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Remdesivir-induced Bradycardia and Mortality in SARS-CoV-2 Infection: A Systematic Review and Meta-analysis

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ADMINISTRATIVE INFORMATION

Support - No financial support.

Review Stage at time of this submission - Data analysis.

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 22 June 2023 and was last updated on 22 June 2023.

INTRODUCTION

Review question / Objective To assess the relationship between remdesivir-induced bradycardia and mortality in patients infected with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Rationale Understanding the relationship between remdesivir-induced bradycardia and mortality in SARS-CoV-2 patients is crucial for patient safety. Identifying risk factors associated with this adverse event can help guide monitoring and treatment strategies. Therefore, we would like to perform a systematic review and meta-analysis to investigate.

Condition being studied The PICO (population, intervention, comparison, outcomes) setting of the current meta-analysis was as following: P: Human infected with Covid-19. I: Remdesivir treatment. C: Placebo. O: Bradycardia happened.

METHODS

Search strategy Two authors made independent electronic searches in the PubMed, Embase, Cochrane CENTRAL, Web of Science and ClinicalTrials.gov with keyword of ("Remdesivir AND bradycardia OR bradyarrhythmia") through the earliest record to Jul 14, 2023.

Participant or population Human participants.

Intervention Remdesivir.

Comparator Placebo.

Study designs to be included Retrospective study.

Eligibility criteria The following criteria were included: (1) prospective or retrospective cohort study. (2) Investigating the bradycardia after Remdesivir treatment (3) The participants confer

Covid-19 infected and using Remdesivir treatment (4) Additional therapies agents was allowed.

Information sources Two authors made independent electronic searches in the PubMed, Embase, Cochrane CENTRAL, Web of Science and ClinicalTrials.gov with keyword of ("Remdesivir AND bradycardia OR bradyarrhythmia") through the earliest record to Jul 14, 2023.

Main outcome(s) The main objective was to assess the association between Remdesivir and bradycardia as the primary outcome.

Additional outcome(s) The secondary outcomes aimed to evaluate the risk factors associated with Remdesivir-induced bradycardia. The potential risk factors assessed included hypertension, diabetes, ICU admission, and beta-blocker usage.

Data management Data extraction was performed by two authors independently. The extracted data included demographic information, study design, specifics of Remdesivir and placebo treatment regimens, as well as values of primary and secondary outcome measures.

Quality assessment / Risk of bias analysis The studies included in our meta-analysis consisted of both prospective and retrospective cohort studies. The quality assessment was conducted using the widely used Newcastle-Ottawa Quality Assessment scale (NOS), which assesses the quality and bias of cohort and case-control studies.

Strategy of data synthesis The meta-analysis employed a random-effects model due to the heterogeneity of the target populations in the included studies. Comprehensive Meta-Analysis software, version 3, was used for the analysis. Statistical significance was defined as a two-tailed p-value less than 0.05. Hedges' g and 95% confidence intervals (CIs) were used to quantify the primary outcomes, with effect sizes of 0.2, 0.5, and 0.8 indicating small, moderate, and large effects, respectively. Odds ratios and their 95% CIs were used to examine the secondary outcome of treatment-related adverse event rates. Heterogeneity among studies was evaluated using the I2 and Cochran's Q statistics, with I2 values of 25%, 50%, and 75% indicating low, moderate, and high heterogeneity, respectively.

Subgroup analysis Subgroup analyses based on the patients' risk factors and Remdesivir induced bradycardia were performed.

Sensitivity analysis To confirm the robustness of the meta-analysis, the sensitivity analyses were performed using one-study removal method to see if there was a significant change in the summary effect size after removing a particular trial from the analysis.

Language restriction No language limit.

Country(ies) involved Taiwan.

Keywords Remdesivir, Bradycardia, Mortality, meta-analysis, systematic review.

Contributions of each author

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