Balancing between sepsis, AKI and gentamicin in the emergency department

Chapter 8

Impact for society

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Aminoglycosides, such as gentamicin, are antibiotic drugs that are considered harmful to the kidneys when not used properly. Therefore, there is frequent hesitation in administering these drugs in severely ill patients with sepsis despite there being an indication. However, in a world with increasing antibiotic resistance it is important to keep all antibiotic options open since the options for appropriate empirical antibiotic therapy with the commonly used broad spectrum antibiotics are becoming fewer. Since aminoglycosides kill bacteria rapidly and there is a low resistance rate, it is important to establish the safety and to optimise the use of these agents as the role of aminoglycosides in the treatment of sepsis will possibly increase in the future era with increasing antibiotic resistance.

Previously, the toxicity of aminoglycosides on the kidneys was mostly studied in ICU patients. However, patients often present themselves with sepsis in the emergency department (ED) and the patients in the ED are often less severely ill.

It is likely that the results of ICU studies cannot be extrapolated to ED patients, because the spectrum of sepsis as seen in these patients in the ED differs.

Our studies were the first to evaluate the effect of a single dose of gentamicin in patients with sepsis in the ED. In two different studies, we established that it is safe to administer a single dose of gentamicin to patients with sepsis in the ED with regard to renal function.

Subsequently, we showed that underdosing of gentamicin is a common finding in the ED. In addition, even when the aimed dose of gentamicin is administered, we measured insufficient gentamicin blood levels in a large number of patients, which consequently could lead to potential treatment failure and eventually to worse outcome. After these findings, simulations were executed to determine which dose would be needed to reach adequate gentamicin blood levels. Using the results of these simulations, a new dosing regimen for gentamicin was introduced by the Antibiotic Committee of the Maastricht University Medical Center+. The dose of gentamicin was increased from 5 mg/kg to 7 mg/kg body weight. After the implementation of this new

dosing regimen, gentamicin blood levels were measured again and we found that a gentamicin dose of 7 mg/kg turned out to be sufficient in the majority of patients.

We established that a single dose of gentamicin is safe with regard to renal function. In addition, we showed ways to optimise the use of gentamicin in the ED, which other hospitals and physicians can use to optimise their own antibiotic treatment protocols. Since sepsis is a life-threatening condition and the incidence of sepsis is increasing over the years, adequate antibiotic treatment is of the utmost importance. The findings of our studies are useful for all physicians of all specialties treating patients with sepsis and can help to make a well-informed choice on appropriate and adequate antibiotic therapy in patients with sepsis.

Due to the possible serious side effects of aminoglycosides, since 2018 the Dutch Health and Youth Care Inspectorate (IGJ) demands that informed consent should be obtained when aminoglycosides are administered. However, we showed that a single dose of gentamicin is safe with regard to renal function. Therefore, maybe such a strict disposition is not necessary for only one dose.

The findings of our studies were published in peer-reviewed journals and if possible as an open access manuscript to make them freely accessible via the internet for a broad public, including developing countries. The general public can benefit from the results of our studies due to more appropriate and adequate antibiotic therapy in terms of antibiotic coverage, in a time with worldwide increasing antibiotic resistance.