ISSN 2515-8260 Volume 10, Issue 04, 2023

A STUDY TO EVALUATE THE OUTCOME OF INFANTS BORN TO MOTHERSRECEIVED MAGNESIUM SULFATE

Dr.Nituparna Saha, SR, R G Kar Medical College and Hospital, Kolkata.
Dr.Shabarna Roy, Associate Professor, R G Kar Medical College and Hospital, Kolkata.
Dr.Nairit De, 3rd year PGT, R G Kar Medical College and Hospital, Kolkata.
Dr.Shibani Pal, Corresponding Author, R G Kar Medical College and Hospital, Kolkata.

ABSTRACT

Objectives: The aim of the study is to detect the effect of magnesium sulphate on neonates when given antenatally, detect gross neurological effect of magnesium among them.

Method: We studied neonates at our institution who were stratified by exposure to magnesium sulfate and compared by various neonatal outcome variables. The exposed population(n=75) was compared for various neonatal outcome variables with the non-exposed group(n=75).

Results: The study included comparable number of distributions in gestational age variation: 9.3%; early preterm, 13.3% each of moderate and late preterm, 62.7% term and 1.3% post-term. The proportion of perinatal asphyxia was found to be significantly higher among the group with antenatal magnesium sulphate (p=0.014); neonatal convulsions were found to be significantly lower (p=0.001). Different neurological events like requirement of intubation at delivery, hypotonia, hyporeflexia were found to be higher in proportion among exposed group but not statistically significant. Significant number of babies in MgSO4 group got admitted in SNCU (p=0.004) but intensive care was not required. NICU care were mostly required for non-exposed group (p=0.02). Use of nasal-CPAP (p=0.02) and invasive ventilation (p=0.034) were significantly higher among non-exposed group. Neonatal death was higher among non-exposed group; not statistically significant (p=0.26) Mean cord blood Mg2+ value was 2.73 mg/dl for those exposed and 2.26 mg/dl for non-exposed group.

Conclusions: Antenatal magnesium has significant effect on immediate outcome after birth and is slightlyhazardous due to perinatal depression. This study depicts the need for studies of antenatal magnesium-sulfate protocols which may lead to maternal and neonatal benefits.

Keywords: Magnesium sulphate, newborn, preterm, neuroprotection and neurological outcomes.

INTRODUCTION

Drugs taken by pregnant mother reach the fetus by crossing placenta and have direct effect on the fetus or baby either directly by causing damage or may have some beneficial effect on baby. [1] Magnesium sulphate is an important drug used for several purposes in antenatal period has shown many effects on newborn baby: mostly in neuroprotection and cardiovascular system. But this medicine has some adverse effects as well.[2]

Magnesium is one of the intracellular cations that helps in normal neuromuscular activity along with extracellular calcium. It also acts as a cofactor for various enzymes, transporter and nucleic acids that are essential for normal cellular function, replications, and metabolic pathways. [3] There is significant reduction of inflammatory cytokines and oxygen free radicals occur by magnesium sulphate, which is significant during hypoxic reperfusion damage.[4] Cerebral vasodilatation, inhibition of calcium influx by magnesium is the key factor of neuroprotection exerted by the drug.[5] This vasodilatation and prevented calcium influx ultimately causes inhibition or delay of ischemic cell death during or after cerebral ischemic events.[6] The risk of cerebral palsy is high in preterm infants along with other neurodevelopmental co morbidities.[7]
Antenatal magnesium sulphate is considered in many institutes in women who are at risk of preterm delivery between 24 and 30 weeks of gestations for the purpose of neuroprotection of the fetus. When preterm delivery is expected within 24 hours, magnesium sulphate is started as close to four hours before expected delivery time as possible irrespective of parity, reason of preterm birth, mode of delivery and antenatal corticosteroid applications.[8] Though the circulatory control of magnesium sulphate is on immature neonatal circulation is still not clear.[9] However, there is major concerns regarding the fetal safety with perinatal $MgSO_4$ administrations and the thought that emerged over 50 years is persisting. [10,11] The clinical consequences of hypermagnesemia among newborns include lethargy, drowsiness, flushing, nausea, vomiting, muscles weakness, loss of deep tendon reflexes, hypotension, apnea, coma, cardiac arrest.[12] But whether neonates are prone to those adverse outcomes of antenatal $MgSO_4$ therapy not well established.[11] Many studies have established the beneficial effects of magnesium sulphate regarding preterm neuroprotection though marginal neuroprotection with neonatal morbidity and mortality have also been proved in some studies. [13]
In Western countries, many studies have been conducted in last several years showing the preventive action antenatal magnesium sulphate on preterm brain and in India few studies have been conducted till now. This study from eastern India tried to compare the action of antenatal magnesium sulphate on neonatal brain so that policies regarding antenatal magnesium sulphate can be given routinely.

