

Comparative effect of magnesium sulfate and indomethacin to magnesium sulfate only for Tocolysis in preterm labor in pregnant women in Kosar Hospital, 2019-2021

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Abstract

Background:Preterm labor is one of the most common pregnancy complications, and it can have catastrophic effects, including preterm birth and accompanying complications. This study's objective is to compare the efficacy of Magnesium Sulfate and Indomethacin vs Magnesium Sulfate alone in avoiding preterm labor in pregnant women at Kosar Hospital in 2019–2021. **Methods:**In this interventional study, which was conducted as a double-blind, randomized clinical trial on 200 pregnant women with gestational ages ranging from 24 to 32 weeks who were referred to Qazvin's Kosar Hospital. Patients were divided into two equal groups and given magnesium sulfate and indomethacin (group A) or magnesium sulfate alone (group B). The data then was analyzed with SPSS statistical software and statistical tests. **Results:**According to the study's findings, the average time interval between receiving the drug and childbirth in group A was 774.71±505.91 hours and in group B it was 545.77±503.32 hours, which was statistically significant ($P < 0.05$). Besides that, the mean gestational age at the time of pregnancy termination was 35.30±2.50 weeks in group A and 35.03±2.65 weeks in group B, which was not statistically significant ($P > 0.05$). The type of intervention, on the other hand, had a significant relationship with the number of labors during the first 7 days after starting the drug ($P > 0.05$). **Conclusion:**The results showed that magnesium sulfate and indomethacin were more effective than magnesium sulfate alone in inhibiting and delaying preterm labor. There were similarities in comparing the findings of our study with other studies. **Keywords:**Preterm labor, Magnesium Sulfate, Indomethacin **Financial disclosures:**None

Introduction

Preterm labor is one of the most important problems in pregnancies, and it can have serious consequences, such as premature birth and its complications (1, 2). In the past, fetal mortality was high in preterm labor. However, these days, with the identification of these pregnancies and proper care of the mother and fetus, the fetal mortality rate in these pregnancies has been reduced; but even so, further research is needed (3, 4). Premature birth, in addition to causing economic, psychological, and psychological problems in the family, also results in the loss of financial and human resources (5). It has received special attention in recent years because it is a painful and stressful experience for both infants and parents (6). Premature infants are readmitted at a rate of 11 per 1000 live births that were alive three months after discharge, which is significantly higher than the rate for term babies (7). Given that a decrease in infant mortality rates indicates an improvement in public health (8), measures to reduce the number of preterm births are especially important factors (9). Nowadays, treatment methods such as taking progesterone orally or injecting it, or taking drugs with vasodilating properties such as Nifedipine, are common (10, 11), but determining the most effective treatment in this field necessitates research. It is a clinical trial with a comparative intervention. For many years, magnesium sulfate has been known to be effective in this field (12); Magnesium sulfate, chemically known as $MgSO_4$, is an injectable drug with clinical applications that include seizure prevention

in preeclampsia, preterm labor, and, on rare occasions, the treatment of cardiac arrhythmias. Both the injectable and oral forms are used to treat hypomagnesemia, as well as bronchodilators and osmotic laxatives. Its cellular effect was mediated by inhibiting the release of acetylcholine at the nerve-muscle junction, thereby inhibiting calcium entry into cells due to increased intracellular magnesium. Its anticonvulsant effect is due to the blocking of calcium neurons via the glutamate duct (which is only found in the CNS) and its anticonvulsant effect on the cerebral cortex without causing CNS depression in the mother and fetus. Indomethacin is also available in pill, capsule, and suppository form as a nonsteroidal anti-inflammatory drug (NSAID). Indomethacin is a powerful analgesic and anti-inflammatory drug that is also used to prevent uterine contractions. Indomethacin works by inhibiting the enzyme cyclooxygenase to convert arachidonic acid to prostaglandin. Prostaglandins play a significant role in both term and preterm labor. Despite extensive researches, no single drug has been introduced as the first line of treatment, and the choice of drug is based on drug availability, effectiveness, maternal and neonatal complications, and drug price. Due to the huge importance of the subject in this study, the effect of Magnesium Sulfate and Indomethacin suppository with the administration of Magnesium Sulfate alone in inhibiting preterm delivery in women aged 24 to 32 weeks at Kosar Hospital in Qazvin in 2019 and 2021 years was compared.

