Polymyxin B and haemofiltration in an adolescent with leukaemia

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Keywords: clearance, haemofiltration, polymyxin B, sieving coefficient

Sir, Sandri et al.1 described the clearance of polymyxin B recently in two patients during continuous venovenous haemodialysis, but data during haemofiltration are not available.

An adolescent with relapsed (high-risk) acute lymphocytic leukaemia received a stem cell transplant and developed persistent shock within 24 h. The patient was anuric and received renal replacement therapy (RRT), as well as vasopressors and polymyxin B for presumptive multidrug-resistant, Gram-negative bacterial sepsis. The polymyxin B dose was variable during the first week of RRT due to changing renal function and support. A dose of 100 mg (1 mg/kg/day) polymyxin B by intravenous infusion was given on days 11 and 12 of RRT. On day 13 of RRT (continuous venovenous haemofiltration via a Prismaflex system with an M100 haemofilter and PrismaSol BGK 4/2.5 replacement fluid: blood flow 220 mL/min, pre-filter replacement rate 1500 mL/h and post-filter replacement rate 500 mL/h), trough concentrations of polymyxin B by HPLC2 drawn pre-filter (after replacement fluid), post-filter (before replacement fluid) and in the ultrafiltrate were 123.3, 117.2 and 0 ng/mL, respectively; these levels were measured when the haemofilter had been in use for ~42 h. The extraction ratio was 0.05, the sieving coefficient was 0 and the haemofilter clearance [extraction ratio × blood flow × (1 − haematocrit)] was 8 mL/min; RRT clearance was thus exclusively via haemofilter adsorption. Further data regarding haemofilter sieving and adsorption of polymyxin B are needed.

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Darunavir and telaprevir drug interaction: total and unbound plasma concentrations in HIV/HCV-coinfected patients with cirrhosis

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Sir, Telaprevir is an NS3/4A protease inhibitor approved for the treatment of chronic hepatitis C virus (HCV) genotype 1.1 Telaprevir is primarily metabolized by cytochrome 450 3A4 (CYP3A4). Also, telaprevir is a potent inhibitor of CYP3A4 and intestinal P-glycoprotein, resulting in increased concentrations of CYP3A substrates.1 Darunavir is mainly metabolized by CYP450 and ritonavir is a potent CYP450 inhibitor. Significant drug–drug interactions have been described in healthy volunteers between telaprevir (750 mg/8 h) and darunavir/ritonavir (600/100 mg/12 h), resulting in decreases in plasma concentrations of both drugs (darunavir: Cmax = 40%, AUC = 40% and Cmin = −42%; telaprevir: Cmax = −36%, AUC = −35% and Cmin = −32%).2,3

Based on these data, co-administration of darunavir/ritonavir and telaprevir is not recommended.1 However, a darunavir/