MATERIALS AND METHODS

Study setting

We conducted a prospective cohort study among babies born to the pregnant women who have received antenatal injection in Department of Obstetrics and Gynecology and later transferred to Sick Newborn Care Unit of Department of Pediatric Medicine; and subsequently followed up at 6months of age in the Outpatient Department of Pediatric Medicine of R. G. Kar Medical College and Hospital from January 2019 to June 2020.
Sample size was calculated using the formula
$N= [(Z_1 - \alpha/2)^2 * SD^2]/L^2$ wherein
N is estimated Sample size, $(Z_1 - \alpha/2)$ is standard normal deviation z score value at 1- level, its value is taken as 1.96 considering 95% confidence interval, SD is standard deviation; it is taken as obtained from another study carried out in Burdwan Medical College in 2015 where data waspublished at Indian Journal of Pharmacology showed standard deviation as 397.82.[14]

L is precision in absolute terms is taken as 90 in our study. Thus, the sample size is calculated as follows.

$N= (1.96^2 * 397.82^2) / 90^2 = 75.05$

Hence, 75 newborns were included as study subjects. Gestational-age matched comparison group who are not receiving injection magnesium sulphate were taken as control and they were 75 in number.

Mother receiving injection magnesium sulphate for the treatment of preeclampsia, impending eclampsia, eclampsia and preterm delivery in labor room or operation theatre was chosen as subjects. Pregnant mother who are receiving some other drug for long duration along with magnesium sulphate, had received magnesium sulphate before coming to our hospital, multiple pregnancy and newborns with congenital anomalies were excluded from the study.

Ethics and consent perspective

Participation to the study was entirely voluntary. The guardians provided consent prior to participation and the written information obtained was held in confidence after entire procedure being explained in lucid local language. Ethical permission was taken from the institutional Ethical Committee before the commencement of the study (memo no. RKC/299 dated 18/01/2019) and the study was conducted in accordance with the Helsinki Declaration.

Study procedure

Personal information of the mother was taken from hospital record sheet. Deliveries were attended not only for sample collection but also for any resuscitation purpose and it was provided if required and APGAR score was noted for each delivery at 1minute and 5minute. The babies were there after followed up till discharge irrespective of being sick or healthy.

For each delivery, Gestational age, Birth weight, APGAR at 1 minute, APGAR at 5 minutes, Respiratory distress, Bradycardia, Hypotonia, Hyporeflexia, Features of sepsis, Shock, admission in sick neonatal care unit (SNCU) or neonatal intensive care unit (NICU), Significant respiratory distress and respiratory support provided, vitals, number of episodes of convulsions, previous stillbirth and neonatal death were recorded in our case pre-designed case record sheet.

Blood samples were collected and sent to biochemistry laboratory as per the following protocol. Deliveries were attended and cord blood were collected in clot vial from placental end and then sent to Biochemistry laboratory immediately, if possible, otherwise stored in 2°-8° C for next day. Baby being born to those mothers was assessed at birth and thereafter based on our study variable. If any child developed convulsion during neonatal period, blood had been drawn at that moment to get magnesium value which was compared with that of cord blood value. (See Supplementary file1; 28)

Data analysis

Statistical analysis performed using IBM SPSS Statistics 22 for Windows based on information. Numerical data was analyzed by descriptive statistics. Independent–samples T test was performed for continuous variables, and they were expressed as means +/- standard deviation. Chi square test (Or Fischer's exact test) was performed for categorical data. Statistical significance was defined as p value <0.05.

