INPLASY PROTOCOL

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Support: **No**

Review Stage at time of this submission: **Formal screening of search results against eligibility criteria.**

Conflicts of interest: **No.**

Meta analysis of milrinone in the treatment of persistent pulmonary hypertension in newborns

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Review question / Objective: **What are the efficacy and safety of milinone for persistent pulmonary hypertension in newborns?**
Condition being studied: **Persistent pulmonary hypertension of the newborn (PPHN) is caused by a variety of causes of neonatal birth after persistent pulmonary vascular resistance increases, pulmonary pressure more than systemic pressure, make the transition from fetal circulation to normal "adult" circulation failure, leading to the pulmonary artery catheter and (or) patent foramen of blood from right to left shunt, eventually appear serious and difficult to correct hypoxemia and other symptoms of clinical syndrome.It is commonly seen in overdue and full-term children, with an incidence of about 2‰ and a fatality rate of 4% ~ 33%.Cyclic nucleotide phosphodiesterase (PDE) is a kind of enzyme that can hydrolyze phosphodiester bonds in cAMP and cGMP, thus inhibiting pulmonary vasodilation.Two subtypes, PDE3 and PDE5, are crucial in the pathogenesis of PPHN.Milinone is a selective PDE3 inhibitor, which can inhibit the degradation of cAMP in the smooth muscle of pulmonary vessels. CAMP can promote the absorption of calcium ions in the sarcoplasmic reticulum, thus causing pulmonary vasodilation and ultimately reducing pulmonary artery pressure.In 2010, Bassler conducted a systematic evaluation on the treatment of neonatal PPHN with milinon, but no randomized controlled trial was found in literature retrieval at that time, and the evaluation effect was uncertain.In recent.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 04 May 2020 and was last updated on 04 May 2020 (registration number INPLASY202050014).

INTRODUCTION

Review question / Objective: **What are the efficacy and safety of milinone for persistent pulmonary hypertension in newborns?**

Condition being studied: Persistent pulmonary hypertension of the newborn (PPHN) is caused by a variety of causes of neonatal birth after persistent pulmonary vascular resistance increases, pulmonary pressure more than systemic pressure, make the transition from fetal circulation to normal "adult" circulation failure, leading to the pulmonary artery catheter and (or) patent foramen of blood from right to left shunt, eventually appear serious and difficult to correct hypoxemia and other symptoms of clinical syndrome.It is commonly seen in overdue and full-term children, with an incidence of about 2‰ and a fatality rate of 4% ~ 33%.Cyclic nucleotide phosphodiesterase (PDE) is a kind of enzyme that can hydrolyze phosphodiester bonds in cAMP and cGMP, thus inhibiting pulmonary vasodilation.Two subtypes, PDE3 and PDE5, are crucial in the pathogenesis of PPHN.Milinone is a selective PDE3 inhibitor, which can inhibit the degradation of cAMP in the smooth muscle of pulmonary vessels. CAMP can promote the absorption of calcium ions in the sarcoplasmic reticulum, thus causing pulmonary vasodilation and ultimately reducing pulmonary artery pressure.In 2010, Bassler conducted a systematic evaluation on the treatment of neonatal PPHN with milinon, but no randomized controlled trial was found in literature retrieval at that time, and the evaluation effect was uncertain. In recent.

METHODS

Participant or population: Randomized controlled trial to evaluate the efficacy and safety of milrinone in the treatment of PPHN compared to conventional treatment.

Intervention: Milrinone combined with conventional treatment for PPHN compared to conventional treatment.

Comparator: Conventional treatment.

Study designs to be included: Randomized controlled trials and specific random methods must be reported.

Eligibility criteria: Randomized controlled trials evaluated the efficacy and safety of milrinone in the treatment of PPHN compared to conventional treatment.

Information sources: The two authors of this paper searched independently in PubMed, Cochrane Library, EMbase, cnki, Chinese biomedical literature database, wanfang database and Chinese scientific and technological journal database (vep) respectively, and the retrieval period was from the establishment of the database to April 1, 2020.English term for "milrinone, Corotrope, Primacor, Win47203, pulmonary hypertension, persistent pulmonary hypertension, pulmonary artery hypertension, PPHN, newborn and infant".The study will not be limited to any country or region, and will be limited to English and Chinese.References to all selected studies and grey literature will be reviewed.

Main outcome(s): Treatment effective rate and incidence of adverse reactions.

Additional outcome(s): Mechanical ventilation time, increased blood oxygen saturation and partial oxygen pressure, and decreased pulmonary artery pressure.

Quality assessment / Risk of bias analysis: The quality of the included literature was evaluated using the improved Jadad scoring criteria, which ranged from 1-3 to low quality and from 4 to 6 to high quality. The risk of bias tool of the Cochrane consultation (RevMan 5.3) was used.The criteria include seven items: random sequence generation, allocation hiding, blinding of participants and researchers, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other sources of bias.

Strategy of data synthesis: The two authors independently extracted and screened the searched literature. The inclusion of controversial documents is decided by a third party.The data extracted included: first author, time of publication, basic characteristics of study subjects (sample

size, age, etc.), intervention measures and outcome indicators. Review Manager 5.3(RevMan 5.3) was used for Meta analysis of the extracted data.P < 0.05 was statistically significant.Heterogeneity was evaluated by χ^2 test and the degree of heterogeneity was calculated by I^2. If there is no obvious heterogeneity among the studies (P > 0.10, I^2 < 50%), the fixed effect model is used for analysis.If there is significant heterogeneity between studies (P≤0.10, I^2 ≥50%), the source of heterogeneity will be further analyzed. After the exclusion of obvious statistical heterogeneity, the random effect model will be used for Meta analysis. Descriptive analysis was conducted for data that could not be meta-analyzed.

Subgroup analysis: None.

Sensibility analysis: If necessary, sensitivity analysis using standards will be performed.

Country(ies) involved: China.

Keywords: Milrinone ;persistent pulmonary hypertension;Newborn ;Meta analysis.

Contributions of each author:
Author 1 - Liu Xin - selection of studies and data extraction, writing of the project.analysis of results.
Author 2 - He Haiying - selection of studies, analysis of results.
Author 3 - Wu Haihuan - selection of studies, analysis of results.
Author 4 - Xin Yuemei - selection of studies and data extraction, writing of the project.