BARTS HEALTH NHS TRUST

ED & CDU Guidelines: Paracetamol Overdose in Adults

TRUST CORE/LOCAL GUIDELINES	
REVIEWED	2012
APPROVAL/ADOPTED	2012
DISTRIBUTION	Emergency Department – all staff, all areas
RELATED POLICIES	Paracetamol overdose
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THIS DOCUMENT REPLACES	First document

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1. APPLICATION

These guidelines apply to adults presenting to Barts Health ED's (> 16 years). They apply to the treatment of paracetamol overdose in the ED and CDU provided by all ED staff. The evidence suggests that pregnant women should be treated on a similar protocol to non-pregnant adults and the risks of NAC are far less than those of hepatic failure. The guideline applies to all oral formulations of paracetamol, *but not to IV*; in those cases advice from National Poisons Information Service (NPIS) is suggested. The vast majority of patients requiring a brief period of in hospital care will be discharged in 6 – 24 hours, making the group ideal for CDU placement. The number of patients requiring further in-patient care beyond this is very small and represents a very high-risk group that are demonstrating marked hepatotoxicity.

2. SUMMARY NOTES

Paracetamol (acetaminophen) is a commonly used analgesic, which works by inhibiting CNS prostoglandin synthesis. One metabolite is hepatotoxic (NAPQI) in high concentrations, but in low amounts is detoxified by glutathione (GSH). Paracetamol is commonly taken in OD and the potential for hepatic failure is significant. Treatment aims to restore GSH and is highly effective if commenced within 8 hours of ingestion with minimal risk of subsequent organ failure.

Symptoms:
< 8 hours – nausea / vomiting common. Metabolic acidosis / coma if paracetamol levels > 800 mg/L
12-36 hours – usually none, occasionally abdominal pain, RUQ pain
24-72 hours – hepatic failure - coagulopathy, deranged LFTs, hypoglycaemia, RUQ pain, jaundice, N& and ARF (predicted by proteinurea, haematurea, loin pain),

3. GUIDELINE

a. Details of Overdose

Date of ingestion	**Time of ingestion**	**Time since ingestion**
Body weight (kg)	**Amount ingested (mg)**	**Dose ingested (mg/kg) Max weight is 110 kg for calculation**

Risk assessment is based on amount ingested in mg/kg paracetamol and time since ingestion.

If the patient's weight is >110 kg, the amount ingested and the antidote dose should be calculated to a maximum weight of 110 kg rather than the patient's actual weight.

For pregnant patients the amount ingested should be calculated using the patient's pre-pregnancy weight and the antidote dose should be calculated using the patient's actual pregnant weight.

b. Risk Assessment

Risk of liver damage (i.e. a peak ALT more than 1000 iu/litre) in relation to OD size	
Based on the dose of paracetamol ingested (mg/kg body weight):	
Less than 150 mg/kg	Unlikely
More than 250 mg/kg	Likely
More than 12 g total	**Potentially fatal**

Since August 2012 all patients are treated based on the previous 'high risk' toxicity line on the nomogram.

c. Treatment Pathways

Activated charcoal should be administered (300ml, 50 gm) orally to patients presenting <u>within 1 hour</u> of ingestion and >150 mg/kg ingested.

The initial assessment, initial obs, all blood tests and the decision to start NAC, or not, should be made in EA or Cubicles. *If the patient is to be treated with NAC prior to obtaining a paracetamol level then NAC should be started **BEFORE** the patients goes to CDU.*

Most patients can be managed on CDU as the SOP is designed for < 24-hour turnaround.

Salicylate levels should not performed routinely – only by clinical suspicion.

If the paracetamol level was obtained 4-16 hours post ingestion and the level is under the treatment line and patient symptom free then NAC is ceased (if already started earlier) and discharge to psychiatric review.

Known time of ingestion

<4 hours

Activated charcoal 50G if <1 hour and >150mg/kg ingested
Don't take paracetamol concentration until 4 hours

Paracetamol concentration (and VBG, LFT, INR) at **4 hours** post-ingestion

Treat according to nomogram when paracetamol concentration available

4 - 8 hours

Paracetamol concentration (and U&E, LFT, INR) **on arrival**

Treat according to nomogram when paracetamol concentration available

8- 16 hours

Start NAC treatment if >75mg/kg ingested

Paracetamol concentration (and U&E, LFT, INR) **on arrival**

Commence / continue / stop treatment according to nomogram

16-36 hrs

Start NAC treatment if >75mg/kg OR evidence of hepatotoxicity

U&E, LFT, INR, paracetamol concentration **on arrival**

Commence / continue NAC if paracetamol detected or INR>1.3 or ALT>150

If INR<1.3 and ALT<150, repeat bloods in 12 hrs. If repeat blds INR 1.4 or more or ALT >150 d/w NPIS