METHODS

Study design

Between 2019 and 2021, this research was performed at Qazvin's Kosar Hospital (Kosar hospital which we chose patients was the only women's specialty hospital in Qazvin state, which means that more than 12 hospitals in the state refer their patients with preterm labor to this center. As a result, patients can select from more than 12 centers). In this interventional study, which was conducted as a double-blind, randomized clinical trial, 200 women with preterm labor symptoms referred to this center were chosen and evaluated via convenience sampling. Patients were divided into two groups randomly: A ($n = 100$) and B ($n = 100$).

Magnesium Sulfate was administered intravenously to group A first at a dose of 4-6 gr, then at a dose of 2 gr/h for 12 hours after the uterine contractions stopped, or for up to 48 hours. Furthermore, they were given a 100mgr rectal Indomethacin suppository every 12 hours until the uterine contractions stopped, or for a maximum of 48 hours. Group B received Magnesium Sulfate intravenously at a dose of 4-6 g, followed by 2 gr/h for 12 hours after the uterine contractions stopped or for a maximum of 48 hours. Group B received a placebo suppository, which was similar to the Indomethacin suppository. Then, the required information was entered into the checklist, and the data were entered into SPSS V24 statistical software and analyzed using the analytical, statistical method.

findings :

According to the findings of the study, the majority of patients were between the ages of 21 and 25. The mean age of the referring women was 27.12 ± 5.43 years, and their BMI was 27.41 ± 3.53 . Also, maternal gravid was between 1 to 5, and the mean maternal gravid was 1.85 ± 0.92 , and 22 of them (11%) had a history of preterm delivery. There was no statistically significant difference between the two groups regarding baseline characteristics such as maternal age, gravidity, and history of preterm delivery. In addition, the maternal gravid was between 1 and 5, with a mean maternal gravid of 1.85 ± 0.92 , and 22 of them (11%) had a history of preterm delivery. In terms of baseline characteristics such as maternal age, gravidity, and history of preterm delivery, there was no statistically significant difference between the two groups. However, there was a statistically significant difference between the two groups in the two variables of BMI and gestational age at the time of admission, so the patients in the group who received Magnesium Sulfate alone had a higher BMI and higher gestational age at the time of admission compared to the group of patients who were receiving Magnesium Sulfate and Indomethacin ($P < 0.05$).

The mean time interval between receiving the drug and delivery in group A (Magnesium Sulfate + Indomethacin) was 774.71 ± 505.91 and in group B (Magnesium Sulfate) was 545.77 ± 503.32 hours.

According to the Whitney U-MANN test, the relationship between the type of intervention and the time

interval between receiving the drug and delivery was statistically significant ($P < 0.05$).

Also, 15% of the patients in the group receiving Magnesium Sulfate versus 8% of the patients in the group receiving Magnesium Sulfate and Indomethacin gave birth within 48 hours after starting the drug. According to the Chi-square test results, this difference was not statistically significant ($P > 0.05$). According to the test results, 31% of the patients in the group receiving Magnesium Sulfate versus 15% of the patients in the group receiving Magnesium Sulfate and Indomethacin had spontaneous delivery within seven days after receiving the tocolytic drug, which according to the test results, Chi-Square This difference was statistically significant ($P < 0.05$).

Also, no significant differences were observed between the two groups in any of the secondary outcomes, according to the results of logistic regression and according to the data displayed in Table 1, among the variables of maternal age, gestational age at admission time, gravidity, BMI, and type of intervention. Only the variables of intervention type and gestational age at the time of Referrals could predict spontaneous delivery within seven days of starting the tocolytic drug.

After adjustment, the type of intervention was still significantly related to the rate of spontaneous delivery within 7 days of starting the tocolytic drug. (Figure-1) (Exp (B)=2.08, $P = 0.048$).

