Clinical update no. 553

19 February 2019

Case: 27yr male

INTENTIONAL OVERDOSE OF 20 X PARACETAMOL APPROX 30HRS AGO. DENIES ANY OTHER DRUG OR ALCOHOL USE. STATES FEELING DEPRESSED, [illegible]

	12:10	18:00	
Sodium	134L	134L	
Potassium	4.0	4.0	
Chloride	95	98	
Bicarbonate	26	22	
Anion Gap	17H	18H	
Urea	4.0	4.1	
Creatinine	81	65	
Est. of GFR	>90	>90	
Glucose	4.9	5.2	
Osmol-calc	276L	277L	
Bili Tot.	128H	101H	
ALT	5895H	6750H	
AST		17547H	
ALKP	188H	147H	
Old GGT			
New GGT	473H	437H	
Protein	79	68	
Albumin	49	40	
Globulin			
Ammonia	275H		(10-50)
PT	26H	39H	
INR	2.2H	3.3H	
APTT	30	36	
Fibrinogen		1.2L	
pH	7.44	7.47H	
pCO2	44	34L	
HCO3	27.1	26.0	
Base Excess	5.7H	1.0	
Lactate	3.3H		
Paracetamol	<2.6 mg/L		

There was delayed presentation. He progressed to hyper-acute liver failure and was transferred to a liver unit.

He was given N-Acetylcysteine, with loading 200 mg/kg and then ongoing infusion; vit K 10mg, 50% dextrose infusion, hypertonic saline and CRRT. LFTs normalised.

Guideline summary

Updated guidelines for the management of paracetamol poisoning in Australia and New Zealand

https://www.mja.com.au/journal/2019/212/4/updated-guidelines-management-paracetamol-poisoning-australia-and-new-zealand

1 Paracetamol dosing that may be associated with acute liver injury

Acute single ingestion*	Repeated supratherapeutic ingestion†
≥ 10g or ≥ 200 mg/kg (whichever is less)	≥ 10 g or ≥ 200 mg/kg (whichever is less) over a single 24-hour period Or ≥ 12 g or ≥ 300 mg/kg (whichever is less) over a single 48-hour period Or ≥ a daily therapeutic dose† per day for more than 48 hours in patients who also have abdominal pain or nausea or vomiting

Acetylcysteine infusions

Standard two-bag regimen*†

- Initial infusion
  - acetylcysteine 200 mg/kg (maximum 22 g) in glucose 5% 500 mL (child, 7 mL/kg up to 500 mL) or sodium chloride 0.9% 500 mL (child, 7 mL/kg up to 500 mL) intravenously, over 4 hours
- Second acetylcysteine infusion
  - acetylcysteine 100 mg/kg (maximum 11 g) in glucose 5% 1000 mL (child, 14 mL/kg up to 1000 mL) or sodium chloride 0.9% 1000 mL (child, 14 mL/kg up to 1000 mL) intravenously, over 16 hours†‡
- If ongoing acetylcysteine is required, continue at the rate of the second infusion (eg, 100 mg/kg over 16 h). Higher ongoing infusion rates (eg, 200 mg/kg over 16 h) may be required for massive paracetamol ingestions and a clinical toxicologist should be consulted

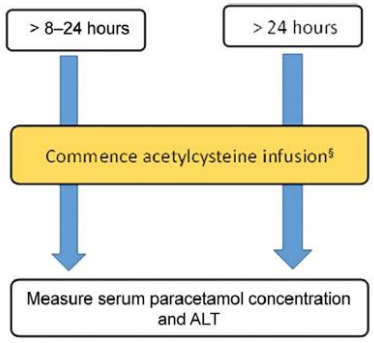
This modifies the old regimen. Instead of 50 mg/kg over 15-60 minutes and then 150mg/kg over 4hr, the same dose of 200 mg/kg is given in 1 bag over 4hr. The slower initial infusion rate reduces side effects, notably non-IgE anaphylactoid reactions and vomiting. This 4hr infusion is followed by the second bag giving 100 mg/kg over 16 h.

Immediate release paracetamol ingestion

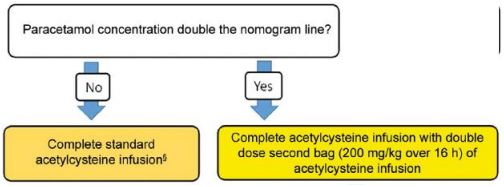
Give charcoal if safe to do so for toxic ingestions presenting at <2hr, or up to 4hr if >30g taken.

