

# Intravenous colistin combination antimicrobial treatment versus monotherapy: a meta-analysis

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## Background

There is conflicting data regarding the effectiveness of colistin combination regimens for the treatment of patients with multi-drug resistant infections. The aim of this study was to evaluate whether IV colistin in combination with other antibiotics (IVCC) was associated with lower mortality compared to colistin monotherapy (IVCM) and identify factors influencing outcomes.

## Methods

PubMed and Scopus were searched till November 2016. Studies were included if they evaluated adult patients with MDR/XDR Gram-negative infections and reported comparative mortality data (adjusted and unadjusted) for patients receiving IVCC versus IVCM. Studies were excluded if primary administration routes for colistin other than IV were used (e.g. oral, topical solutions, intraventricular or intrathecal, intramuscular, inhaled) or the comparator group in combination therapy did not receive colistin. A daily mean/median colistin dose or reported administered dose in the methodology of >6 million international units (MIU) was considered high, acknowledging that patients with decreased renal function receiving lower doses could have been included in the high dose regimens. Random effects meta-analyses were performed.

## Results

Thirty-two studies (29 observational, 3 RCTs) were included. The overall quality of data was low (median MINORS score 12, range 6-17; all RCTs open label, unclear allocation concealment, and variable random numbers generation) and characterized by the lack of adjusted data. The majority of the studies were not designed to evaluate the outcome of the meta-analysis and focused mainly on infections due to *A. baumannii* and *K. pneumoniae*. Colistin was administered at variable doses, with or without a loading dose, and in combination with several antibiotics. Overall, IVCC was not associated with lower mortality than IVCM [32 studies, 2328 patients, RR 0.91, 95% CI 0.81-1.02, I<sup>2</sup> 8%]. IVCC was associated with lower mortality when high dose (>6 MIU) colistin was employed (figure 1, 0.80, 0.69-0.93), in studies conducted in Asia (0.82, 0.71-0.95), in patients with bacteremia (0.75, 0.57-0.98), and in patients with *Acinetobacter* infections (0.88, 0.78-1.00).

## Conclusion

Overall, low quality data suggest that IVCC did not lower mortality in patients with MDR Gram negative infections. However, there is some evidence for a benefit observed with high IV colistin doses.

**Figure.** Forest plot depicting the risk ratios (RR) of mortality among patients treated with IVCC versus IVCM.

