# Use of Magnesium Sulphate in Persistent Pulmonary Hypertension of Newborn

M A A Mamun[1], S Begum[2], M Hussain[3], A Jabbar[4]

**Abstract**

**Background :** One of the common causes of respiratory distress in neonate is persistent pulmonary hypertension of newborn (PPHN) and has been estimated to occur in 2 per 1000 live born term infants.

**Objective :** To evaluate the effect of injectable Magnesium Sulphate ($MgSO_4$) in the treatment of Persistent Pulmonary Hypertension of Newborn.

**Methodology :** It was a prospective, nonrandomized, clinical study conducted from August 2015 to July 2017 among 25 neonates having moderate to severe PPHN in the Pediatric Cardiac Intensive Care Unit (CICU) of Dhaka Shishu (Children) Hospital. Injectable Magnesium Sulphate was used along with other supportive management. Outcome measures include drop of pulmonary vascular resistance and increase oxygenation. Side effects of Magnesium Sulphate were observed and outcome was recorded. Data were analyzed by using SPSS version 17.

**Results :** There was significant improvement of oxygenation and decrease in pulmonary vascular resistance at 72 hours after use of $MgSO_4$ (p=000). Complications were present in 28% cases which include hypotension in 16% patients, urinary retention in 8% and altered GI function in 8% cases. Mortality was 16% among study population.

**Conclusion :** MgSO4 is effective in improving oxygenation and reduction of pulmonary vascular resistance in PPHN.

**Key Wards :** Magnesium Sulphate, PPHN, neonate.

DOI: https://doi.org/10.3329/nimcj.v10i2.45430
Northern International Medical College Journal Vol. 10 No. 2 January 2019, Page 370-372

[1] Dr. Mohammad Abdullah Al Mamun
Associate Professor
Dept. of Pediatric Cardiology
Bangladesh Institute of Child Health, Dhaka Shishu (Children) Hospital

[2] Dr. Sheuly Begum
Associate Professor
Dept. of Gynae and Obstetric
Enam Medical College and Hospital

[3] Prof. Manzoor Hussain
Professor and Head

[4] Dr. Abdul Jabbar
Registrar

3,4
Dept. of Pediatric Cardiology
Bangladesh Institute of Child Health, Dhaka Shishu (Children) Hospital

**Correspondence**
Dr. Mohammad Abdullah Al Mamun
Associate Professor
Dept. of Pediatric Cardiology
Bangladesh Institute of Child Health, Dhaka Shishu (Children) Hospital
E-mail: mamundsh@gmail.com

## Introduction

Persistent Pulmonary Hypertension of newborn (PPHN) may result when pulmonary vascular resistance fails to fall after birth. The blood pressure in the arteries of the lungs (pulmonary arteries) is normally much lower than the blood pressure in the rest of the body. Before a baby is born the muscle surrounding the pulmonary arteries is tightly constricted resulting in a very high pressure in these arteries. After birth the arteries dilate and the pressure drops. PPHN is characterized by increased pulmonary vascular resistance and right-to-left shunting through the foramen ovale, with or without a patent ductus arteriosus, causing arterial hypoxia even with 100% $FiO_2$.[1] Persistent pulmonary hypertension in the newborn (PPHN) is a neonatal emergency which requires immediate intervention.[2,3]

One of the most common presentation of PPHN in newborn is Neonatal Respiratory Distress which is life-threatening and a common emergency responsible for 30-40% of admissions in the neonatal period. Fifteen percent of term infants and 29% of late preterm infants admitted to the neonatal intensive care unit develop significant respiratory morbidity. Newborns with respiratory distress must be evaluated promptly and accurately.[4]

