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Nephrotoxicity during aminoglycoside therapy for infective endocarditis

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Background: Aminoglycosides are commonly used in the treatment of infective endocarditis (IE). Because of it's nephrotoxic potential it's place in the treatment arsenal is currently being debated. What is the potential risk of giving short-term therapy (<10 days) vs longer treatment? Will concomitant vancomycin therapy have an additive nephrotoxicity?

Methods & Materials: A cohort study of 128 consecutive patients with IE treated at Sahlgrenska University Hospital, Gothenburg, Sweden 2007 through 2010 evaluated risk factors for kidney dysfunction during treatment and follow-up. Kidney funtion was assessed by estimated glomerular filtration rate (eGFR) recorded prior to, weekly during treatment, 1 month, 3 months and 1 year post-treatment.

Results: A majority of patients (93%) received received combination therapy with tobramycin, 41% also received vancomycin. There was a mean decrease of eGFR from 88.4 to 78.0 mL/min (-11.8%) from start of tobramycin treatment to 1 week post-treatment. The decrease was accentuated 1 month post-treatment (-12.4%). A gradual reversibility was recorded 3 months, and 1 year post-treatment respectively.

Age, total dose of tobramycin, cardiac surgery, concomitant treatment with potential renal toxic drugs, concomitant vancomycin therapy, and elevated tobramycin serum concentrations were associated with accentuated in-hospital decrease in eGFR.

Major risk factors for permanent decrease in kidney function were established after subgroup analyses of comparable groups. A total dose of >2500 mg tobramycin implicated a decreased reversibility of eGFR during 1-year F/U. Concomitant vancomycin + tobramycin therapy caused a 19% loss in eGFR while no reduction followed sequential vancomycin + tobramycin therapy. Patients with an initial eGFR < 39 mL/min had the same decrease and reversibility of renal function as patients with eGFR ≥40 mL/min. Patients with short-term therapy < 10 days had no long-term decrease in renal function.

Conclusion: Total dose of >2500 mg tobramycin therapy caused a decreased reversibility during 1-year F/U, while short-term therapy < 10 days had no impact on long-term kidney function.

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Implant-associated infection after major orthopaedic surgery: biofilm production of staphylococci

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Background: Staphylococci, especially *S. aureus* and *S. epidermidis* remain the leading pathogens of the implant-associated infection (IAI) after major orthopedic surgery due to their pronounced ability to form the biofilms onto orthopedic devices. The aim of our study was to evaluate the biofilm forming ability of the *S. aureus* and *S. epidermidis* strains collected from patients with IAI.

Methods & Materials: A hundred and five *S.aureus* and hundred and seven of *S. epidermidis* strains were studied. The strains were revealed from cultures of samples of soft tissue, aspirats or exsudate as well as from sonicated explanted devices from 189 patients with orthopedic IAI. Antibiotic susceptibility was evaluated by Kirby-Bauer method. We evaluated biofilm formation by the microtiter plate assay using the crystal violet staining described by Christensen et al. (1985), with minor modifications. All the strains were tested in quadruplicate, and the average resulting OD values for each strain were calculated. The biofilm forming ability of staphylococcal isolates was considered such as strong (OD≥0.2), moderate (0.2>OD≥ 0.15) and weak (OD < 0.15).

Results: The obtained results demonstrate that 32.1% of S. aureus and 68.2% of *S. epidermidis* isolates were meticillin-resistant. The strong biofilm forming ability was detected in 33.4% of all tested staphylococci, but 50.6% of the tested isolates were considered weak biofilm formers. Independent of the sourses from which staphylococci were revealed, its biofilm forming ability appears to depend on the type of staphylococci. The strong biofilm forming ability was detected in 35-55% of *S. epidermidis* and only in 28-29% *S. aureus* obtained from different cultured samples. However found 55% of strains *S. epidemidis* recovered from explanted devices to be intense biofilm formers.

Conclusion: *S. epidermidis* has emerged as one of the most important pathogen in IAI. It was shown *S. epidermidis* to be more frequently meticillin resistant compared to the *S. aureus* among IAI related staphylococci. There are also a significant difference between staphylococcal species in favor of *S. epidermidis* in ability to form biofilms. In addition, more than a half of *S. epidermidis* strains isolated from removed devices tend to have the strong ability to form biofilms.

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