ISSN 2515-8260 Volume 10, Issue 04, 2023

RESULTS

Table 1 showing neonatal outcomes

Parameters	**Exposed**	**Non-exposed**	**P-value***
Early preterm	7	7	NA
Moderate preterm	10	10	NA
Late preterm	10	10	NA
Term	47	47	NA
Post- term	1	1	NA
Cord blood Mg2+(Mean+/- S.D)	2.73+/-0.86	2.26+/-1.41	0.02
SNCU admission	40	22	0.002
NICU admission	8	20	0.001
Neonatal hospital stay(days)	10.78 +/- 1.13	11.54+/-1.23	0.84

Apgar score			
Mean+/- S.D. at 1minute	7.44+/- 1.53	8.52+/-1.33	0.9
Mean+/- S.D. at 5minute	7.46+/-0.9	8.48+/-0.82	0.83
Respiratory distress	18	19	0.84
CPAP support	6	16	0.021
Ventilation support within 24 h of birth	4	12	0.034
Oxygen support	18	23	0.35
Seizures	1	14	0.0004
Prolonged hypotonia	20	17	0.56
Hyporeflexia	12	9	0.48
Bradycardia	10	4	0.03
Sepsis	10	18	0.10
Shock	7	16	0.041
Hypoxic ischemic encephalopathy			0.03
Mild	6	3	
Moderate	6	1	
Severe	3	0	

Neonatal death	5	9	0.26

Table 2 showing adverse outcomes like hypoglycemia/sepsis/shock/ventilator requirement

Parameters	**With MgSO4**		**Without MgSO4**	
Hypoglycemia	1	11.11%	4	23.53%
Features of Sepsis	4	44.44%	6	35.29%
Shock	1	11.11%	4	23.53%
Ventilator support	1	11.11%	5	29.41%

DISCUSSION

Magnesium sulphate has used since last century for the treatment as well as for prevention of preeclampsia and eclampsia. Based on other studies, it is now being used for neuroprotection of child in case of preterm deliveries. Here, we have tried to know the overall effect of the drug on newborn with some special interest on CNS outcome including developmental milestones at 6 months of age.

The study was conducted between two groups 75 in each group where all mothers were given injection MgSO4 before delivery and other group had 75 mothers who didn't receive MgSO4 prior to delivery. Ambedkar et al included 60 in each group whereas Monalisa et al took 100 such mother with magnesium sulphate recipients [15,16]. Shokry et al took 28 mothers with MgSO4 and 20 without MgSO4 recipient mother.[17] Rauf et al included total 107 participants with 46 in test group and 61 in control group. [18] Nelson et al had 117 total newborns with 75 controls for case for his study to look for the association of magnesium sulphate exposure and development of cerebral palsy. [19] So, most of the studies conducted so far, included less than100 participants.

Gestational age distribution

Most of the study was done with preterm babies and was redecided like Shokry et al included mothers from 30 to 34 weeks of gestations whereas it was less than 32 weeks in the study of Rauf et al, less than 30 weeks in the study of Crowther et al and 24 to 34 weeks in the study of Mittendorf et al [17, 18, 20, 21]. But Amedkar et al included the study criteria above 34 weeks gestations.[15] There was no such predetermined criteria in the study of Monalisa et al; still there was no significant variation was showed among two groups.

In our study, we didn't have any prefixed gestational age criteria, not even excluded any

gestational age. We had early preterm 7; which included 9.33% of total population; Moderate preterm 20;13.33%, Late preterm 10; comprised 13.33%, 47 term; consisting of 62.67% and only 1 post term baby (1.33%).

Distributions of perinatal outcomes

Ambedkar et al showed that most of the delivery receiving magnesium sulphate was vaginal delivery with significant proportion ($P < 0.05$) having induction of labor among mild preeclampsia group. Overall number of LUCS was less. [15] The comparison group was taken gestational age matched. In contrary, we found caesarean section was mostly prevalent among those who have received MgSO4 (74.67%) as compared to the without MgSO4 group (38.67%) and it is significant with P=0.002 and Z=3.06.

