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ePoster Viewing

**Antimicrobials: antimicrobial PK/PD, pharmacogenomics, pharmacoeconomics and general pharmacology, drug interaction studies**

**Stability of amoxicillin/clavulanic acid and amoxicillin reconstituted in isotonic saline**

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**Introduction :** An increasing proportion of intensive care units use extended or continuous infusion when administering broad spectrum beta-lactam antibiotics , in order to increase PK/PD target attainment. Only 1 previous study assessed the stability of amoxicillin/clavulanic acid at room temperature (RT) in a concentration of 20 mg/mL amoxicillin and 4 mg/L clavulanic acid in polyolefin infusion bags. It was found to be stable for a maximum of 4h because of limited stability of clavulanic acid. One study tested the stability of amoxicillin solution at RT and found this to be stable for 24h. However, interactions can occur between drugs and containers, with the possible adsorption onto the surface of the container, leading to loss of drug. Therefore, for each plastic material used and each drug, stability needs to be confirmed. We hypothesized that stability may be improved by dilution.

**Objectives:** The aim of this study was to assess the stability of amoxicillin as a 10 mg/L solution, and amoxicillin/clavulanic acid as a 10/2 g/L solution in isotonic saline in a polypropylene infusion bag at RT (25°C).

**Methods:** Amoxicillin 1000 mg (Clamoxyl®) and amoxicillin/clavulanic acid 1000 mg/200 mg (Augmentin®) were obtained as the commercial powder preparation for injection from GlaxoSmithKline (Wavre,Belgium). The antibiotics were reconstituted with 20 mL of 0.9 % sodium chloride for injection according to local practice and were then mixed with 80 mL 0.9% sodium chloride solution in a polypropylene infusion bag in order to reach a 10 g/L solution (2 g/L for clavulanic acid). We prepared three solutions for each antibiotic and all samples from each infusion bag were analyzed in fivefold. The infusion bags were stored at 25°C. The amoxicillin solution was sampled immediately after preparation and up to 12h later. The amoxicillin/clavulanic acid solution was sampled immediately after preparation and up to 6h later. Amoxicillin and clavulanic acid concentrations were determined using stability indicating high performance liquid chromatography coupled to tandem mass spectrometry. The solution was considered stable if the percentage of intact molecule was  $\geq 90\%$ , as specified by the European Pharmacopeia.

**Results:** The results are shown in figure 1. When dissolved without clavulanic acid, amoxicillin was stable until 12h storage at RT which is in line with previously reported results. The combination of amoxicillin and clavulanic acid was much less stable; the concentration of clavulanic acid fell below 90% after only 3h, which is slightly less than the findings from a previously published study which found stability to be limited to 4h at RT.

**Conclusions :** Amoxicillin as a 10g/L NaCl 0.9% solution was stable for >12h at 25°C which may allow administration as continuous infusion. When combined with clavulanic acid stability was insufficient to allow continuous infusion, but prolonged infusion up to 2h may be an option.