**Nephrotoxicity of TDM-guided amphotericin B infusions in intensive care patients.** Geersing, TH[1]; Van der Voort, PHJ[2]; Spronk, PE[3]; Franssen, EJF[1]

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**Background:** Continuous administration of conventional amphotericin B (CCAB) and therapeutic drug monitoring (TDM) may limit amphotericin B associated nephrotoxicity. Amphotericin B is used in intensive-care units (ICUs) for pre-emptive treatment of invasive fungal infections. In this study we investigated the incidence of nephrotoxicity in critically ill patients treated with TDM-guided CCAB.
**Methods:** In a retrospective cohort study we compared patients pre-emptively treated with CCAB with ICU patients who did not receive CCAB using a multiple linear regression analysis. ICU patients of two large teaching hospitals (OLVG Oost and Gelre Apeldoorn) were included between 2008 and 2018. Exclusion criteria were patients admitted on ICU for less then three days, patients receiving CCAB less then three days and patients receiving CCAB for other indications than preventing candida peritonitis. Also patients with continuous venovenous hemodialysis (CVVHD) on ICU admission, in the non CCAB cohort, and CVVHD at the start of CCAB were excluded. Primary endpoint was the change in creatinine, in CCAB-treated patients during CCAB-use and in the control group during ICU admission.
**Results:** A total of 3053 patients were included, 185 in the treatment arm and 2868 controls.

| Difference mean creatinine and Baseline creatinine | Correlation coëfficiënt | β | P-value |
|---|---|---|---|
| **CCAB vs control** | 1,223 | 0,005 | 0,783 |
| **Corrected for confounders*** | -3,292 | -0,011 | 0,485 |
| **Amphotericin B blood level**** | -3,003 | -0,008 | 0,851 |
| **# days CCAB**** | -2,441 | -0,104 | 0,002 |
| **# mg CCAB**** | 0,011 | 0,019 | 0,607 |

* age at admission (1), baseline creatinine (2), APACHEIV predicted mortality (3) and baseline ventilation (4).
** corrected for confounders: (1),(2),(3),(4), mean Amfotericin B blood level, # days CCAB and # mg CCAB.

Treatment with CCAB shows no significant influence on creatinine (β coefficient = -0.011, P 0.485). Increasing amphotericin B levels, CCAB-days or mg administered CCAB did not increase creatinine.
**Conclusion:** TDM-guided CCAB does not enhance nephrotoxicity in critically ill patients.

**Keywords:** amphotericin B, continuous administration, nephrotoxicity