

What is the right gentamicin dose for multiple trauma patients? A Monte Carlo simulation exploration study

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ABSTRACT

Background: The appropriate dose of gentamicin is important to prevent and treat infections. The study aimed to determine the optimal dose of gentamicin to achieve the probability of pharmacokinetic/pharmacodynamic (PK) targets for efficacy and safety in multiple trauma patients.

Methods: PK parameters of gentamicin in multiple trauma patients were gathered to develop a one-compartment PK model for prediction. The Monte Carlo simulation method was performed. The 24-h area under the concentration time curve to the minimum inhibitory concentration ratio (AUC_{24h}/MIC) ≥ 50 was defined for the infection prevention target. AUC_{24h}/MIC ≥ 110 or the maximum serum concentration to MIC ratio $\geq 8-10$ was for the treatment of serious Gram-negative infection target. The risk of nephrotoxicity was the minimum serum concentration ≥ 2 mg/L. The optimal dose of gentamicin was determined when the efficacy target was $>90\%$ and the risk of nephrotoxicity was lowest.

Results: The optimal gentamicin dose to prevent infection when the MIC was <1 mg/L was 6–7 mg/kg/day. A higher dose of gentamicin up to 10 mg/kg/day could not reach the target for treating serious Gram-negative infection when the expected MIC was ≥ 1 mg/L. The probability of nephrotoxicity was minimal at 0.2–4% with gentamicin doses of 5–10 mg/kg/day for 3 days.

Conclusions: Once daily gentamicin doses of 6–7 mg/kg are recommended to prevent infections in patients with multiple trauma. Gentamicin monotherapy could not be recommended for serious infections. Further clinical studies are required to confirm our results.

Key Words: Gentamicin, multiple trauma, pharmacodynamics, pharmacokinetics, surgical site infection

INTRODUCTION

Surgical site infections (SSIs) have been reported as high as 50% in trauma patients with Gustilo-Anderson Type-III open bone fractures.^[1,2] Contaminated traumatic wounds can lead to nonunion of bone, osteomyelitis, and life-threatening complications, including sepsis.^[3,4] Therefore, early antibiotic prophylaxis is strongly recommended for preventing complications from infection.^[5,6] The Eastern Association for the Surgery of Trauma recommends a combination of ceftazidime and gentamicin in trauma patients with type II and III open fractures.^[7] This combination showed to reduce

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