

Bleeding time after magnesium sulphate infusion in cases of preeclampsia

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ABSTRACT

Background: preeclampsia is a pregnancy-associated multisystem disorder that affects 3-5% of all pregnancies. It remains a leading cause of maternal and neonatal morbidity and mortality in the world. Magnesium sulphate is the drug of choice in the management of impending eclampsia and eclampsia. Magnesium sulphate has an anti-coagulating effect, which has been used early in preeclampsia to delay the advance of the disease. This action however, is considered as a disadvantage, because it can prolong the bleeding time. The prolongation of bleeding time may precipitate postpartum haemorrhage. **Objective:** the objective of this study was to observe the effects of magnesium sulphate on bleeding time in patients with preeclampsia. **Patients and Methods:** a study was conducted between April 2018 and February 2019. Fifty patients with preeclampsia were included in the study. Bleeding time was measured through modified Ivy method. These measures were recorded before, immediately and 24 hours after discontinuation of magnesium sulphate. **Results:** after magnesium sulphate therapy; bleeding time is increased, haemoglobin level and haematocrit level are decreased.

Conclusion: bleeding time in patients with severe preeclampsia was prolonged with magnesium sulphate infusion. This is clinically important because it worsens the present condition and causes possible complications.

Keywords: C-reactive protein, gestational diabetes.

INTRODUCTION

Magnesium Sulphate is a drug that belongs to the miscellaneous group of anti-convulsants. Magnesium prevent or controls convulsions by blocking neuromuscular transmission and decreasing the amount of acetylcholine liberated at the endplate by the motor nerve impulse^(1,2).

The daily requirements of magnesium are 4 to 6 mg/Kg body weight/day in adults⁽³⁾. The recommended daily allowance in pregnancy is 450 mg/day^(4,5).

Magnesium is absorbed in the proximal part of the small intestine and to some extent from the colon⁽⁶⁾. Magnesium is mainly excreted through the kidney once it is absorbed, but the unabsorbed fraction is excreted through faeces⁽⁷⁾.

Magnesium Sulphate has been extensively used in cases of preeclampsia; it has many benefits in such patients e.g.:

- Prophylaxis against eclampsia^(8,9).
- Hypotensive.
- As a tocolytic agent.

Magnesium Sulphate acts by:

- ✓ Blocking the neuromuscular transmission and decreasing the amount of acetyl choline liberated at the endplate by the motor nerve impulse⁽¹⁰⁾.
- ✓ Reducing cerebral irritability, but does not cause deep sedation⁽¹¹⁾.
- ✓ Causing some peripheral vasodilatation and decreased responsiveness of vascular smooth muscles to sympathomimetic amines⁽¹²⁾.
- ✓ Having anti-coagulating effect, which has been used early in preeclampsia to delay the advance of the disease^(13,14). This action, however, is considered as a disadvantage, because it can

prolong the bleeding time through the following mechanism: It stimulates prostacyclin, which is a potent platelet aggregation inhibitor that inhibits adenosine diphosphatase, which is required by platelets to induce aggregation⁽¹⁵⁾.

All through the magnesium sulphate therapy, the patient must be monitored carefully in order to avoid toxicity. This entails the following^(16,17):

1. Urine output: Which should not be below 100 ml/4 hours, as magnesium sulphate is mainly excreted by the kidney.
2. Patellar reflex: Avoid its sluggishness or absence, as it is the first sign of toxicity.
3. Respiratory rate: Should not below 12/minute.
4. Serum level of magnesium: Therapeutically effective plasma levels of magnesium are 4-7 mEq/L. Patellar reflex disappears when the plasma level reaches 10 mEq/L. When plasma magnesium level rises above 12 mEq/L, respiratory depression and paralysis develops and arrest follows⁽¹⁸⁾.

