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Development of an on-line application to support a programme aimed to evaluate antimicrobial dosing optimization without therapeutic drug monitoring in critically ill patients in Brazil

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Background: Enhancing the quality of prescribing and administration of antibiotics should be considered a key priority for improving therapeutic outcomes and suppressing the increasing rates of resistance that is presently observed worldwide. The availability of therapeutic drug monitoring (TDM) for many of the commonly used antibiotics is a rarity in a considerable number of centers around the world. Alternatively, the use of a widely available web based application utilizing population PK models and sophisticated simulation algorithms may have the potential to be a valuable tool in optimizing PKPD indices. The aim of this study was to describe the process of modifying an on-line dose optimization application to meet the needs of a program designed to evaluate the adaptation of published population PK models for dose optimization in the absence of TDM into the care of Brazilian critically ill patients.

Material/methods: Piperacillin and tazobactam PK models are coded into Individually Designed Optimum Dosing Strategies (ID-ODSTM) on - line using the R language to provide the necessary background for the high - level computations to estimate concentration - time profiles for 5000 virtual patients per simulation. The user provides patient demographic and laboratory information (including MICs) via a user friendly html interface in international units. PTAs for up to 200 short and extended infusion regimens from 2000 to 8000 mg of piperacillin at 50 mg intervals given every 12, 8, 6 and 4 hours for the target $fT>MIC$ of 50% for MICs up to 32 $\mu\text{g/ml}$ in serum are established assuming 70% protein binding and lognormal distribution for all pharmacokinetic parameters.

Results: PTAs for all simulated regimens are evaluated and a subset reaching 90% or more is separated for further analysis to provide the dosing regimen that achieves the optimal target at the pre-specified MIC with the least amount of drug in mgs to be administered in a 24 h time period. Once computation is accomplished, clinically relevant information including patient demographics, suggested dosing regimens, PTAs, and creatinine clearance will be displayed using uncomplicated and adequately descriptive plotting designs and in the Portuguese language (Figure 1. and 2.).

Conclusions: The development of this modified application provides the foundations for a multi-model based, point of care clinical decision support tool on the web and mobile devices for clinicians focusing on optimizing antimicrobial therapy. In the absence of available and affordable TDM, this system will be used to evaluate the adaptation of published population PK models for dose optimization into the care of the Brazilian critically ill patients. By setting the application to give the dosing regimen that uses the lowest amount of drug per day, the cost will also be kept to the minimum necessary to provide optimal exposure.

Piperacillin and Tazobactam

Piperacillin and Tazobactam

Idade (anos)

Altura (cm)

Peso (kg)

Sexo

Creatinina (mg/dl)

CIM (mg/L)

Modelo

Identificação do paciente

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