INPLASY PROTOCOL

To cite: Cang et al. Carbapenems versus β-lactam and β-lactamase inhibitors for treatment of Nosocomial Pneumonia: a systematic review and meta-analysis. Inplasy protocol 202340113. doi: 10.37766/inplasy2023.4.0113

Received: 30 April 2023

Published: 30 April 2023

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Support: **None.**

Review Stage at time of this submission: **Preliminary searches.**

Conflicts of interest:
None declared.

Carbapenems versus β-lactam and β-lactamase inhibitors for treatment of Nosocomial Pneumonia: a systematic review and meta-analysis

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Review question / Objective: **(1) Participants: Patients had to be diagnosed with HAP (including VAP). Pneumonia had to be diagnosed based on clinical and radiographic criteria: purulent tracheal secretions with at least one respiratory sign or symptom of pneumonia, including new-onset fever or hypothermia, leukocytosis, or decline in oxygenation and including new or worsening infiltrates on chest radiographs within 48 h of hospital admission. HAP was defined as a patient with pneumonia who remained in hospital ≥48 h after hospital admission. VAP was defined as pneumonia with onset ≥48 h after endotracheal intubation and mechanical ventilation. (2) Interventions: The experimental group had to be treated with carbapenems. (3) Comparaors: The control group had to be treated with BLBLIs. (4) Outcomes: The primary outcomes were mortality and clinical response. Secondary outcomes were the microbiologic response and adverse effects (AEs). (5) Study design: a randomized control trial (RCT).**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 April 2023 and was last updated on 30 April 2023 (registration number INPLASY202340113).

INTRODUCTION

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mechanical ventilation. (2) Interventions: The experimental group had to be treated with carbapenems. (3) Comparaors: The control group had to be treated with BLBLIs. (4) Outcomes: The primary outcomes were mortality and clinical response. Secondary outcomes were the microbiologic response and adverse effects (AEs). (5) Study design: a randomized control trial (RCT).

Condition being studied: β-lactam and β-lactamase inhibitors (BLBLIs) have been used empirically in nosocomial pneumonia, but their efficacy and safety are controversial. We carried out a meta-analysis to evaluate the efficacy and safety of carbapenems versus BLBLIs against nosocomialpneumonia.Seven randomized controlled trials comprised of 3306 patients were identified. We included new BLBLIs in this meta-analysis, and we found no significant difference in the prevalence of mortality, clinical cure, clinical failure, or microbiologic clinical cure in patients treated with carbapenems or BLBLIs. However, we found that patients treated with carbapenems may suffer resistance to P. aeruginosa. Patients treated with carbapenems were less likely to experience SAEs than patients treated with BLBLIs. We conducted a sensitivity analysis on mortality, and the result was stable. We conducted a subgroup analysis according to the type of carbapenems, the classification of microorganisms and the categorization of AEs and found no difference between IMI versus TZP or meropenem versus a novel BLBLI.

METHODS

Participant or population: Patients had to be diagnosed with HAP (including VAP). Pneumonia had to be diagnosed based on clinical and radiographic criteria: purulent tracheal secretions with at least one respiratory sign or symptom of pneumonia, including new-onset fever or hypothermia, leukocytosis, or decline in oxygenation and including new or worsening infiltrates on chest radiographs within 48 h of hospital admission. HAP was defined as a patient with pneumonia who remained in hospital ≥48 h after hospital admission. VAP was defined as pneumonia with onset ≥48 h after endotracheal intubation and mechanical ventilation.

Intervention: The experimental group had to be treated with carbapenems.

Comparator: The control group had to be treated with BLBLIs.

Study designs to be included: A randomized control trial (RCT).

Eligibility criteria: (1) Participants: Patients had to be diagnosed with HAP (including VAP). Pneumonia had to be diagnosed based on clinical and radiographic criteria: purulent tracheal secretions with at least one respiratory sign or symptom of pneumonia, including new-onset fever or hypothermia, leukocytosis, or decline in oxygenation and including new or worsening infiltrates on chest radiographs within 48 h of hospital admission. HAP was defined as a patient with pneumonia who remained in hospital ≥48 h after hospital admission. VAP was defined as pneumonia with onset ≥48 h after endotracheal intubation and mechanical ventilation. (2) Interventions: The experimental group had to be treated with carbapenems. (3) Comparaors: The control group had to be treated with BLBLIs. (4) Outcomes: The primary outcomes were mortality and clinical response. Secondary outcomes were the microbiologic response and adverse effects (AEs). (5) Study design: a randomized control trial (RCT).
Exclusion criteria: (1) abstracts, conference papers; (2) studies with incomplete data or using different control drugs; (3) articles not written in English.

Information sources: Not reported.

Main outcome(s): Mortality, clinical cure, clinical failure, microbiologic clinical cure rates, resistance by P. aeruginosa, side-effects of antibiotic treatment.

Quality assessment / Risk of bias analysis: Cochrane Collaboration's risk of bias tools.

We evaluated the confidence in the evidence for each outcome by employing the GRADE approach, which considers study design, risk of bias, inconsistency, indirectness, imprecision.

Strategy of data synthesis: Review Manager 5.4 was used for this meta-analysis . Treatment effects were calculated with the risk ratio (RR) and the corresponding 95% confidence interval for dichotomous outcomes. Cochran's Q statistic (significance level, $P < 0.01$) and I2 statistic were employed to assess heterogeneity. According to the Cochrane Handbook, I2 can be considered "non-important" (60%) . Heterogeneity can be xategorized into three types: clinical heteogeneity, methodological heterogeneity and statistical heterogeneity. Although statistical heterogeneity was not present, there was still clinical heterogeneity, and therefore, the radom-effects model was employed to improve the reliability of the result. Results were assessed using forest plots.

Subgroup analysis: Subgroup analyses were conducted according to the type of carbapenems, the classification of microorganisms and categorization of AEs.

Sensitivity analysis: Sensitivity analysis was undertaken to ascertain the results of the meta-analysis by excluding each individual study.

Country(ies) involved: China.

Keywords: carbapenem antibiotics, β-lactam, β-lactamase inhibitors, nosocomial pneumonia, systematic review meta-analysis.

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