "a residency student at Shahrekord University of Medical Sciences, Shahrekord, Iran, whose proposal was approved by the Ethics Committee of Shahrekord University of Medical Sciences, Shahrekord, Iran (IR.SKUMS.REC.1395.31).

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Availability of Data and Materials

The data supporting the findings of this study are available from the corresponding author (SS).

Conflict of Interest

The authors declared no conflicts of interest.

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Authors' Contributions

Study design: T.N. and S.S.;

Sampling: T.N.;

Writing the main manuscript text and preparing tables: F.S. and S.S.

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[DOI: 10.53208/ajpr.5.1.3]

All authors reviewed the manuscript.

References

1. World Health Organization. Preterm birth fact sheet. Geneva: World Health Organization; [cited 2023 May 10]. Link
2. Liang X, Lyu Y, Li J, Li Y, Chi C. Global, regional, and national burden of preterm birth mortality, 1990–2019: a systematic analysis. EClinicalMedicine. 2024;76:102890. [DOI: 10.1016/j.eclinm.2024.102840]
3. Cao G, Liu J, Liu M. Global, regional, and national incidence and mortality of neonatal preterm birth, 1990–2019. JAMA Pediatr. 2022;176(8):787–796. [DOI: 10.1001/jamapediatrics.2022.1622]
4. Bradley E, Blencowe H, Moller AB, Okwaraji YB, Sadler F, Gruending A, et al. Born too soon: global epidemiology of preterm birth and drivers for change. Reprod Health. 2025;22(Suppl 2):105. [DOI: 10.1186/s12978-025-02033-x]
5. Jaju PB, Kalghatgi RN, Warke HS, et al. Effectiveness and Safety of Isoxsuprine Hydrochloride as Tocolytic Agent in Arresting Active/Threatened Preterm Labor and Its Role in Maintenance Tocolysis: A Prospective, Open-Label Study. Am J Perinatol. 2021;38(3):291–295. [DOI: 10.1055/s-0039-1696720]
6. Alavi A, Rajaee M, Amirian M, Mahboobi H, Jahanshahi KA, Faghihi A. Effect of Maintenance Therapy with Isoxsuprine in the Prevention of Preterm Labor: Randomized controlled trial. Electron Physician. 2015;7(4):1144–1149. [DOI: 10.14661/2015.1144-1149]
7. Csapo AI, Herczeg J. Arrest of premature labor by isoxsuprine. Am J Obstet Gynecol. 1977;129(5):482–491. [DOI: 10.1016/0002-9378(77)90084-9]
8. Raymajhi R, Pratap K. A comparative study between nifedipine and isoxsuprine in the suppression of preterm labour. Kathmandu Univ Med J (KUMJ). 2003;1(2):85–90. Link
9. Robertson PA, Herron M, Katz M, Creasy RK. Maternal morbidity associated with isoxsuprine and ritodrine therapy for preterm labor. Eur J Obstet Gynecol Reprod Biol. 1981;11(6):371–378. [DOI: 10.1016/0028-2243(81)90086-1]
10. Crowther CA, Brown J, McKinlay CJD, Middleton P. Magnesium sulphate for preventing preterm birth in threatened preterm labour. Cochrane Database Syst Rev. 2014;(8): CD001060. [DOI: 10.1002/14651858.CD001060.pub2]
11. Cox SM, Sherman ML, Leveno KJ. Randomized investigation of magnesium sulfate for prevention of preterm birth. Am J Obstet Gynecol. 1990;163(3):767–772. [DOI: 10.1016/0002-9378(90)91065-K]
12. Elliott JP, Morrison JC, Bofill JA. Risks and Benefits of Magnesium Sulfate Tocolysis in Preterm Labor (PTL). AIMS Public Health. 2016;3(2):348–356. [DOI: 10.3934/publichealth.2016.2.348]
13. Shennan A, Suff N, Jacobsson B; the FIGO Working Group for Preterm Birth; Simpson JL, Norman J, Grobman WA, Bianchi A, Mujanja S, Valencia CM, Mol BW. Int J Gynaecol Obstet. 2021;2(1):31–532. [DOI: 10.1002/ijgo.13856]
14. Shepherd ES, Goldsmith S, Doyle LW, Middleton P, Marret S, Rouse DJ, Pryde P, Wolf HT, Crowther CA. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. Cochrane Database Syst Rev. 2024;5(5):CD004661. [DOI: 10.1002/14651858.CD004661.pub4]
15. Toghroli H, Saeieh SE, Rezapour-Nasrabad R, Rahimzadeh M, Ataei M, Faraji A. Comparative study of the tocolytic effects of magnesium sulfate and indomethacin on pregnancy duration and neonatal outcomes in preterm labor: a clinical trial. International Journal of Pharmaceutical Research. 2020;12(3):559–564. [DOI: 10.31838/ijpr/2020.12.03.08]
16. Faraji R, Asgharnia M, Dalil Heirati F, Nemati F. A Comparison between magnesium sulfate and nifedipine for Preterm labor prevention. J Babol Univ Med Sci. 2013;15(4):88–92. [DOI: 10.18869/acadpub.jbums.15.4.88]
17. Sariri E, Vahdat M, Nasiri E. Comparison of celebrex and magnesium Sulfate in Prevention of Preterm Labor. Iran J Obstet Gynecol Infertil. 2006;9(1):27–32. [DOI: 10.22038/ijogi.2006.5987]
18. Zethelius M, Bergman L, Ekelund AC, Vala CH, Jacobsson B, Kuusela P, et al. Can universal cervical length screening with vaginal progesterone for a short cervix reduce preterm birth? A systematic review and meta-analyses. Acta Obstet Gynecol Scand. 2026. [DOI: 10.1111/aogs.15118]
19. Salari Z, Mirzaei S, Ravari A, Mirzaei T. The comparison between vaginal progestrone and Isoxuprine tab on duration of latent phase after

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[DOI: 10.53208/ajpr.5.1.3]

controled preterm labor. J Rafsanjan Univ Med Sci. 2012;11(4):301–312. Link
20. Seehusen DA, Grogan SP. Magnesium sulfate for prevention of preterm birth. Am Fam Physician. 2015;91(7):444–445. Link
21. Lotfalizadeh M, Teymoori M. Comparison of nifedipine and magnesium sulfate in the treatment of preterm. Iran J Obstet Gynecol Infertil. 2010;13(2):7–12. [DOI: 10.22038/ijogi.2006.5987]
22. Yogol NS, Shakya R, Thapa P. Ritodrine and isoxsuprine in management of preterm labor. J Nepal Med Assoc. 2009;48(176):265–268. [PMID]
23. Flenady V, Wojcieszek AM, Papatsonis DN, Stock OM, Murray L, Jardine LA, et al. Calcium channel blockers for inhibiting preterm labour and birth. Cochrane Database Syst Rev. 2014; CD002255. [DOI: 10.1002/14651858.CD002255.pub2]

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