



Does MgSO₄ Treatment Affect Maternal Aspartate Aminotransferase to Platelet Ratio Index (APRI) Score in Preterm Labor?

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Abstract

Aim: This study evaluated the association between magnesium sulfate treatment for fetal neuroprotection on APRI scores in pregnant women with the preterm birth threat.

Material and Methods: Thirty-one pregnant women hospitalized and received MgSO₄ for preterm birth risk in the Obstetrics and Gynecology Department, between 2019-2022 were included, and the patient records were evaluated retrospectively. The fetal neuroprotective MgSO₄ treatment protocol included administering a loading infusion dose of 4 grams/30 minutes followed by a 1 gram/hour infusion for 24 hours to pregnant women hospitalized for a threat of preterm labor. In addition, the electrocardiography, hemogram, and hepatic and renal functions were evaluated upon hospitalization before MgSO₄ administration, and patients were monitored closely. Women who gave birth before completion of 24 hours of MgSO₄ administration, multiple pregnancies, patients with comorbid deteriorated liver or kidney functions, preeclampsia, intrauterine growth retardation, fetal abnormalities, gestational diabetes mellitus, chorioamnionitis, adolescent and advanced age pregnancies or any other obstetric complications were excluded from analyses. The APRI score was calculated and compared between the results of the biochemical analyses performed at initiation (basal) and 12th hour of MgSO₄ administration.

Results: The mean APRI score at the 12th hour of administration (0.45±0.07) was significantly higher than the basal values (0.31±0.07) (p<0.001), but hemoglobin, hematocrit, and platelet values were similar (p>0.05 for all).

Conclusions: Magnesium sulfate treatment for preterm birth threat significantly increases APRI score at the 12th hour of administration.

Keywords: APRI score, MgSO₄ treatment, neuroprotective effect, preterm birth

INTRODUCTION

Preterm birth is a significant cause of newborn morbidity and mortality and the most frequent reason for antenatal hospitalization. In addition, premature neonates are vulnerable to long-term complications, particularly cerebral palsy. Randomized-controlled trials and meta-analyses revealed that antenatal magnesium sulfate (MgSO₄) administration for fetal neuroprotection when preterm birth is anticipated might decrease the neurological morbidities, including cerebral palsy and severe motor dysfunction. The MgSO₄ administration within 24 hours of risk of preterm delivery is also recommended by the

American College of Obstetricians and Gynecologists (ACOG), World Health Organization (WHO), and several other associations (1-6).

The aspartate aminotransferase (AST) to platelet ratio index (APRI) score is a non-invasive scoring system. It is frequently used to assess liver inflammation and cellular damage and grade hepatic fibrosis. It is calculated using the AST and platelet values in routine blood sample analyses. The APRI score is more frequently used for gastrointestinal conditions but has come into gynecology-obstetrics practice recently, and this non-invasive bioindicator provides valuable information in clinical applications (7-10).

CITATION

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The MgSO₄ treatment has rare side effects and is safe for both mother and fetus when administered in the therapeutic range. It is primarily eliminated from kidneys, but there is no precise data regarding its use in hepatic failure (11). Also, there is no data on neuroprotective MgSO₄ administration on maternal APRI scores. Thus, this study aimed to evaluate the changes in APRI scores in pregnant women who received MgSO₄ for neuroprotective purposes.

MATERIAL AND METHOD

Thirty-one pregnant women hospitalized and received MgSO₄ for preterm birth risk in the Obstetrics and Gynecology Department of the Ankara Liv Hospital of Yuksek Ihtisas University, Faculty of Medicine, between 2019-2022 were included, and the patient records were evaluated retrospectively. The study protocol was approved by the Ethics Committee of Yuksek Ihtisas University (Date: 18/05/2023; Approval No: 2023/03/07).

The fetal neuroprotective MgSO₄ treatment protocol included administering a loading infusion dose of 4 grams/30 minutes followed by a 1 gram/hour infusion for 24 hours to pregnant women hospitalized for a threat of preterm labor. In addition, the electrocardiography, hemogram, and hepatic and renal functions were evaluated upon hospitalization before MgSO₄ administration, and patients were monitored closely. Hourly urine excretion and deep-tendon reflexes were followed for any adverse event. Women who gave birth before completion of 24 hours of MgSO₄ administration, multiple pregnancies, patients with comorbid deteriorated liver or kidney functions, preeclampsia, intrauterine growth retardation, fetal abnormalities, gestational diabetes mellitus, chorioamnionitis, adolescent and advanced age pregnancies or any other obstetric complications were excluded from analyses. Demographic characteristics of the patients, medical and obstetric histories, weeks of gestation, hemogram and biochemical test results, delivery types were collected retrospectively from patient records. Fetal well-being of all hospitalized patients was checked with ultrasound and NST during hospitalization.

