Case Report

Dosage of once-daily gentamicin in spinal cord injury patients

S Vaidyanathan^{*1}, JWH Watt¹, G Singh¹, BM Soni¹ and P Sett¹

¹Regional Spinal Injuries Centre, District General Hospital, Southport, UK

Introduction: In patients with spinal cord injury (SCI), serum creatinine does not accurately reflect the level of renal function. Therefore, in SCI patients, the dose of potentially nephrotoxic drugs should be adjusted on an individual basis from the estimated creatinine clearance.

Case report: A 41-year-old male with tetraplegia due to cervical spinal cord injury underwent extended pyelolithotomy for staghorn calculus in the right kidney. The blood urea level was 9.9 mmol/l; creatinine was 112 μ mol/l (reference range: 0–135). We were conscious of this patient's renal disease, and therefore, administered only 3 mg/kg of gentamicin (240 mg) instead of the standard dose of 5 mg/kg body weight. Despite taking this precaution, the gentamicin level measured 22.5 h after the initial dose, was in the potentially toxic range—3.3 mg/l.

Conclusion: We recommend that even the first dose of gentamicin in the once-daily regimen, which is 5 mg/kg, should be individualised in SCI patients based on age, sex, weight, height, level of spinal cord injury, and renal function.

Spinal Cord (2000) **38**, 197–198

Keywords: gentamicin; spinal cord injury; creatinine clearance; nephrotoxicity; tetraplegia

Introduction

A meta-analysis showed that treatment with single daily doses of aminoglycosides seems to be more effective, less nephrotoxic, and as ototoxic as multiple doses daily.¹ The protocol on once-daily dosing of gentamicin recommends *the first dose of 5 mg/kg with a maximum of 400 mg, which can be given regardless of renal function.* The blood level of gentamicin is then estimated between 12–24 h after the initial dose. (A summary of the protocol can be obtained from the authors). This protocol may not be applicable to all spinal cord injury (SCI) patients as exemplified by this case report.

Case report

A 41-year-old male with tetraplegia due to cervical spinal cord injury underwent extended pyelolithotomy for staghorn calculus in the right kidney. His height was 70.5 inches; weight: 79.5 kg. This patient had stones in the left kidney as well. The blood urea level was 9.9 mmol/l; creatinine was 112 μ mol/l (reference range: 0–135). We were conscious of this patient's renal disease, and therefore, administered only 3 mg/kg of gentamicin (240 mg) instead of the standard dose of

5 mg/kg body weight. The gentamicin level was measured 22.5 h after the initial dose; *it was in the potentially toxic range—3.3 mg/l.* His blood creatinine increased to 160 μ mol/l; urea was 11.5 mmol/l; his potassium level rose to 6 mmol/l. The 24 h urine output, however, remained greater than 2.4 l. There was no co-administration of high-dose furosemide (>160 mg daily on one or more days), other nephrotoxic antibiotics, or non-steroidal anti-inflammatory drugs (e.g. diclofenac).

This patient was not administered any further doses of gentamicin. He was given 50% dextrose and human actrapid insulin through separate intravenous infusions; he received intravenous infusion of 500 ml of 1.26% sodium bicarbonate daily for 3 days. Microbiology of urine showed *Pseudomonas aeruginosa*; this was treated with meropenem given intravenously at a dose of 250 mg every 12 h. After a week, blood tests showed that creatinine level had fallen to 80 μ mol/l; urea level had decreased to 3.5 mmol/l.

Discussion

Nephrotoxicity is defined as a rise in serum creatinine of >45 μ mol/l, if the initial serum creatinine concentration was <270 μ mol/l.² Gentamicin nephrotoxicity is characterised by: reduced creatinine clearance rates,

*Correspondence: S Vaidyanathan, Regional Spinal Injuries Centre, District General Hospital, Southport, Merseyside, PR8 6PN, UK

Table 1 Dosage of once-daily gentamicin in SCI patients based on estimated creatinine clearance

Estimated creatinine clearance	Daily dose of gentamicin
> 80 ml/min	4.0 mg/kg body weight
Between 50 and 80 ml/min	3.25 mg/kg body weight
Between 30 and 50 ml/min	2.5 mg/kg body weight
Below 30 ml/min	2.0 mg/kg body weight

increased urinary flow rate, glycosuria and enzymuria.³ SCI patients constitute a discrete therapeutic population. The clearance and volume of distribution of gentamicin in SCI patients were different from those in able-bodied patients.⁴ In SCI patients, serum creatinine may be within normal limits, or only maximally elevated despite significant reduction in creatinine clearance. For any given level of serum creatinine, the measured creatinine clearance is lower in SCI patients than in able-bodied controls.⁵ Thus in the presence of SCI, serum creatinine may not accurately reflect the level of renal function, and should not be used as the sole guidance for dosing antibiotics that are excreted via the kidney.

