Editorial

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Is Therapeutic Drug Monitoring of Teicoplanin Useful?

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Vancomycin and teicoplanin are the glycopeptides currently in use for the treatment of infections caused by beta-lactam-resistant gram-positive organisms [1]. Teicoplanin, a glycopeptide antibiotic, has a lower possibility than vancomycin to cause renal toxicity, and causes fewer anaphylactoid reactions [2]. Teicoplanin has been found to be comparable to vancomycin in efficacy [1]. As teicoplanin can be administered once daily intramuscularly as well as intravenously, it can be used for outpatient therapy of methicillin-resistant staphylococcal infections [1]. Teicoplanin completely excreted unchanged in the urine by glomerular filtration, and doses should be reduced appropriately in patients with renal dysfunction. Its pharmacokinetics include a prolonged terminal half-life of 150 to 180 h, which is important during long-term therapy [1].

Usual dose and dosing interval of teicoplanin for IV injection or infusion consist initially 400 mg every 12 hours for 3 doses and subsequently 200 mg once daily (400 mg once daily for severe infections) [1, 3]. Higher doses are recommended in patients over 85 kg, or in severe burns or methicillin-resistant *Staphylococcus aureus* (MRSA) infection [1, 3]. For streptococcal endocarditis, initially 6 mg/kg every 12 hours for 3 doses, then 6 mg/kg once daily are typical [1, 3]. For enterococcal endocarditis, initially 10 mg/kg every 12 hours for 3 doses, then 10 mg/kg once daily are standard. For child, initially 10 mg/kg every 12 hours for 3 doses, subsequently 6 mg/kg once daily (10 mg/kg once daily for severe infections or in neutropenia) is a typical regimen [1, 3].

Vancomycin level monitoring is common in the hospitals with increasing minimal inhibitory concentration (MIC) of *S. aureus* ("MIC creep") [1]. For complicated infections (bacteremia, endocarditis, osteomyelitis, meningitis, and hospital-acquired pneumonia) and for infections caused by strains with MICs of >1 μg/mL, trough levels of 15 to 20 μg/mL are recommended [1]. Larger vancomycin doses are associated with increased nephrotoxicity [1], and monitoring of vancomycin trough serum levels is recommended in the view of avoiding nephrotoxicity [4].

Therapeutic drug monitoring (TDM) of teicoplanin is not routine because of the lack of evidence for dose-related adverse effects of teicoplanin [3]. However, measuring of teicoplanin plasma concentrations may help to optimize therapy in some patients. Data of teicoplainin TDM are largely lacking [1]. Harding et al. [5] reported the probability of successful treatment increased with mean pre-dose (trough) serum concentration of teicoplanin and reported that a mean daily dose of 4 mg/kg was associated with treatment failure when compared to a

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mean daily dose of 6 mg/kg [5]. Also, Harding et al. [5] suggested successful treatment of *S. aureus* septicemia with teicoplanin requires trough plasma teicoplanin concentration of >10 mg/L as a result of simulation. According to previous reports, higher trough concentrations > 20 mg/L and > 30 mg/L of teicoplanin are considered to be needed for MRSA endocardtis and osteomyelitis, respectively [6, 7].

Nah et al. [8] investigated the TDM of teicoplanin in clinical setting with Korean patients. They reported that there is the suboptimal concentration (< 10 mg/L) of plasma teicoplanin level in nearly half of the study patients in spite of the majority of the patients received loading dose as recommended (400 mg every 12 hours for three times), and emphasized the importance of loading dose and routine TDM of teicoplanin [8]. This article focused the roles of TDM for the optimal efficacy of therapeutic drug, not for avoiding adverse effects of a drug.

An area under curve (AUC)/MIC value of ≥400 was associated with a successful outcome with human pharmacodynamic study for vancomycin [9]. The vancomycin target was identified in patients with pulmonary infections [9]. However, established pharmacodynamic targets were not available for teicoplanin [10]. An AUC/MIC value of teicoplanin to *Staphylococcus* considered important pharmacodynamics parameter [10]. There is no information about MIC values of pathogens and AUC/MIC values and a peak concentrations in the study by Nah et al. [8]. The TDM for vancomycin therapy has been shown to be a cost-effective procedure [11]. However, cost effective study of teicoplanin TDM is still largely lacking. Nah et al. [8] reported the first study about teicoplanin TDM in Korea, which emphasize the importance of loading dose and TDM of teicoplanin. The limitations of this study include that the association between plasma concentrations of teicoplanin and clinical therapeutic effects are not evaluated.

We can expect the usefulness of teicoplanin TDM in the same respect of vancomycin TDM. However, we are currently in need of data of pharmacokinetics, clinical pharmacodynamics and TDM of teicoplanin in clinical setting, because of its current significant role for anti-MRSA treatment.

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