



Retrospective Evaluation of Repeated Supratherapeutic Ingestion (RSTI) of Paracetamol

Harry Egan¹, Geoffrey Isbister², Jennifer Robinson², Betty Chan³, **Angela Chiew**³

¹Prince of Wales Hospital Clinical School, University of NSW

²Department of Clinical Toxicology and Pharmacology, Calvary Mater Newcastle and Clinical Toxicology Research Group, University of Newcastle

³Department of Clinical Toxicology, Prince of Wales Hospital

Objective: Repeated supratherapeutic ingestion (RSTI) of paracetamol can result in acute liver injury. Management guidelines vary, in Australia acetylcysteine treatment is recommended in patients with a paracetamol concentration >20 mg/L and/or ALT >50 U/L. Laboratory investigation are repeated after at least 8 h and treatment ceased if ALT remains <50 U/L or static and paracetamol concentration <10 mg/L. To investigate patients presenting with RSTI of paracetamol and determine whether an admission ALT<50 U/L rules out those who will develop hepatotoxicity (ALT >1000 U/L).

Methods: Retrospective review of all paracetamol RSTI presentations to two toxicology services over a 4-year period. Patients were included if they ingested >4 g per 24 h of paracetamol for a period >8 h, regardless of ingestion intent. Data collected included demographics, ingestion history, pathology results, treatments and outcomes.

Results: 266 patients were identified, 145(55%) females and median age 43 y (IQR: 30-56 y). The median ingested dose was 9 g per 24 h (IQR: 6-12 g) over a median time of 2 d (IQR:1-5 d). The table summarises clinical presentation and outcomes stratified according to peak ALT. Paracetamol was taken in 180 (67%) for pain, flu symptoms in 22(8%), chronic opioid/paracetamol combination abuse in 30 (11%), and 46 (17%) intentional staggered ingestions. Paracetamol was detected in 192 (72%) on presentation with a median concentration of 14 mg/L (IQR: 7-27 mg/L). The median ALT on admission in those who developed hepatotoxicity compared to those who didn't was significantly higher 1182 U/L (IQR: 598 – 4251 U/L) vs. 30 U/L (IQR: 18-59 U/L) respectively (p=<0.0001). All 17 who developed hepatotoxicity had an ALT >50 U/L on arrival. Five presenting with an ALT <50 U/L developed a peak ALT between 50-1000 U/L. 139 (52%) received intravenous acetylcysteine, of which 64 received an abbreviated course, with a median length of infusion of 11 h (IQR:7-14 h). 127(48%) didn't receive acetylcysteine, 42 had a repeat ALT all remained unchanged.

Conclusion: Our results confirm that those with acute liver injury secondary to RSTI of paracetamol will have an elevated ALT on presentation. The Australian guideline for RSTI appear useful in ruling out patients who don't require acetylcysteine.



	Peak ALT < 1000	Peak ALT > 1000 IU/L
Number of patients	249	17
Median average dose ingested per 24 hrs (g/24 hrs) (IQR)	8.6 (n=246) (6 – 12)	7.8 (6 - 11)
Median days ingested (days) (IQR)	2 (2 – 5)	3 (1.5 -8.5)
Median presenting paracetamol concentration (mg/L) (IQR)	14 (n=178)* (7 - 27)	17 (n=14)^ (11 – 54)
Median presenting ALT (IU/L) (IQR)	30 (18 – 59)	1182 (598 - 4251)
Number ALT < 50 on presentation (%) (95% CI)	172 (69%) (95% CI: 63 -74%)	0 (0%) (95% CI: 0 -18%)
Number treated with acetylcysteine (%) (95% CI)	65 (26%) (21 -32%)	16 (94%) (73 -100%)

*67 undetectable paracetamol concentration and 4 not ordered.

^3 undetectable paracetamol concentration.