

Role of magnesium Sulfate in Preterm labour- A prospective study

Shazia Chowdhary¹, Reema Khajuria², *Rohini Jaggi³

¹ Senior Resident, SMGS Hospital, GMC Jammu, J&K, India.

² Associate Professor, SMGS Hospital, GMC Jammu, J&K, India

³ Senior Resident, SMGS Hospital, GMC Jammu, J&K, India.

*Corresponding Author: Dr. Rohini Jaggi

Email id: dr.rohini@gmail.com

Introduction:

Labour is a series of events that take place in the genital organs in an effort to expel the viable products of conception out of the uterus through the vagina into the outer world (**DC Dutta, 9th Edition**). A normal labour occurs between 37 to 42 completed weeks of pregnancy in which fetus presents by vertex, begins spontaneously and terminates naturally without artificial aid and without any complications. Sometimes it may occur prior to 37 weeks when it is called preterm labour.

Preterm labour refers to the onset of regular uterine contractions of at least four in 20 minutes or eight in 60 minutes with progressive change in cervical effacement of 80% or more and cervical dilatation >1cm (**Williams, 21st Edition**), between the age of viability and 37 completed weeks of gestation.

The period of viability varies in different countries from 20 to 28 weeks depending upon the facilities available for newborn care and the likelihood of survival. In India, the age of viability has been fixed administratively at 28 weeks, when the fetus weighs approximately 1000 grams (**IMA guidelines on fetal viability Dec, 2017**)

Prematurity is a significant cause of perinatal mortality and morbidity and risk is inversely related to gestational age at birth. The global annual incidence of preterm birth in 2014 was 10.6% of all live births. And the estimated preterm birth rate in India was 13.6% (11.1- 16.1%) in 2014 (**Lancet Glob Health, 2019**).

Complications related to preterm births were the leading cause of death and account for more than 15% of deaths in children younger than 5 years of age (**Liu L et al., 2015**). Survivors often have long-term consequences with respect to their growth, health and psychosocial functioning (**Teune MJ, 2011**) (**Moster D, 2008**).

Magnesium sulphate has been a commonly used drug (**Lewis DF, 2005**). The tocolytic effects of MgSO₄ were initially reported by **Hall DG et al., (1959)**. However the major use of MgSO₄ in obstetrics has been to prevent seizures in women with either eclampsia or pre-eclampsia (**Duley L et al., 2010**).

Toxicity is extremely rare with correct preparations and careful clinical monitoring. Clinical monitoring during MgSO₄ infusion includes detailed charting of pulse rate, blood pressure, respiratory rate, knee jerk, urinary output. 1g of calcium gluconate (10 ml in 10% of solution) is an effective antidote which is easily available in cases of toxicity. It should be given slow intravenously to avoid bradycardia and hypotension.

Moreover it is associated with fewer side effects and can be effectively used in patients with cardiovascular disorders and diabetes mellitus where other agents like ritodrine are contraindicated.

This study is planned to assess the tocolytic affect of magnesium sulphate so as to decrease the load of premature births thus decreasing the neonatal morbidity and mortality.

Aims and objectives:

- To determine the efficacy of magnesium sulphate to arrest the preterm labour and to carry the pregnancy till term, if possible.
- To prolong the labour for at least 48-72 hours so as to give the benefit of antenatal corticosteroids.

SOURCE OF DATA:

The current study was a hospital based prospective longitudinal study. It was conducted on the patients admitted in labour room with diagnosed preterm labour pains in the Post-Graduate Department of Obstetrics and Gynaecology, Shri Maharaja Ghulab Singh Hospital, Government Medical College Jammu. It was conducted after approval from institutional ethical committee of Government Medical College, Jammu.

STUDY TYPE: Interventional Study

STUDY DESIGN: Prospective Longitudinal Study

PERIOD OF STUDY:

1st November 2019 – 31st October 2020.

INCLUSION CRITERIA:

- Gestational age between 28⁺⁰ – 33⁺⁶ weeks.
- Uterine contractions atleast 4 in 20mins or 8 in 60mins.
- Intact fetal membranes.
- Cervical dilatation of <4cms.

EXCLUSION CRITERIA:

- Absent fetal membrane.
- Any signs and symptoms of chorioamnionitis
- Maternal disorder or any complication like heart disease, uncontrolled gestational hypertension, uncontrolled diabetes mellitus, ante-partum hemorrhage or any other medical disorders.
- Fetal disorder like AFD, IUGR, IUD, oligo or polyhydramnios.