In the study of Monalisa et al, the distribution of birth weight was not very much significant, and she excluded neonate with birth weight <1000 grams and in the study of Ambedkar et al, low birth weight was observed in 45.8% in the severe preeclampsia group and 36.7% with mild preeclampsia group who received magnesium sulphate but that was not statistically significant (P=0.07). [16, 15]

In our study also, we have found that birth weight of the neonates was more or less equally distributed among the patients of the two groups. We have found 48% and 54% LBW babies in MgSO4 group and without MgSO4 group respectively.

Monalisa et al had shown that APGAR score decreased significantly with high dose of magnesium given to mother that is Pritchard regimen; <7 score of APGAR at 1 minute was observed in 5 % of low dose magnesium recipients whereas 64.29% of high dose MgSO4 recipients (P=0.00) and at 5 minutes it was 2.5% vs 57.14% (P =0.021). APGAR score of ≤3 at 1 minutes and 5 minutes was recorded as 1.25% vs 42.86% (P = 0.002) and 0% vs 5% (P= 0.003) respectively. But, in a study conducted by Bouet et al, APGAR score of <7 at 5 minutes was found to be significantly (P=0.01) more (36.4%) among 'No magnesium sulphate group' than magnesium sulphate recipient group (11.7%). Rauf et al also has shown low APGAR score both at 1minute and 5 minutes among magnesium received group though statistically not significant (P=0.112 for 1 minute and 0.09 for 5 minute). [21, 18]

The occurrence of overall perinatal asphyxia was found to be significantly higher among MgSO4 recipient group (20.0%) than non-recipient group (4%) with 'p value' being 0.014. But, when individual class of asphyxia was reviewed, no statistical significance can be showed. Mild asphyxia was found among 8.0% in MgSO4 group than non MgSO4 group where it was exactly half in number (4.0%) (p=0.49); moderate birth asphyxia was prevalent among 8.0% of MgSO4 group whereas it was only 1.3% among comparison group (p=0.116) and lastly severe perinatal asphyxia was found in 4.0% in MgSO4 group with 0.0% among the other group (p=0.24).

Intubation at delivery room was required in 78.5% of newborn with antenatal higher dose magnesium exposure, found in the study of Monalisa et al and it was obviously significant with P= 0.01. Study conducted by Mina Abbasi also showed that intubation at delivery room to be significantly more among babies born to mother with high dose serum magnesium (5% VS 2%)

(P=0.03). We have also seen that intubation was also higher among magnesium recipient group (45%) in the study of Bouet et al in comparison to non-recipient group (18%) though it was not statistically significant. Another significant result has been obtained from the study of Rauf et al that need for neonatal resuscitations including intubation was higher (47.8%) among magnesium group (P= 0.015). [16, 22, 21, 18]

This study could not show any statistical significance though intubations at the time of deliver was higher among the babies with MgSO4 group (1.3%) as compared to the babies without MgSO4 group (0.0%) (Z=1.01, p=0.3).

Still birth was 30% in high dose magnesium recipient in study conducted by Monalisa et al (P=0.008) and we didn't get a single still birth in either group.[16]

Distribution of different neonatal events

 Hypotonia has been found to affect the newborn in numerous cases where exposure to antenatal magnesium sulphate. In a large retrospective cohort study by Abbasi Ghanvati et al, occurrence of neonatal hypotonia corresponded to increasing neonatal magnesium level significantly (P= <0.001). Ambedkar et al also found the occurrence of neonatal hypotonia to be higher about 11% in MgSO4 exposed group (P=0.028). In the study of Das et al, 85% neonatal hypotonia was found to be associated with higher dose of antenatal magnesium sulphate than compared to low dose MgSO4 (5%) (P=0.012). Another significant result has been obtained from Rauf et al where hypotonia was found in 8.7 % of magnesium recipient group with 0% among control group (P=0.03). [23, 15, 16, 18]