Despite its undesirable, sometimes even life-threatening side effects, the role of magnesium sulphate in the management of severe preeclampsia and eclampsia has been well established for seizure prophylaxis. Also, it lowers the blood pressure^(19,20).

Kyncz and Cibils⁽²¹⁾ observed that blood loss increased among patients with preeclampsia who received magnesium sulphate infusion. The bleeding time was checked before infusion of magnesium and at completion of infusion and it was found that bleeding time more than doubled among patients who need the drug. This finding was also reported in previous works⁽²²⁾.

AIM OF THE STUDY

If Magnesium Sulphate therapy in cases of preeclampsia is associated with a significant prolongation of the bleeding time^(23,24), its use in this indication might lead to severe post partum haemorrhage which is potentially life threatening particularly in those already compromised patients with contracted blood volume^(25,26).

PATIENTS AND METHODS

Study design:

The study included pregnant patients with severe preeclampsia to evaluate the effect of magnesium sulphate on the bleeding time.

Study period:

April 2018 to February 2019.

Study setting:

The study included fifty pregnant patients with severe preeclampsia, recruited from the attendants of the Antenatal Care clinic and Emergency Room of the Etay Al-baroud Hospital.

Approval of the Medical Ethics Committee and signing a written informed consent was done.

Inclusion criteria:

- 1) Duration of pregnancy > 38 weeks .
- 2) Diastolic blood pressure \geq 110 mmHg.
- 3) Proteinuria \geq 2+.
- 4) With or without lower limb oedema .

Exclusion criteria:

- 1) History of intake of acetyl salicylic acid or any other drug that may alter the bleeding time during pregnancy.
- 2) Thrombocytopenic patients (Platelet Count < 120 thousands /cmm).
- 3) Major trauma to the genital tract during vaginal delivery.

Data collection technique and tools:

Those women enrolled in this study, underwent admission procedures:

1. Full history taking.
2. Thorough general examination.
3. Thorough obstetrical examination.
4. Laboratory tests :
 - a) Complete blood picture included : haemoglobin concentration, haematocrit value and platelet count.
 - b) Fasting blood sugar.
 - c) Blood urea and serum creatinine.
 - d) Liver enzymes { Aspartate Aminotransferase (AST) and Alanine Transaminase (ALT) }.
 - e) Complete urine analysis (including protein in urine).
 - f) Bleeding time using **modified Ivy method**⁽²⁷⁾:

A sphygmomanometer cuff is applied to the patient's upper arm, and is inflated to 40 mm Hg. This pressure must be maintained during the test. Test area is selected on the volar surface of the forearm (approximately 5-10 cm from elbow groove) that is devoid of hair and superficial veins : This area is cleaned with alcohol pad .In rapid succession, two incisions are done , each one 9 mm long and 1 mm deep, using template slit and blade. Two stopwatches are started and the wounds are blotted every 30 seconds with filter paper without touching the wound edges .The first stopwatch is stopped when blood exuding from the first incision no longer stains the filter paper. The same procedure is done for the second wound using the second stopwatch. The average bleeding time is calculated. It is approximated to the nearest half minute .The sphygmomanometer cuff is released and a butterfly bandage is applied to each wound.

All the selected patients received 4 grams of magnesium sulphate in 250 cc glucose 5% intravenously at the beginning as bolus dose followed by 6 grams in 500 cc glucose 5% every 6 hours postpartum.

Follow up was observed with the respiratory rate , urine output and knee jerk were monitored for any signs of toxicity: Urine output below 100 cc / 4 hours, respiratory rate less than 16 cycles / minute or disappearance of the knee jerk. Measurement of blood pressure every hour. The drug was stopped if the blood pressure was less than 100/60 mmHg.

The bleeding time was measured immediately after discontinuation of the drug and 24 hours later. In the present study, the bleeding time was considered prolonged if it was equal 10 or more minutes.