METHOD:

The current study was conducted in 96 patients admitted to the SMGS hospital during the study period, with the complaints of labour pain fulfilling the inclusion and exclusion criteria. After taking the informed written consent, detailed history and clinical examination of the patient including vitals, systemic examination, per-abdomen and per-vaginum examination was done. All base-line investigations and a USG abdomen was done. Patients were catheterized and monitoring chart was maintained including Fetal heart sound, uterine contractions, pulse rate, blood pressure, respiratory rate, knee jerk and urinary output. After proper selection of patient an initial loading dose of 4gm of MgSO₄ in 20% solution was given intravenously slowly over 15-20 mins. That was followed by continuous intravenous infusion at the rate of 2gm/hr. Intravenous infusion of MgSO₄ was continued for 12 hours after the uterine quiescence was achieved i.e <4 contractions/hr with absence of cervical change. Therapy was discontinued in patients who developed adverse effects and in those whose contractions were not subsided within two hours of initiation of therapy and were allowed to progress. Two doses of Inj. Betamethasone 12mg intramuscularly; 24 hours apart were given. Drug to delivery interval was assessed and tocolysis was considered successful in those whose uterine quiescence was achieved and no change in cervical dilatation was seen with prolongation of pregnancy for more than forty eight hours atleast.

Statistical Methods: The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean±SD and categorical variables were summarized as frequencies and percentages. Graphically the data was presented by bar and pie diagrams. Chi-square test or Fisher's exact test, whichever appropriate, was applied for comparing categorical variables. A P-value of less than 0.05 was considered statistically significant.

Results:

The present prospective longitudinal study was conducted on 96 patients with preterm labour admitted in labour room of Post-Graduate Department of Obstetrics and Gynaecology, Shri Maharaja Ghulab Singh Hospital, Government Medical College Jammu. Following observations were made during the culmination of our study.

Age (Years)	Number	Percentage
--------------------	---------------	-------------------

20-24	40	41.7
25-29	46	47.9
30-34	8	8.3
≥ 35	2	2.1
Total	96	100
Mean±SD (Range)=25.3±3.54 (20-36)		

Mean age was 25.3±3.54.

46 cases (47.9%) were in age group of 25-29 years which constitute majority of cases where as 40 cases (41.7%) were in the age group of 20-24 years. Other 8 cases(8.3%) were in 30-34 years and there were just 2 cases(2.1%) beyond 35 years.

Parity	Number	Percentage
Nulli para	49	51.0
Para 1	35	36.5
≥ Para 2	12	12.5
Total	96	100

The majority of patients i.e 49 cases(51%) were nulliparous. 35 cases (36.5%) were para 1 and other 12 cases (12.5%) were para 2 or more.

Gestational age (Weeks)	Number	Percentage
28-30	5	5.2
30-32	15	15.6
32-34	76	79.2
Total	96	100
Mean±SD (Range)=32.6±1.34 (28.3-33.9)		

The above table shows distribution of cases according to gestational age and is as follow:
 The majority of cases were between 32-34 weeks of gestation i.e 76 cases (79.2%).
 15 cases (15.6%) were in 30-32 weeks of gestation and remaining 5 cases(5.2%) were between 28-30 weeks of gestation. The calculated mean gestational age was 32.6 ± 1.34 .

Table 4: Cervical dilatation of study patients		
Cervical dilatation	Number	Percentage
1 cm	29	30.2
2 cm	37	38.5
3 cm	30	31.3
Total	96	100

As shown above in the table; 37 patients (38.5%) had cervical dilatation of 2cm which constitutes maximum number followed by 30 patients (31.3%) who had dilatation of 3cm and 29 patients (30.2%) with cervical dilatation of 1cm.

Table 5: Cervical effacement (%) of study patients		
Cervical effacement (%)	Number	Percentage
25%	34	35.4
50%	31	32.3
60%	20	20.8
70%	11	11.5
Total	96	100

The maximum number of cases had cervical effacement of 25% which was seen in 34 cases (35.4%). 31 cases (32.3%) had 50% effacement followed by 20 cases (20.8%) who had 60% cervical effacement and remaining 11 cases (11.5%) had 70% effacement.

Table 6: Station of head of fetus		
Station	Number	Percentage
-3	21	21.9
-2	35	36.5
-1	34	35.4
0	6	6.3
Total	96	100

The above table shows distribution of patients according to station of head which is as follow:
 21 cases (21.9%) were having station of head at -3
 35 cases (36.5%) had station at -2 and 34 cases (35.4%) had station at -1 and these constitutes maximum number of patients.
 Whereas only 6 cases (6.3%) had head station at 0.

Table 7: Time taken for uterine contractions to subside in study patients		
Time (Minutes)	Number	Percentage
≤ 60 Minutes	21	24.7
61-120 Minutes	64	75.3
Total	85	100
Mean±SD (Range)=89.7±23.12 (50-120 Minutes)		

Table 7 shows the distribution of cases according to the time taken by the uterine contractions to subside after initiation of therapy. In majority of cases i.e 64 cases (75.3%) uterine contractions subsided between 61 to 120mins.

In 21 cases (24.7%) uterine contractions subsided in almost an hour and in remaining 11 cases contractions did not subside at all.

