
Assessment of Maternal-Fetal outcomes by Doppler Flow Velocity Waveforms in Preterm Labor Patients Undergoing Magnesium Sulfate Tocolysis

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Abstract

Background: Preterm labor is frequency uterine contractions, progressive effacement and dilation of the cervix prior to term gestation. Prevention and treatment of preterm labor is important because it is one of the most important causes of perinatal morbidity and mortality. The etiology of preterm labor is poorly understood.

Aim of the Work: to evaluate the influence of antenatally administered magnesium sulfate (MgSO₄) given to women at risk of preterm birth on the cerebral blood flow and systemic hemodynamic in preterm infants.

Patients and Methods: This was a prospective observational interventional study conducted from October 2016 to February 2017 on (40) patients undergoing preterm labor at AL Zahraa hospital AL Azhar university and New Cairo Hospital, after informed a written consent was taken from every patient after counseling them the procedure of the study.

Results: In our study we found that the best blood level of magnesium sulfate at which contractions stopped (cut off) is (>4.18) mg/dl which equal (6.82) gm of administrated magnesium sulfate with sensitivity (94.74%) and specificity (100%), positive predictive value (PPV) was (100%) and negative predictive value (NPV) was (50%).

Conclusion: Maternal magnesium sulphate (Mgso₄) decreases the cerebral perfusion pressure and blood flow, and this likely protects the germinal matrix against the development of circulatory stress in the early post natal period. Magnesium sulphate achieved the primary outcome (prevention of delivery for 48 hours, with uterine quiescence) at cut-off value of (\geq 4.18) mg/dl which equal (6.82) gm with sensitivity (94.74%), specificity (100%), positive predictive value (100%) negative predictive value (50%).

Key words: Doppler flow velocity waveforms, preterm labor, magnesium sulfate tocolysis, maternal-fetal outcome

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Introduction

Although survival of preterm infants in intensive care has increased substantially in recent decades, the risk of their developing brain lesions with subsequent poor neurodevelopment remains high. Because of their poorly developed autoregulatory control mechanisms, cerebral blood flow may fluctuate considerably with spontaneous variations in systemic blood pressure (BP) ⁽¹⁾.

A number of immaturity-related factors, e.g., ductus arteriosus shunting and respiratory distress syndrome (RDS), may further potentiate systemic circulatory oscillations and endanger cerebrovascular integrity in preterm infants⁽²⁾. Thus, the circulatory liability of prematurely born infants is considered to be a primary cause of the development of both hemorrhagic and ischemic brain injuries⁽³⁾.

Doppler sonography is a non-invasive procedure that detects the heartbeat of a fetus. This technology can be used to evaluate pulsations in the fetal heart and to examine blood vessels for signs of abnormalities. A medical practitioner can use Doppler sonography to see the flow of blood from the placenta to the baby, or within the baby's body. This procedure can be very helpful in determining whether the placenta is delivering a sufficient blood supply to the developing baby. It also helps medical practitioners ensure the well-being of the baby, as well as to determine whether there is a need for early delivery or for other medical procedures to ensure good fetal health⁽⁴⁾.

Prevention of preterm delivery and preventive stabilization of both the cerebral and systemic hemodynamics in the fetus and neonate are clearly major clinical challenges for perinatal care. Tocolytic agents, such as magnesium sulfate (MgSO₄) reduce slightly the incidence of preterm delivery⁽⁵⁾, but may additionally have independent influences on the neurologic outcome of the exposed infants⁽⁶⁾.

In fact, clinical studies indicate that antenatal MgSO₄, originally used for the treatment of maternal preeclampsia and eclampsia⁽⁷⁾ may decrease the incidence of brain injuries among very low birth weight infants⁽⁴⁾.

The mechanism of the cerebral effects of this tocolytic is still unclear, but because this drug has potent effects on maternal systemic and cerebral circulation and readily cross the placenta, they may also exert a significant effect on the perinatal circulation during transition. Although these hemodynamic effects may prove to be important for preterm infants with immature circulatory control systems, they are still poorly understood⁽⁸⁾.

Aim of the work

1. Evaluate the influence of antenatal administered magnesium sulfate (MgSO₄) given to women at risk of preterm birth on the cerebral blood flow and systemic hemodynamic in preterm infants.
2. Evaluation of pregnant women at risk of preterm labor by Doppler study on fetal middle cerebral, umbilical and maternal uterine arteries before and after magnesium sulfate administration.
3. Evaluation of maternal, fetal and neonatal outcomes.