Discussion

In order to lessen the negative effects of infancy and improve survival and quality of life for infants, it is imperative that preterm labor be prevented and treated. The ultimate goal of controlling preterm labor is not only to extend the pregnancy but also to improve neonatal outcomes and reduce mortality rates. This attitude will have a significant long-term impact on the cost of health and social care. Although no tocolytic drug with minimal adverse effects on the mother and fetus and also improving neonatal outcomes has been introduced to date, this study aimed to compare the effect of concomitant administration of Magnesium Sulfate and Indomethacin suppository with Magnesium Sulfate alone on preterm delivery in Kosar hospital between 2019 and 2021.

The mean time interval between receiving the drug and delivery was longer in group A (Magnesium Sulfate + Indomethacin) than in group B (Magnesium Sulfate), indicating that type A intervention was more effective at inhibiting preterm delivery in patients than type B intervention. The relationship between the type of intervention and the time interval between receiving the drug and delivery was statistically significant.

According to the findings of the Lewis et al. (1995) study, the combined group (Magnesium Sulfate and Indomethacin) had a greater effect on increasing the duration of tocolysis than the Magnesium Sulfate group alone, with a difference of more than 370 hours compared to 70 hours in the Magnesium Sulfate group only, a difference that was statistically significant.

Compared to patients in the group receiving Magnesium Sulfate and Indomethacin, more patients in the group receiving Magnesium Sulfate delivered within 48 hours and 7 days after receiving the drug. In the first 48 hours, this difference was not statistically significant, but in the interval of seven days, this difference was significant. According to Borna and Saeedi (2007), Celecoxib was 81 percent effective at delaying delivery for more than 48 hours, while Magnesium Sulfate was 87 percent effective, neither of which was statistically significant (13). According to Abaasaelizadeh et al. (2014), 32% of pregnant women gave birth after 24 hours and 60% after 48 hours in the Magnesium Sulfate group, while 37% of pregnant women gave birth after 24 hours and 63% of patients gave birth after 48 hours in the Indomethacin group, indicating that no significant difference between the two groups existed (15).

Despite the fact that no significant difference was observed between the study groups within 48 hours of receiving the drug in each of the studies mentioned, the rate of delivery in the groups was higher than the results of our study, which was due to differences in entry criteria.

Additionally, contrary to our findings, when Mesdaghinia et al. (2012) compared the effects of Indomethacin and Magnesium Sulfate on preterm labor, labor delays were comparable in both groups, and no cases

of preterm labor were admitted within 48 hours. (17). According to Taj Aramesh et al. (2012), when comparing the effects of Indomethacin and Magnesium Sulfate on delaying preterm delivery, 37 percent of patients treated with Indomethacin gave birth within the first 72 hours, while 9 percent of patients treated with Magnesium Sulfate gave birth within the first 72 hours, a significant difference between the two groups (18). In contrast to the preceding study, this distinction Seven days after initiating the drug was significant in our study.

There was no significant difference between the two groups in terms of adverse effects on mothers, and there was no significant relationship between the type of intervention and secondary outcomes such as NICU hospitalization, gestational age at the end of pregnancy, or neonatal Apgar score. According to the findings of the study conducted by Vermillion et al. (2000), there was no statistically significant difference in the mean gestational age between the Indomethacin group and the control group between the groups. (26). According to Klauser et al(2014) .’s study comparing the effects and side effects of Nifedipine (N), Magnesium Sulfate (M), and Indomethacin (I) for the treatment of preterm labor, the gestational age at delivery was comparable in all three groups. There were no significant differences in efficacy or maternal safety between the three tocolytic factors (16). The logistic regression model’s output indicated that the type of intervention had a significant relationship with the rate of spontaneous delivery within 7 days of receiving the drug. In this case, Magnesium Sulfate and Indomethacin suppository are more effective when administered together.

Data analysis revealed that concomitant administration of Magnesium Sulfate and Indomethacin had a greater effect on inhibiting and delaying preterm labor than Magnesium Sulfate alone. Other parameters (neonatal Apgar score, drug side effects, gestational age at the end of pregnancy, etc.) were slightly different between the two groups, and due to the significance of the average time interval between drug administration and delivery and the type of delivery in the two groups, prescribing Magnesium Sulfate and Indomethacin suppository have more beneficial effects in this field.