Mean time taken for uterine quiescence was 89.7±23.12.

Table 8: Interval between drug administration and delivery		
Interval (Hours)	Number	Percentage

< 48 hours	14	14.6
48-72 hours	50	52.1
>72 hours	32	33.3
Total	96	100
Mean±SD (Range)=61.2±23.24 (6-120 hours)		

The above table showing the duration of time between drug administration and delivery and it was found that 14 cases (14.6%) delivered within 48 hours while 50 cases (52.1%) delivered between 48-72 hours which constitutes majority of deliveries. And other 32 patients (33.3%) delivered after 72 hours.

Mean interval between drug and delivery was 61.2±23.24.

Table 9: Success of tocolysis in study patients		
Tocolysis	Number	Percentage
Successful	82	85.4
Failure	14	14.6
Total	96	100

In 82 patients delivery was postponed by ≥ 48 hours thus successful tocolysis was achieved in 85.4%. Where as other 14 patients delivered before 48 hours giving the failure rate of 14.6%

Table 10: Success of tocolysis in study patients as per parity					
Parity	Successful tocolysis		Failed tocolysis		P-value
	No.	%age	No.	%age	
Para 0	47	95.9	2	4.1	0.008*
Para 1	27	77.1	8	22.9	
\geq Para 2	8	66.7	4	33.3	

Total	82	85.4	14	14.6	
-------	----	------	----	------	--

***Statistically Significant (P-value<0.05)**

Table 10 shows relationship of parity with respect to tocolytic response. It was found that out of 49 nulliparous patients 47 (95.9%) delivered after 48 hours and 2 patients (4.1%) delivered within 48 hours. Where as 27 patients of total 35 cases who were para 1 delivered after 48 hours giving success rate of 77.1% and failure in 22.9%. Similarly the success rate in \geq para 2 is 66.7%.

Chi-square test was used for p value and it was observed that difference was statistically significant with $p = 0.008$.

Table 11: Success of tocolysis in study patients as per gestational age (weeks)					
Gestational age (weeks)	Successful tocolysis		Failed tocolysis		P-value
	No.	%age	No.	%age	
28-32	16	80.0	4	20.0	0.678
32-34	66	86.8	10	13.2	
Total	82	85.4	14	14.6	

It was observed that success rate was 86.8% with gestational age between 32-34 weeks who delivered after 48 hours and failure rate of 13.2% as 10 patients delivered prior. In gestational age of 28-32 weeks success rate was 80.0% and failure was seen in 20.0%. Value of significance calculated and was found statistically insignificant.

Table 12: Success of tocolysis in study patients as per cervical dilatation					
Cervical dilatation	Successful tocolysis		Failed tocolysis		P-value
	No.	%age	No.	%age	
1 cm	28	96.6	1	3.4	0.011*
2 cm	33	89.2	4	10.8	
3 cm	21	70.0	9	30.0	
Total	82	85.4	14	14.6	

***Statistically Significant (P-value<0.05)**

The above table shows distribution of patients according to cervical dilatation at the time of initiation of therapy and time taken for delivery. It was found that cases with cervical dilatation of 1cm had high success rate 96.6% and less failure rate i.e 3.4% as compared to those with more cervical dilatation like 2cm and 3cm had success

rate of 89.2% and 70.0% and failure of 10.8% and 30.0% respectively. The p value was calculated and was found statistically significant (0.011).

Table 13: Success of tocolysis in study patients as per cervical effacement					
Cervical effacement (%)	Successful tocolysis		Failed tocolysis		P-value
	No.	%age	No.	%age	
25%	33	97.1	1	2.9	0.002*
50%	28	90.3	3	9.7	
60%	15	75.0	5	25.0	
70%	6	54.5	5	45.5	
Total	82	85.4	14	14.6	

***Statistically Significant (P-value<0.05)**

As shown above in table, 33 cases (97.1%) out of 34 cases with cervical effacement of 25% achieved successful tocolysis with failure rate of 2.9%. In patients with cervical effacement of 50%, the successful tocolysis was achieved in 90.3% patients and failure of 9.7% . The success and failure rate was 75% and 25% in patients with effacement of 60% and 54.5% and 45.5% with 70% cervical effacement respectively.

The p value was found to be 0.002 which was statistically highly significant.

Table 14: Success of tocolysis in study patients as per station of head					
Station of head	Successful tocolysis		Failed tocolysis		P-value
	No.	%age	No.	%age	
-3	21	100.0	0	0.0	<0.001*
-2	34	97.1	1	2.9	
-1	26	76.5	8	23.5	
0	1	16.7	5	83.3	
Total	82	85.4	14	14.6	

***Statistically Significant (P-value<0.05)**

Table 14 shows success of tocolysis as per station of head at the start of therapy:

The success rate was 100% when head was at station -3. Rate of success and failure was 97.1% and 2.9% when head was at -2 station. The success rate declined with station -1 and 0 as 76.5% and 16.7% and failure rate was 23.5% and 83.3% respectively.