Patients and Methods

This prospective observational interventional study was conducted from October 2016 to February 2017 on (40) patients undergoing preterm labor at AL Zahraa hospital Al Azhar university and New Cairo Hospital, after informed a written consent was taken from every patient after counseling them the procedure of the study.

Inclusion criteria:

Primigravida Women between (28-36) weeks depending on 1st day of last normal menstrual period (LMP) or early ultra sound U/S with singleton pregnancy.

Exclusion criteria:

1. Multi fetal gestation.
2. Not Sure of date (LMP).
3. Medical complications of pregnancy (diabetes-hypertension-kidney or liver disease - heart disease – chestdisease -Preeclampsia).
4. Evidence of fetal distress.

Methods

Every patient was submitted into these data:

A-Personal history:

The patient's name, age, address, occupation and phone number.

B- Menstrual history:

1st day of last menstrual period, expected date of delivery, gestational age (28-36) wks.

C- Present history:

At least two uterine contractions were happened for 30 seconds during 10 minutes.

D-Past history:

1. Medical disorders as hypertension, diabetes, heart, chest, liver or kidney diseases.

2. Surgical history.

E- Family history of preterm labor.

Examination

1-General examination:

- **Maternal vital signs (temperature, blood pressure, heart rate respiratory rate).**

2-Abdominal examination:

- **Uterine contractions frequency/duration/intensity are evaluated continuously using cardio-tochography (CTG).**

- **Ultra sound:confirm the fetal presentation, assess amniotic fluid volume and estimate fetal weight.**

3-Trans Vaginal Ultra Sound (TVUS)

- **To evaluate the cervical length when the diagnosis of labor is uncertain (<2.5cm).**

4- **Full investigations for mother were done (CBC-ABO-RH-FBS-urine analysis-liver and kidney function test).**

5- **Pulse-wave Doppler measurements** were made from the fetal middle cerebral artery, the fetal umbilical artery, and the maternal uterine arteries before the initiation of magnesium sulfate tocolysis.

6- All patients received prophylaxis antibiotics of 1.5 gm ceftriaxone and (500) ml hydration with lactated ringers solution before magnesium sulphate infusion.

7- This protocol consisted of (4) gm bolus of magnesium sulfate infused IV over 30 min, a continuous infusion of (2) g/hr until uterine contractions stopped⁽⁹⁾.

- **During the treatment, patient were monitored for urine output, deep tendon reflexes, and respiratory rate per minute.**

- **Monitoring of uterine contraction and fetal heart rates by CTG.**

8- All patients received intramuscular corticosteroid for premature fetal lung prophylaxis: (Dexamethazone: four doses of 6 mg 12 hours apart).

9- After contractions have been stopped, the Doppler flow measurements were repeated.

10- Serum magnesium levels were measured.

11- The pre-therapy and intra-therapy Doppler flow studies were then compared to determine significant changes.

Technique

The examination was performed in a supine, slightly left lateral tilted position through the examination to avoid supine hypotension.

Ultrasonographic and Doppler flow velocity waveforms studies were done with Pulse Wave Doppler after real time colour flow localization of the umbilical and middle cerebral arteries by Samsung somoacex US (S12GM3HJ3401K) 2013.

Umbilical Artery Doppler

The patients placed in a semi-recumbent position with a left lateral tilt, and then the uterine contents are quickly scanned by the real time ultrasound in order to select an area of amniotic cavity with several loops of umbilical cord. Ideally these cord loops should not be close to the cord insertion. Using a Pulsed Wave Doppler, the characteristic sound and shape of the umbilical artery wave form was demonstrated and identified.

Three separate readings or more were averaged before the final values obtained, with three waveforms for each reading. Because of the potential effect of fetal breathing movements on waveform variability, recording were performed during periods of fetal apnea. Both the resistance index (RI) and (PI) were calculated.

Middle Cerebral Artery Doppler

The standard plane for measuring the biparietal diameter was visualized. This plane included the thalamus and the cavum septum pellucidum, the colour and flow mapping function were then superimposed and the middle cerebral artery can be seen pulsating at the level of the insula. The middle cerebral artery can be seen running from the internal carotid artery in a lateral direction into the Sylvian tissue.

