

Ertapenem is used off-label to treat osteoarticular infections but there are few pharmacokinetic (PK) data to guide optimal dosing strategies in patients who may be obese with multiple co-morbidities including diabetes and peripheral vascular disease” Chambers et al (2018).

Abstract:

PURPOSE: Ertapenem is used off-label to treat osteoarticular infections but there are few pharmacokinetic (PK) data to guide optimal dosing strategies in patients who may be obese with multiple co-morbidities including diabetes and peripheral vascular disease.

METHODS: Participants undergoing lower limb amputation or elective joint arthroplasty received a dose of intravenous ertapenem prior to surgery. Eight plasma samples were collected over 24 h, together with at least one bone sample per patient. Ertapenem concentrations in plasma and bone were measured using liquid-chromatography/mass-spectroscopy and analysed using non-linear mixed effects PK modelling.

RESULTS: Plasma and bone concentrations were obtained from 10 participants. The final population PK model showed that a fat free body mass was the most appropriate body size adjustment. Ertapenem diffused rapidly into bone but concentrations throughout the 24 h dosing period were on average 40-fold higher in plasma, corresponding to a bone to plasma ratio of 0.025, and highly variable between individuals. Simulations demonstrated a high probability of target attainment (PTA) for free plasma concentrations when the minimum inhibitory concentrations (MIC) were ≤ 0.25 mg/L. By contrast, at MICs of 0.5 mg/L and ≥ 1 mg/L, the fractions of patients attaining this target was $\sim 80\%$ and 40% , respectively. In bone, the PTA was $\leq 45\%$ when the MIC was ≥ 0.25 mg/L.

CONCLUSION: Local bone and free plasma concentrations appear adequate for osteoarticular infections where Enterobacteriaceae are the main causative pathogens, but for Staphylococcus aureus and other bacteria, conventional dosing may lead to inadequate PTA.

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Reference:

Chambers, J., Page-Sharp, M., Salman, S., Dyer, J., Davis, T.M.E., Batty, K.T. and Manning, L. (2018) Ertapenem for osteoarticular infections in obese patients: a pharmacokinetic study of plasma and bone concentrations. *European Journal of Clinical Pharmacology*. December 4th. .

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