The p value was < 0.001 which was statistically highly significant.

Table 15: Side effects of drug in study patients		
Side effects	Number	Percentage
Hot flushes	20	20.8
Nausea	12	12.5
Headache	2	2.1
Palpitations	2	2.1
Dizziness	2	2.1

The majority of patients had no significant side effects. Among those who developed side effects, hot flushes were experienced by 20.8% patients followed by nausea in 12.5%. 2.1% had complaints of headache and another 2.1% had palpitations and dizziness.

Table 16: Distribution of study patients as per mode of delivery		
Mode of delivery	Number	Percentage
Vaginal delivery	84	87.5
LSCS	12	12.5
Total	96	100

87.5% of study patients delivered vaginally and 12.5% had undergone cesarean delivery. Of which 4 cases underwent LSCS for preterm breech while 3 other were having liquor meconium stained and 2 because of fetal bradycardia . 2 had non-reactive CTG and 1 because of loops of cord around neck.

Table 17: Showing neonatal APGAR score at birth		
APGAR score	Number	Percentage
< 7	12	12.5
≥ 7	84	87.5
Total	96	100

The APGAR score at birth was $\geq 7/10$ in 87.5% of neonates and remaining 12.5% had APGAR score less than 7.

Table 18: Neonatal outcome of study patients

Neonatal outcome	Number	Percentage
NICU admissions	27	28.1
RDS	5	5.2
Birth asphyxia	1	1.0
VLBW	1	1.0
Neonatal death	7	7.3

Total number of NICU admissions were 28.1% of which 7.3% neonates died due to complications of prematurity. 5.2% died of RDS, 1.0% because of birth asphyxia and another 1.0% due to VLBW.

Discussion:

Prematurity and related complications are the leading cause of perinatal morbidity and mortality worldwide. Of which RDS is one of the major cause that can be prevented by giving antenatal corticosteroids for fetal lung maturity. Identifying the susceptible patients, giving them proper therapy as with tocolytic drugs can reduce the neonatal morbidity and mortality.

In developing countries like ours where sophisticated neonatal care units are not commonly available, yet pediatric units have to cater to a huge number of premature neonates, but we can contribute by reducing the incidence of preterm births.

Numerous studies have been conducted worldwide in search of an ideal tocolytic drug but none has been found yet. Likewise this study was conducted to see the efficacy of magnesium sulphate as a tocolytic drug.

In our study, 96 patients were taken as study population who came to labour room with complaints of preterm labour. These patients were selected randomly and were given magnesium sulphate intravenously as described earlier.

In present study the majority of patients (47.9%) were in the age group of 20-25 years followed by 41.7% were in age group of 20-24 years. The mean age of patients participating in the study was 25.3 ± 3.54 which was comparable to mean age of 26.6 ± 6.8 in study conducted by **Lyell DJ et al., (2007)**. This mean age was also comparable to 24.53 ± 5.83 of study conducted by **Abasalizadeh S et al., (2014)** and 24.24 ± 4.15 of **Shirazi A et al., (2015)** study.

In our study 51% were nulliparous which constitutes maximum number of patients and were comparable with 53.83% primiparous patients in study conducted by **Shirazi A et al., (2015)** and somewhat comparable with 57% of study conducted by **Kawagoe Y et al., (2011)**. Thus the present study shows that the risk of preterm labour is more in young primi patients and these results were similar to studies conducted by **Lyell DJ et al., (2007)**, **Glock JL et al., (1993)**, **Jirapinyo M et al., (2010)** and **Nemani S et al., (2018)** who in their respective studies had reported that preterm labour usually develops in younger females and this may be associated with primiparity.

The success rate as per parity was found to be 95.9% in nulliparous women which was found to be in declining trend with respect to increasing parity. Thus success rate was 77.1% and 66.7% in para 1 and ≥ 2 para respectively with failure rate of 22.9% and 33.3% in para 1 and para ≥ 2 . These results were statistically significant (p value 0.008) and were comparable with **Shirazi A et al., (2015)** study where success and failure rate was 95.92% and 4.08% respectively in primiparous patients and 80.95% and 19.05% respectively in multiparous.

In our study the mean gestational age was 32.6 ± 1.34 weeks which were similar to 32.65 ± 3.71 weeks of **Shirazi A et al., (2015)** study and **Taherian AA et al., (2007)** had found mean gestational age for magnesium sulfate group as 32.06 weeks. The mean G.A was somewhat comparable to 30.8 ± 2.3 of a study conducted by **Lyell DJ et al., (2007)**. In present study it was observed that the majority of patients around 79.2% had G.A between 32-

34 weeks, **Nemani S et al., (2018)** had also found that most of the patients in their study were between 32-34 weeks and around 66% had G.A >32weeks.

