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EDITORIAL

Glomerular hyperfiltration, the devil in disguise

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Glomerular hyperfiltration is an underdiagnosed condition leading to augmented renal clearance. This condition passes unnoticed, and can lead to serious underdosing of renally excreted antibiotics. In the present issue, Dylan de Lange pays attention to this condition. His contribution is worth reading for its clinical relevance.[1]

A typical case of glomerular hyperfiltration is as follows. A 24-year-old previously healthy man was admitted to hospital after a severe motor accident. At the trauma site he was found to be comatose and was intubated. Apart from an instable thoracic-3 vertebral fracture, which was fixated at day three, and some other less important injuries, his cerebral trauma was the most severe of his injuries. He underwent early hemicraniectomy to evacuate an acute subdural hematoma with mass effect. After repositioning of the cranial bone flap three weeks later, a subduro-peritoneal drain was inserted, because his neurological condition deteriorated. He subsequently developed fever. Several blood cultures showed growth of *S. epidermidis* and the pre-emptive vancomycin treatment was continued.

The patient's renal function appeared to be normal, on admission his serum creatinine was 73 µmol/L and after five weeks of intensive care treatment with persistently decreased consciousness (maximal EMV score of 8), the serum creatinine decreased to 40 µmol/L. Vancomycin blood levels were measured. Initial intravenous dose was twice 1000 mg but this dose had to be increased to 4-times 1300 mg to attain trough levels above 15 mg/L. Of note, this patient additionally exhibited intermittent sympathetic hyperactivity (fever, tachycardia, hypertension, tachypnoea, hyperhidrosis and dystonic posturing) which was successfully treated with hydration, enteral propanolol and intravenous clonidine.[2]

This young patient with severe traumatic brain injury had augmented renal clearance with subtherapeutic vancomycin concentrations. In such cases, augmented renal clearance is a devil in disguise. The first reason for this is that the condition passes unnoticed with routine clinical monitoring. Therefore, awareness on the part of the physician is crucial. Patients at risk include younger patients with apparently 'normal' renal function who exhibit sympathetic hyperactivity after major trauma, especially head injury, burns or during early sepsis. The precise mechanism is not well known, but the condition is associated with high catecholamine concentrations, fluid loading and low plasma albumin concentration and is reported in up to forty percent of septic and eighty five percent of the young trauma patients with normal renal function.[3-7]. The second pitfall is the augmented renal clearance of water soluble antibiotics and other solutes. For example, subtherapeutic concentrations of vancomycin[8-9], β-lactam antibiotics,[10] meropenem,[11] piperacilline/tazobactam[11] and levetiracetam[9] are reported in the literature.

How do we incorporate this knowledge into daily practice? Several measures seem necessary. First, in younger patients with trauma, early sepsis and burns, a higher initial dose of antibiotics should be considered to saturate an increased distribution volume. Subsequently, the non-toxic renally excreted antibiotics such as β-lactams, carbapenems and fluoroquinolones should be dosed more frequently or continuously (β-lactams), to prevent concentrations falling below the minimum inhibitory concentration due to augmented renal clearance. With non-toxic drugs, the risk of underdosing is higher than that of overdosing. Second and ideally, therapeutic drug monitoring should be performed. If this option is not available, creatinine clearance from a 2-4-hours urine collection period should be done at regular intervals to monitor augmented renal clearance and guide antibiotic dosing. Glomerular filtration may be markedly increased, creatinine clearances of 310 and of 375 mL/min/1.73 m^2 have been reported.[11,12] Third and finally, toxic antibiotics such as aminoglycosides, which demonstrate concentration-dependent killing, should be given more frequently in cases of augmented renal clearance, and therapeutic drug monitoring should be performed, not only in patients with diminished renal function but also in those with apparently

normal renal function. The same strategy is recommended for vancomycin for which continuous infusion may be considered as well.[4]

The message here is, be aware of glomerular hyperfiltration in younger patients with trauma, sepsis and burns with apparently normal renal function; measure 2-4 hours creatinine clearance regularly, administer antibiotics more frequently and perform therapeutic drug monitoring, not only in patients with diminished but also in those with apparently normal renal function. This strategy is likely to increase treatment success.

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