If paracetamol not detected and normal bloods, discharge for psychiatry treatment

16-36 hrs

Start NAC treatment if >75mg/kg OR evidence of hepatotoxicity

U&E, LFT, INR, paracetamol concentration **on arrival**

Commence / continue NAC if
Paracetamol detected or
ALT > 3 x normal and INR > 1.3 or
ALT > 3 x normal and INR < 1.3
If INR > 1.3 with normal ALT consider other cause for raised INR

Unknown ingestion time
or
Staggered overdose
(ingestion over > 1 hour)

Start NAC treatment if >75mg/kg ingested
U&E, LFT and INR **on arrival**.

Give full 21 hrs NAC treatment if condition below not met.

In staggered overdose only do paracetamol levels if >24 since last tablet ingested. In this case- if no detected levels and UE, LFT, INR normal and patient asymptomatic, stop NAC and refer to psychiatry.

d. Essential Investigations Required

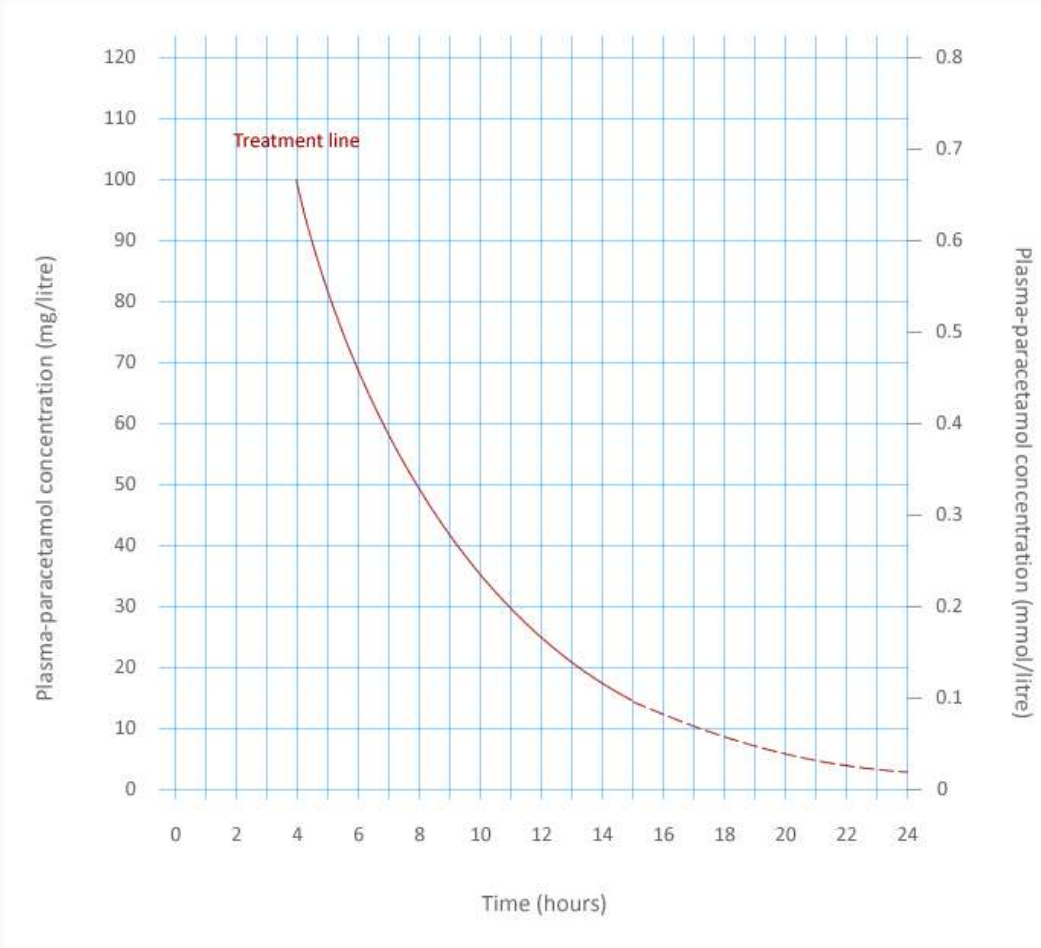
Arterial blood gases are NOT required unless the venous bicarbonate is abnormal.