In our study success of tocolysis as per gestational age was found to be 80.0% in G.A between 28-32 weeks and 86.8% in G.A between 32-34 weeks and the p value was statistically not significant but the results were comparable to study conducted by **Nemani S et al., (2018)** who observed that magnesium sulphate is more effective drug in gestational age >32 weeks and is less effective to arrest preterm labour in <32 weeks period of gestation.

In our study 38.5% of patients had cervical dilatation of 2cm, 31.3% had 3cm where as remaining 30.2% had cervical dilatation of 1cm which was comparable with 30% cases with cervical dilatation of 2-3 cm of study conducted by **Nemani S et al., (2018)**.

The success rate of tocolysis in relation to cervical dilatation in our study was 96.6% with cervical dilatation of 1cm as compared to 89.2% and 70.0% at dilatation of 2cm and 3cm respectively. Thus success rate declined with increasing dilatation of cervix which was statistically significant (p value 0.011) and this was consistent with success rate of 94.11% with cervical dilatation of 1 cm of **Mahajan A and Marwah P (2014)** study. And they also concluded that success rate came down with increasing dilatation i.e 44.4% with dilatation of 2-3cm. Various other studies conducted by **Steer and Petrie (1977)** and **Madden C et al., (1990)** have shown the similar results of increasing failure rate with progressive dilatation of cervix.

In our study 35.4% patients had cervical effacement of 25%. 32.3% had 50% effacement, 20.8% had effacement of 60% and remaining 11.5% cases had cervical effacement of 70%. The success rate of tocolysis was 97.1% in patients with effacement of 25% which was comparable to results of **Mahajan A and Marwah P (2014)** study who concluded that success rate was 91.68% with cervical effacement upto 20%. In the present study success rate of tocolysis declined with increasing cervical effacement and the p value (0.002) was statistically highly significant which was again consistent with **Mahajan A and Marwah P (2014)** study who also observed a decline in success rate with increased cervical effacement. In another study by **Tchilinguirian NG et al., (1983)** it was found that tocolytic efficacy declines as cervical effacement increases to 50%.

In present study it was observed that success of tocolysis varies as per head of station. Maximum tocolysis was seen when head is high up at -3 station. The success rate declines with the descent of head from 100% at -3 station to 16.7% at station 0. The p value (0.001) was statistically significant. Though there is not much literature evaluating success of tocolysis as per station of head but in study by **Madden C et al., (1990)** it was observed that success rate of tocolysis was 50% if initial modified Bishop's score is >4 and success rate was 88% with score less than or equal to 4.

The mean time taken by uterine contractions to subside was 89.7 ± 23.12 minutes in our study and 24.7% cases achieved uterine quiescence within 60 minutes of administration of therapy. Where as 75.3% achieved quiescence between 1-2 hours. The results were comparable to study conducted by **Nemani S et al., (2018)** where it was found that mean time taken was 74 minutes and 29.17% patients had achieved uterine quiescence in 30 min - 1 hour. Where as in 66.67% of cases; uterine contractions were subsided between 1-2 hours and other 4.17% had achieved quiescence within 30 minutes.

In present study the mean interval between drug administration and delivery was 61.2 ± 23.24 hours. 14.6% cases delivered within 48 hours whereas majority 52.1% delivered between 48 - 72 hours and remaining 33.3% delivered after 72 hours.

It was found that a total 82 patients delivered after 48 hours of administration of therapy, thus the efficacy of magnesium sulphate tocolysis was 85.4%. Other 14 cases delivered within 48 hours giving the failure rate of 14.6%. These results were comparable with various studies as below:

Studies:	Prolongation of delivery >48 hours
Nemani S et al., (2018)	89.58%
Morales WJ et al., (1993)	85%
Mahajan A and Marwah P (2014)	82%
Lyell DJ et al., (2007)	87%
Shirazi A et al., (2015)	89.01%
Kawagoe et al., (2011)	90%
Present study	85.4%

In our study majority of patients had not experienced any adverse effects. Of many who experienced; most of them complaint of hot flushes 20.8% and results were comparable to 26% of **Lyell DJ et al., (2007)** study. But it was not of that severity to warrant discontinuation of therapy. Nausea was another major complaint in 12.5% of patients and very few patients experienced palpitations, headache and dizziness and results were comparable to studies of **Mahajan A and Marwah P (2014)** and **Saha S (2002)**. Various other studies like **Holander DI et al., (1987)**, **Beall MH et al., (1985)** have shown that magnesium sulphate has less side effects than other tocolytic drugs.