Three readings were averaged; with the average of three waveforms calculated for each reading. Both the (RI) and (PI) were calculated.

Uterine Arteries Doppler: Trans vaginal Doppler.

Doppler Values:

UA, UTA and MCA (RI) and (PI) values were expressed numerically in approximation to the second decimal. Paired T test was used to compare values before and after course.

1ry outcomes of this study for mothers include: (stopped contractions- gestational age of delivery-mode of delivery)

For baby include: (Apgar score- O₂ saturation-umbilical cord magnesium sulfate concentration-BP)

2ry outcomes include: ICU admission.

Statistical analysis of the data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level.

The used tests were

1- Mean value (\bar{x}) = $\frac{\sum X}{n}$

Where X = the sum of all observations.

n = the number of observations.

2- The standard deviation S.D. = $\sqrt{\frac{\sum (x-\bar{x})^2}{n-1}}$

Where

$\sum (X_i - \bar{X})^2$ = the sum of squares of differences of observations from the mean.

3 - Paired t-test

It is used during comparison between the results before

and after treatment in the same group. The "t" is calculated as follows:

$$t = \frac{X_d}{\frac{S.D_d}{\sqrt{n}}}$$

Where

X_d = Mean of the difference.

$S.D_d$ = Standard deviation of the difference.

n = Number of cases.

4- Receiver operating characteristic curve (ROC)

It is generated by plotting sensitivity (TP) on Y axis versus 1-specificity (FP) on X axis at different cut off values. The area under the ROC curve denotes the diagnostic performance of the test. Area more than 50% gives acceptable performance and area about 100% is the best performance for the test. The ROC curve allows also a comparison of performance between two tests.

5-Sensitivity

The capacity of the test to correctly identify diseased individuals in a population "TRUE POSITIVES". The greater the sensitivity, the smaller the number of unidentified case "false negatives".

6- Specificity

The capacity of the test to correctly exclude individuals who are free of the disease "TRUE NEGATIVES". The greater the specificity, the fewer "false positives" will be included

7- Positive Predictive value (PPV)

The probability of the disease being present, among those with positive diagnostic test results

8- Negative Predictive value (NPV)

The probability that the disease was absent, among those whose diagnostic test results were negative

Results

Table (1): Demographic data of the studied women (n= 40).

	Range	Mean \pm SD
Age (years)	16.0 – 30.0	21.60 \pm 4.17
BMI (Kg/m ²)	19.0 – 32.0	27.05 \pm 3.32
Pulse (Beat/min)	65.0 – 80.0	72.72 \pm 4.66
Blood pressure systolic (mmHg)	100.0 – 120.0	110.30 \pm 5.91
Blood pressure diastolic (mmHg)	60.0 – 90.0	74.60 \pm 9.07
Gestational age(weeks)	28.0 – 36.0	33.60 \pm 2.74

Table (2): Maternal Doppler flow velocity wave form changes in studied women.

Total number=40	Magnesium sulphate administration		p-value
	Before	After	
Right uterine artery			
RI	0.44 \pm 0.05	0.47 \pm 0.04	0.003*(HS)
PI	0.68 \pm 0.08	0.63 \pm 0.09	0.007*(HS)
Left uterine artery			
RI	0.47 \pm 0.05	0.46 \pm 0.05	0.298(NS)
PI	0.68 \pm 0.09	0.65 \pm 0.11	0.695(NS)

This table shows that there is a highly significant difference as regard right uterine artery RI, PI before and after treatment with p-value (0.003), (0.007) respectively.

As regard left uterine artery RI, PI there is insignificant differences before and after treatment with p-value (0.298), (0.695) respectively.

Table (3): Fetal Doppler flow velocity wave form changes in studied women.

Total number=40	Magnesium sulfate administration		P-value
	Before mgso4	After mgso4	
Fetal middle cerebral			
RI	0.75 \pm 0.05	0.69 \pm 0.05	<0.001*(HS)
PI	1.65 \pm 0.26	1.78 \pm 0.18	0.005*(HS)
Fetal umbilical artery			
RI	0.60 \pm 0.03	0.60 \pm 0.03	0.323(NS)
PI	0.90 \pm 0.08	0.91 \pm 0.08	0.649(NS)

This table shows that there is a highly significant differences in fetal middle cerebral artery RI, PI before and after treatment with p-value (<0.001), (0.005) respectively.

