



Piperacillin-Tazobactam effectiveness by comparison of dose regimens for septic burn patients requiring vasopressors by applying pharmacokinetics-pharmacodynamics (PK/PD) approach

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Introduction Piperacillin combined with tazobactam is largely prescribed to septic patients undergoing intensive care of nosocomial infections caused by Gram-negative strains. Recommended dose cannot achieve the target after the intermittent infusion, once serum levels result below those required for effectiveness against MIC strains higher than clinical breakpoint. outcome [1].

Objective

Rational of study was to investigate piperacillin efficacy in burn patients receiving the dose regimens recommended in our hospital based on PK/PD approach against nosocomial susceptible Gram-negative strains.

Methods

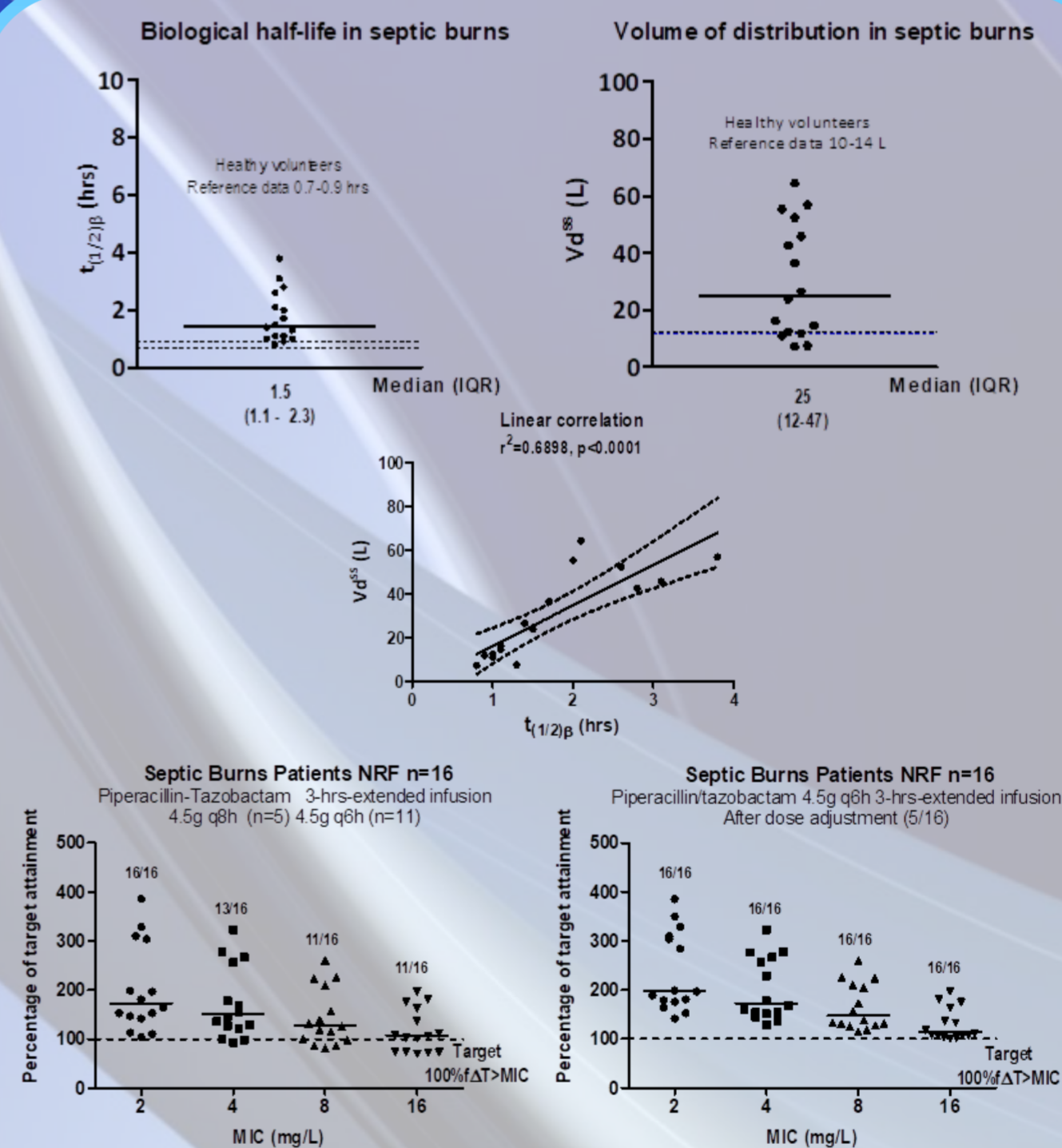
- Ethical approval was obtained and no conflicts of interest to declare for all authors were obtained.
 - Critically ill burn patients (12M/4F) with renal function preserved were included in the protocol.
- Patients undergoing therapy with TAZOCIN by 3hrs-extended infusion: 4.5g q8h (G1: 5 patients) or 4.5g q6h (G2:11 patients)
- Blood sampling for serum measurements: at the steady state 3rd and 5th hrs of start piperacillin infusion, done by LC-UV [2].
 - Pharmacokinetics (PK): noncompartmental data analysis: PK-data of septic patients compared with healthy volunteers [3].
 - PK/PD approach: target attainment (PTA) based on the predictive index of drug efficacy ($\%f\Delta T > MIC$) for the therapeutic target, $100\%f\Delta T > MIC$, considered [4].

References: [1] Silva Junior *et al.* (2017). [2] Sanches *et al.* (2013). [3] Occhipinti *et al.* (1997). [4] Abdul-Aziz *et al.* (2016)

Results

Characteristics of patients at admission were:

- 32 (24-41) yrs, 70 (62-75) kg body weight, 22 (14- 37) % total burn surface area, SAPS3 62 (35-67), medians (IQR). Inhalation injury (13/16), MV-vasopressors in all of them. *SAPS Simplified Acute Physiology Score*
- PK-changes that impact drug effectiveness was found.
- Target was attained for 11 patients by eradication of nosocomial pathogens up to MIC 16 mg/L after 4,5g q6h.
- Dose adjustment was required for target attainment in 5/16 patients receiving 4.5g every 8 hours at the initial therapy.
- Clinical and microbiological cure occurred for all patients after dose adjustment.



Conclusion

- Superiority of the dose regimen Piperacillin/Tazobactam 4.5g q6h over 4.5g q8h after 3hours extended infusion was demonstrated, once after dose adjustment clinical cure was reached in the rest of them.
- Then, piperacillin serum monitoring must be done routinely in critically ill septic burn patients to reach soon the desired outcome based on PK/PD approach done in a real time, an important tool considered for cure of infections, and to avoid the microbial resistance.