The Effect of the time of administration on the Clearance of Aminoglycosides in General Ward and ICU patients

Erik van Maarseveen¹, Wai Hong Man¹, Johannes Proost², Cees Neef³, Daniël Touw⁴

1 Department of Clinical Pharmacy, University Medical Center Utrecht, The Netherlands
2 Department of Pharmacokinetics, Groningen, University of Groningen, Faculty of Mathematic and Natural Sciences, The Netherlands
3 Department of Clinical Pharmacy, Maastricht University Medical Center, The Netherlands
4 Apotheek Hoogte Ziekenhuizen & HagaHospital The Hague, The Netherlands

Objective
To determine whether time of administration affects the clearance of aminoglycosides in ICU and general ward patients.

Introduction
• Patients with a low renal clearance of aminoglycosides (AMG’s) are at increased risk of developing AMG-related nephrotoxicity;
• With the introduction of once-daily-dosing (ODD) the time of administration could affect treatment outcomes;
• Multiple studies have demonstrated an effect of the time of administration on the clearance of AMGs;
• However, this effect has never been studied in a large population of critically ill or general ward patients on ODD. Therefore, we examined the relation between time of administration and clearance of AMGs in these patients.

Methods
In this retrospective analysis ICU and general ward patients, admitted at any hospital in The Hague (The Netherlands) between Jan 2001 and Dec 2009, who were treated with i.v. tobramycin (TOB) or gentamicin (GEN) were included. Patients had to be over 18 years of age, have an estimated creatinine clearance higher than 25 mL/min and receive a once daily dose larger than 4 mg/kgLBM. Finally, a peak level drawn 0.5-1 h and a second level drawn 6-14 h after end of infusion had to be available. Patients were divided into three groups by time of administration: 6:00-12:55 (morning), 13:00-18:00 (afternoon) and 21:00-3:00 (night). Pharmacokinetic parameters were calculated using an iterative 2-stage Bayesian procedure (MWPharm 3.80) and a local pharmacokinetic model. AMG clearance, AUC and volume of distribution were compared by a Student’s t-test. A p-value less than 0.05 was considered to be statistically significant.

Results
A total of 389 ICU patients and 207 general ward patients were divided into the morning, afternoon and night groups. No significant differences were found in patient characteristics between the three groups in both populations (Table 1). There were no statistically significant differences in clearance, AUC and volume of distribution between the morning, afternoon and night groups in both populations.

Conclusions
This large retrospective study shows that the time of administration had no influence on clearance, AUC and volume of distribution of TOB and GEN in ICU and general ward patients. Consequently, an effect on treatment outcomes is unlikely.

Recommendations
AMGs should be started as soon as possible in case of (suspected) severe hospital-acquired pneumonia or sepsis and subsequent dosages should thereafter consequently be administered every 24 hours in order to minimize toxicity without compromising efficacy.

References

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