As regard fetal umbilical artery there is insignificant differences.

Table (4): Side effects of magnesium sulfate on the studied women.

Total number=40	Yes	
	No.	%
NO side effects	15	37.5
Allergic reaction (<i>itching, chest tightness, choking in the throat, nasal congestion</i>)	12	30.0
Palpitations	1	2.5
Severe drowsiness	2	5.0
Sweating	10	25.0

Table (5): Primary neonatal outcomes.

Primary fetal outcomes	Range	Mean \pm SD.
Apgar score at 1 min	3.0 – 7.0	5.24 \pm 1.01
Apgar score at 5 min	1.0 – 9.0	8.08 \pm 1.82
Oxygen saturation %	68.0 – 92.0	84.05 \pm 5.55
Fetal serum mgso4(mg/dl)	1.43 – 5.04	3.64 \pm 0.86
Blood pressure systolic(mmhg)	25.0 – 56.0	46.50 \pm 8.52
Blood pressure diastolic(mmhg)	15.0 – 32.0	27.90 \pm 3.99
Neonatal RDS		
No	28	70.0%
Yes	12	30.0%

This table shows that the mean Apgar score at 1 min is (5.24) and at 5min is (8.05) as regard oxygen saturation the mean level is (84.05), mean systolic and diastolic neonatal blood pressure is (46.05),(27.9) respectively and the mean Fetal serum Mgso4 is (3.64). Regarding Respiratory Distress Syndrome there are 12 cases representing (30%).

Table (6): Secondary neonatal outcomes.

Secondary outcomes	No.	%
Neonatal Intensive care unit		
No	28	70.0
Yes	12	30.0

This table shows that (30%) of neonates are admitted to NICU.

Table (7): Maternal outcomes.

Maternal Outcomes	No.	%
Mode of delivery		
Cesarian Section	4	10.0
Vaginal delivery	36	90.0
Delivery <48 hours after MgSO4 infusion		
No	38	95.0
Yes	2	5.0
Stopped contractions		
No	2	5.0
Yes	38	95.0

Blood pressure systolic (mmHg)	100.0 – 120.0	110.30 ± 5.91
Blood pressure diastolic (mmHg)	60.0 – 90.0	74.60 ± 9.07
Maternal Heart Rate (beat/minute)	114.0 – 138.0	125.10 ± 5.45

This table shows that 90% of patients delivered by vaginal delivery. Delivery in less than 48 hours after treatment is only in 5% of patients as 95% of patients showed stopped contraction.

Mean systolic and diastolic blood pressure after treatment are (110.3),(74.6) mmHg respectively and mean maternal heart rate is (125.10) beat/minute.

Table (11): Cut off for Maternal serum MgSo4 to diagnosed stopped contractions and labor >48 hours

	Cut off in blood (mg/dl)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
MgSO4	≥4.18	94.74	100.0	100.0	50.0

This table shows that the best blood level at which contraction stopped is (≥4.18) mg/dl which equal (6.82) gm of administrated magnesium sulfate.

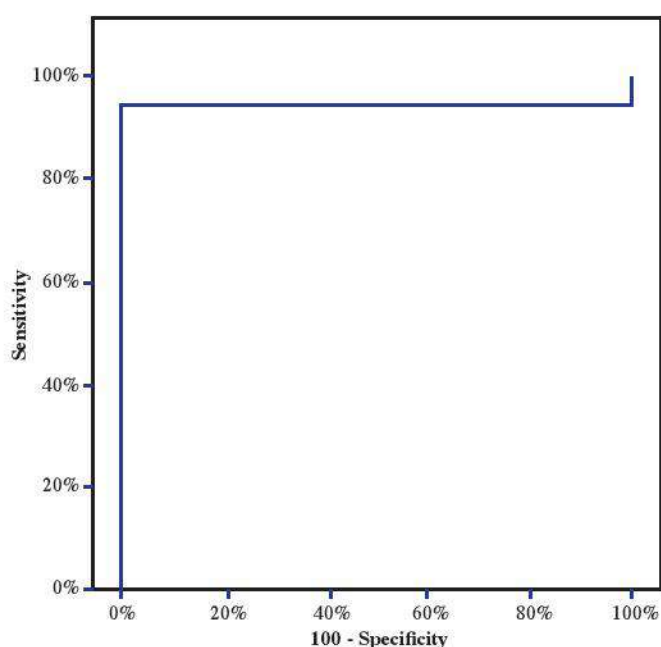


Figure (1):

Cut off for Maternal serum MgSo4 to diagnosed stopped contractions and labor >48 hours.