Primary treatment of the neonate with PPHN depends on the underlying disorder. A variety of treatment options includes surfactant, sedation, alkalinization, vasodilatation e.g (tolazoline, inhaled nitric oxide, magnesium sulfate, adenosine, bosentan, sildenafil), high frequency jet-ventilation (HFJV) and extracorporeal membrane oxygenation (ECMO).[5] The aim of treatment is to lower pulmonary vascular resistance, maintain systemic blood pressure, reverse right to left shunt and improve arterial oxygen saturation.[6] There is strong evidence for the use of inhaled nitric oxide (NO) and ECMO in the treatment of PPHN. However, many developing countries and resource limited centers do not have the funds or the technical

expertise required for these expensive therapies.[7]

Magnesium sulphate is a natural Ca channel blocker that antagonizes Ca ion entry into smooth muscle cell thus promoting vasodilatation. It is safe and cheaper alternative for first line treatment in moderate PPHN.[8,9] A recent study concluded that where Nitric Oxide facilities are not available, Magnesium Sulphate ($MgSO_4$) is a cheap alternative for first line treatment of moderate PPHN.[10] Very few data are available in our country regarding outcome and treatment of PPHN in Bangladesh. Therefore, this study was conducted to find out the effectiveness of Magnesium Sulphate in PPHN.

## Materials and Methods

It was an prospective, nonrandomized, clinical study, conducted from August 2015 to July 2017 in the Cardiac Intensive Care Unit (CICU) of Dhaka Shishu (Children) Hospital. During this period neonates having respiratory distress and/or cyanosis were screened and with pre and post ductal $O_2$ saturation difference>10% were undergone echocardiography. Moderate to severe PPHN were identified among 25 neonates and were treated with Magnesium Sulphate with a loading dose of 100mg/kg over 30 min followed by 20-50 mg/kg/h for 5 hours for 3 days. No other vasodilator drug was administered before or during the treatment. Pre-ductal and post ductal peripheral capillary oxygen saturation ($SpO_2$) was monitored. Outcome measures include drop of pulmonary vascular resistance measured by right ventricular systolic pressure, increased partial pressure of oxygen in arterial blood ($PaO_2$), mechanical ventilator duration and time interval to improve, measured by drop of Right ventricular systolic pressure (RVSP)<25 mmHg and increase $PaO_2$>30 mmHg. Side effect was observed in the patient and outcome was recorded. Consent from the parents and permission from Ethical Review Committee of Dhaka Shishu (Children) Hospital was taken. Data were analyzed by using SPSS version 17.

## Result

Mean age of study neonates were32.12±14.26 hours. There was significant improvement of oxygenation from diagnosis to 72 hour after treatment (p=0.000) [Table I].

Paired samples t test was done to assess the comparison. Statistically significant improvement was found at 72$^{th}$ hour regarding drop of right ventricular systolic pressure (RVSP) [Table II].

Complications were present in 28% cases. Hypotension developed in 4 patients, urinary retention develops 2 patients and altered GI function was found in 2 patients (Table-III).

Mean time was taken to improve was 86.66±34.98 hours, mean hospital stay was 9.48±3.39 days and 16% cases died (Table-IV).

**Table I : Assessment of improvement of oxygenation from diagnosis to 72$^{th}$ hour after treatment**

| Time | $PaO_2$ (mean ±SD) | *P* value | $SpO_2$ (mean ±SD) | *P* value |
|---|---|---|---|---|
| At diagnosis | 45.74±13.62 | 0.000 | 64.56±7.04 | 0.08 |
| At 6$^{th}$ hour | 48.26±12.60 | | 70.72±8.49 | |
| At diagnosis | 45.74±13.62 | 0.000 | 64.56±7.04 | 0.000 |
| At 12$^{th}$ hour | 51.46±11.86 | | 72.84±6.37 | |
| At diagnosis | 45.74±13.62 | 0.000 | 64.56±7.04 | 0.000 |
| At 24$^{th}$ hour | 55.14±10.87 | | 79.12±6.53 | |
| At diagnosis | 45.74±13.62 | 0.000 | 64.56±7.04 | 0.000 |
| At 36$^{th}$ hour | 58.689.19 | | 82.64±5.83 | |
| At diagnosis | 45.74±13.62 | 0.000 | 64.56±7.04 | 0.000 |
| At 48$^{th}$ hour | 66.70±8.56 | | 87.80±7.91 | |
| At diagnosis | 45.74±13.62 | 0.000 | 64.56±7.04 | 0.000 |
| At 72$^{th}$ hour | 88.38±7.15 | | 91.95±7.96 | |

