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Renal impairment following aminoglycoside therapy in cystic fibrosis

Cystic fibrosis (CF) is a chronic respiratory, life limiting illness in the Caucasian population. Chronic infection with *Pseudomonas aeruginosa* occurs in more than 80% of adults and this contributes to deterioration in lung function over time.[1] A reported long term complication includes renal impairment from presumed cumulative aminoglycoside antibiotics. Aminoglycosides are highly effective against *Pseudomonas aeruginosa* and effectively penetrate the sputum of patients with CF, achieving more effective bacterial killing.[2] The nephrotoxicity of aminoglycosides is reported to be caused by proximal tubular alteration of cell function and cell necrosis.[3]

The study by Smyth *et al*[4] demonstrates increased renal toxicity measured by plasma creatinine following a case controlled analysis of patients undergoing gentamicin therapy for the treatment of cystic fibrosis exacerbation. The authors did not specify the timing of plasma creatinine measurements in relation to gentamicin dosing (ie, was it collected before the gentamicin dose was given or at an interval following the dose). This would have been important to clarify whether renal impairment was present prior to dosing or occurred subsequently. Of further interest is the measurement of creatinine levels following cessation of gentamicin to elucidate whether renal impairment was persistent or document evidence of renal function recovery. Plasma creatinine reflects glomerular function rather than tubular function, which was not measured in this study. Plasma creatinine levels are subject to factors such as dehydration, nutrition and body size, and may not be a sensitive test in detecting renal impairment until well established disease has occurred.[5]

The challenge in quantifying renal impairment in cystic fibrosis is to describe the site of damage (ie, renal tubules versus renal glomeruli) and manifestations of early injury. Early and more accurate measurements of glomerular filtration rate may be attained by measuring the protein, cystatin C,[6] or by utilising nuclear medical scans which provide validated measures by renal clearance of exogenous filtration markers, most commonly diethylenetriaminepentaacetate (DTPA).[7] With regard to tubular injury, excretion of urinary proteins have been proposed as early markers of aminoglycoside induced tubular toxicity. Steinkamp *et al*[8] demonstrated that acute tubular injury measured by excretion of urinary enzymes achieve almost complete recovery after 4 weeks from cessation of aminoglycosides. Ideally, prospective studies should measure renal function (both glomerular and tubular) in aminoglycoside naïve cystic fibrosis subjects and document early renal changes following aminoglycoside administration in a dose dependent manner.

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Authors' response

We welcome Dr Tai's comments on our paper. We described a case control study of acute renal failure in cystic fibrosis (CF)[1] and not a study designed to measure the prevalence, severity or risk factors for renal impairment. Patients with acute renal failure (ARF) were reported to us from 20 UK CF centres and clinical data were extracted retrospectively from the case notes. We therefore adopted a pragmatic definition of ARF (raised plasma creatinine for age with or without oliguria). We agree that substantial renal impairment may occur before a rise in creatinine is seen. However, our intention was to investigate those patients with renal failure requiring dialysis (needed in 13/24 cases) or close monitoring of renal function.[2]

In an earlier paper, we have published the maximum plasma creatinine values seen in patients with ARF, recorded after gentamicin, where this was administered (median creatinine 674 mmol/l (range 124–1972)).[2] At follow-up, 22 of 24 patients had made a full recovery, with a normal plasma creatinine. One patient required long term dialysis (biopsy evidence of diabetic nephropathy prior to ARF) and another long term antihypertensive treatment.

The design of this study did not allow us to assess whether renal impairment was present prior to ARF. The prevalence of renal impairment in adults with CF is reported as 31–42% but the prevalence in children is unknown.[3] We agree that a well designed study of the prevalence and risk factors for renal impairment in children with CF would be useful. We would suggested measuring GFR, using the chromium 51 ethylene diamine tetra acetate (EDTA) test.[4]

Six patients with ARF in our series had biopsy evidence of acute tubular necrosis and two had hypomagnesaemia, which suggests tubular damage.[2] We have previously shown that there is a smaller elevation in proximal tubular enzymes with once daily tobramycin administration than with traditional three times daily treatment.[5] Measures of proximal tubular impairment could be included in a future study of renal impairment in children with CF.

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Bronchial asthma on Mount Kilimanjaro is not a disadvantage

Every year, an increasing number of people travel to high altitude and travellers with asthma are becoming more common in remote environments.[1] It is well recognised that certain situations at high altitude, such as exercising in cold air, may provoke symptoms.[2] However, the mountain