Falsely elevated calcineurin-inhibitor trough levels: a case series of catheter adsorption

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Background: Treatment with calcineurin inhibitors is essential in the management of transplant patients. Oral administration is generally preferred, however intravenous (IV) administration is considered in patients with impaired/variable gastrointestinal absorption. Because of the narrow therapeutic index and intra-/inter-patient variability, tacrolimus (TAC) and cyclosporin A (CSA) trough levels are regularly monitored.

Methods: TAC and CSA concentrations are measured using Chemiluminescent Microparticle ImmunoAssay (Abbott) and Electrochemiluminescence ImmunoAssay (Roche), respectively. Two transplant patients, treated intravenously because of malabsorption, were included in this study. For the first patient, at ICU, IV TAC therapy had been guided by trough concentrations, ranging from 1.3 to 8.2 ng/mL, after which he was transferred to the haematology department and was switched back to oral TAC administration. Irregular TAC levels were found post-switch (21.2 to 34.0 ng/mL), up to 415% of the highest baseline trough level. The second patient initially received IV TAC but was switched to oral CSA treatment because of irregular TAC levels and subsequently to IV CSA. In the next 2 months, unexpectedly elevated CSA levels were found (606 to 730 ng/mL), which were first attributed to incorrect sampling times.

Results: For both patients, analytical interferences on the TAC/CSA measurements were excluded using an in-house developed LC-MS/MS method. As blood collections were performed from the central venous catheters (CVC), all different CVC lumina, in parallel with peripheral blood collection, were sampled. Lab analyses showed that at least one lumen was contaminated due to previous IV TAC administration (first patient). Samplings from the two lumina of the CVC, confirmed CSA contamination of both CVC lumina: 572 and 308 ng/mL, versus 134 ng/mL from peripheral blood sampling (second patient).

Conclusions: Although blood collection using central venous access is more patient friendly, these case series indicate that the use of multi-lumen CVC (previously) used for drug administration is a serious risk for (cross-)contamination and inappropriate dose adjustments. Even flushing procedures cannot overcome adsorption on certain catheter materials. Hence, peripheral sampling should always be favoured for TDM-samplings or alternatively, capillary (micro)sampling. Additionally, standardized guidelines for TDM in catheter patients are needed.

Key words: Tacrolimus, Cyclosporin A, adsorption, pre-analytical error