The importance of a fast-track pharmacology for the proper management of antibiotic therapy in intensive care units

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Introduction

Multidrug-resistant (MDR) organisms are common in patients in intensive care units (ICU) (1). As a result, these patients have substantial mortality rates (40–65%), particularly if they have a high severity of illness score, sepsis and septic shock (2, 3).

Given this background, immediate and appropriate antibiotic therapy – defined as timely commencement of pharmacologic treatment with appropriate spectrum for the pathogen(s) – is mandatory to improve the clinical outcome of ICU patients (4). Antibiotic therapy for ICU patients is initially empirical, but it is revised when the results of the microbiological tests are available. Previously, results were obtained in 48–96 hours after collection of specimens, however, in recent years, a number of novel technologies for the microbiological diagnosis of infections have been developed, providing results in a shorter time frame compared with conventional diagnostic approaches (5, 6). They include multiplex polymerase chain reaction (PCR), matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) and lateral flow assays or immuno-chromatographic methods. These technological improvements opened the era of „fast-track microbiology", a concept firstly introduced by Mulatero et al. in 2011 (6). He proposed the following definition: "fast microbiology is based on a premise of faster results, reducing the time needed for a result, to allow earlier and optimized patient management". There is no universal consensus on the definition of 'fast', but it is reasonable to describe it as obtaining the result within a working day shift (i. e. 8 h).

Pharmacologic issues of antibiotics in ICU patients

Beyond microbiology, successful treatment of severe infections in ICU is based on a proper antimicrobial stewardship program (7). This includes the selection of the most appropriate antibiotic agent(s), ensuring the adequate exposure, whilst taking into consideration both pathophysiologic changes of ICU patients and physicochemical properties of the antimicrobial agent(s) administered to reach optimal pharmacokinetic/pharmacodynamic (PK/PD) targets (8–10).

Indeed, a basic understanding of PK is important for clinicians when prescribing drugs. This is particularly true for antibiotics since under-dosing may result in treatment failure, increasing the likelihood of the development of antimicrobial resistance (9). The achievement of optimal antibiotic exposure is difficult in clinical practice because most of these drugs are administered according to standard dosing regimens. They do not take into account pathophysiologic and/or iatrogenic factors that are likely to affect the PK in ICU patients. This makes the management of antibiotic therapy extremely challenging in these patients (9, 10). The main effects of altered pathophysiology in ICU patients on the antibiotics PK are summarized in Table 1.

Therapeutic drug monitoring: analytical aspects

Therapeutic drug monitoring (TDM) is the clinical practice of measuring drugs with the aim of optimizing the individual dosage regimens. This approach is usually adopted in patients treated with narrow therapeutic index drugs, such as the aminoglycoside antibiotics. However, there is increasing evidence of TDM use for drugs with a wide therapeutic index, especially in the ICU setting. Nevertheless, in order to consider TDM clinically useful, validated bioanalytical assays with a rapid turnaround time for the quantification of anti-infective drugs in biological matrices are essential. Historically, the analytical approach for TDM in serum or plasma used gas chromatography or high performance liquid chromatography (LC)

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Cit. zkr: Klin Farmakol Farm 2023;37(3):86-88
Článek přijat redakcí: 24. 7. 2023