All patients were observed during labour and the amount of blood lost postpartum was measured by: The hemoglobin concentration and haematocrit value were estimated immediately postpartum and compared with estimated at admission, The amount of blood lost within first 4 hours after delivery was roughly estimated by collecting all the sanitary containing the discharges and blood coming per vagina. These pads were weighed and the original weight of the pads is subtracted, visual estimation of the amount of blood lost (mild, moderate or severe) based on obstetric experience.

RESULTS

The clinical data of the selected cases are shown in table (1). Their ages ranged from 23 to 34 years with a mean of 29.2 ± 3.434 . The gravidity ranged from 1-4 pregnancies with a mean of 1.48 ± 0.735 and parity ranged from 0-4 deliveries with a mean of 0.32 ± 0.55 . The duration of pregnancy ranged between 38 and 40 weeks.(figure 1,2).

Table (1): Clinical data of the studied group

Duration of pregnancy (in weeks):		
21	21	42.0
18	18	36.0
11	11	22.0
38		
39		
40		
Range	38-40	
Mean ± SD	38.8 ± 0.782	

	On admission	Immediately after discontinuation	24 hrs after discontinuation
Range (minutes)	2-7	4-14	3-8
Mean ± SD	4.2 ± 1.02	8.67 ± 1.86	4.34 ± 0.91
T		19.6	1.8
P		0.0001 *	0.077 NS

	Frequency	
	Number	%
Age distribution (in years):		
20-	6	12.0
25-	19	38.0
30-35	25	50.0
Range	23-34	
Mean ± SD	29.2 ± 3.434	
Gravidity :		
1	32	64.0
2	13	26.0
3	4	8.0
4	1	2.0
Range	1-4	
Mean ± SD	1.48 ± 0.735	
Parity :		
0	36	72.0
1	12	24.0
2	2	4.0
3	0	0.0
4	0	0.0
Range	0-2	
Mean ± SD	0.32 ± 0.551	

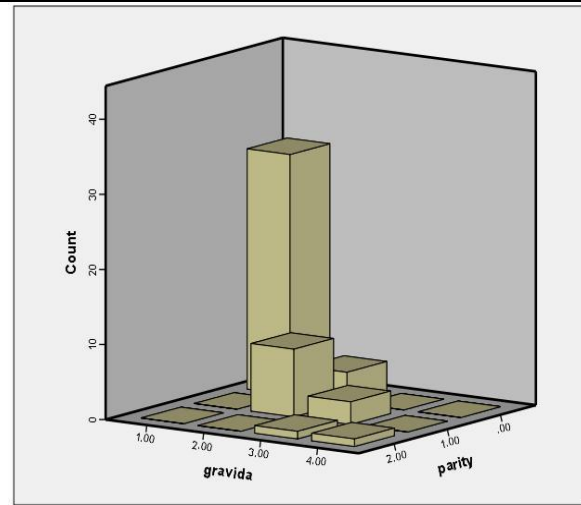


Figure (1): Clinical data of studied group.

The bleeding time before magnesium sulphate infusion ranged between 2-7 minutes, with a mean of 4.2 ± 1.02 minutes. It increased significantly immediately after discontinuation of magnesium sulphate to range between 4-14 minutes, with a mean of 8.67 ± 1.86 minutes.

Bleeding time, 24 hours after discontinuation of the drug, ranged between 3-8 minutes, with a mean of 4.34 ± 0.91 minutes. The bleeding time at 24 hours after discontinuation nearly returned to the normal value similar to that at admission i.e. the difference was statistically insignificant as shown in Table (2).

Table (2): Bleeding time (minutes) before administration of magnesium sulphate, immediately and 24 hours after discontinuation of the drug

Increase in bleeding time	Number	%
< 50 %	3	6.0
50-100%	27	54.0
> 100%	20	40.0

* Statistically significant.
 NS = Statistically non- significant.
 SD = standard deviation

Table (3): Distribution of patients according to the increase in bleeding time

On admission the haemoglobin concentration ranged between 9 - 12.5 g/dl , with a mean of 10.22 ± 0.827 . It decreased after labour to range between 7.5 - 11 g/dl , with a mean of 9.32 ± 0.896 g/dl as shown in table (4) figure (3).

