INPLASY PROTOCOL

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None declared.

Comparison between aggressive and non-aggressive intravenous hydration protocol in patients with acute pancreatitis: A systematic review and meta-analysis of randomized controlled trials

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Review question / Objective: **To systematically review the treatment harms and benefits between the aggressive and non-aggressive hydration protocol in patients with acute pancreatitis from the randomized controlled trials.**
Condition being studied: **Acute pancreatitis, the inflammation of the pancreas, probably increases the mortality risk. An adequate and sufficient intravenous fluid supplement is the cornerstone therapy for acute pancreatitis . However, the comparisons between different hydration strategies regarding the amount of fluid remains controversial.**
Information sources: **We searched the PubMed, Embase and the Cochrane Library to identify the relevant randomized controlled trials without the language limitation from the database inception to November 15, 2022. The updated search will be performed before we submit the final report to the medical journals. The search strategy was developed by the evidence-based medicine researcher and librarian. The important keywords with MeSH terms included "acute pancreatitis", "normal saline" and "Lactated Ringer's solution". To make our search more comprehensive, we also manually reviewed the reference lists from the included studies, the previous review articles and published guideline of acute pancreatitis.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 November 2022 and was last updated on 15 November 2022 (registration number INPLASY2022110068).

INTRODUCTION

Review question / Objective: **To systematically review the treatment harms and benefits between the aggressive and non-aggressive hydration protocol in patients with acute pancreatitis from the randomized controlled trials.**

Condition being studied: Acute pancreatitis, the inflammation of the pancreas, probably increases the mortality risk. An adequate and sufficient intravenous fluid supplement is the cornerstone therapy for acute pancreatitis . However, the comparisons between different hydration strategies regarding the amount of fluid remains controversial.

METHODS

Participant or population: Adults with acute pancreatitis.

Intervention: Aggressive hydration protocol.

Comparator: Non-aggressive hydration protocol.

Study designs to be included: Randomized controlled trials.

Eligibility criteria: After removal the duplicated records from different databases, two independent reviewers (XWL and CHW) will identify the included studies based on the following PICOS: (1) participants: adults with acute pancreatitis; (2) interventions: aggressive fluid resuscitation defined as a. fluid administration (normal saline or Lactated Ringer's solution) at a rate greater than 10 ml/kg/hour; b. fluid bolus 20 ml/kg for 2 hours then 3 ml/kg/hour in the first 24 hour or c. fluid administration ≧ 4,000 ml in the first 24 hour; (3) comparisons: non-aggressive fluid resuscitation defined as a. fluid administration at a rate lower than 10 ml/kg/hour; b. fluid bolus 10 ml/kg for 2 hours then 1.5 ml/kg/hour in the first 24 hour or c. fluid administration < 4,000 ml in the first 24 hour (4) primary outcome: all-cause death rate. Other secondary outcomes, such as the rate of fluid overload, sepsis, acute respiratory failure, acute kidney failure, pancreatitis necrosis, length of hospital stay, clinical progression, systemic inflammatory response syndrome (SIRS) subsided in 48 hours, persistent SIRS (lasting >48 hours), and changes in BUN or hematocrit, will be also evaluated if they had been reported from the included studies; (5) design: randomized controlled trials.

Information sources: We searched the PubMed, Embase and the Cochrane Library to identify the relevant randomized controlled trials without the language limitation from the database inception to November 15, 2022. The updated search will be performed before we submit the final report to the medical journals. The search strategy was developed by the evidence-based medicine researcher and librarian. The important keywords with MeSH terms included "acute pancreatitis", "normal saline" and "Lactated Ringer's solution". To make our search more comprehensive, we also manually reviewed the reference lists from the included studies, the previous review articles and published guideline of acute pancreatitis.

Main outcome(s): The primary outcome was the all-cause mortality risk, and the secondary outcomes included the risk of fluid overload, sepsis, acute respiratory failure, acute kidney failure, pancreatitis necrosis, length of hospital stay, clinical progression, systemic inflammatory response syndrome (SIRS) subsided in 48 hours, persistent SIRS (lasting >48 hours), and changes in blood urea nitrogen, hematocrit and C-reactive protein levels.

Quality assessment / Risk of bias analysis: The risk-of-bias assessment will be performed by two independent reviewers. We will use the Cochrane Collaboration's tool 2.0 which contains randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, selection of the reported result, and overall bias, to evaluate the methodological quality of the included randomized controlled trials.

Strategy of data synthesis: We will use the Review Manager Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) to conduct a random-effects meta-analysis due to the expected clinical heterogeneity among included trials. The pooled risk ratio (RR)

and mean difference (MD) with 95% confidence interval (CI) will be calculated for categorical and continuous outcomes, respectively. If multiple scales are employed to measure the same continuous outcome, we will use the standardized mean difference (SMD) to express the results. The I2 statistic will be used to determine the extent of statistical heterogeneity among the included trials, and a value > 50% is considered as significant heterogeneity. Funnel plots will be constructed to visually examine the presence of publication bias if there are at least 10 included trials in the meta-analysis.

Subgroup analysis: Subgroup analyses will include the severity of the pancreatitis (e.g., severe or non-severe pancreatitis according to revised Atlanta classification), age (e.g., ≧50 or <50 years old), baseline SIRS status (e.g., yes or no), and fluid types (e.g., normal saline or Lactated Ringer's solution).

Sensitivity analysis: To determine the robustness of the results of our main analyses, we will conduct a sensitivity analysis by only including RCTs with low risk of bias.

Country(ies) involved: Taiwan.

Keywords: acute pancreatitis; hydration; systematic review and meta-analysis.

Contributions of each author:

Author 1 - Xiu-Wei Li - Author 1 conducted the study selection, data extraction, risk-of-bias assessment, meta-analysis and drafted the manuscript.
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