Mode of delivery was an other important factor and in our study it was found that 87.5% women delivered vaginally which was comparable to 84.78% of **Nemani S et al., (2018)** study. Only 12.5% of cases required cesarean delivery. Of which 4 cases underwent LSCS for preterm breech while 3 other were having liquor meconium stained and 2 because of fetal bradycardia . 2 had non-reactive cardiotocography and 1 because of loops of cord around neck. **Mahajan A and Marwah P (2014)** in their study also observed rate of vaginal delivery was high around 74% and cesarean rate was 26%.

The aim of the tocolysis ideally should be to delay delivery to a maximum time, if not; delivery should be delayed by sufficiently enough time to enable transfer of fetus in utero to higher centers and to give benefit of corticosteroids for fetal lung maturity i.e atleast 48 hours. The fetal lung maturity is indirectly interpreted by the improved neonatal APGAR score (Appearance, Pulse, Grimace, Activity and Respiration) at birth.

In our study APGAR score of $\geq 7/10$ was observed in 87.5% of neonates and the results were comparable to study of **Mahajan A and Marwah P (2014)** who observed that 84% of neonate had APGAR score of 8 or more. The overall success rate of achieving live birth rate in our study was 92.7% and observation was supported by study conducted by **Saha S. (2002)** who concluded live birth of 89.3%. Only 7 babies could not be saved despite all the efforts and intense care; most of them belonged to failure group of tocolysis. This accounts for perinatal mortality of 7.3%. Although 28.1% required NICU admission at birth due to prematurity and related complications but most of them survived and were discharged satisfactorily after few days. In **Nemani S et al., (2018)** study the rate of perinatal mortality was 15.22%

Magnesium sulphate given to mother crosses the placenta to achieve equilibrium in fetal serum and less so in amniotic fluid. Moreover studies by **Crowther CA et al., (2003)**, **Marret S et al., (2008)**, **Rouse DJ et al., (2008)** and **Doyle LW et al., (2009)** have shown neuro-protective effect of magnesium in low birth weight infants.

The limitations of study includes:

- Invasive procedure like catheterization because strict e4monitoring charts has to be maintained to find out any signs of toxicity. And IV cannula as it was continuous infusion therapy thus patients had to be on bed.
- Due to Covid pandemic relatively small number of cases and also short duration of study are considered as limitations of study.

Conclusion:

The success of such therapy depends on proper selection of cases, judicious administration of therapy and strict monitoring. In our study we concluded that intravenous magnesium sulphate is an effective tocolytic drug for postponement of delivery for atleast 48 hours. This is the minimum time required to give benefit of corticosteroids for fetal lung maturity, to possibly decrease the risk of respiratory distress syndrome in premature infants.

I would also like to mention that several additional and potentially large comparative randomized clinical studies are still required in search of an ideal tocolytic drug.

References:

1. **Abasalizadeh S, Fakhraei MA, Ghojazadeh M, Abasalizadeh F, Raouf S, Javadi EHS et al.** Compare the efficacy of Indomethacin and magnesium Sulphate in prevention of preterm labor. *Int J Curr Res Aca* 2014; 2(8):244-51.
2. **Amon E, Midkiff C, Winn H, Holcomb W, Shumway J, Artal R.** Tocolysis with advanced cervical dilatation. *Obstet Gynecol* 2000;95(3):358-362.
3. **Andrew W. Helfgott, Donald C. Willis and Jorge D. Blanco.** Is hydration and sedation beneficial in the treatment of threatened preterm labor? A preliminary report. *Journal of maternal-fetal medicine* 1994;3(1):37-42.
4. **Beall MH, Edgar BW, Paul RH, Smith-Wallace T.** A comparison of ritodrine, terbutaline, and magnesium sulfate for the suppression of preterm labor. *Am J Obstet Gynecol* 1985;153(8): 854-59.

