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Evaluation of vancomycin MIC creep in Staphylococcus aureus infections - a meta-analysis

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Evaluation of vancomycin MIC Creep in *Staphylococcus aureus* infections – a meta-analysis

Background: Vancomycin is currently the primary option treatment for methicillin-resistant *Staphylococcus aureus* (MRSA). However, an increasing number of MRSA isolates with high minimum inhibitory concentrations (MICs), within the susceptible range (vancomycin MIC creep) are being reported worldwide. Resorting to a meta-analysis approach, this study aims to comprehensively assess the evidence of vancomycin MIC creep, between 2006 and 2016.

Material/methods: The studies to be included in the meta-analysis approach were retrieved from Pubmed database, from January 2006 to January 2016. Search query was defined. The abstracts of the collected articles were reviewed and a study was considerable to be eligible for inclusion if it was written in English and it is possible to know values of vancomycin MIC, details of the applied MIC

methodologies, number of studied isolates, year and local of the study investigation. MetaXL 1.0, a tool for meta-analysis in Microsoft Excel, was used to pool individual prevalence from each study.

Results: Literature search identified 646 studies. After title and abstract analysis, 550 were excluded and 96 full-text articles were reviewed. Of these, 50 studies were included in the meta-analysis.
Considering all the studies included in the pool, the mean of vancomycin MIC was 1.20 mg/L and 1.19 mg/L, when determined by the BMD (Broth Microdilution) and Etest method, respectively. The analysis of the distribution of MRSA isolates with vancomycin MIC ≥ 2 mg/L showed a decrease over time, either with BMD or Etest methods. The Spearman's correlation coefficient results (-0.95 to BMD and -0.75 to Etest) showed no evidence of MIC creep.
Regarding the analysis of the pooled mean of vancomycin MIC by region, it was observed that in Europe with both BMD and Etest method was 1.10 mg/L. In Asia, with the BMD method was 1.17 mg/L and with the Etest method was 0.98 mg/L. In USA, these values are slightly increased, with values of 1.37mg/L and 1.49mg/L for the BMD method and Etest method, respectively.

Conclusions: This study is the first meta-analysis evaluating the trends of vancomycin MIC determined with different MIC methods, in a worldwide perspective, including single and large multicenter studies. The performed meta-analysis evaluated the trend of vancomycin MIC over time, and no statistically evidence of MIC creep phenomenon was detected. These findings must be considered when interpreting vancomycin susceptibility and during the discussion of the need to find alternative antistaphylococcal agents for patients with elevated but susceptible vancomycin MIC values.