**Table II : Assessment of comparison in improvement regarding RVSP after treatment at 72$^{th}$ hour**

| Drug | RVSP (mean ± SD) | *P* value |
|---|---|---|
| Magnesium sulphate (n=21) ($MgSO_4$) | At diagnosis = 53.03±9.20 | 0.000 |
| | At 72th hour = 34.69±9.88 | |

RVSP - Right ventricular systolic pressure

**Table III: Complication of Magnesium Sulphate (n=25)**

| Complications | Number | Percent |
|---|---|---|
| Absent | 18 | 72 |
| Present | 7 | 28 |
| Hypotension | 4 | 16 |
| Urinary retention | 2 | 8 |
| Altered GIT Function | 2 | 8 |

(Multiple response)

**Table IV : Outcome**

| Outcome | | |
|---|---|---|
| Time taken to improve (hours) [mean ± SD], n=21 | | 86.66±34.98 |
| Duration of mechanical ventilator [mean ± SD], n=12 | | 112.10±20.48 |
| Hospital Stay (days) [mean ± SD], n=21 | | 9.48±3.39 |
| Outcome | Improved | 21(84%) |
| | Died | 4(16%) |
| Neuro developmental assessment at discharge | Normal | 21(100%) |

## Discussion

In this study we found that pulmonary vascular resistance (measured by echocardiographic evaluation)dropped remarkably by $MgSO_4$. Shaltouta et al[10] also found significant drop in pulmonary vascular resistance in their study.

In this study improvement of oxygenation measured by changes in partial pressure of oxygenation and ventilator duration. A

significant improvement of patients' oxygenation parameters were noted at 72 hours which was comparable with other studies.[10-12] Ulsa et al[13] in a recent randomized clinical trial also showed that $MgSO_4$ was effective in the improvement of oxygenation in PPHN. Marked improvement in partial pressure oxygen at 6 hours and maximum improvement at 24 hours were found by Chandran et al[11]. In this study oxygenation was started to improve at 6 hours but significantly improved after 12 hours. Mean ventilatory time support was 112.10±20.48 hours which was comparable with Tolsa et al[12].

Raimondi et al[9]concluded that where nitric oxide facilities are not available, magnesium sulphate is a cheap alternative for first line treatment of moderate PPHN. Chandran et al[11] found $MgSO_4$ to be a safe and effective pulmonary vasodilator. They concluded that MgSO4 could be used as a first-line vasodilator in developing countries because of its low cost, high efficacy and easy administration. Tolsa et al[12] and Daffa et al[14] also concluded that $MgSO_4$ may be considered as an alternative treatment in PPHN when no other modalities are available.

At high serum concentrations, magnesium is a muscle relaxant, a sedative, and a potent vasodilatory drug. Blood pressure was monitored and hypotension was observed in 4 of our patients (16%). In response to hypotension MgSO4 infusion was temporarily discontinued and saline infusion was given. Shaltouta et al[10] reported 20% hypotension in their study in case of $MgSO_4$. No systemic hypotension were noted by Tolsa et al[12]. Chandranet al[11] in their study maintained mean blood pressure with short periods of dopamine alone or in combination with dobutamine. Dopamine was commenced at 5-10 µg/kg/min before the loading dose of $MgSO_4$ to prevent systemic hypotension. The slight decrease in heart rate was also found and easily corrected by dobutamine support.

