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Mortality of Continuous infusion versus intermittent bolus of Meropenem: A System Review and Meta-analysis of Randomized Controlled Trials

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ADMINISTRATIVE INFORMATION

Support - Nil.

Review Stage at time of this submission - Data extraction.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 08 November 2023 and was last updated on 08 November 2023.

INTRODUCTION

Review question / Objective To investigate the association between continuous infusion of meropenem and mortality rates.

Rationale Meropenem, the time-dependent antibiotics is widely utilized for the treatment of diverse bacterial infections. Traditionally, these antibiotics have been administered as intermittent bolus doses at specific time intervals. Performing a continuous infusion can provide constant therapeutic levels, potentially improving bacterial eradication reduced mortality rate in the critical illness population. Therefore, we would like to investigate the association between continuous infusion of meropenem and mortality rates.

Condition being studied The PICO (population, intervention, comparison, outcome) setting the current meta-analysis was as the following; P: Human participants, I: Continuous infusion of meropenem, C: intermittent bolus of meropenem, and O: Mortality.

METHODS

Search strategy Two authors (MY, Ai and CY, Liu) independently conducted electronic searches in the Pubmed, Embase Cochrane CENTRAL, ClinicalTrials.gov database using the keywords (Continuous infusion AND Meropenem). The search period covered from each database to the date of 14 August, 2023.

Participant or population Human participants.

Intervention continuous infusion of meropenem.

Comparator Intermittent bolus of meropenem.

Study designs to be included Randomized controlled trials.

Eligibility criteria Generate a recruited study list, the following inclusion criteria will be used: (1) Enrolled human participants in the randomized control trials (RCTs). (2) RCTs that investigated the mortality rate between continuous infusion and intermittent bolus of meropenem to treat severe infection.

Information sources Two authors (MY, Ai and CY, Liu) independently conducted electronic searches in the Pubmed, Embase Cochrane CENTRAL, ClinicalTrials.gov database using the keywords (Continuous infusion AND Meropenem). The search period covered from each database to the date of 14 August, 2023.

Main outcome(s) The primary outcomes were the mortality rate between the administration continuous infusion and intermittent bolus of meropenem. We also analyzed the different subgroup mortality trend in different meropenem, mixing with other beta-lactam agents, different continuous infusion dose. The outcome was measured and quantified using odds ratios. The sensitivity test and public bias were also evaluated.

Additional outcome(s) The secondary outcomes we investigated the clinical success and improvement between continuous infusion and intermittent bolus of meropenem. The treat-related adverse events were also analyzed in our study.

Data management Two independent authors (M.-Y.A. and C.-Y.L.) extracted data from the recruited studies, encompassing demographic data, study design, details and values of the primary and secondary outcomes.

Quality assessment / Risk of bias analysis In order to assess the methodological rigor of the studies included in our investigation, we used the Cochrane risk-of-bias tool for randomized trials, version 2 (RoB 2). This tool comprises six primary components: randomization process, adherence to the intervention, handling of missing outcome data, outcome measurement, selective reporting, and an overall assessment of bias.

Strategy of data synthesis Due to the diversity in target populations across the studies included, we conducted the current meta-analysis using a random-effects model in Comprehensive Meta-Analysis software, version 3 (Biostat, Englewood, NJ). We considered a two-tailed p-value below 0.05 as indicative of statistical significance. For quantifying the primary outcomes, specifically changes in fatigue scores, we opted for Hedges' g and 95% confidence intervals (CIs). Effect sizes of 0.2, 0.5, and 0.8 on Hedges' g were categorized as small, moderate, and large, respectively. In investigating the secondary outcome, which pertained to treatment-related adverse event rates, we employed odds ratios and their corresponding 95% CIs. To assess the extent of heterogeneity among the studies, we relied on the I2 and Cochran's Q statistics. An I2 value of 25%, 50%, and 75% was considered indicative of low, moderate, and high heterogeneity, respectively.

Subgroup analysis Subgroup analyses based on the meropenem dosage and continuous infusion effect on mortality.

Sensitivity analysis In order to validate the robustness of the meta-analysis, sensitivity analyses were conducted through the one-study removal method. This approach involved systematically assessing whether the removal of a specific trial from the analysis resulted in a substantial alteration of the summary effect size.

Language restriction No language limit.

Country(ies) involved Taiwan.

Keywords continuous infusion, Meropenem, mortality, bacterial eradication.

Contributions of each author
Author 1 - Ming-Ying Ai.
Author 2 - Wei-Lun Chang.
Author 3 - Chia-Ying Liu.