INPLASY PROTOCOL

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None declared.

Intravenous pentamidine for Pneumocystis jirovecii pneumonia prophylaxis in immunocompromised patients without human immunodeficiency virus: a systematic review and meta-analysis

Chiu, CY[1]; Ching, P[2].

Review question / Objective: **Breakthrough PJP rate and adverse reactions in HIV-uninfected immunocompromised patients who received intravenous pentamidine.**
Rationale: **Trimethoprim-sulfamethoxazole (TMP-SMX) is a first-line Pneumocystis jirovecii pneumonia (PJP) prophylaxis agent, but intravenous pentamidine (IVP) every 4 weeks (Q4W) is commonly used in human immunodeficiency virus (HIV)-uninfected immunocompromised hosts because IVP is not associated with cytopenia and delayed engraftment. Breakthrough PJP rate on TMP-SMX prophylaxis, incidence of adverse reactions, and adverse events requiring discontinuation of TMP-SMX have been described in the literature. However, breakthrough PJP rate and adverse reactions are not well characterized in IVP.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 December 2022 and was last updated on 18 December 2022 (registration number INPLASY2022120072).

INTRODUCTION

Review question / Objective: **Breakthrough PJP rate and adverse reactions in HIV-uninfected immunocompromised patients who received intravenous pentamidine.**

Rationale: **Trimethoprim-sulfamethoxazole (TMP-SMX) is a first-line Pneumocystis jirovecii pneumonia (PJP) prophylaxis agent, but intravenous pentamidine (IVP) every 4 weeks (Q4W) is commonly used in human immunodeficiency virus (HIV)-uninfected immunocompromised hosts because IVP is not associated with**

cytopenia and delayed engraftment. Breakthrough PJP rate on TMP-SMX prophylaxis, incidence of adverse reactions, and adverse events requiring discontinuation of TMP-SMX have been described in the literature. However, breakthrough PJP rate and adverse reactions are not well characterized in IVP.

Condition being studied: HIV-uninfected immunocompromised patients who received IVP for PJP prophylaxis.

METHODS

Search strategy: (intravenous pentamidine) AND (pneumocystis pneumonia [Mesh]) AND (prophylaxis [Mesh]) NOT (human immunodeficiency virus [Mesh]).

Participant or population: Clinical studies reporting outcomes of IVP for PJP prophylaxis were screened. All study types except case reports and conference abstracts were considered. Studies focused on patients living with HIV (PLHIV) were excluded.

Intervention: HIV-uninfected immunocompromised patients who received IVP for PJP prophylaxis.

Comparator: No comparator because this meta-analysis calculate the incidence of event. at single arm.

Study designs to be included: Retrospective, prospective studies and randomized controlled trial.

Eligibility criteria: HIV-uninfected immunocompromised patients who received IVP for PJP prophylaxis.

Information sources: MEDLINE, Embase, Cochrane Library, and ClinicalTrials.gov were searched.

Main outcome(s): The primary outcome is breakthrough PJP in patients receiving IVP.

Additional outcome(s): The secondary outcomes are the incidence of adverse reactions to IVP and discontinuation rate due to adverse events.

Data management: All analyses were performed using Comprehensive Meta-Analysis (CMA) software, version 3 (Biostat, Englewood, NJ, USA).

Quality assessment / Risk of bias analysis: The methodological quality of enrolled studies was evaluated using Newcastle-Ottawa Quality Assessment Scale for observational studies. Newcastle-Ottawa Quality Assessment Scale contains nine items in three categories (participant selection, comparability, and exposure), which yields a total score between 0 to 9 points.

Strategy of data synthesis: A random effects model was employed. Between-trial heterogeneity was determined by using I2 tests; an I2 > 50% was considered statistically significant heterogeneity. Funnel plots and Egger's test were used to examine potential publication bias. Level of significance was 5%.

Subgroup analysis: Age, geographical region, sample size, frequency of IVP, and use as first-line PJP prophylaxis.

Sensitivity analysis: Leave-one-out method.

Language restriction: Only English literature.

Country(ies) involved: USA (The University of Texas Health Science Center at Houston).

Other relevant information: No.

Keywords: Intravenous pentamidine, Pneumocystis jirovecii pneumonia, prophylaxis, hematopoietic stem cell transplantation, immunocompromised host.

Dissemination plans: Publish this study.

Contributions of each author:
Author 1 - Chia-Yu Chiu was responsible for conceptualization, data curation, formal

analyses, methodology, and manuscript draft.
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