Investigation	Normal Value	Pre-NAC result	Post- NAC result
Creatinine	59-104µmol/L		
ALT	4-59 IU/L		
Venous HCO_3	22-30mmol/L		
INR	0.90 – 1.10		
Paracetamol	<10mg/L		N/A

e. *Deciding whether to treat a paracetamol overdose*

Treatment of paracetamol overdose should be based on this nomogram. Use the below treatment line for all patients. (NB. At > 16 hours post-ingestion, interpret paracetamol concentrations with caution – most patients in this group with <u>any</u> detected paracetamol should be treated). This nomogram is only useful if ingestion has occurred over 1 hour or less. There are no contraindications to NAC. Adverse events are detailed below.

Annex 1: Revised paracetamol overdose treatment nomogram



f. NAC Treatment Regimen (adults only)

All patients requiring treatment are treated with Intravenous N-Acetylcysteine.

Treatment is 150mg/kg in 200mls of 5% dextrose over 60 minutes, then 50mg.kg in 500mls of 5% dextrose over 4 hours and finally 100mg/kg in 1000mls of 5% over 16 hours. The aim is to administer 300mg/kg over 21 hours. The infusions should be continuous with no gaps between doses.

The table below gives some examples of amounts needed for each part of the infusion for various different patient weights (you will need to calculate the amount for each individual patient)

Adult Dosage Table

Adult acetylcysteine prescription (each ampoule = 200mg/mL acetylcysteine)					Please circle appropriate weight and volume.	
Regimen	First Infusion		Second Infusion		Third Infusion	
Infusion fluid	200 mLs 5% glucose or sodium chloride 0.9%		500 mLs 5% glucose or sodium chloride 0.9%		1000 mLs 5% glucose or sodium chloride 0.9%	
Duration of infusion	1 hour		4 hours		16 hours	
Drug dose	150 mg/kg acetylcysteine		50 mg/kg acetylcysteine		100 mg/kg acetylcysteine	
Patient Weight[1]	Ampoule volume[2]	Infusion Rate	Ampoule volume[2]	Infusion Rate	Ampoule volume[2]	Infusion Rate
kg	mL	mL/h	mL	mL/h	mL	mL/h
40-49	34	234	12	128	23	64
50-59	42	242	14	129	28	64
60-69	49	249	17	129	33	65
70-79	57	257	19	130	38	65
80-89	64	264	22	131	43	65
90-99	72	272	24	131	48	66
100-109	79	279	27	132	53	66
≥110	83	283	28	132	55	66

NB. For patients weighing > 110kg, use a body-weight of 110 kg to calculate the dose of NAC.

g. Post N-Acetylcysteine (NAC) treatment

Repeat VBG, INR, LFTs immediately once NAC is complete (**no need to repeat paracetamol concentration**) and insert into the table above. If normal, discharge patient to psychiatric review. Note: NAC can increase the INR but never beyond 1.3. Isolated small elevations in ALT are common and do not confer significant risk, providing all other investigations are normal; these patients can be followed in OP.

Serum Creatinine elevated above baseline	YES / NO
Serum ALT elevated 2 x above baseline	YES / NO
INR >1.3 or a rise in INR of >0.2	YES / NO

If **YES** to ANY of these, then NAC should be continued at a rate of **150mg/kg/24 hours (i.e. third bag's dose and rate)**

If yes to any above question then refer to Medical team and continue NAC treatment in same dose as third bag if one of the abnormalities outlined above is found.

In cases of isolated ALT rise with normal HCO_3, INR and Cr, the need to continue NAC is debatable. Repeat same Investigations in 12 hours and if the only abnormality is ALT with all others within normal range, than d/c for OP f/u unless significant symptoms or psychiatric issues.

The NAC is otherwise continued until the INR is either: normal, in cases of mild toxicity; OR falling towards normal, and is less than 3 in cases of more severe toxicity. There is no clinical advantage to treating transaminase rises with acetylcysteine after this normalisation in INR. If the creatinine is rising in isolation repeat same bloods in 12 hours and discharge if normal. If abnormal refer to Medics and continue NAC.

All discharged patients should be told to re-attend if they develop N,V, RUQ/abdominal pain.

h. Side-Effects expected from NAC

These are common and very rarely severe. Most reactions are allergic or anaphylactoid and occur during the initial bag of NAC. If the patient develops erythema, urticaria, pruitis, flushing then stop the infusion, administer IV antihistamines and restart the infusion to run over 1 hour (if bag 1) or at the prescribed rate (if bag 2 or 3). If the patient develops angioedema or brochospasm then stop the infusion for 1 hour and treat with steroids, antihistamines and bronchodilators.

Anaphylaxis is treated per trust guidelines. Senior and toxicology advice on further treatment should be sought