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The ATOM family symposium - Digoxin overdose and response to antibodies (DORA)

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The optimal indications and dose of digoxin specific antibody (Digoxin Fab) is ill-defined in both acute and chronic digoxin poisonings. This part of the Australian Toxicology Monitoring Study (ATOM) aimed to investigate the pharmacokinetics and dynamics of digoxin and response to digoxin Fab. This is a prospective cohort study of patients recruited through the New South Wales Poisons Information Centre (NSW PIC) and 3 toxicology centres since September 2013. We also developed a Physiologically Based Pharmacokinetic (PBPK) Model of digoxin poisoning to support interpretation of findings from this cohort.

Free digoxin concentrations dropped to zero within an hour of Fab administration in all patients. When large doses of digoxin Fab were used, there was a gross excess of free digoxin Fab but it disappeared from the central compartment quickly. The free digoxin concentrations rebound to some degree in all patients within 10-40h, but many patients do not get recurrent toxicity. The PBPK model fitted the acute poisoning data well and indicated that the rate and extent of rebound may be overestimated by more simple 2 compartment models.

Digoxin Fab appeared to be effective for cardiac complications of acute digoxin poisoning, the only death occurring when digoxin Fab was not available. In contrast it had only modest effects in chronic poisoning reflecting the multiple comorbidities and other medication in this elderly group of patients. Full or even half neutralising doses appear to be excessive and wasteful in many patients. This was demonstrable in both the PBPK model and the patient data, where direct measurement of unbound digoxin antibodies was made. In both scenarios, Digoxin Fab may be given in staggered doses in the first 24-48h, titrated against ECG changes and clinical response.