Case report

Amikacin - treatment of an urinary tract infection in a hemodialysis patient – what may be eventually missed?

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Abstract

The study is presenting a clinical case of a diabetic patient on regular haemodialysis treatment with an exacerbated urinary infection, demonstrated by fever, microhematuria, disuria and significant bacteriuria. The urinary bacterial infection (Pseudomonas aeruginosa $>10^5$, sensitive to amikacin) was treated ineffectively by an aminoglucoside (amikacin) until pH of the urine was changed to slight alkaline level – the appropriate media in which aminoglucosides are effective and reasonably applied. The successful treatment after alkalization proved that pH of the media is of great importance for aminoglucoside's therapy and must not be neglected. *Hippokratia 2006; 10(1):39-40*

Key words: *urinary tract infection, aminoglucosides, acid or alkaline media, diabetes mellitus, haemodialysis*

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Introduction

The aminoglycoside antibiotics are bactericidal agents, used predominantly to treat infections caused by gram negative bacteria. Aminoglycosides are also active against some Gram positive bacteria, but in such cases they are not considered agents of primary choice. Enterococcal infections may be treated with a combination including penicillin, ampicillin, or vancomycin. Aminoglycosides may also be used as adjunctive therapy for staphylococcal infections. [1, 2]. The aminoglycosides exhibit similar pharmacokinetics, pharmacodynamics as well as physical, chemical and toxic characteristics. They are concentration dependent antibiotics, i.e. when aminoglycoside concentration increases, the extent of bacterial killing action increases also. While the postantibiotical effect increases with concentration dependent antibiotics, this is not always true about the aminoglycosides. Some data suggest that the postantibiotical effect in Gram negative bacteria may vanish over time with multiple doses of aminoglycoside [3, 4].

Considering the dosing, tobramycin and gentamicin initially have been usually dosed 80 mg every 8 hours or 1.5 mg/kg every 8 hours. Some clinicians have also attempted to individualize the aminoglycoside dose and dosage interval tailored to individual patients needs using pharmacokinetic models. Single daily dosing (SDD) uses daily doses ranging from 3 to 7 mg/kg/day. This treatment regime is designed to produce higher peak concentrations than seen with conventional dosing. The use of the 24 hour dosing interval is tailored to create a period during the dosage interval where there will be essentially no aminoglycoside present. It is believed that the "aminoglycoside-free period" will reduce accumulation of aminoglycosides in tissues such as the inner ear and kidney and will reduce drug related toxicity [3, 4, 5]. The "aminoglycoside-free interval" should also assist in overcoming "adaptive resistance". One large aminoglycoside dose once daily, instead of several divided doses given on multiple occasions through the day, may result in less net transfer of aminoglycoside from the blood to the tissue. Smaller and more frequent doses do not facilitate drug transport into the tissue and ultimately produce higher tissue concentrations than SDD [4, 5]. Thus, between saturation of the amount of aminoglycoside moving into the tissue and the use of an "aminoglycoside-free period," SDD strategies should be less toxic to the patient because of reduction in aminoglycoside tissue accumulation [5].

Aminoglycosides are primarily eliminated unchanged by the kidney through glomerular filtration for approximately 85 to 95% of the dose administered. That is why chronic renal failure requires reduction of the daily aminoglycosides dose and prolonged period of application.

Case report

We present a 68 year-old patient with the following diagnoses: Diabetes mellitus-insulin dependent type; Diabetic nephropathy, retinopathy and neuropathy; Secondary recurrent chronic pyelonephritis; Adenoma prostate; End stage renal disease - on hemodialysis treatment;. Secondary anaemia and hypertention; Uremic, hypertonic and febrile encephalopathy; Uremic and hypertonic cardiomyopathy; Cardiac failure; Psoriasis; Psoriatic arthri-

tis; Urethral catheter for drainage of the urine.

The diabetes had been proved 11 years ago, and a few years later hypertension had been diagnosed. Since year 2001 psoriatic disease and secondary recurrent chronic pyelonephritis had started. 2 years later a low degree cardiac failure and anemia had developed as well. Adenomatous Hyperplasia of prostate had been registered 1 year ago and urinary obstruction developed in the last two months. Two weeks ago the patient had started regular dialysis treatment, because of terminal chronic renal failure.

The patient was admitted urgently in our clinic because during his last regular haemodialysis session he complained of severe fatigue, disorientation, hypertension - 200/100 mm Hg, fever with high temperature – 38.2^0 C. A blood culture for microbiology was taken and some antipyretics were administered. At the end of the session the status of the patient worsened and the patient became unconscious. The glucose blood level was slightly above the normal range – 6.8 mmol/l. Consulting neurologist concluded that there was a temporary disturbance in consciousness, related to the hypertonic reaction and the fever and recommended infusion of mannitol and antihypertensive treatment. The next day the patient regained consciousness but had an almost permanent higher temperature, reaching 39^0 C. The urine in the collecting bag was cloudy and its color was palepink (microhematuria). A randomly selected antibacterial therapy with cephazolin in appropriate doses was started and the urethral catheter was replaced with a new one. On two consequent days urine cultures for microbiology were sent (meanwhile the blood culture was negative). Five days later according to the results, which showed presence of pseudomonas aeruginosa $>10^5$, sensitive to amikacin, the treatment was changed and amikacin was started. At the fourth day from the start of aminoglycoside's therapy the temperature continued to be high and we decided to check urine pH. Not too much surprisingly pH was in the range of 5 - 5.5 and the patient was given oral sodium bicarbonate in high doses to alkalize the pH of the medium (urine) where amikacin had to act. Three days later pH of the urine was in the range of 7.2 – 7.6 and the body temperature decreased to normal levels. The next 3 urine cultures were sterile and the patient's status improved. The antibiotic treatment combined with alkalization of the urine has worked well. The patient was discharged in good health, considering his overall state, with normal body temperature, sterile urine and continuing ambulatory haemodialysis treatment.

Discussion and conclusions

The aminoglycoside antibiotics are predominantly used to treat infections caused by Gram negative bacteria and their effectiveness is much higher than in cases of Gram positive agents. Antibiotic activity of the aminoglycosides is pH dependent. Aminoglycosides are much more active in an alkaline pH.

Their antibacterial action at standard concentrations can be eliminated as the pH reaches 5 to 5.5 and it would be a mistake of the "medical art" to use them without taking into account pH level of the media where the antibiotic has to act [6, 7]. Small changes in the pH of the medium will affect the ratio of ionized and non-ionized aminoglycosides. That is quite important because only the non-ionized aminoglycosides are active. pH is particularly important in therapy of urinary tract infections. Alkalization of the urine with bicarbonate or carbonic anhydrase inhibitors (e.g., acetazolamide) may dramatically increase the antimicrobial effect of the aminoglycosides on bacterial pathogens [7, 8]. Our experience, described in this case report, proved once again that simple fact and we would like to remember the nephrologists and urologists how important could be such a formally negligible detail for a successful treatment.

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