No patient experienced decrease heart rate in our study. Urinary retention develops in 2 patients and altered GI function was found in 2 patients. Chandran et al[11] found that feeding was well tolerated in their study. However, other side effects of $MgSO_4$ (flaccidity and hypocalcaemia) were not found in the present study.

Despite a better understanding of the underlying pathophysiology and the various treatments that have been proposed, pulmonary hypertension remains a potentially fatal complication among newborns. In this study mortality was 16%.

In the study done by Chandran et al it was found that all infants who were survived had normal neurological findings at discharge from the hospital.[11] The neurodevelopmental assessment was normal at 6 and 12 months of age in the study done by Tolsa et al.[12] In our study Neurodevelopmental assessment was also found normal in all infants at discharge.

## Conclusion

Magnesium Sulphate is effective in improving oxygenation and reduction of pulmonary vascular resistance in PPHN.

## Acknowledgement

This study was funded by Ministry of Science and Technology, Government of People's Republic of Bangladesh.

## References

1. Askin DF. Fetal-to-neonatal transition- what is normal and what is not? Neonatal Netw. 2009;28:e33-40
2. Edwards MO, Kotecha SJ, Kotecha S. Respiratory distress of the term newborn infant. PaediatrRespir Rev 2013;14:29-36.
3. Walsh-Sukys MC, Tyson JE, Wright LL, Bauer CR, Korones SB, Stevenson DK et al. Persistent pulmonary hypertension of the newborn in the era before nitric oxide: practice variation and outcomes. Pediatr2000;105:14–20.
4. Hibbard JU, Wilkins I, Sun L. Consortium on Safe Labor. Respiratory morbidity in late preterm births. JAMA 2010;304:419-425.
5. Konduri GG, Kim UO. Advances in the diagnosis and management of persistent pulmonary hypertension of the newborn. PediatrClin North Am 2009;56:579-600.
6. Kinsella JP, Abman SH. Inhaled nitric oxide therapy in children. Paediatr Respir Rev 2005;6:190-98.
7. Chambers CD, Hernandez-Diaz S, Van Marter LJ, Werler MM, Louik C, Jones KL, et al. Selective serotonin-reuptake inhibitors and risk of persistent pulmonary hypertension of the newborn. N Engl J Med 2006;354 :579-87.
8. Shaltout F, Hegazy R, Aboulghar H, Motelb LA. Magnesium sulphate versus sildenafil in the treatment of persistent pulmonary hypertension of the newborn. IntClinPediatr2012;1:19-24.
9. Raimondi F, Migliaro F, Capasso L. Intravenous magnesium sulphate versus inhaled nitric oxide for moderate persistent pulmonary hypertension of newborn. A multicentre, retrospective study. J Trop Pediatr2008;54:196-199.
10. Shaltouta F, Hegazya R, Aboulghara H, Motelb LA. Magnesium Sulphate Versus Sildenafil in the Treatment of Persistent Pulmonary Hypertension of the Newborn. Int J ClinPediatr. 2012;1(1):19-24.
11. Chandran S, Haqueb ME, Wickramasinghe HT, Wint Z. Use of magnesium sulphate in severe persistent pulmonary hypertension of the newborn. J Trop Pediatr. 2004;50:219-223.
12. Tolsa JF, Cotting J, Sekarski N, Payot M, Micheli JL, Calame A. Magnesium sulphate as an alternative and safe treatment for severe persistent pulmonary hypertension of the newborn. Archives of Disease in Childhood 1995; 72: F184-F187.
13. Uslu S, Kumtepe S, Bulbul A, Comert S, Bolat F, Nuhoglu A. A comparison of magnesium sulphate and sildenafil in the treatment of the newborns with persistent pulmonary hypertension: a randomized controlled trial. J Trop Pediatr. 2011;57(4):245-250.
14. Daffa SH, Milaat WA. Role of magnesium sulphate in treatment of severe persistent pulmonary hypertension of the neoborn. Saudi Med J. 2002 Oct;23(10):1266-9.