Table (4): Comparison between haemoglobin level (g/dl) before and after labour

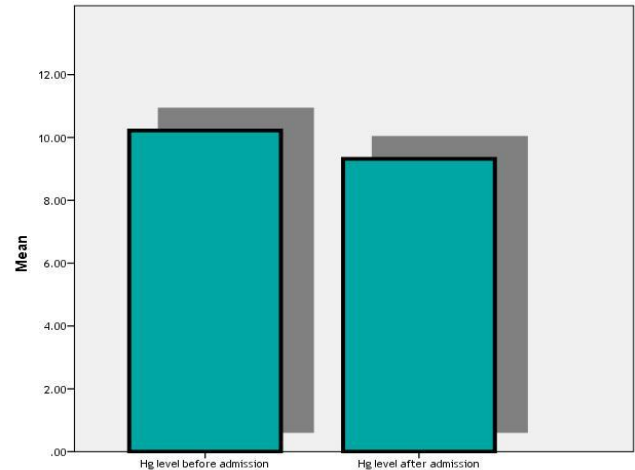


Figure (3): Comparison between haemoglobin level before and after labour

	Before	After
Range (minutes)	9 – 12.5	7.5 – 11
Mean \pm SD	10.2 ± 0.83	9.32 ± 0.89
T	18.9	
p	0.0002	

On admission the haematocrit value ranged between 29-45% , with a mean of 34.27 ± 2.974 % . It decreased after labour to range between 27-40 % with a mean of 30.84 ± 3.0396 % as shown in table (5) figure (4).

Table (5): Comparison between Haemaocrit value (%) before and after labour

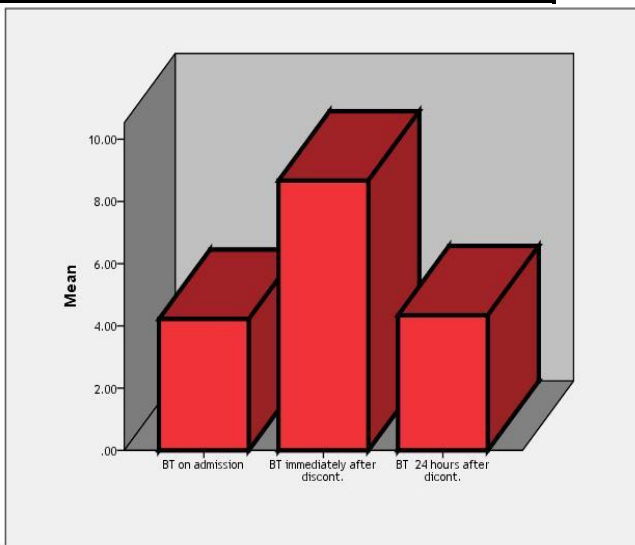


Figure (2): Comparison between bleeding time before infusion, immediately and 24 hours after discontinuation

	Before	After
Range	29-45	27-40
Mean \pm SD	34.3 ± 2.97	30.8 ± 3.04
T	19.395	
p	0.0003*	

* Statistically significant.