Though proportion of hypotonia was higher among the patients with MgSO4 group (26.7%) as compared to the patients without MgSO4 group (22.7%) but it was not significant (Z=0.35, p= 0.51) In comparison, hyporeflexia was not found in many studies. Only Das et al have shown significant association of neonatal hyporeflexia with higher dose of antenatal magnesium sulphate (P=0.025%). [24] But our study did not prove significant hyporeflexia among MgSO4 group though it is more among this group (16% VS 12.5%) (p= 0.54)

 Bradycardia was also found to be significantly higher among the group with high dose of magnesium in the above study (P=0.022) but we didn't find any significant association of bradycardia among MgSO4 group (13.3%) than without MgSO4 group (5.3%) with 'p value' of 0.16. [16]

 The occurrence of respiratory distress was comparable among two groups in the study of Ambedkar et al though statistically significant (P= 0.143). Higher rate of respiratory depression was observed in association with high magnesium level (P=0.02).[15] In the study of Shokry et al, no significant difference was found regarding respiratory distress.[17] In the study of Greenberg et al, there was significant difference found in two groups where 35.7% of MgSO4 exposed group to 0% of non-exposed group (P=0.06%).[24]

Here, evidence of respiratory distress was almost less equally distributed among two groups.

48.6% of MgSO4 group and 51.4% of without MgSO4 group (p=0.84).

 In the study of Shokry et al, the occurrence of neonatal seizure was significantly higher among control group (35%) than magnesium sulphate group (3.6%) (P=0.011). [17] But it was not statistically significant in the study done by Rauf et al though higher percentage was found to suffer from neonatal convulsion among control group (4.9%) than magnesium sulphate group (2.2%) (P=0.63).[18] Similarly, we have also found that history of convulsions was significantly higher among the babies without MgSO4 exposure (18.7%) than babies with MgSO4 exposure (1.33%) with p value of 0.001. Also, the use of anticonvulsants was found to be higher in without MgSO4 group (8.0%) as compared to MgSO4 group (1.3%) (Z=2.38, p= 0.016).

 NICU admission rate was significantly higher among high dose magnesium group as found in Das et al study (P=0.03).[16] Similar findings have been found in other 'studies also; like Ambedkar et al has showed 21.7% NICU admission requirement in magnesium recipient group than control group which was only 5% (P= 0.007).[15] In the study of Greenberg et al, these percentage was 14.7% VS 5.1% with (P= 0.04%). [24] In contrary, we have found, proportion of NICU admission was significantly higher among the neonates without MgSO4 exposure (26.67%) than with MgSO4 group (10.67%) with the 'p value' of 0.02 whereas SNCU admission rate was much higher among exposed group (53.33%) than non-exposed (29.3%) with 'p value' of 0.004. That means MgSO4 is causing some perinatal adverse effects but that is not severe enough to demand intensive care.

 Need for respiratory support was much higher among magnesium sulphate group as found in the study of Rauf et al (97.8% VS 88.5%) with P value of 0.006; among them mechanical ventilator as well as CPAP requirement was higher in exposed group though oxygen hood use was higher in non-exposed group.[18] Significant respiratory rate was much higher among high dose magnesium sulphate group (P = 0.00) found in the study of Das et al but it was not so significant in the study of Greenberg et al though support requirement was higher in MgSO4 exposed group (39.3% VS 25%) with P value found to be >0.99.[18, 24] Shokry et al also could not find any significance in the use of mechanical ventilator though they found higher percentage in control group (35%) than exposed group (32%) (P= 0.83).[17] No particular association has been found in the study of Abbassi- Ghanavati in relation to serum magnesium level(P = 0.3). [23]

We have found respiratory depression was not associated with MgSO4 therapy and the rate of oxygen therapy was not associated with it. Uses of nasal CPAP as well as invasive mechanical ventilation uses were found to be significantly higher among without MgSO4 group (21.0% for CPAP and 16.0% for invasive ventilations) with 'p value' of 0.021 and 0.034 respectively. So, MgSO4 is not causally associated with respiratory depression.

 Neonatal death was very much associated in context of antenatal magnesium sulphate use.

