

Dose optimization of β -lactam antibiotics in children: from population pharmacokinetics to individualized therapy

Abstract

Introduction: β -Lactams are the most widely used antibiotics in children. Their optimal dosing is essential to maximize their efficacy, while minimizing the risk for toxicity and the further emergence of antimicrobial resistance. However, most β -lactams were developed and licensed long before regulatory changes mandated pharmacokinetic studies in children. As a result, pediatric dosing practices are poorly harmonized and off-label use remains common today.

Areas covered: β -Lactam pharmacokinetics and dose optimization strategies in pediatrics, including fixed dose regimens, therapeutic drug monitoring, and model-informed precision dosing are reviewed.

Expert opinion/commentary: Standard pediatric doses can result in subtherapeutic exposure and non-target attainment for specific patient subpopulations (neonates, critically ill children, e.g.). Such patients could benefit greatly from more individualized approaches to dose optimization, beyond a relatively simple dose adaptation based on weight, age, or renal function. In this context, Therapeutic Drug Monitoring (TDM) and Model-Informed Precision Dosing (MIPD) emerge as particularly promising avenues. Obstacles to their implementation include the lack of strong evidence of clinical benefit due to the paucity of randomized clinical trials, of standardized assays for monitoring concentrations, or of adequate markers for renal function. The development of precision medicine tools is urgently needed to individualize therapy in vulnerable pediatric subpopulations.