5. **Chau AC, Gabert HA, Miller JM.** A prospective comparison of terbutaline and magnesium for tocolysis. *Obstet Gynecol* 1992; 80(5):847-51.
6. **Chawanpaiboon S, Vogel JP, Moller AB, Lumbiganon P, Petzold M, Hogan D et al.** Global, regional, and national estimates of levels of preterm birth in 2014: a systemic review and modeling analysis. *Lancet Glob Health* 2019;7(1):37-46.
7. **Chesley LC, Tepper I.** Some effects of magnesium loading upon renal excretion of magnesium and certain other electrolytes. *J Clin Invest* 1958;37(10):1362-372.
8. **Crowther CA, Hiller JE, Doyle LW, Haslam RR.** Effect of magnesium sulfate given for neuroprotection before preterm birth: a randomized controlled trial. *JAMA* 2003;290(20):2669-76.
9. **Cunningham FG, Gant NF, Leveno KJ, Gilstrap III LC, Hauth JC, Wenstrom KD.** Preterm birth. In: Williams Obstetrics. 21st edition. McGraw Hill publication. USA. 2001;27. pp. 689-728.
10. **Doyle LW, Crowther CA, Middleton S.** Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. *Cochrane Database of Systematic Reviews* 2009; 1: CD 004661.
11. **Duley L, Gulmezoglu AM, Henderson-Smart DJ, Chou D.** Magnesium sulphate and other anticonvulsants for women with pre-eclampsia. *Cochrane Database Syst Rev* 2010;2010(11):CD000025.
12. **Formin VP, Gibbs SG, Vanam R, Monmiya A, Hurd WW.** Effects of magnesium sulfate on contractile force and intracellular calcium concentration in pregnant human myometrium. *Am J Obstet Gynecol* 2006;194(5):1384-390.
13. **Glock JL, Morales WJ.** Efficacy and safety of nifedipine versus magnesium sulfate in the management of preterm labor: A randomized study. *Am J Obstet Gynecol* 1993;169(4):960-64.
14. **Goldenberg RL, Culhane JF, Iams JD, Romero R.** Epidemiology and causes of preterm birth. *Lancet* 2008;371(9606):75-84.
15. **Goldenberg RL, Suzanne P, Janet, Garry R, William W, Stephen T.** Bed rest in pregnancy. *Obstetrics and Gynecology* 1994;84:131-36.
16. **Hall DG, McGaughey HS, Corey EL, Thornton WN.** The effects of magnesium therapy on the duration of labour. *Am J Obstet Gynecol* 1959;78(1):27-32.
17. **Hayes E, Moroz L, Pizzi L, Baxter J.** A cost decision analysis of 4 tocolytic drugs. *Am J Obstet Gynecol* 2007;197(4):383.
18. **Himpens E, Vanden Broeck C, Oostra A, Calders P, Vanhaesebrouck P.** Prevalence, type, distribution and severity of cerebral palsy in relation to gestational age: a meta-analytic review. *Dev Med Child Neurol* 2008;50(5):334-40.
19. **Hiralal Konar.** Normal labor. In: DC Dutta's textbook of Obstetrics. 9th edition. New Delhi: Jaypee Brother Medical Publishers (P) Ltd;2018. pp. 108.
20. **Hollander DI, Nagey DA, Pupkin MJ.** Magnesium sulphate and ritodrine hydrochloride: a randomized comparison. *Am J Obstet and Gynecol* 1987;156(3):631-37.
21. **Jirapinyo M, Thuvasethakul P, Leelaphiwat S.** Prospective study in premature labor with magnesium sulfate. *Asia Oceania J Obstet Gynaecol* 1990;16(2):91-96.
22. **Kawagoe Y, Sameshima H, Ikenoue T, Yasuhi I, Kawarabayashi T.** Magnesium sulfate as a second-line tocolytic agent for preterm labor: a randomized controlled trial in Kyushu Island. *J Pregnancy* 2011;2011(965060)1-6.
23. **Klauser CK, Briery CM, Martin RW, Langston L, Magann EF, Morrison JC.** A comparison of three tocolytics for preterm labour: a randomized clinical trial. *J Matern Fetal Neonatal Med* 2014;27(8):801-06.
24. **Lettieri L, Vintzileos AM, Rodis JF, Albini SM, Salafra CM.** Does idiopathic preterm labour resulting in preterm birth exist ? *Am J Obstet and Gynecol* 1993;168(5):1480-485.
25. **Lewis DF.** Magnesium sulfate: the first-line tocolytic. *Obstet Gynecol Clin North Am* 2005;32(3):485-500.
26. **Liu L, Oza S, Hogan D, Perin J, Rudan I, Lawn JE et al.** Global, regional, and national causes of child mortality in 2000-13, with projections to inform post-2015 priorities: an updated systemic analysis. *Lancet* 2015;385(9966):430-40.
27. **Lyell DJ, Pullen K, Campbell L, Ching S, Druzin ML, Chitkara U et al.** Magnesium Sulfate Compared With Nifedipine for Acute Tocolysis of Preterm Labor: A Randomized Controlled Trial. *Obstet Gynecol* 2007;110(1):61-67.