The bleeding time discontinuation of magnesium sulphate infusion increased in all cases . the magnitude of this increase is shown in table(3). In most of the cases (> 93%), the bleeding time was prolonged by > 50% of its original value as shown in table (3)

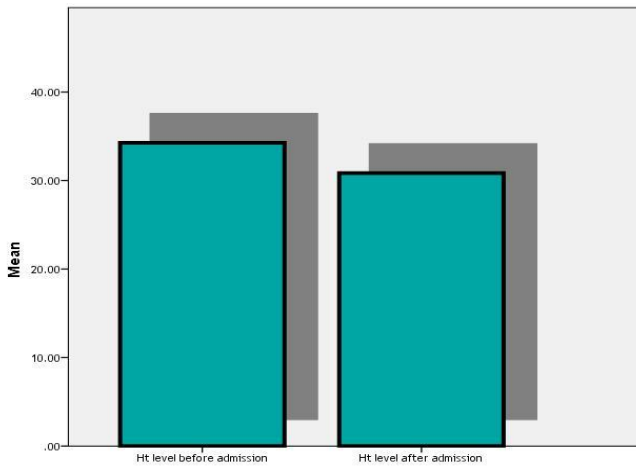


Figure (4): Comparison between haematocrit value before and after labour

DISCUSSION

Preeclampsia is a disease characterized by hypertension, proteinuria, and/or oedema developing after the 24th week of gestation and rarely develops earlier in cases of trophoblastic disease. Patients with preeclampsia have a contracted blood volume and therefore, any significant bleeding may result in a life-threatening condition for these patients. The role of magnesium sulphate in management of severe preeclampsia and eclampsia has been well established for seizure prophylaxis and control⁽²⁸⁾.

Magnesium sulphate acts by blocking the neuromuscular transmission and decreasing the amount of acetylcholine liberated at the endplate by the motor nerve impulse. Also, it reduces the cerebral irritability without causing deep sedation. However, it was noticed that the bleeding time is prolonged in cases that received magnesium sulphate infusion⁽²⁹⁾.

Several studies have demonstrated the relationship between magnesium sulphate infusion in preeclamptic patients and prolonged bleeding time. **Canten et al.**⁽³⁰⁾ noted that magnesium appears to have both in vivo and in vitro antiaggregant properties through stimulation of prostacyclin, which is a potent platelet aggregation inhibitor.

In the present study, it was noted that there was a 102.4% increase in the bleeding time in 14 out of 50 cases, i.e. 28%. This finding is similar to that reported in some earlier studies⁽³¹⁾.

During labour and postpartum, the amount of blood lost was observed and only one case among the fifty cases had postpartum haemorrhage of a mild degree. She lost about 700 cc blood (the haemoglobin decreased from 10 grams to 7 grams). This observation is very important and must be considered during management of any preeclamptic patient on magnesium sulphate who already has a compromised blood volume. Previous studies attribute this increased incidence of postpartum haemorrhage with the use of magnesium sulphate to its antiaggregant effect or due to its tocolytic

effect⁽³²⁾, which makes induction of labour usually necessitate higher doses of oxytocin.

The bleeding time was estimated another time 24 hours after discontinuation of magnesium sulphate. It was found that at that time it nearly returned to the normal level ranging from 2 to 10 minutes.

In the present study, the dose of magnesium sulphate given was variable according to the stage of labour at admission and the response to induction of labour. However, this variability was not accompanied by any difference in the degree of increase in bleeding time, i.e. no correlation between the total magnesium sulphate dose and percentage increase in bleeding time.

In this study, cases with any disorder were excluded in order to correlate the bleeding time prolongation with the effect of magnesium sulphate. The haemoglobin concentration and haematocrit value diminished in some cases which delivered vaginally than those delivered caesarean so caesarean section had no marked effect on haemoglobin and haematocrit value. Cases of caesarean section which complicated intraoperative had excluded.

CONCLUSION

In conclusion this study suggests that magnesium sulphate causes prolongation of the bleeding time when given through infusion in preeclamptic patients, and so it can increase the incidence of postpartum haemorrhage. Also, it can lower the blood pressure.

The present work emphasized the beneficial therapeutic role of magnesium sulphate to prevent and control seizures in severe preeclamptic patients.

Despite such therapeutic role, the accompanying prolongation of bleeding time may precipitate postpartum haemorrhage. Active measure to control such bleeding should be ready at hand when managing cases of severe preeclampsia.

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