Discussion

Preterm birth (PTB) is still the leading cause of perinatal morbidity and mortality. Early-term complications such as respiratory distress syndrome, necrotizing enterocolitis, and intraventricular hemorrhage are frequent problems in preterm infants. Frequent late-term complications include visual impairment, hearing loss, and cerebral palsy⁽¹⁰⁾.

Although the rate of other obstetric complications has declined with the development of contemporary obstetric understanding, the treatment methods developed for preterm labor (PTL) have so far

failed to reduce the number of PTBs. However, some benefits are gained through prolongation of pregnancy to enable corticosteroid administration to accelerate fetal lung maturation. The least harmful drug for the mother and fetus, and the most effective tocolytic medication should be selected and administered without any delay after diagnosing the existence of any preterm pattern⁽¹¹⁾.

Tocolytics can be used alone and/or in combination. Each tocolytic agent, in addition to their success in stopping the premature uterine contractions, presents maternal and fetal adverse effects. The use of these drugs requires close monitoring of patients during their administration⁽⁹⁾.

Magnesium sulfate is the most commonly used first-line tocolytic in North America although it has not been demonstrated to be superior to saline infusion, and its use has been a source of controversy. Magnesium sulfate requires intravenous administration, has potential for over medication with serious maternal adverse effects and may be associated with adverse neonatal effects⁽¹²⁾.

In the present study we aimed to evaluate the influence of antenatal administrated magnesium sulfate (MgSO4) given to women at risk of preterm birth on the cerebral blood flow and systemic hemodynamic in preterm infants we conclude 40 patients undergoing preterm labor.

In the present study, the mean age, body mass index (BMI) and gestational age of the studied patients were (21.60±4.17) years,(27.05±3.32) kg/m²,(33.60±2.74) was respectively, All cases were primigravida.

Also pulse and blood pressure were measured to all patients at first visits. The mean and SD of pulse rate were (72.72 ± 4.66) beat/minute. The mean and SD of systolic and diastolic blood pressure were (110.30 ± 5.91) and (74.60 ± 9.07) mmHg respectively as shown in table ⁽⁴⁾.

In the current study the mean systolic and diastolic blood pressure after treatment with magnesium sulphate were (110.3 ± 5.90) , (74.6 ± 9.07) mmHg respectively and the mean maternal heart rate was (125.10 ± 5.54) as shown in table ⁽⁴⁾.

Uterine artery Doppler flow velocity wave form changes in our study were highly significant in right uterine artery RI and PI before and after treatment with magnesium sulphate with p-value (0.003), (0.007) respectively however there were no significant changes in left uterine artery RI and PI with P value (0.298), (0.695) respectively as shown in table ⁽⁵⁾.

This is in agreement with **Güden et al.** ⁽¹¹⁾ study that showed The PI of the right uterine and the RI were significantly high following the treatment with magnesium sulphate ($p=0.001$ and $p=0.018$) respectively. However, no changes were observed in the left uterine artery PI and RI ($p=0.072$ and $p=0.901$) respectively.

In addition to **Abd El-Hamed Sedek** ⁽¹³⁾ who found that there was a significant differences in right uterine artery Doppler parameters before and after administration of MgSo4 in the studied patients in PI and RI with p-value (0.001) and (0.002) respectively.

These changes in uterine arteries PI had been explained as vasodilation in magnesium sulphate treated uterine arteries and thus the increase in blood flow. The changes that occur in these vessels were described as physiological changes that occur with the removal of preterm labor stress on the fetus ⁽¹¹⁾.

In contrary to our result, Souza et al. ⁽¹⁴⁾ showed that **Loading dose of Magnesium Sulphate (MgSO4) causing significant reduction in the PI and S/D ratio in both uterine arteries p-value (0.005), this differences may be due to that the included patients were preclampsic**

As regard fetal umbilical artery RI and PI in the current study we found that there were insignificant changes before and after treatment with mag-

nesium sulphate with p- value (0.323) (0.649) respectively as shown in table ⁽⁶⁾.

