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RESEARCH ARTICLE

The Effect of Magnesium Sulfate Therapy on Bleeding Time in Women with Threatened Preterm Labor

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ABSTRACT

Magnesium sulfate is widely used in obstetrics and is drug of choice in two important complications of pregnancy, preeclampsia and preterm labor. The antagonistic effects of magnesium sulfate on calcium ion and on platelet aggregation may lead to changes in bleeding time. This study was conducted to evaluate the effect of magnesium sulfate on bleeding time in women with threatened preterm labor. A group of 40 patients with signs of preterm labor were treated with magnesium sulfate (4 grams in 200 ml D.W.5% in 20 minutes followed by maintenance dose of 2 grams per hour infusion) and template bleeding time (with IVY method), platelet count and mean arterial pressure were obtained before and 2 hours after magnesium sulfate infusion. The data were analyzed using paired t-test. The mean bleeding time before and after treatment were 161.1+50.6 and 169+61.8 seconds respectively and the mean platelet count was 179,925 and 185,250 respectively. The mean arterial pressure was 86.9+9 mmHg before treatment compared to 81.9+8.3 mmHg after treatment. According to the data presented in this study, there was no significant difference in bleeding time and platelet count before and after treatment with magnesium sulfate whereas the mean arterial pressure was significantly different (p<0.001) before and after treatment with magnesium sulfate.

Keywords: *Magnesium sulfate, Preterm labor, Bleeding time, Platelet count*

Magnesium is a divalent cation involved in adenosine triphosphate transfer reactions and antagonizes some of the effects of calcium ion. For platelet aggregation to occur; both adenosine triphosphate and calcium are required [1]. Previous studies have shown magnesium ion to possess platelet antiaggregant properties [1]. Magnesium sulfate is widely used in obstetrics and is drug of choice in two important complications of pregnancy, preeclampsia and preterm labor [2-3].

The bleeding time is a commonly-used diagnostic test that evaluates platelet-related hemorrhagic disorders. Previous research reported the prolongation of bleeding time in patients with preeclampsia receiving magnesium sulfate [3-5]. Also, some abnormalities have been reported in platelet function and bleeding time in pre-eclamptic patients without magnesium sulfate administration [6-7]. The administration of magnesium sulfate to patients with possibility of preterm labor as tocolytic agent usually is done without bleeding time measurement.

The magnesium sulfate administration to prevent preterm labor in threateneded preterm labor is routine in our center and therefore this study was conducted to clarify the effect of magnesium sulfate on bleeding time and platelet count in threatened preterm labor patients admitted to Mirza Kochak Khan Hospital.

MATERIALS AND METHODS

The study population was the pregnant patients admitted to Mirza Kochak Khan Hospital from March 20, 2002, to March 20, 2003, for threateneded preterm labor.

The inclusion criteria were 20-36 weeks gestation with at least one uterine contraction (with duration >30 seconds) in 10 minutes.

The exclusion criteria were vaginal bleeding, amniotic sac rupture, intrauterine fetal death, fetal growth restriction, chorioamnionititis (mother body temperature ≥ 38°c, uterine tenderness, and offensive odor vaginal

Table 1. Characteristics of the patients with threatened preterm labor treated with magnesium sulfate in Mirza Kochak Khan Hospital in 2002-2003 (n =40)

Patient characteristics	Mean ± standard deviation
Age (years)	25.6±5.6
Gestational age (weeks)	33.5±1.5
Gravidity	2.4±2
Parity	1.0±1.6

secretion, or FHR ≥160/min), cervical dilatation ≥ 3cm, a history of platelet or clotting disorders, ingestion of aspirin or any other drug known to prolong bleeding time during the preceding 30 days, liver disease or other concurrent medical disorder, thrombocytopenia, the initial bleeding time longer than 420 seconds.

All the patients were informed about the procedure and written consent was obtained from each individual patient.

For each eligible patient for the study, a template bleeding time, an initial platelet count and arterial blood pressure were recorded.

An automated sphygmomanometer cuff (Riester, Empire Wandmodell, Germany) was used to obtain blood pressure readings on the left arm at the level of the heart, while the patient was in a supine position. The hospital laboratory using a single instrument did the platelet counts.

Magnesium sulfate (Pasteur Institute, Tehran, Iran) was administered as an intravenous bolus (4 grams) mixed in 5% dextrose solution and infused over 20 minutes. Magnesium was maintained with a continuous infusion of 2 g/h.