The APRI score was calculated from the results of the biochemical analyses performed at initiation (basal) and 12th hour of MgSO₄ administration, using the formula by Wai et al. (12), as follows:

$$APRI = \frac{AST (IU/L) / AST (ULN)}{Platelet (10^9/L)} \times 100$$

Statistical Analyses

Descriptive analyses were presented using mean±standard deviation after controlling for normal distribution assumptions using normality tests and visual inspections of histograms and detrended Q-Q plots for continuous

variables, and frequency and percent for categorical variables. Continuous variables were compared with the Wilcoxon signed-rank test between two consecutive measurements. Statistical analyses were done in SPSS 25 (IBM Inc., Armonk, NY, USA), and a type-I error level of 5% was considered a statistical significance threshold.

RESULTS

A total of 31 patients were included in the study. The mean age of patients, the gestational week at MgSO₄ administration, and neonate birth weight were 29.2±5.6 years, 28.5±1.9 weeks, and 1225.2±307.6 grams, respectively. Seventeen (54.8%) patients were nulliparous, while 14 (45.2%) patients were multiparous. Eight (25.8%) patients had a spontaneous vaginal delivery, and the remaining 23 (74.2%) patients had cesarean section delivery. The sociodemographic and clinical characteristics of patients are presented in Table 1.

Table 1. Demographic and clinical characteristics of patients

	Mean±SD
Age, years	29.16±5.60
Gestational age, weeks	28.45±1.91
Birth weight, grams	1225.16±307.60
	n (%)
Parity	
Nulliparous	17 (54.8)
Multiparous	14 (45.2)
Delivery mode	
Normal	8 (25.8)
C/S	23 (74.2)

Biochemical analyses revealed that the AST levels at the 12th hour were significantly higher than the basal levels (p<0.001). However, there were no significant differences between basal and 12th-hour hemoglobin (p=0.97), hematocrit (p=0.21), and platelet (p=0.25) levels. The APRI score at the 12th hour was significantly higher than the APRI score at basal measurements (p<0.001) (Table 2).

Table 2. Biochemical analyses at initiation and 12th hour of MgSO₄ administration

	Basal	12 th hour	P
	Mean±SD	Mean±SD	
Magnesium (mEq/L)	-	4.8±0.4	-
Hemoglobin g/dL	11.3±1.4	11.3±1.3	0.97
Hematocrit (%)	32.2±3.2	33.3±3.6	0.21
Platelet (×10 ⁹ /L)	241.6±19.2	240.3±18.4	0.25
AST (IU/L)	29.7±6.7	42.8±5.4	<0.001
APRI Score	0.31±0.07	0.45±0.07	<0.001

DISCUSSION

This is the first study that evaluates the effects of MgSO₄ on the maternal APRI scores when administered for neuroprotection in preterm labors. The analyses showed

that MgSO₄ administration significantly increases the APRI scores at 12th hours of administration following the loading dose. Our findings showed that APRI score of the pregnant patients can change with the administration of MgSO₄. Results of this study may support the current clinical practice and usage of APRI score in the patient follow up in the treatment of magnesium sulfate.

The MgSO₄ administration is the first choice of intervention to manage severe preeclampsia and eclampsia. However, it has been more used for neuroprotective purposes in recent years. Many tocolytic drugs for women are used in preterm labor to prolong pregnancy and reduce birth damage associated with prematurity. It has a neuroprotective effect in the newborn, when magnesium sulfate (MgSO₄) is used prenatally in mothers at risk of preterm delivery. Therefore, MgSO₄ is frequently used for tocolytic purposes.

The research showed that in-utero exposure to MgSO₄ before early preterm delivery decreases the incidence and severity of cerebral palsy. It is also considered safe or might cause more favorable or manageable side effects when administered in therapeutic doses (13-14). No complications were observed in our study due to MgSO₄ administration.