In consistent with our result **Güden et al.** ⁽¹¹⁾ found that no statistically significant difference was observed in umbilical artery PI and RI and systole to diastole (S/D) rates ($p=0.358$, $p=0.556$, and $p=0.534$) respectively.

Another study by **Keeley et al.** ⁽¹⁵⁾ showed that there is no significant changes in umbilical artery PI and RI before and after treatment with magnesium sulphate with p- value (0.235) and (0.349) respectively.

Also **Wright et al.** ⁽¹⁶⁾ stated that there was no effect of magnesium sulphate on umbilical artery PI and RI Doppler flow in similarity with our result with p-value (0.963) and (0.822) respectively.

This differences may explained by **Houlihan et al.** ⁽¹⁷⁾ showed that there is evidence that magnesium sulfate promotes vasodilatation of the umbilical artery with consequent decrease of vascular resistance.

The study had been done by **Abd El-Hamed Sedek** ⁽¹³⁾ disagree with our result as they found that there was a significant difference between umbilical artery Doppler parameters before and after administration of magnesium sulphate in the studied patients with p-value (0.001) and this is may be due to all patient included were pre-eclampsic also.

Also, **Souza et al.** ⁽¹⁴⁾ reported in their study that patients with normal blood pressure levels the vasodilator effect of magnesium is not evident; in patients with pre-eclampsia this effect is significant.

In the current study fetal middle cerebral artery Doppler flow velocity were highly significant changes in RI and PI before and after treatment with magnesium sulphate with p-value (<0.001) and (0.005) respectively as shown in table (6).

This is in agreement with the study done by **Güden et al.** ⁽¹¹⁾ that showed an increase in the PI of the middle cerebral artery and a decrease in the RI with p- value ($p=0.024$ and $p<0.001$) respectively.

Another study by **Abd El-Hamed Sedek** ⁽¹³⁾ showed an increase in the PI of the middle cerebral artery and a decrease in the RI with p- value ($p=0.021$ and $p<0.003$) respectively.

This is explained by that. The alterations in fetal hemodynamics during magnesium sulfate administration suggest a physiologic normalization process related to the stressed preterm and this explained by that The increase of PI in the middle cerebral artery was attributed to the cerebral blood flow increase during preterm labor and the normalization of middle cerebral artery PI following magnesium sulphate treatment, thus the cessation of preterm labor.

In contrary our result **Sayin et al.** (18) study their result showed a significant decrease in middle cerebral artery PI. due to that they found in women between the 26th and 32nd weeks middle cerebral artery PI did not significantly change after 48 h. However, in women between the 32nd and 36th weeks the middle cerebral artery PI significantly differed in the treatment groups compared to controls after 48 h and concluded that these effects on blood flow are particularly significant in women between 32nd and 36th weeks this differences may be due to the increase in the blood pressure of the included patients as all cases included were also pre-eclamptic.

As regard the maternal adverse effect in our study we found that (30%,n=12) of studied patients showed allergic reactions after treatment,(25%,n=10) shows sweating,(5%,n=2) had sever drowsiness and only (2.5%,n=1) who showed palpitations rest of patients had no side effects as shown in table (7).

This result were in agreement with **Bain et al.** (19) who reported that maternal adverse effects of magnesium sulphate include flushing (22%), increased warmth (7%) and sweating (5%) due to the peripheral vasodilatory effects of magnesium.

In another study by **Lyell et al.** (12) they found that several maternal side effect occurred like Shortness of breath in (14%) of patients, Pulmonary edema and Hypotension in (3%) and Chest pain in (8%) other side effect like also occurred Nausea in (32%), Lethargy in (29%),vomiting in (26%),flushing in (22%),dizziness in (17%),blurring of vision in (13%).

Fetal primary outcomes after treatment with magnesium sulphate in the present study we found that the mean Apgar score at one and five minutes were (5.24±1.01).(8.08±1082) respectively, oxygen saturation was (84.05±5,55), Fetal serum magnesium sulfate concentration was (3.64±0.86) mg/dl as shown in table (8).