Shokry found higher mortality in MgSO4 group with P value being 0.48; though Monalisa et al found 5% death in higher magnesium group and it was statistically significant also (P = 0.043).[17, 16] Whereas, Ambedkar et al did not found any neonatal death in their study.[15] No significant result has been found in the study of both Abbassai et al and Bouet et al (more in control group with P value being 0.06). [23, 22] But, Rauf et al found significant mortality among exposed group (P=0.015). We got 5 deaths among the MgSO4 i.e. 6.8% but it was much less than other group i.e. 9 (12.2%) though it was not significant.[18]

 Regarding sepsis, shock and hypoglycaemia, no single study has showed any association. Only Greenberg has mentioned about sepsis that was also more among non-exposed group, though not significant (P= 0.06).[25] Similarly, we have also found sepsis to be more prevalent among without MgSO4 group but not statistically significant (p=0.14). But proportion of shock was significantly higher among this group also (p=0.017)

Distribution of Cord blood magnesium

 The mean cord blood magnesium level was 2.73mg/dl for those who received MgSO4 according to Pritchard regimen and 2.26 mg/dl for those who did not get exposed to it. There is significant association has been found in two groups with ‘p value’ of 0.02. We had an objective to compare the level of magnesium in cord blood to that of serum for those children who are suffering from neonatal convulsions. But, among our study populations those who were exposed to antenatal magnesium sulphate, only 1 child has such history, and no magnesium deficiency were found. So, we cannot be confirmed regarding this objective base on only 1 result. Similarly for comparison group also we didn’t find any magnesium deficiency.

Limitations

In our study number of study population included, are quite less. Inclusion of more number of antenatal mothers with magnesium sulphate exposure is expected to produce better analysis.

 Sepsis, shock, hypoglycaemia was more common among non-exposed group and these could be responsible for poor neurological outcome. This aspect could not be analysed properly.

Financial support and sponsorship:

Non-funded project.

Conflicts of interest:

There are no conflicts of interest among the authors.

Author contributions

NS and SP designed the research; SR and NS conducted the research; SP and NS treated all the infants, NG analyzed data; NG and SR wrote the paper and all authors have checked the final content before submission.

REFERENCES

1. Boyle RJ; Effects of Certain Prenatal Drugs on the Fetus and Newborn; Pediatrics in Review; January 2002;23(1); 17-24 available at http://pedsinreview.aappublications.org/content/23/1/17 accessed on 30th June 2020
2. Bain ES, Middleton PF, Crowther CA; Maternal adverse effect of different antenatal magnesium sulphate regimens for improving maternal and infant outcomes: a systemic review; BMC Pregnancy and Childbirth; 2013; 13, 195 available at http://www.biomedcentral.com/1471-2393-/13/195 accessed on 30th June 2020
3. Magnesium: Reference Range, Interpretation, Collection and Panels ; available at http://emedicine.medscape.com/article/2088140-overview accessed on 30th June, 2020.
4. Thordstein M, Bagenholm R, Thiringer K. Kjellmer I. Scavengers of free oxygen radicals in combination with magnesium ameliorate perinatal hypoxic-ischemic brain damage in the rat. Paediatr Res 1993; 34:23-26 available at https://www.nature.com/articles/pr1993726 accessed on August 2020

5. Mazur A. Maier J.A.M.;Magnesium; Encyclopedia of Food and Health; 2016 available at http://www.sciencedirect.com/topics/medicine-and-dentistry/magnesium accessed on 30th June 2020
6. Mildvan AS. Role of magnesium and other divalent cations in ATP-utilizing enzymes. Magnesium 1987;6:28-33 available at https://pubmed.ncbi.nlm.nih.gov/3029516 accessed on August 2020
7. Hafstrom M, Kallen K, Serenius F, et al. Cerebral Palsy in extremely Preterm. Pediatrics. 2018; 141(1) available at https://pediatrics.aappublications.org/content/141/1/e20171433 accessed on July 2020

8. Magnesium Sulphate for Neuroprotection of the Fetus in Women at risk of Preterm Birth; South Australian Perinatal Practice Guideline; Public-14-A2 available at https://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/resources/policies/magnesium+sulphate+for+neuroprotection+of+the+fetus+in+women+at+risk+of+preterm+birth+-+sa+perinatal+practice+guidelines accessed on July 2020