28. **Madden C, Owen J and Hauth JC.** Magnesium tocolysis: Serum levels versus success. *Am J Obstet Gynecol* 1990;162(5):1177-80.
29. **Mahajan A, Marwah P.** Arrest of preterm labor: A comparative study between magnesium sulfate and isoxsuprine. *International Journal of Basic and Applied Medical Sciences* 2014;4(3):19-25.
30. **Marret S, Marpeau L, Be´nichou J.** Benefit of magnesium sulfate given before very preterm birth to protect infant brain. *Pediatrics* 2008;121(1):225-26.
31. **McCubbin JH, Sibai BM, Abdella TN, Anderson GD.** Cardiorespiratory arrest due to acute maternal hypermagnesaemia. *Lancet* 1981;1(8228):1058.
32. **Menon R.** Spontaneous preterm birth, a clinical dilemma: Etiologic, pathophysiologic and genetic heterogeneities and racial disparity. *Acta Obstetrica et Gynecologica Scandinavica* 2008;87(6):590-600.
33. **Mizuki J, Tasaka K, Masumoto N, Kasahara K, Miyake A Tanizawa O.** Magnesium sulfate inhibits oxytocin-induced calcium mobilization in human puerperal myometrial cells: possible involvement of intracellular free magnesium concentration. *Am J Obstet Gynecol* 1993;169(1):134-39.
34. **Morales WJ, Madhav H.** Efficacy and safety of indomethacin compared with magnesium sulfate in the management of preterm labor: a randomized study. *Am J Obstet Gynecol* 1993;169(1):97-102.
35. **Moster D, Lie RT, Markestad T.** Long-term medical and social consequences of preterm birth. *N Engl J Med* 2008;359(3):262-73.
36. **Nemani S, Dasari MM, Mudadla V, Balla S.** Role of magnesium sulphate in preterm labour. *IAIM* 2018;5(2):168-73
37. **Pritchard JA.** The use of magnesium ion in the management of eclamptogenictoxemias. *Surg Gynecol Obstet* 1955; 100(2):131-40.
38. **Rouse DJ, Hirtz DG, Thom E, Varner MW, Spong CY, Mercer BM et al.** A randomized controlled trial of magnesium sulphate for the prevention of cerebral palsy. *N Engl J Med* 2008;359(9):895-905.
39. **Saha S.** Role of magnesium sulphate in suppression of preterm labour. *Am J Obstet Gynaecol* 2002;32(2):53-57.
40. **Sakhavar N, Mirteimoori M, Teimoori B.** Magnesium Sulfate versus HCG (Human Chorionic Gonadotropin) in Suppression of Preterm Labour. *E Medical Journal* 2008;9(3):134-40.
41. **Shirazi A, Ansari NH, Ahmed M.** Comparison of efficacy for tocolysis of preterm labor between magnesium sulphate and nifedipine. *PJMS* 2015; 9(4):1177-80.
42. **Sibai BM.** Magnesium sulphate is the ideal anticonvulsant in pre eclampsia-eclampsia. *Am J Obstet Gynecol* 1990;162(5):1141-145.
43. **Spisso KR, Harbert GM, Thiagoriajah S.** The use of magnesium sulfate as the primary tocolytic agent to prevent premature delivery. *Am J Obstet Gynecol* 1982;142(7):840-45
44. **Stallworth JC, Yeh S, Petrie RH.** The effect of magnesium sulphate on fetal heart rate variability and uterine activity. *Am J Obstet Gynecol* 1981; 140(
45. **Steer CM, Petrie RH.** A comparison of magnesium sulfate and alcohol for the prevention of premature labour. *Am J Obstet Gynecol* 1977;129(1):1-4
46. **Taherian AA, Dehdar P.** Comparison of efficacy and safety of nifedipine versus magnesium sulfate in treatment of preterm labor. *J Res Med Sci.* 2007;12(3):136-42.
47. **Tchilinguirian NG, Najem R, Sullivan GB, Craparo FJ.** The use of ritodrine and magnesium sulfate in the arrest of premature labor. *Int J Gynaecol Obstet* 1984;22(2):117-123
48. **Teimoori B, Sakhavar N, Merteimori M, Naroule B, Ghasemi-rad M, Saroonehrigi M et al.** Efficacy and Safety of progesterone versus magnesium sulfate in the management of preterm labour: A Randomized study. *Gynecol Obstetrics* 2011;1:1.
49. **Teune MJ, Bakhuizen S, Bannerman CG, Opmeer BC, Van Wassennaer AG, Morris JM.** A systemic review of severe morbidity in infants born late preterm. *Am J Obstet Gynecol* 2011;205(4):374.
50. **Tica VI, Tica AA, Carlig V, Banica OS.** Magnesium ion inhibits spontaneous and induced contraction of isolated uterine muscle. *Gynecol Endocrinol* 2007;23(7):368-72.
51. **Wilkins IA, Lynch L, Mehalek KE, Berkowitz GS, Berkowitz RL.** Efficacy and side effects of magnesium sulphate and ritodrine as tocolytic agents. *Am J Obstet Gynecol* 1988;159(3):685-89.

52. **Witlin AG, Friedman SA, Sibai BM.** The effect of magnesium sulphate therapy on the duration of labor in women with mild pre eclampsia at term: a randomised double-blind, placebo-controlled trial. *Am J Obstet Gynecol* 1997;176(3):623-27.
53. **Wolf HT, Hegaard HK, Greisen G, Huusom L, Hedegaard M.** Treatment with magnesium sulphate in preterm birth: A systemic review and meta-analysis of observational studies. *J Obstet Gynecol* 2012;32(2):135-40.
54. **Zuspan FP.** Treatment of severe pre-eclampsia and eclampsia. *Clin Obstet Gynecol*1966;9(4):954-72.