While secondary fetal outcomes as we reported (30% n=12) of neonates needed admission to neonatal intensive care unit because of neonatal respiratory distress syndrom as shown in table (9).

Lyell et al. (12) in agreement with our study they reported that (23%) showed neonatal respiratory distress syndrome, (5%) had sepsis,(1%) died and (52%) admitted to neonatal intensive care unit due to neonatal complications.

In another studies by **Abasalizadeh et al.** (20) they reported that (42%) of neonates showed respiratory distress syndrome, (26%) showed necrotizing enterocolitis (NEC), (22%) showed Sepsis.

This explained by some investigators have speculated that magnesium sulfate may slow gastrointestinal function, leading to feeding issues, and may lead to significant respiratory suppression (21).

In disagreement with our study **Abasalizadeh et al.** (20) reported that in patients received magnesium sulfate one minute Apgar score was (2.99) and five minute Apgar score was (2.64).

After treatment and on follow up of patients during study period we found that (90.0%) delivered by normal vaginal delivery but (10%) had C.S because of contracted pelvis, (95%) of patients deliver after more than 48 hours after magnesium sulphate infusion while only (5%) deliver in less than 48 hours as (95%) of patients Stopped contractions after treatment.

This explained by **Phillippe et al.** (22) as they demonstrated that magnesium inhibited extracellular calcium entry, intracellular calcium release, cytosolic calcium oscillations, and phasic contractions of myometrial smooth muscle.

In agreement with our result **Lyell et al.** (12) reported that, patients received MgSO₄ had delayed delivery, only (7%) patients out of deliver in 48 hours they showed that prevention of delivery for 48 hours with attainment of uterine quiescence occurred in (93%) in patients received magnesium sulphate.

On the other hand,the study done by **Kawagoe et al.** (23) disagree with our result as they reported that (57%) of patients received magnesium sulphate delivered by Cesarean section, (14%) Deliver in less than 48 hours.Because of massive genital bleeding of unknown causes, which occurred after

12 hours of magnesium infusion without improvement of uterine contractions.

In the current study we found that the best blood level of magnesium sulphate at which contraction stopped is (≥ 4.18) mg/dl which equal (6.82) gm of administrated magnesium sulphate with sensitivity (94.74%) and specificity (100%), positive predictive value (PPV) was (100%) and negative predictive value (NPV) was (50%) as shown in table (11).

In another study by **Khani et al.** (23) agree with our result as they showed that the cut off point for magnesium sulfate was (4.7) mg/dL as specificity, sensitivity, positive and negative predictive values were (95%), (50%), (66.5%) and (83.33%) respectively.

In our study we reached to that magnesium sulphate is a good tocolytic agent (as 95% of preterm women stopped contractions), if given in a suitable dose (4) gm bolus of magnesium sulfate infused IV over 30 min, a continuous infusion of 2 g/hr, to allow enough time for pregnant women to receive intramuscular dexamethazone for premature fetal lung prophylaxis and provide time for safe transport of the mother, if indicated, to a facility that has an appropriate level of neonatal care if the patient delivered preterm, with specificity, sensitivity, positive and negative predictive values were (95%), (50%), (66.5%) and (83.33%) respectively.

Conclusion

1. Maternal magnesium sulphate (Mgso4) decreases the cerebral perfusion pressure and blood flow, and this likely protects the germinal matrix against the development of circulatory stress in the early post natal period.
2. The decreased maternal uterine artery (PI) values indicated a relative increase in uterine blood flow velocity and this may be one explanation for the success of magnesium sulphate as atocolytic agent.
3. No significant changes in umbilical artery (PI).
4. Magnesium sulphate achieved the primary outcome (prevention of delivery for 48 hours, with uterine quiescence) at cut-off value of (≥ 4.18) mg/dl which equal (6.82) gm with sensitivity (94.74%), specificity (100%), positive predictive value (100%) negative predictive value (50%).

Recommendations

Our study recommended that:

1. Administration of magnesium sulphate at cut off value (≥ 4.18) mg/dl which equal (6.82) gm to women at risk of preterm birth with close monitoring of patient would achieve the tocolytic effect with the least morbidity for both mother and fetus.
2. Other further studies for more evaluation of magnesium sulphate as atocolytic agent in preterm labor.
3. Other further studies to assess fetal neuroprotection of magnesium sulphate.

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