Adherence to guidelines for therapeutic monitoring of glycopeptide and aminoglycoside antibiotics

Sascha Karlen\textsuperscript{a}, Stefan P. Kuster\textsuperscript{b}, Emmanuel Eschmann\textsuperscript{c}, Stefan Weiler\textsuperscript{c}, Jürg Blaser\textsuperscript{c}

\textsuperscript{a} Medical Informatics Research Centre, Directorate of Research and Teaching, University Hospital, Zurich, Switzerland; \textsuperscript{b} Division of Infectious Diseases and Hospital Epidemiology, University Hospital and University of Zurich, Switzerland; \textsuperscript{c} Division of Clinical Pharmacology and Toxicology, University Hospital, Zurich, Switzerland

**Introduction**

Guidelines for therapeutic drug monitoring (TDM) have been established for glycopeptide and aminoglycoside antibiotics because of their narrow therapeutic windows, in order to ensure therapeutic efficacy and to avoid toxic overdosing with nephro- or otoxicity. The purpose of this quality control study was to determine adherence to TDM guidelines for the aminoglycoside gentamicin and the glycopeptides vancomycin and teicoplanin in order to assess the need for improvements.

**Methods**

We included all inpatients admitted to the University Hospital Zurich over a 3-year period from 1 January 2012 to 31 December 2014. All electronic orders of intravenously administered gentamicin, vancomycin and teicoplanin, and the corresponding TDM laboratory orders, were analysed retrospectively. Medication orders during intensive care stays were not electronically available and were therefore excluded.

Institutional guidelines released in 2011 provided recommendations for initial monitoring at intervals no longer than 72 h for gentamicin, 60 h for vancomycin and 96 h for teicoplanin. Shorter initial TDM intervals have been advised for patients with impaired renal function and for three times as opposed to once-daily dosing of gentamicin. Guidelines released in 2014 proposed shorter intervals for gentamicin and teicoplanin. In this analysis, however, these shortened intervals have not been considered.

Courses of drug therapy may be prescribed as single or multiple subsequent orders (e.g., for dose adjustments). Therefore, subsequent prescriptions separated by ≤24 h were considered as single continuous courses of therapy. To analyse the adherence to guidelines we measured the time period between the start of drug therapy and the initial TDM.

**Results**

Drug therapies administered to 115 509 inpatients were analysed, including 470 courses of gentamicin therapy consisting of 1045 orders, 2396 courses of vancomycin with 6168 orders and 807 courses of teicoplanin with 2184 orders.

Treatment was administered for less than 72 h in 40% (188/470) of gentamicin, 41% (985/2396) of vancomycin and 26% (209/807) of teicoplanin courses.

Treatment lasting ≥72 h was monitored according to guidelines for gentamicin in 72% (203/282) of courses, for vancomycin in 67% (939/1411) and for teicoplanin in 63% (379/598).

Treatment lasting ≥96 h was monitored within 72 h for gentamicin in 74% (178/241) of courses, for vancomycin in 74% (907/1224) and for teicoplanin in 50% (275/552).

Treatment of ≥120 h was not monitored at all for gentamicin in 7% (14/208), for vancomycin in 7% (68/1046), and for teicoplanin in 13% (66/512) of courses.

**Conclusion**

Physicians’ adherence to TDM guidelines was only 72% or below, with the best compliance for gentamicin. Overall TDM adherence has room for improvement and quality assurance actions have to be considered. Educational programs require a continuous effort. As a complementary measure computerised decision support might be implemented. Automated reminders could be displayed in the medical record whenever TDM is overdue. The same algorithms might also be applied to other therapies that have to be monitored according to guidelines. Studies are needed to evaluate the impact of these concepts on patients’ safety, treatment efficacy and overalerting of physicians.

**Disclosure statement**

No potential conflict of interest relevant to this article was reported.