9. Rantonen T, Kaapa P, Gronlund J, Ekblad U, Helenius H, Kero P, et al. Maternal magnesium sulphate treatment is associated with reduced brain-blood flow perfusion in preterm infants; Crit Care Med; 2001;29;1460-1465 available at https://pubmed.ncbi.nlm.nih.gov/11445708/ accessed on July 2020
10. Usman Sana, Foo Lin, Tay Jasmine; Use of magnesium sulphate in preterm deliveries for

neuroprotection of the neonate; The Obstretician and Gynecologist 2017; 19:21-28 available at https://obgyn.onlinelibrary.wiley.com/doi/fu///10.1111/tog.12328 accessed on July 2020

11. Shephard E, Salam RA, Manhas D, Synnes A, Middleton P, Makrides M, et al; Antenatal magnesium sulphate and adverse neonatal outcomes: A systemic review and meta-analysis PLoS Med 16(12):e1002988 available at https://journal.plos/org/plosmedicine/article?id=10.1371/journal.pmed.1002988 accessed on August 2020

12. Van Laecks S. Hypomagnesemia and hypermagnesemia. Acta Clin Belg. 2019; 74(1):41-47 available at https://www.tandfonline.com/doi/abs/10.1080/17843286.2018.1516173 accessed on August 2020

13. Nassar AH, Sakhel K, Maarouf H, Naassan GR, Usta IM; Adverse maternal and neonatal outcomes of prolonged course of magnesium sulphate tocolysis; Acta Obstet Gynecol Scand;2006; 85; 1099-1103 available at https://www.ajog.org/article/S0002-9378(04)01442-5/abstract accessed on August 2020

14. Dutta DC; Hypertensive Disorders in Pregnancy ; A Textbook of Obstetrics ; 7th edition; Konar H editor, Kolkata, New Central Book Agency (P) Ltd; 2013; 219-240

15. Amedkar A, Prasad M, Chauhan AR; Neonatal Effect of Maternal Magnesium Sulphate in Late Preterm and Term Pregnancies; The Journal of Obstetrics and Gynecology of India; 2019 Jan- Feb; 69(1): 25-30 https://doi.org/10.1007/s13224-017-1074-4

16. Das M, Ray Chowdhury P, Mondal B, Mitra D, Bandopadhyay D, Pramanik S;Assessment of serum magnesium levels and its outcome in neonates of eclamptic mothers treated with low dose magnesium sulphate regimen; Indian Journal Pharmacology; 2015;47(5); 502-508 https://www.ncbi.nim.nih.gov/m/pubmed/26600638 accessed on December 2018

17. Shokry M, Elsedfy G, Bassiouny M, Anmin M, Abozid H; Effects of antenatal magnesium sulphate therapy on cerebral and systemic hemdynamics in preterm newborns; Acta Ostetricia et Gynecologica; 2010; 89; 801-806 from https://obgyn.onlinelibrary.wiley.com accessed on July 2020

18. Rauf M, Sevil E, Eru C, Yavuz S, Cemil C; Antenatal Magnesium Sulphate Use for Fetal Neuroprotection: Experience from a Tertiary Care Hospital in Turkey; Biomedical Research, An International Journal of Medical Sciences; 2017; vol 28; Issue 4 from https://www.biomedres.info/biomedical-research/antenatal-magnesium-sulphate-use-forfetal-neuroprotection-experience-from-a-tertiary-care-Hospital-in-turkey.html accessed on August 2020

19. Nelson KB, Grether JK; Can Magnesium Sulphate Reduce the Risk of Cerebral Palsy in Very Low Birthweight Infants; Pediatrics; February; 1995; 95;(2); 263-269 available at https://pediatrics.aappublications.org/content/95/2/263 accessed on July 2020

20. Crowther A , Hiller JE, Doyle LW, Haslam RR; Australian Collaborative Trial of

Magnesium Sulphate (ACTOMgSO4) Collaborative Group. Effect of magnesium sulphate given for neuroprotection before preterm birth : a randomised controlled trial; JAMA 2003; 290;2669-2676 available at https://pubmed.ncbi.nlm.nih.gov/14645308 accessed on August 2020

