Vancomycin Loading Dose and the Incidence of Nephrotoxicity in Adult Patients: A Systematic Review and Meta-Analysis

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Introduction

- Vancomycin is a widely used treatment for methicillin-resistant staphylococcus aureus (MRSA) infections, requiring attainment of a certain serum concentration to exert its antibacterial effect.
- Loading dose is a suggested strategy to help reach target steady state concentration more rapidly and is associated with better therapeutic level attainment[6].
- The lack of high-quality studies on improved outcomes and inconsistencies among evidence on the correlation between vancomycin loading dose and nephrotoxicity are possible reasons for reluctance to use loading dose.
- The objective of this systematic review and meta-analysis was to evaluate available studies and assess the incidence of nephrotoxicity in patients given a vancomycin loading dose.

Methods

- PubMed and Embase databases were searched through 26 February 2020 for clinical trials and observational cohort or case-control studies on adult patients initially treated with intermittent infusion vancomycin.
- Inclusion criteria: reported the number of patients receiving and not receiving loading dose and the incidence of nephrotoxicity between both groups.
- Exclusion criteria: conference abstracts or posters, studies not published in the English language, duplicates, studies with significantly overlapping population with other studies.
- Heterogeneity among studies was assessed with χ^2 test and I^2 statistics. Mantel-Haenszel random-effect model was used for pooling odds ratios (OR) and 95% confidence intervals (CI) for all primary outcomes.
- Bias was assessed using a funnel plot, the Newcastle-Ottawa quality assessment scale and the Cochrane risk-of-bias tool for randomized trials.

References

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Results

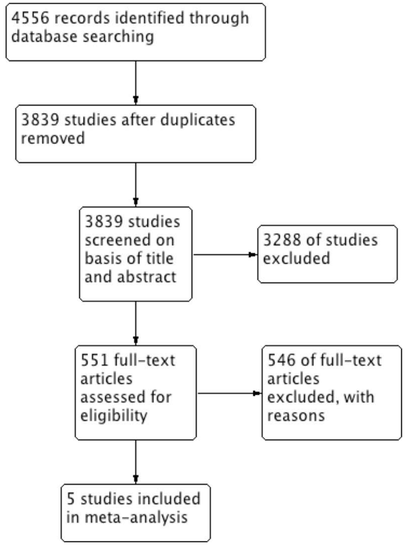

Figure 1. Flow diagram of study selection process

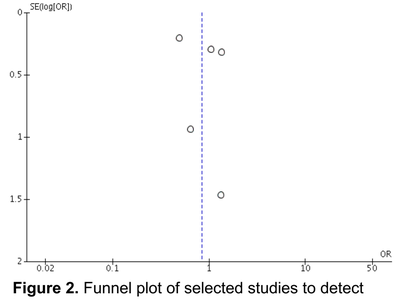

Figure 2. Funnel plot of selected studies to detect heterogeneity and bias

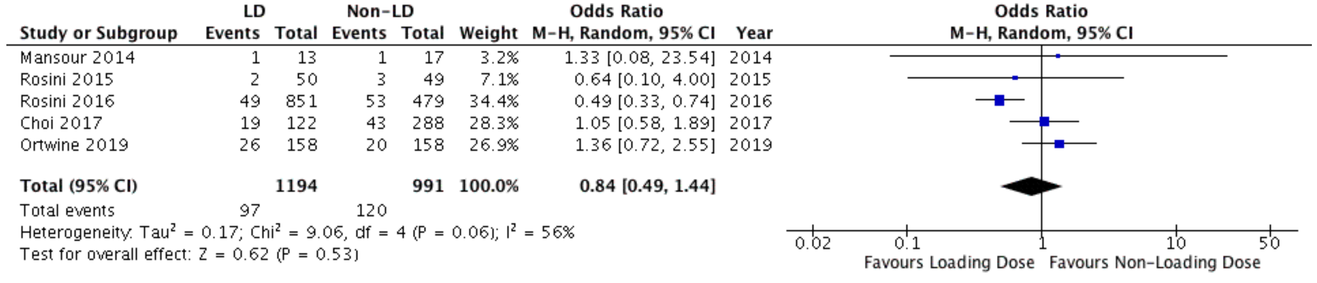

Figure 3. Pooling of primary outcomes from included studies using Mantel-Haenszel random-effect model with odds ratios (OR) and 95% confidence intervals (CI)[1-6].

Study	Selection				Comparability	Outcome			Score
	Representation of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	
Mansour 2014	★	★	★	★		★	★		6
Rosini 2016	★	★	★	★		★	★		6
Choi 2017	★	★	★	★		★	★		6
Ortwine 2019	★	★	★	★	★	★	★		7

Table 1. Newcastle-Ottawa scale assessment for included cohort studies.

Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Binding of participants and personnel (performance bias)	Binding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Rosini 2015	+	?	-	-	+	+	+

Table 2. Risk of bias assessment for included randomized controlled trials (RCTs).

Conclusions

- No significant difference in the incidence of vancomycin-induced nephrotoxicity was observed between patients who received and not received a vancomycin loading dose (OR 0.84, 95% CI 0.49 – 1.44).
- Meta-analysis using data adjusted for confounding factors was not possible because only one study (Ortwine 2019) reported adjusted effect estimates. In this study, no statistically significant association between loading dose and nephrotoxicity was observed when adjusting for confounding variables (OR 1.295, 95% CI 0.657 – 2.553).
- Additional studies that are prospective in nature are needed to address potential confounding factors.

Disclosures

No extramural support, financial or otherwise, was received in completion of this systematic review and meta-analysis