# Population Pharmacokinetic Study of Amoxicillin-Treated Burn Patients Hospitalized at a Swiss Tertiary-Care Center

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## Abstract

**Purpose:** The objective of this study was to investigate the population pharmacokinetics (PK) of amoxicillin in ICU burn patients and the optimal dosage regimens.

**Methods:** This was a prospective study involving 21 consecutive burn patients receiving amoxicillin. PK data were analyzed using nonlinear mixed-effects modeling. Monte-Carlo simulations assessed the influence of various amoxicillin dosage regimens with identified covariates on the probability to achieve a target (PTA) value of time during which free amoxicillin concentrations in plasma exceeded the MIC (*f*T>MIC).

**Results:** A two-compartment model best described the data. Creatinine clearance ($CL_{CR}$) and body weight (BW) influenced amoxicillin CL and central volume of distribution ($V_1$), respectively. The median $CL_{CR}$ (Cockcroft-Gault formula) was high (128 ml/min), with 25% of patients having $CL_{CR}$ of > 150 ml/min. The CL, $V_1$, and half-life ($t_{1/2}$) values at steady state for a patient with a $CL_{CR}$ of 110 ml/min and BW of 70 kg were 13.6 liters/h, 9.7 liters, and 0.8 h, respectively. Simulations showed that a target *f*T>MIC of ≥ 50% was achieved (PTA > 90%) with standard amoxicillin dosage regimens (1 to 2 g every 6 to 8 h [q6–8h]) when the MIC was low (<1 mg/liter). However, increased dosages of up to 2 g/4 h were necessary in patients with augmented $CL_R$ or higher MICs. Prolonging amoxicillin infusion from 30 min to 2 h had a favorable effect on target attainment.

**Conclusions:** In conclusion, this population analysis shows an increased amoxicillin CL and substantial CL PK variability in burn patients compared to literature data with nonburn patients. Situations of augmented $CL_{CR}$ and/or high bacterial MIC target values may require dosage increases and longer infusion durations. (This study has been registered at ClinicalTrials.gov under identifier NCT01965340.)

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