Interpret the nomogram for acute ingestion of immediate release paracetamol taken at a known time, The treatment threshold is a 4hr level above 150 mg/L (note the units used).

Commence NAC if presentation >8hr post ingestion; then check paracetamol level and ALT to decide whether to continue or stop.



For levels more than double the treatment line give a higher dose of NAC in the 2nd bag – 200 mg/kg over16hr instead of the usual 100 mg/kg over 16hr.



Two hours before the NAC infusion is scheduled to end check ALT. Also get a paracetamol level if the initial level was >2x the nomogram line. Continue NAC beyond 20hr if ALT >50 U/L (or increasing if baseline ALT >50) OR if paracetamol level >10 mg/L.

Multiple or staggered immediate release paracetamol ingestions

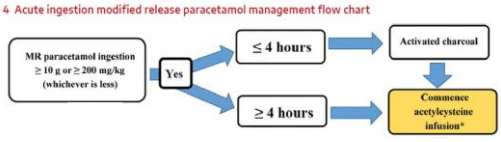
Treat as per acute ingestion using the earliest time of ingestion to interpret the nomogram. Make sure a level is taken at at least 4hr post last ingestion time, and repeat an initial level if taken within 4hr of last ingestion time. NAC should commence within 8hr whenever possible, which may require empric treatment pending levels.

Modified release paracetamol ingestions

All modified release ingestion >10g or >200 mg/kg should get charcoal if <4hr (and at >4hr if massive ingestion) and should get a full 20hr NAC infusion. Do not use the nomogram to determine the need to commence NAC. Levels can guide the need for higher dose or prolonged infusion. Use higher dose NAC if taken >30g or > 500 mg/kg or the level is >2x the nomogram line.

If ingestion is <10 g or 200mg/kg then decide treatment based on 2 levels taken 4hr apart.

4 Acute ingestion modified release paracetamol management flow chart



Paediatric liquid paracetamol ingestion

If >6years of age or present at >4hr then follow the adult guideline.

If an ingestion >200 mg/kg of liquid paracetamol is suspected, then a 2-4hr level < 150 mg/L means NAC is not required.

If a 2-4hr level is > 150 mg/L then treat only if a repeat level at 4hr post ingestion is > 150.

Repeated supratherapeutic ingestion

There is little evidence to guide management. Minor subclinical ALT elevation is common.

If low paracetamol level and normal ALT then risk is low.

If paracetamol >20 mg/L or ALT >50 U/L then start NAC and repeat levels at 8hr. Cease NAC at 8hr if paracetamol <10 mg/ and ALT <50. Small fluctuations in ALT ±20 do not mandate prolonged NAC. ALT will generally rise markedly if liver toxicity is developing.

Cessation of acetylcysteine

If ongoing acetylcysteine is required, continue at the rate of the second infusion (eg, 100 mg/kg over 16 h). Higher ongoing infusion rates (eg, 200 mg/kg over 16 h) may be required for massive paracetamol ingestions and a clinical toxicologist should be consulted

Cessation of acetylcysteine

- In patients who require acetylcysteine beyond 20 hours, acetylcysteine can be ceased if all the following criteria have been met:
  - ALT or AST are decreasing;
  - INR < 2.0; and
  - patient is clinically well

And

- For modified release ingestions and patients with an initial paracetamol concentration greater than double the nomogram line, paracetamol concentration < 10 mg/L (66 µmol/L)

NAC infusion beyond 20hr is at the same rate as the 2nd bag, and is indicated if paracetamol level toward end of 20hr is >10 mg/L and ALT >50 or rising (small fluctuations in ALT of ±20 don't mandate prolonged NAC). Repeat testing each 12hr if NAC infusion is continued >20hr.

Hepatotoxicity and subsequent liver failure

A small number have ALT >1,000 U/L, with a minority going on to fulminant liver failure. Most recover with standard treatment.

Consult a liver unit if INR >3.0, renal failure/ oliguria, persisting acidosis pH < 7.3 or lactate >3, hypotension, hypoglycaemia, thrombocytopaenia or encephalopathy or altered consciousness with GCS <15 not related to drug ingestion.