21. Mittendorf R, Dambrosia J, Pryde PG, Lee KS, Gianopoulos, Besigner RE ; Association between the use of antenatal magnesium sulphate in preterm labour and adverse health outcomes in infants; Am J Obstet Gynecol; 2002 186; 1111-1118 https://www.ncbi.nlm.nih.gov/m/pubmed/12066082 accessed on December 2018

22. Bouet PE, Brun S, Madar H, Baisson AL, Courtey V, Lachambre GG, Lasocki S, Sentilhes L; Implementation of an antenatal magnesium sulphate protocol for fetal neuroprotection in preterm infants ; Nature research; 2015;5;14732 available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4586759/ accessed on July 2020

23. Ghanavati MA, Alexander JM, Mclntire DD, Sarvarni RC, Leveno KJ; Neonatal Effect of Magnesium Sulphate Given to Mother; Am Journal of Perinatology; 2012; 29; 795-80 http://www.ncbi.nlm.nih.gov/m/pubmed/22773290/ accessed on December 2018

24. Greenberg MB, Penn AA, Whitaker KR, Kogut EA, El-Sayed YY, Caughey AB, Lyell DJ; Effect of magnesium sulphate exposure on term neonates, Journal of Perinatology; 2013;33; 188-193 available at https://www.natures.com/articles/jp201295 accessed on August 2020

25. Rouse DJ, Hirtz DG, Thom E, Varner MW, Spong CY, Mercer BM; A randomised controlled trial of magnesium sulphate for the prevention of cerebral palsy; N Engl J Med; 2008;359; 895-905 https://www.nejm.org/doi/full/10.1056/NEJMoa0801187 accessed on December 2018

26. Conde-Agudelo A, Romero R; Antenatal magnesium sulphate for the prevention of cerebral palsy in preterm infants <34 weeks gestations: A Systemic Review and Meta analysis; Am J Obstet Gynecol; 2009; June; 200(6): 595-609 https://www.nci.nlm.nih.gov/pmc/articles/PMC3459676/

27. Denver Developmental Screening website available at https://denverii.com/ accessed on September 2020

28. Fenton TR, Lyon AW, Rose MS; Cord blood calcium, phosphate, magnesium and alkaline phosphatase gestational age specific reference intervals for preterm infants; BMC Pediatrics; 2011; 11:76 available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3179922/ accessed on January 2019

SUPPLEMENTARY FILE: 1

Measurement of Cord blood magnesium : [28]

Name: Colorimetric method

Principle: Magnesium formed a colored complex when reacts with Magon sulfonate in alkaline solutions: and the intensity of the color formed is proportional to the concentration of magnesium in the sample.

Reagents:

ISSN 2515-8260 Volume 10, Issue 04, 2023

R	Xylidol Blue Thioglycolic acid DMSO	0.1 mmol/L 0.7 mmol/L 3000mmol/L
Magnesium calculation	Magnesium aqueous primary standard 2 mg/dl	

Samples: Serum heparinized plasma; without hemolyzed and separated from cells as early as possible. (Not in oxalate or EDTA as anticoagulant)
Procedure:
1. Assay conditions: Wavelength 546 nm, temperature 37° C, Cuvette 1 cm light path
2. Adjust the instrument to zero with distilled water
3. Pipette into a cuvette:

Blank Standard Sample

	Blank	Standard	Sample
R (ml)	1.0	1.0	1.0
Standard (microL)	-	10	-
Sample(microL)	-	-	10

4. Mix and incubate for 5 minutes at room temperature or 3 minutes a 37°C
5. Read the absorbance (A) of the samples and calibrator, against the blank. The color is stable for at least 30 minutes.
Calculation:
[(A)Sample- (A) Blank]/[(A)Standard-(A) Blank] *2(Standard concentration= mg/dl magnesium in sample

ISSN 2515-8260 Volume 10, Issue 04, 2023

Conversion factors:
Mg/dl * 0.412=mmol/L , 0.5 mmol/L = 1.0 mEq/L = 1.22 mg/dl =12.2 mg/L
Reference Values: Cord blood magnesium Normal range: 1.4 – 2.3 mg/dl (0.6 – 1) milimol/L [48]