TDM-guided clinical pharmacological advices for personalization of antimicrobial treatment in critically ill children

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Drug pharmacokinetic in the first decade of life and early childhood is unexpectedly different from that displayed in adults and attaining therapeutic concentrations frequently challenges prescribing physicians.
Moreover, pediatric population is traditionally burdened by a lack of information for dose selection. In particular for anti-infective therapies, few guidelines can effectively inform on the most appropriate dose to choose in different clinical scenarios.
In recent years therapeutic drug monitoring (TDM) has been gaining relevance in personalizing drug regimens in antibiotic chemotherapies, with the intent both of ensuring an adequate plasmatic exposure according to PK/PD principles and avoiding toxicities related to high antibiotic concentrations. However, in order to provide a significant impact on the pharmacological management, TDM results have to be carefully interpreted in light both of the patient pathophysiological characteristics (taking into account clearance variability, site of infection, drug interactions) and microbiological susceptibility of the isolated pathogen, and a clinical pharmacological advice (CPA) suggesting dose adjustments should be provided.
The objective of this retrospective evaluation is to assess the role of clinical pharmacological advices based on therapeutic drug monitoring in tailoring antimicrobial therapies in the critically ill children. This work involved 47 pediatric patients treated with meropenem (n=16 patients; male/female:5/11; mean age: 10.7±5.0 yrs; mean weight: 37.7±21.6 kg), linezolid (n=16 patients; male/female: 11/5; mean age: 9.6±5.4 yrs; mean weight: 37.8±24.2 kg) and the antifungal agent voriconazole (n=15 patients; male/female: 6/9; mean age: 10.2±4.8 yrs; mean weight: 36.6± 17.8 kg) who underwent real-time TDM.
At first TDM 68.7%, 37.5% and 66.6% of patients treated with meropenem, linezolid and voriconazole respectively, were underexposed. In particular trough concentrations (Cmin) expressed as median and IQ range were 3.93 [2.5-13.5] mg/L for meropenem (desired range: 8-12 mg/L), 3.29 [0.83-5.89] mg/L for linezolid (desired range: 2-7 mg/L) and 0.74 [0.37-1.48] mg/L for voriconazole (desired range: 1-5.5 mg/L) respectively. The posologic regimen was 126.7 [78.6-161.9] mg/kg daily, 25.63 [20.4-30.0] mg/kg daily and 8.9 [7.9-10.1] mg/kg daily for meropenem, linezolid and voriconazole respectively.
The median number of CPAs for each patient was 1 [1-2] for meropenem, 2 [1-2] for linezolid and 2 [1-4.5] for voriconazole.
After dose adjustments, in those patients having further CPAs, median Cmin improved at 9.34 [6.2-13.4] mg/L for meropenem, 3.7 [2.0-4.9] mg/L for linezolid and 1.99 [1.2-2.2] mg/L for voriconazole.
In conclusion, clinical pharmacological interpretation of therapeutic drug monitoring results may allow a personalization of antimicrobial drug exposure in the pediatric population and can fill the gap between the paucity of pharmacokinetic studies devoted to identify the most appropriate antibiotic dosages and the needs of clinical practice.