Conclusion:

Our study found that Magnesium Sulfate and Indomethacin were more effective at preventing and delaying preterm labor than Magnesium Sulfate alone. Comparing our study’s findings to those of other studies revealed some similarities. Following the current research process and in order to improve performance in the field of future studies, it is recommended that interventional studies be conducted with a larger sample size and control of all significant variables in order to obtain more accurate results. Separate studies can also be conducted to determine the effect of the type of intervention on other aspects of labor, such as the type of labor, complications, and pain, with the results being combined with those from the current study.

DECELERATION

Conflicts of interest : The authors declare no conflict of interest.

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Ethical approval : This study was approved by the ethics committees of the collaborating hospital. Informed consent was obtained from all participants.[IR.QUMS.REC.1398.102].

Contribution of each authors to the submitted manuscript: In this study, Sh.Hoorshad is contributed in the following parts: conception and design of the study; acquisition of data; analysis and interpretation of data collected; and final approval and guarantor of the manuscript. H. Pakniat helped come up with the idea for and design of the study and gave the manuscript his final approval. M. Sadeghi Ivraghi was the submitting author; she devised the study’s concept and design; she was an editor; she assisted in the writing of the article; and she gave the manuscript her final approval and guarantee. M.Dadashaliha, who is the corresponding author of this article, took part in the conception and design of the study; analysis and interpretation of data collected; drafting of the article; and final approval and guarantor of the manuscript.

Figure 1 .Comparison of the average time interval in hours between receiving tocolytic medication and giving birth in the two groups.

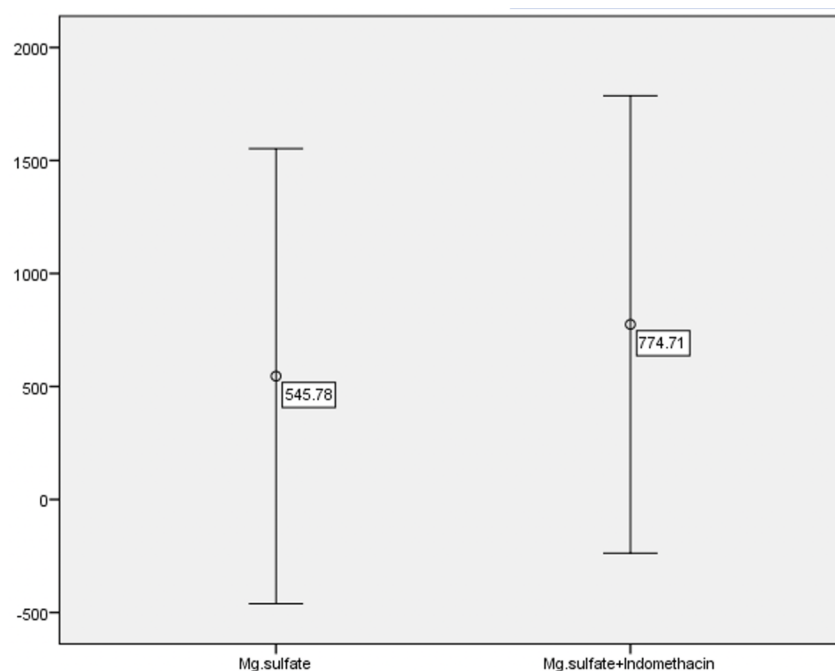


Table 1. Results of logistic regression to determine the predictors of delivery within 7 days after starting tocolytic drug

	B	S.E.	Exp(B)	Sig.
Type of Intervention	0.735	0.371	2.085	0.048
Maternal age	-0.008	0.036	0.992	0.816
Gestational age at the time of referral	-0.291	0.103	0.747	0.005
Gravidity	0.283	0.223	1.327	0.204
BMI	-0.062	0.051	0.939	0.224
Constant	10.783	3.908	48189.401	0.006

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