As serum creatinine concentration is likely to overestimate renal function in SCI patients who have decreased muscle mass, gentamicin dosing needs to be determined on an individual basis from the estimated creatinine clearance (see Appendix 1).⁶ This method of calculating creatinine clearance in a SCI patient is practical, simple, requires minimal patient information, and is less cumbersome than collecting a 24-h urine sample.

Although the protocol for once-daily gentamicin dosing schedule recommends an initial dose of 5 mg/kg body weight, even the first dose of gentamicin may need to be reduced in SCI patients, as some SCI patients may have compromised renal function with decreased creatinine clearance level. We suggest that the dosage schedule for once-daily gentamicin as recommended by Prins *et al.*⁷ may be followed for SCI patients (Table 1), with the proviso that the gentamicin dose requires further reduction, if a decline in renal function is anticipated as in patients undergoing extracorporeal lithotripsy.⁸ We were aware that this tetraplegic patient had renal disease, and therefore, administered only 3 mg/kg of gentamicin (240 mg) instead of the standard dose of 5 mg/kg body weight. Despite taking this precaution, the gentamicin level remained in the potentially toxic range after a period of 22.5 h. His creatinine clearance, as estimated from the pre-operative serum creatinine level, was 47 ml/min. Had we followed the regime proposed by Prins *et al.*⁷ with the stipulation that the dose requires further reduction to compensate for possible, transient decline in renal function, in the immediate post-operative period following Gil-Vernet intra-sinus pyelolithotomy, it is likely that we would

have avoided the potential mishap in our tetraplegic patient.

References

- 1 Ferriols-Lisart R, Alos-Alminana M. Effectiveness and safety of once-daily aminoglycosides: a meta-analysis. *Am J Health Syst Pharm* 1996; **53**: 1141–1150.
- 2 Prins JM, Weverling GJ, van Ketel RJ, Speelman P. Circadian variations in serum levels and the renal toxicity of aminoglycosides in patients. *Clin Pharm Therap* 1997; **62**: 106–111.
- 3 Whiting PH, Brown PA. The relationship between enzymuria and kidney enzyme activities in experimental gentamicin nephrotoxicity. *Renal Failure* 1996; **18**: 899–909.
- 4 Gilman TM, Brunnemann SR, Segal JL. Comparison of population pharmacokinetic models for gentamicin in spinal cord-injured and able-bodied patients. *Antimicrob Agents Chemother* 1993; **37**: 93–99.
- 5 Kaji D, Strauss I, Kahn T. Serum creatinine in patients with spinal cord injury. *Mt Sinai J Medicine* 1990; **57**: 160–164.
- 6 Griver AR, Prince RA, Darouiche RO. A simple method for administering vancomycin in the spinal cord injured population. *Arch Phys Med Rehabil* 1997; **78**: 459–462.
- 7 Prins JM *et al.* Validation and nephrotoxicity of a simplified once-daily aminoglycoside dosing schedule and guidelines for monitoring therapy. *Antimicrob Agents Chemother* 1996; **40**: 2494–2499.
- 8 Eterovic D, Juretic-Kuscic L, Capkun V, Dujic Z. Pyelolithotomy improves while extracorporeal lithotripsy impairs kidney function. *J Urol* 1999; **161**: 39–44.

Appendix 1

Estimated creatinine clearance in SCI patients adapted from Griver *et al*⁶

Lean body weight (LBW)

Males = 50 kg + 2.3 (height – 60 inches)

Females = 45.5 kg + 2.3 (height – 60 inches)

Estimated creatinine clearance

Paraplegic subjects:

$$\frac{(140 - \text{age}) \times \text{LBW}}{72 \times \text{serum creatinine (mg/dl)}} \times 0.8$$

Tetraplegic subjects:

$$\frac{(140 - \text{age}) \times \text{LBW}}{72 \times \text{serum creatinine (mg/dl)}} \times 0.6$$

Female SCI subjects:

Creatinine clearance (calculated as above) $\times 0.85$