Several mechanisms were suggested for the neuroprotective features of MgSO₄ administration, including stabilization of cerebral circulation by stabilizing blood pressure and normalizing cerebral blood flow, prevention of excitatory injury by stabilizing neuronal membranes and blockade excitatory neurotransmitters, such as glutamate. Moreover, MgSO₄ is a robust antioxidant with significant anti-inflammatory effects (15).

Several previous studies reported data on the effects of MgSO₄ administration on the immune and inflammatory responses. In one of those, Sugimoto et al. showed that MgSO₄ administration decreases the TNF- α and IL-6 production, which has roles in inflammatory processes (16), which was also demonstrated by other studies (17). Another study by Haruka Suzuki-Kakisaka reported reductions in the levels of TNF- α and IL-6 (18). An animal model has recently evaluated the lipopolysaccharide-simulated inflammation in brain tissue during pregnancy and reported that MgSO₄ administration decreased proinflammatory cytokine production (19). Another study found that maternal MgSO₄ administration prevents brain damage in the neonate, but without any decreases in the cerebral IL-1 β levels, contrary to other studies, which suggests that the neuroprotective effects of MgSO₄ administration are not mediated by the inhibition of inflammatory cytokine production (20). Nevertheless, a recent study reported that MgSO₄ administration increases the inflammatory indexes, contrary to others. Orgul et al. evaluated 63 pregnant women hospitalized for preterm labor, and reported that MgSO₄ administration increases the inflammatory indexes including neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and

systemic immune-inflammation index at 6th hour of administration, which contradicts with other studies regarding the inflammatory characteristics of magnesium, and concluded that preterm labor is an inflammatory process per se, might be affected from many factors, and may change rapidly (21).

A recent study has evaluated the effects of MgSO₄ on the hepatic ischemia/reperfusion damage in a rat model, and the results from 32 adult female Wistar-Albino rats revealed that MgSO₄ administration pretreatment moderately decreased the liver damage through its anti-inflammatory and anti-oxidant effects (22).

There are only limited number of studies on the effects of MgSO₄ treatment on the liver functions. In one of those studies from 2018, the effects of MgSO₄ treatment on liver functions in major depressive disorder cases were evaluated, and no significant effects were found (23). In contrary to that study, we found that AST levels were increased 12 hours after the initiation of MgSO₄ infusion. Nevertheless, this increase was temporary, and we observed normal hepatic functions at the postpartum 2nd day. The increase in the APRI score following MgSO₄ administration that we observed has not been reported in the literature. Although the MgSO₄ is metabolized from kidneys, our results also suggests that it might have effects also on liver. Further studies with larger sample sizes may warrant better elucidation of these effects.

Recently; The APRI score, which is frequently the subject of research in inflammation, malignancies, cardiovascular diseases, and infections such as covid 19, continues to be the subject of new research in the field of obstetrics. Especially in viral infections such as covid 19, the APRI score, which can show the severity of the infection, continues to be interesting (24,25). In our study, it will be instrumental in putting forward the idea that the APRI score can be put into practical use in the field of obstetrics. If these findings are supported by larger studies, a low-cost and practical scoring system will contribute to the clinic. In a similar article in which some non-invasive and low-cost biomarkers, such as APRI, determined from blood parameters, were examined in preterm births in obstetric practice. The idea of integrating such low-cost biomarkers into clinical usage was discussed (26).

Besides its promising results, our study is not without some limitations. First, the sample size is relatively low due to the study design, and our results needs confirmation by further studies with larger sample sizes. In addition, another limitation is that the study was a single center study. Supporting our findings with multicenter studies will provide broader contributions to the literature. Last but not least, we could only evaluate the short-term outcomes of MgSO₄ treatment, thus long-term outcomes need to be evaluated in future studies with longer follow-up periods.

Nevertheless, despite its limitations, our study will also be beneficial in terms of opening up new horizons for

clinicians. It is a research that gives us the idea that a treatment protocol such as MgSO₄ that can cause potential toxicity can be predicted with a simple non-invasive biomarker and necessary precautions can be provided.

CONCLUSION

The APRI score significantly increases at the 12th hour of MgSO₄ infusion administered for neuroprotective purposes in preterm labors. Further prospective studies may be helpful to understand the pathophysiological effect of neuroprotective magnesium sulfate administration on maternal APRI Score levels.

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Conflict of Interest: The authors have no conflicts of interest to declare.

Ethical approval: This study was accepted by the Yuksek Ihtisas University Faculty of Medicine Ethics Committee (Date: 18/05/2023; Approval No: 2023/03/07).

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