INPLASY PROTOCOL

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None declared.

The efficacy of prone position ventilation in treating pediatric acute respiratory distress syndrome: a systematic review and meta-analysis

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Review question / Objective: **Pediatric acute respiratory distress syndrome (PARDS) is a life-threatening condition that may impact the quality of life in survivors and cause serious socio-economic and psychological consequences on their families. Today, there are few data to guide the early adjuvant treatment of PARDS. In this meta-analysis, we aimed to evaluate the role of prone position ventilation (PPV) in the treatment for PARDS patients more comprehensively.**
Information sources: **We systematically searched the Embase, Ovid Medline, PubMed and the Cochrane Library and etal in terms of the English-written studies. In addition, we searched the Chinese database of CNKI, Wanfang and VIP database and etal. Briefly, the keywords for search including "pediatric" (also searched "infant", "child", and "neonatal"), "prone position" and "acute lung injury" (also searched "respiratory distress syndrome" and "severe pneumonia"). Besides, we searched Google scholar for grey literature. All the databases were searched due to 24th March 2021. After the literature search, all the studies were imported into Endnote (Clarivate Analytic, version X9) for excluding duplicate studies and screening the abstract.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 December 2022 and was last updated on 17 December 2022 (registration number INPLASY2022120070).

INTRODUCTION

Review question / Objective: **Pediatric acute respiratory distress syndrome (PARDS) is a life-threatening condition that may impact the quality of life in survivors and cause serious socio-economic and psychological consequences on their families. Today, there are few data to guide the early adjuvant treatment of PARDS. In this meta-analysis, we aimed to evaluate the role of prone position ventilation (PPV) in the treatment for PARDS patients more comprehensively.**

Condition being studied: Pediatric Acute Respiratory Distress Syndrome (PARDS) is a kind of acute progressive hypoxic respiratory failure caused by various non-cardiogenic factors inside and outside the lungs in children. Its pathophysiological characteristics are increased pulmonary capillary permeability, alveolar protein exudative pulmonary edema, atelectasis, lung consolidation, decreased lung compliance, increased intrapulmonary shunt, and imbalance of ventilation/blood flow ratio. The main clinical manifestations are respiratory distress, cyanosis, and refractory hypoxemia.

PARDS is a common critical disease in pediatrics, causing serious socio-economic and psychological consequences on their families. The current treatment plan is limited and the mortality is high. In 2004, the PARDS Cooperation Group in China conducted a clinical survey on the intensive care units of 25 children's hospitals. This results showed that the PARDS prevalence rate was 1.42%, the case fatality rate was as high as 62.9%, ,the relative risk (RR) of death exceeded 9 times the average level of intensive care units in China. According to other epidemiological studies, the annual average incidence of PARDS was 2.0 to 12.8 per 100,000 people, and the mortality was 18 to 35%. Prone position ventilation (PPV) was proposed by Bryan in 1974. It is a prone position to improve the ventilation of the dorsal lung tissue during mechanical ventilation, thereby making the whole lung ventilation more uniform. As an important lung protective ventilation strategy, PPV has been widely used in adults with respiratory failure. One study showed that physiological indicators such as arterial blood oxygen saturation, oxygen partial pressure and oxygenation index (OI) were significantly improved after changing the position. In recent years, related researches about PPV in the treatment of various types of respiratory failure patients with mechanical ventilation have inconsistent results. Overall, most studies confirmed the positive effect of PPV in mechanical ventilation of patients with respiratory failure. So far, there is still considerable controversy about whether PPV should be routinely used in patients with PARDS. PPV has been routinely carried out in adult patients and achieved good results. In view of children have lighter weight and better cardiopulmonary compensation than adults, we speculate whether PPV should be routinely implemented in PARDS patients. We plan to conduct a meta-analysis on this issue through evidence-based medicine methods to evaluate the efficacy of PPV in treating PARDS patients, so as to provide the evidence for the further clinical application.

METHODS

Participant or population: The inclusion criteria were: 1) the age of patients were below 18 years old; 2) the pediatric acute lung injury (PALI) and PARDS was diagnosed based on the Berlin definition, in which the PARDS was defined as an acute diffuse, inflammatory lung injury, with PaO2/FiO2 ratio ≤ 300; 3) Study design was limited in case-control studies, cohort studies, and randomized control trials. The reviews, meta-analyses, and conference abstracts were further screening for inclusion. The exclusion criteria included: 1) studies not focus on PARDS or PALI in pediatric patients; 2) no comparison between prone position with other position; 3) no available assessment data of the outcome; 4) animal experiment.The inclusion criteria were: 1) the age of patients were below 18 years old; 2) the pediatric acute lung injury (PALI) and PARDS was diagnosed based on the Berlin definition, in which the PARDS was defined as an acute diffuse, inflammatory lung injury, with PaO2/FiO2 ratio ≤ 300 [11]; 3) Study design was limited in case-control studies, cohort studies, and randomized control trials.

