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CORRESPONDENCE

High systemic tobramycin concentrations after selective decontamination of the digestive tract in a critically ill patient with septic shock and multiple organ failure

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Dear Editor,

Selective decontamination of the digestive tract (SDD) is a strategy to reduce the number of nosocomial infections in patients admitted to the ICU by eradicating potentially pathogenic aerobic micro-organisms from the gastrointestinal tract.[1] SDD consists of the topical administration of tobramycin, amphotericin-B and colistin in the oropharynx and gastrointestinal tract. This is considered a safe therapy since these antibiotics are non-absorbable after oral administration. In critically ill patients, systemic detection of tobramycin (>0.05 mg/l) has been described. However, serum levels above 1 mg/l have been found less frequently[2-4] and in these patients, no adjustment of the SDD regime was performed.

We describe a case of high serum tobramycin levels (>1 mg/l) in an ICU patient with septic shock and multiple organ failure receiving SDD and our subsequent therapeutic interventions.

A 75-year-old woman was admitted to the ICU for severe septic shock with multiple organ failure, based on faecal peritonitis due to perforation of the sigmoid colon. She had had a right hemicolectomy with ileotransversostomy two days earlier. She had a relaparotomy on the same day and the perforation of the sigmoid colon was sutured. Because of acute kidney injury, continuous venovenous haemofiltration (CVVH) was started on day 2. SDD was started on day 3. The regimen consisted of 0.5 g mouth paste (2% colistin, 2% tobramycin and 2% amphotericin-B) and 10 ml suspension via the gastric tube (100 mg colistin, 80 mg tobramycin and 500 mg amphotericin-B, prepared by combining a colistin plus tobramycin suspension with an amphotericin-B suspension) four times a day.

The course of her illness was complicated. A second relaparotomy was performed on day 11, due to faecal leakage and suture dehiscence from the initial surgical site of the right hemicolectomy. She received both a temporary ileostoma and an external fistula on the remaining part of the transverse colon, descending colon and rectosigmoid. For this reason, rectal SDD suppositories (40 mg amphotericin-B, 40 mg tobramycin and 40 mg colistin) twice daily were added to the SDD regimen on day 16. She suffered from ongoing systemic inflammatory response syndrome (SIRS), needed drainage of several abdominal fluid collections and was continuously treated with various antibiotics (teicoplanin, vancomycin, linezolid, piperacillin / tazobactam).

During CVVH, no tobramycin levels were measured. Spontaneous diuresis increased and on day 42 the CVVH was stopped. However, the serum creatinine remained high (171 µmol/l on day 45) and we therefore determined the systemic tobramycin concentration, which was 2.3 mg/l (immunoassay, Roche) on day 45. Prolonged high tobramycin trough levels are correlated with an increased risk of nephrotoxicity, due to accumulation and damage to the renal tubular cells. Further, high tobramycin levels are associated with ototoxicity. For these reasons, the dosing frequencies of the SDD suspension and SDD suppositories were halved in our patient on day 47 to twice daily for the suspension and once daily for the suppository. The dose frequency of the mouth paste was not adjusted. On day 53 the tobramycin serum concentration was 1.4 mg/l and tobramycin was excluded from the SDD suspension administered via the gastric tube. On day 55 the tobramycin serum concentration was still 1.6 mg/l and on day 58 the SDD suppositories, mouth paste and suspension were all stopped, which resulted in a tobramycin serum level of 0.6 mg/l at day 60. Three months after admission to the ICU, the patient was discharged to a rehabilitation centre. No adverse events were reported.

Detectable serum levels (>0.05 mg/l) have been described in patients using SDD[2,3] and are associated with tobramycin leakage due to an impaired gut barrier in conditions as sepsis,

shock or major surgery.[2] Additionally, impaired renal function has been related to decreased clearance of systemic tobramycin.[2,3]

Our patient had several risk factors for increased absorption and decreased clearance of tobramycin. Sepsis, ongoing SIRS, acute kidney injury and major gastrointestinal surgery may all have contributed to her high tobramycin serum levels. After removing tobramycin out of the oral suspension, the tobramycin serum level remained high. This suggests relevant mucosal absorption of tobramycin suppositories and/or mouth paste.

Analogue to the national SWAB guidelines,[5] we advise to monitor systemic tobramycin levels during CVVH. Further we advise to monitor systemic tobramycin levels once a week in ICU patients with impaired kidney function (eGFR <30 ml/min) and in ICU patients with abdominal sepsis receiving SDD. Based on the literature,[3] we also advise to monitor systemic tobramycin levels in patients on prolonged treatment with SDD (>14 days) and when SDD is administered via several routes.[1] In patients with high tobramycin serum levels (>1 mg/l), we advise adjusting the dose frequency of SDD, excluding tobramycin from the SDD suspension, and lastly to stop SDD altogether. .

Transparency declarations

None to declare.

Ethics

The ethics committee of the Martini Hospital gave permission for submission of this correspondence. Further, this manuscript maintains the patient's privacy.

Disclosure

All authors declare no conflict of interest. No funding or financial support was received.

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