A second template bleeding time, arterial blood pressure and platelet count were obtained 2 hours after the initial magnesium bolus administration. A single investigator did all the measurements to minimize technical variance.

The bleeding time was measured using IVY method. A sphygmomanometer cuff was inflated on the patients arm to 40 mmHg. The arm was supported at the level of the heart, and a muscular area on the volar aspect distal to the antecubital area was identified and swabbed with alcohol. The incision was made by depth of 3 mm and blood was blotted with filter paper every 30 seconds until no blood stained the paper. The mean bleeding time was obtained. The normal bleeding time using this method is 1-7 minutes. The data were analyzed using paired t-test with $p<0.05$ being significant. The minimum sample size required for the test was calculated using a power of 80%, 95% confidence and standard deviation of 96 seconds to detect difference of 60 seconds in bleeding time. The minimum sample size was found to be 40.

The project protocol was approved by the Ethical Committee at Tehran University of Medical Sciences.

RESULTS

The mean age of the 40 patients was 25.6 (17-40) years. Other characteristics of the patients are shown in Table 1.

The mean bleeding time 2 hours after magnesium sulfate administration was 169 seconds (range 90-360 sec) and pretreatment value was 161.1 seconds (range 85-275 sec), which are not significantly different (Table2).

Also, there is not a significant difference between the mean platelet count before (179925 per mm3; range 150000-287000) and 2 hours after (185250 per mm^3; range 130000-283000) magnesium sulfate administration (Table2).

The mean arterial pressure was 86.9 (range 57-103) mmHg and 81.9 (range 67-103) mmHg for pre- and post-treatment respectively. In this study, there was no need for changing the dose of magnesium sulfate since the contractions were well inhibited.

DISCUSSION

Magnesium sulfate has long been assumed to have anticoagulant effect via antiplatelet and antithrombotic properties [1,8]. Some laboratory studies have suggested the augmentation of factor IX and VIII activity [9] and increased platelet aggregation and reduction in protein C and S level favoring clot formation [10]. However, other studies have shown magnesium to decrease platelet aggregation [11], decrease endothelin I level, and increase antithrombin III levels [10], resulting in suppressed thrombus formation.

Harnett et al. (2001) have reported that magnesium has no effect on platelet function using thrombelastography after magnesium administration, and also magnesium had no effect on functional fibrinogen level [12]. Rukshin, et al. (2002), have reported that intravenous magnesium sulfate produced marked inhibition of acute stent thrombosis without significant effect on platelet aggregation or bleeding time [13]. The discrepancy between the findings encouraged us to look at bleeding time and platelet count in our patients who

Table 2. Comparison between the values obtained from threatened preterm labor patients before and 2 hours after treatment with magnesium sulfate in Mirza Kochak Khan Hospital in 2002-2003 (n=40)

	Before administration	2 hours after administration	t- test
Bleeding time (seconds)	161.1±50.6	169.0±61.8	NS
Platelet count (in mm^3)	179925±37410	185250±36359	NS
Mean arterial pressure (mmHg)	86.9±9.0	81.9±8.3	$p<0.001$

The values are the mean ± standard deviation
NS -not significant

were receiving magnesium sulfate for threatened preterm labor.

In our study, there was no significant effect of magnesium on bleeding time and no significant effect on platelet count.

There is discrepancy between these findings and previous reports on prolongation of bleeding time after magnesium sulfate administration in preeclampsia [4,5]. This discrepancy might be explained by the reports on platelet dysfunction and bleeding time prolongation in patients with preeclampsia prior to magnesium sulfate therapy [6,7].

However, our findings are in agreement with some other reports on platelet function and bleeding time measurement after magnesium sulfate administration [4,5,12,13]. In this study, it also has been shown that magnesium sulfate administration decrease mean arterial pressure by 5 mmHg. This change in mean arterial pressure is statistically significant ($p<0.001$) and it is in agreement with other previous reports [4].

In conclusion, the current practice of administration magnesium sulfate (a 4 grams bolus followed by 2 g/h) did not influence bleeding time and platelet count in our patients and can be safely used in preterm patients. Reduction in mean arterial pressure without effect on bleeding time and platelet count make magnesium use suitable in preeclampsia patients which may have abnormalities in platelet function and bleeding time [6,7].

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