# Clearance of aspirin and salicylate in a laboratory model of continuous kidney replacement therapy is lower than renal clearance in healthy volunteers.

Harris, O\*; Khan, S\*; Preece, M; Greenwood, IA; Stott, JB; Rhodes, A; Shah, N; Leaver, S; Lonsdale, DO

\*joint first-author

Abstract

**Background and aims**

Aspirin use in critical care is common, either as a treatment initiated as part of a critical illness or as part of a patient’s regular medication. For those with significant critical illness leading to kidney failure, continuous kidney replacement therapy (CKRT) may be initiated as part of organ supportive critical care. It is recognised that CKRT removes aspirin and salicylate, however data is lacking on the extent of drug clearance from CKRT outside of the setting of case reports in salicylate poisoning1.

In a laboratory model of renal replacement therapy, we aimed to describe the clearance of aspirin and salicylate at conventional doses of continuous veno-venous haemofiltration (CVVH) and explore where in a filtration circuit the drug is lost.

**Methods**

CKRT using an Aquarius system (Nikkiso Medical) and a 4L jar of aspirin or salicylate in solution (500 mg/L) was used as a laboratory CKRT model. CKRT was run at a range of clinically relevant filtration rates (15-55 ml/kg/hr) and blood pump speeds (80–300 ml/min) with samples taken from the aspirin solution and effluent at 30-minute intervals. Drug concentrations were measured using UV spectrophotometry (Jenway) at 233 nm (aspirin) and 296 nm (salicylate).

**Results**

At standard CVVH CKRT effluent rates (25 ml/kg/hr), salicylate clearance was 0.8 L/hr and aspirin clearance was 1.92 L/hr. Clearance was proportional to effluent rate, for example aspirin clearance was 1.2 L/hr at 15 ml/kg/hr effluent rate and 2.8 L/hr at 55 ml/kg/hr (p=0.01). Altered blood pump speed did not meaningfully impact on drug clearance. There was a discrepancy in salicylate measured from the solution in the jar and that measured in the effluent, suggesting salicylate is eliminated not only via haemofiltration but also in adherence to the filter and tubing of the circuit.

**Conclusion**

We have successfully used a laboratory model of CKRT to measure drug clearance by this therapy, in isolation from residual patient elimination pathways. CKRT at effluent rates recommended in critical care provided salicylate clearance of 0.8 L/hr in this laboratory model. This compares to a renal clearance of 2.5 L/hr in healthy volunteers2. It is therefore likely that standard doses of aspirin provide therapeutic concentrations of aspirin/salicylate during CKRT. Further studies that account for the complexities of in-vivo operation of CKRT and residual patient elimination pathways are needed to confirm these findings and explore potential accumulation/toxicity.

1. Papacostas MF, Hoge M, Baum M, Davila SZ. Use of continuous renal replacement therapy in salicylate toxicity: A case report and review of the literature. *Heart & Lung.* 2016;45(5):460-463.

2. Levy G. Pharmacokinetics of salicylate elimination in man. *J Pharm Sci.* 1965;54(7):959-967.