

Piperacillin-vancomycin effectiveness by PK/PD approach in septic burn patients receiving the empiric dose regimen recommended for renal failure

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Introduction: Critically ill burn patients present pharmacokinetics (PK) changes at the earlier stage of septic shock that can impact the desired outcome. Additionally, these patients usually present renal insufficiency and antibiotic drug effectiveness depends on adequate dose adjustments according to renal function and drug serum levels.

Objective: To investigate drug effectiveness and safety of combined therapy of vancomycin with piperacillin/tazobactam to avoid renal toxicity of vancomycin or neurotoxicity of the β -lactam.

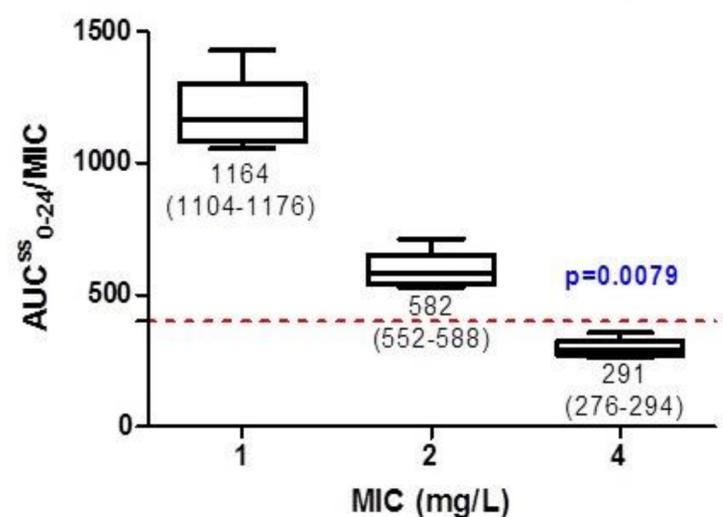
Methods: Septic burn patients with renal dysfunction receiving adjusted dose regimen were considered. Therapy started with vancomycin 1g q24h (1-hour infusion) and piperacillin/tazobactam 2.25g q6-8h (3-hours infusion). Three blood samples were collected (2 mL/each) at the same time dose interval for drug serum measurements through liquid chromatography. PK data was based on noncompartmental analysis. PK/PD approach was performed based on recommended predictive index: $AUC/MIC > 400-600$ for vancomycin; $100\% fT > MIC$ for piperacillin.

Results: Ten adult burn patients (2F/8M) were investigated: 33 (31-42) years, medians (quartiles), 69 (60-80) kg, total burn surface area 43 (32-49) %; creatinine clearance was 31 (23-40) mL/min. The burn agent was fire, inhalation injury occurred in 6/10 patients. Tracheal intubation and vasoactive drugs were required for all patients, but hemodialysis for none. Pharmacokinetics was altered in a different manner for hydrophilic antimicrobials in burn patients with renal failure. Vancomycin target was attained against isolated gram-positive pathogens, MIC 2 mg/L (*Streptococcus spp*, MIC 0.5 mg/L, *Staphylococcus spp* MIC 0.5-2 mg/L) with renal function-adjusted dose (Figure 1A).

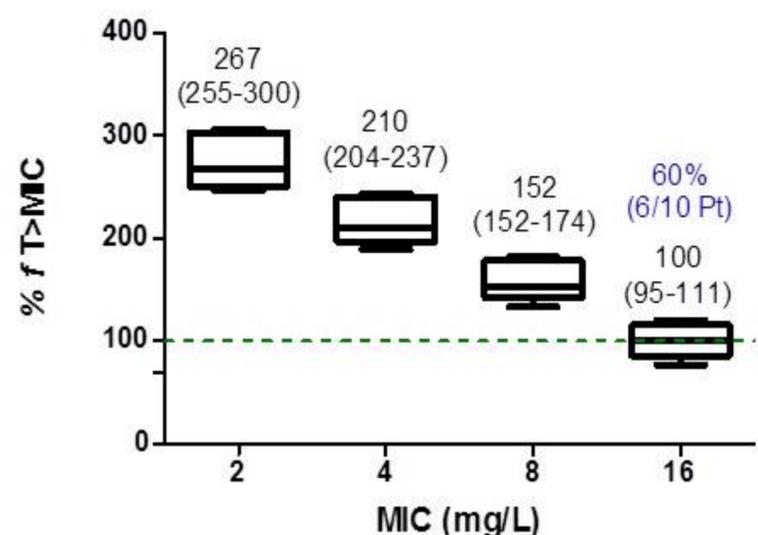
Results: The target was reached to piperacillin empirical dose regimen for all patients against MIC 8 mg/L, strains; while additional dose adjustment was required in 4/10 patients against strains *K. pneumoniae* and *Pseudomonas aeruginosa* with MIC 16 mg/L (Figure 1B). Clinical cure was registered for all patients by eradication of isolated pathogens during the clinical course of septic shock.

Figure 1: Vancomycin and Piperacillin combined therapy in septic burns for drug effectiveness, medians (quartiles, min/max values).

Vancomycin effectiveness - Target $AUC^{ss}_{0-24}/MIC > 400$



Piperacillin effectiveness - Target $100\% fT > MIC$



Conclusion: Drug serum monitoring and PK/PD approach are considered clinically relevant tools to guarantee target attainment for cure of nosocomial infections and safety of combined therapy in critically ill burn patients with renal failure.