Poster Abstracts

PO-65

ANTI-XA ACTIVITY IN APIXABAN OVERDOSE: A CASE REPORT

James Barton[1], Anselm Wong[2,3], Andis Graudins[1,3]

[1]Monash Clinical Toxicology, Monash Health, Victoria, Australia, [2]Austin Clinical Toxicology, Austin Health, Victoria, Australia, [3]School of Clinical Sciences, Department of Medicine, Faculty of Medicine, Nursing and Health Sciences, Monash University, Victoria, Australia

Objectives: Apixaban is a novel oral anticoagulation agent that exerts its effect through direct factor Xa inhibition. We present a case of multi-drug overdose including apixaban with associated apixaban concentrations.

Case Report: A 53 year-old man presented to our metropolitan hospital following a deliberate self-poisoning with 200mg apixaban, 35mg ramipril, 105mg bisoprolol, 280mg atorvastatin, 6mg colchicine, 37.4mg magnesium, 4x500mg paracetamol/9.5mg codeine/5mg phenylephrine and alcohol. He developed hypotension that was treated with noradrenaline. It was felt that this was the result of his ramipril and bisoprolol overdose. He did not develop any significant bradycardia or conduction delays to suggest significant beta-blocker toxicity. Initial coagulation studies, measured 6 hours post overdose, showed an International normalized ratio (INR) of 3.6 (0.8-1.2) (HaemosIL RecombiPlasTin 2G assay), activated partial thromboplastin time (APTT) of 37 (22-32 secs) and Anti-factor Xa activity concentration of 1.73 U/ml (based on low molecular weight heparin, therapeutic range 0.5-1U/ml). Apixaban concentrations were derived directly from anti-factor Xa chromogenic assay (ACT-TOP machine, HaemosIL Liquid Anti Xa assay and Stago apixaban calibrator). His initial and peak apixaban concentration (at 6 hours post-ingestion) was 1022.6 ng/ml and was associated with only minor bleeding from his femoral central line insertion site, which improved with local compression. Vitamin K 10mg (at 9 hours post ingestion) and Prothrombinex-VF 2000 units (at 13 hours post ingestion) were administered without any observed effect on coagulation studies. Apixaban elimination appeared to display first-order kinetics (r^2=0.97) with an elimination half-life of 7.4 hours. His serum apixaban concentration entered the therapeutic dose range at 10 hours post-ingestion and he recovered uneventfully.

Conclusion: A peak INR of 3.6 was seen in our patient correlating with a previous study's (1) linear INR/apixaban concentration relationship. This suggests that the INR may have a role in risk assessment of overdose and the ongoing monitoring of the anticoagulation effect of apixaban, if the anti-Xa assays are not available. There is considerable variation in sensitivity of prothrombin/INR assays to apixaban and this should be taken into account when interpreting these results. Apixaban did not appear to show any saturation absorption kinetics. There was rapid resolution of anticoagulation with no demonstrable benefit of currently available clotting factor replacement.

1. Frost C, Wang J, Nepal S, Schuster A, Barrett Y, Mosqueda-Garcia R et al. Apixaban, an oral, direct factor Xa inhibitor: single dose safety, pharmacokinetics, pharmacodynamics and food effect in healthy subjects. British Journal of Clinical Pharmacology. 2013;75(2):476-487.