Intervention: Prone position ventilation.

Comparator: Supine position ventilation.

Study designs to be included: Study design was limited in case-control studies, cohort studies, and randomized control trials.

Eligibility criteria: All the studies evaluating the efficacy of PPV in treating PARDS were

included in our study. The inclusion criteria were: 1) the age of patients were below 18 years old; 2) the pediatric acute lung injury (PALI) and PARDS was diagnosed based on the Berlin definition, in which the PARDS was defined as an acute diffuse, inflammatory lung injury, with PaO2/FiO2 ratio ≤ 300; 3) Study design was limited in case-control studies, cohort studies, and randomized control trials. The reviews, meta-analyses, and conference abstracts were further screening for inclusion. The exclusion criteria included: 1) studies not focus on PARDS or PALI in pediatric patients; 2) no comparison between prone position with other position; 3) no available assessment data of the outcome; 4) animal experiment.

Information sources: We systematically searched the Embase, Ovid Medline, PubMed and the Cochrane Library and etal in terms of the English-written studies. In addition, we searched the Chinese database of CNKI, Wanfang and VIP database and etal. Briefly, the keywords for search including "pediatric" (also searched "infant", "child", and "neonatal"), "prone position" and "acute lung injury" (also searched "respiratory distress syndrome" and "severe pneumonia"). Besides, we searched Google scholar for grey literature. All the databases were searched due to 24th March 2021. After the literature search, all the studies were imported into Endnote (Clarivate Analytic, version X9) for excluding duplicate studies and screening the abstract.

Main outcome(s): Characteristics of the selected studies - There were 13 studies comparing prone position and supine position in treating PARDS patients. The publish year ranged from 2002 to 2020, and the recruitment year ranged from 1994 to 2017. Finally, 1,252 pediatric patients were included in this study. Among them, 367 pediatric patients were treated by PPV and 885 pediatric patients were treated by supine position ventilation (SPV). The median age ranged from 1.35 year to 4.2 years old, and 49.5% of pediatric patients were girls.

Respiratory assessment in PPV - In terms of PaO2, we found that there was no significant difference between prone position group and supine position group (SMD=0.52, 95%CI=-0.09-1.13, random effect model, P=0.098). However, prone position decrease the PaCO2 compared with SPV group (SMD=-0.84, 95%CI=-1.66--0.02, random effect model, P=0.001). Moreover, there is no significant difference between two groups in terms of blood PH (SMD=-0.19, 95%CI=-0.49- 0.11, random effect model, P=0.225).

In terms of the PaO2/FiO2 score, the PPV could increase PaO2/FiO2 score comparing with SPV (SMD=1.76, 95%CI=0.73- 2.78, random effect model, P=0.001). Similarly, prone position could provide a better oxygenation compared with SPV (SMD=-1.56, 95%CI=-2.87- -0.24, random effect model, P=0.020).

Mortality - In terms of mortality of PARDS patients, prone position could not decrease mortality rate comparing with supine position (RR=1.05, 95%=0.96-1.15, P=0.317).

Quality assessment / Risk of bias analysis: The quality assessment of this study was based on the Cochrane Collaboration, Three of the 13 included studies were regarded as grade A, and the rest 10 studies were graded as B.

Strategy of data synthesis: The Stata version 15.0 software was used for statistical analysis. The RR was used for analyzing the outcome of mortality. For continuous variables, such as PaO2, PaO2/FiO2, OI, blood PH, PaCO2, the standard mean difference (SMD) was used. Both data were reported with 95% confidence intervals (CI) and all the significant P value was set as 0.05. The I2 statistic and χ2 test was used for statistical heterogeneity (I2 ≥ 50% indicating the presence of heterogeneity). When the heterogeneity existed, the random-effects model was used; otherwise, the fix-effect model was applied. Finally, the forest plots were drawn and the funnel plots were used for evaluating the publication bias. Egger's linear regression test was used to assess probable publication bias among the

contained studies. The stability of the joint consequences was inspected by applying a sensitivity analysis, as each study included was deleted in turn, and then summary ORs were recalculated to examine the change between the original and reobtained ORs. P <0.05 was indicated as statistical significance.

Subgroup analysis: Not applied.

Sensitivity analysis: From the results of sensitivity analysis, we saw no material alterations existed in recalculated SMDs when compared with the original SMDs after deleting any single eligible study in all kinds of comparison, which implied that our results were dependable and firm.

Country(ies) involved: China.

Keywords: pediatric; acute respiratory distress syndrome; prone position ventilation; PaO2; oxygenation index.

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