INPLASY

The effects on magnesium sulfate for persistent pulmonary hypertension of newborns: a meta-analysis

INPLASY202380098

doi: 10.37766/inplasy2023.8.0098

Received: 22 August 2023

Published: 22 August 2023

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ADMINISTRATIVE INFORMATION

Support - No.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - The authors declare no conflict of interest. Min Zeng is currently an M.D. student under the supervision of Prof. Yusheng Pang. Her research is centered on explosive myocarditis. Limei Zhang is also an M.D. student of Prof. Yusheng Pang. Her research is centered on cardiac failure. Yusheng Pang is a professor at the Department of Pediatrics, First Affiliated Hospital, Guangxi Medical University, China. Professor Pang's group's current research interest is pulmonary hypertension in children.

INPLASY registration number: INPLASY202380098

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 August 2023 and was last updated on 22 August 2023.

INTRODUCTION

Review question / Objective This study aimed to evaluate the effects of magnesium sulfate on persistent pulmonary hypertension in newborns.

Condition being studied Persistent pulmonary hypertension of the neonate (PPHN) is defined as a cardiopulmonary disease with severe hypoxemia that occurs soon after birth. It is characterized by sustained elevation of pulmonary vascular resistance (PVR), preventing an increase in pulmonary blood flow after birth. The affected neonates fail to establish blood oxygenation, precipitating severe respiratory distress, hypoxemia, and eventually death. The data from the United States shows prevalence for PPHN ranging from 0.4 to 6.8 for every 1,000 live births, whereas the United Kingdom shows fluctuation from 0.43 to 6 for every 1,000 live births [2, 3].PPHN is one of the most common reasons for neonatal intensive care unit hospitalization and is associated with high mortality. Despite advances in neonatal cardiorespiratory treatment and care, PPHN is still one of the main causes of neonatal morbidity and mortality, with a mortality rate of 4–33%. Management of PPHN generally includes optimizing oxygenation, ventilation, and pulmonary vasodilators,e.g(inhaled nitric oxide(iNO), tolazoline, magnesium sulfate(MgSO4), adenosine, sildenafil, bosentan), and extracorporeal membrane oxygenation (ECMO).In resource-restricted countries, these expensive therapies can not be easy to apply. MgSO4 is an effective vasodilator, so it may reduce high pulmonary arterial pressure in PPHN. If MgSO4 is effective for PPHN, it would possibly be a low-cost and

lifesaving therapy. Dehdashtian M et al.[6] conducted a non-randomized, controlled trial of ten newborns who were admitted to the Neonatal Intensive Care Unit (NICU) with PPHN. They were treated with conventional mechanical ventilation, but they did not respond to that and are candidates for ECMO. Then the newborns who did not respond to mechanical ventilation were treated with magnesium sulfate infusion. Nine out of ten babies survived and one of them died. The differences between the mean AaDO2, Oxygen index(OI), and PH after mechanical ventilation and magnesium sulfate administration were significant.MgSO4 has a role in the treatment of PPHN patients who do not respond to ventilation.

METHODS

Search strategy Pubmed, EMBASE, Google Scholar, MEDLINE, OVID, and Web of Science. (sulfate Magnesium)[Title/Abstract]OR(Magnesium sulphate, Heptahydrate)) [Title/Abstract]OR(Heptahydrate Magnesium sulfate) [Title/Abstract] OR (Pulmonary Hypertension, Familial Persistent of the Newborn) [Title/Abstract]OR(ACD-MPV))[Title/Abstract]OR(ACDMPV))[Title/Abstract]OR(Alveolar Capillary Dysplasia With Misalignment Of Pulmonary Veins))[Title/Abstract]OR(Persistent Fetal Circulation))[Title/Abstract]OR (Circulation Persistent Fetal))[Title/Abstract]OR(Familial Persistent Pulmonary Hypertension of the Newborn))[Title/Abstract]OR(Fetal Circulation, Persistent)))[Title/Abstract]OR(Hypertension Pulmonary of Newborn,Persistent))[Title/Abstract]OR (Misalignment of the Pulmonary Vessels)) [Title/Abstract]OR(Persistent Pulmonary Hypertension of Newborn))[Title/Abstract]OR(Alveolar Capillary Dysplasia With Misalignment Of Pulmonary Veins And Other Congenital Anomalies)[Title/Abstract] OR randomized controlled trials[Publication Type].

Participant or population Newborns diagnosed with PPHN according to the American Heart Association and Thoracic Society's guidelines for diagnosis and treatment.

Intervention Treatment with MgSO4.

Comparator Control group was treated with other drugs; MgSO4 group was treated with magnesium sulfate.

Study designs to be included Randomized controlled trials.

Eligibility criteria Inclusioncriteria (1)All babies were admitted to NICU with profound hypoxemia (PaO2<50 mmHg) with adequate ventilatory support before treatment withdrugs. (2)All babies had confirmed the diagnosis by echocardiography. (3)Experimental group treated with magnesiumsulfate. (4)Control group was treated with otherdrugs. (5)Clinical randomized controlledtrial. (6)Outcome indicators including OI,A-aDO2,pH,PaO2,PaCO2, MAP,heartrate,MABP. (7)Study type:RCTs.Exclusion criteria(1)The data is incomplete and unavailable for validity data extraction. (2)Studies from non-RCTs(including animal/cell experiments).(3)Congenital heart diseases,massive intracranial hemorrhage≥Grade 3,and active seizures.

Information sources Searching Pubmed, EMBASE, Google Scholar, MEDLINE, OVID, and Web of Science, only randomized controlled trials were collected to study.

Main outcome(s) The blood magnesium concentration, heart rate, OI, A-aDO2, pH, PaO2, PaCO2, mean airway pressure(MAP), Mean pulmonary arterial blood pressure (MABP).

Quality assessment / Risk of bias analysis Zhang Yan and Zeng Min independently assessed the risk of bias (ROB), following the Cochrane Handbook version 5.1.0 tool for assessing ROB in RCTs.The following seven domains were considered: (1) randomized sequence generation, (2)treatment allocation concealment, blinding of, (3)participants,(4)personnel,(5)incomplete outcome data, (6) selective reporting, and (7) other sources of bias. Following the Cochrane Handbook version 5.1.0 tool for assessing ROB in RCTs.

Strategy of data synthesis Stata software was used for data processing. All variables are continuous variables and are expressed as Means and standard deviation (SD) in studies. Continuous variables in the study will be reported as mean difference (MD=absolute difference between the means of two groups, defined as the difference in means between the treatment and control groups and calculated using the same scale) or standardized mean difference (SMD=mean difference in outcome between groups/standard deviation of outcome between subjects, used to combine data when trials with different scales) with 95% confidence intervals(CI) and analysis. Considering I2>50%, the random effects model was selected, while the fixed effects model was selected with I2<50%.

Subgroup analysis None.

Sensitivity analysis None.

Country(ies) involved China.

Keywords effects; magnesium sulfate;persistent pulmonary hypertension of newborns;meta-analysis;newborns.

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