GUIDELINE

N-ACETYLCYSTEINE (NAC) IV INFUSION FOR PARACETAMOL POISONING

Disclaimer: This document does not override decision based on clinical judgement and experience of the prescriber.

SCOPE

Site	Service/Department/Unit	Disciplines
Sir Charles Gairdner Hospital	Critical Care Areas, Medical & Surgical Wards	Medical, Nursing.

INTRODUCTION

Paracetamol overdose can cause hepatotoxicity and potentially fatal fulminant liver failure. Signs of paracetamol poisoning include vomiting, right upper quadrant tenderness and mental state changes, but potentially life-threatening poisoning may be clinically silent for the first 12 – 24 hours.

NAC (N-acetylcysteine) effectively reduces mortality when started within 8 hours of paracetamol overdose. Prognosis is also improved when therapy is initiated later in the clinical course of hepatotoxicity. If hepatic failure develops, intensive supportive care and consultation with hepatology is required, including consideration of liver transplantation. Hepatocytes will regenerate and return to normal function without long term sequelae if the patient recovers from the initial hepatic insult.[1]

A 2 bag NAC protocol significantly reduces the rate of adverse effects when compared to the traditional 3 bag regimen[2]. The loading dose is given over 4 hours thus reducing the occurrence of anaphylactoid reactions which can occur after rapid NAC loading. [3]

AVAILABILITY

- Acetylcysteine 2g in 10ml (200mg/ml) concentrated injection ampoule for IV infusion only. Must be diluted before use.

INDICATIONS

Single ingestion of immediate release paracetamol >10g or >200mg/kg (whichever is less) AND <500mg/kg, presenting to hospital within 8 hours, where a timed paracetamol level indicates the patient is at risk of hepatotoxicity (i.e. above the treatment nomogram line).

Modifications to this standard management are required in staggered ingestions; repeated supra-therapeutic ingestion; massive ingestion >500mg/kg; slow release preparation ingestion; if the plotted level is twice the treatment threshold of the nomogram; or if NAC is started greater than 8 hours post ingestion[1,4]. Further Toxicology advice should be sought in these scenarios.

CONTRAINDICATIONS

- When a timed paracetamol level indicates low risk for hepatotoxicity (i.e. is below the treatment nomogram in paracetamol overdose).
- Previous anaphylactoid reaction to NAC is NOT a contraindication for future use.

PRECAUTIONS

- Observe for bronchospasm in patients with a history of asthma.
- Critically unwell patients at risk of cerebral oedema should have NAC infused in a smaller volume of fluid with normal saline, not 5% dextrose. This reduces the risk of potentiating further cerebral oedema. Consult with Toxicology in such cases.
- NAC dose should be increased in consultation with Toxicology when patients are on haemodialysis as NAC can be dialysed.

DOSAGE

Acetylcysteine (NAC) is delivered as an intravenous infusion over 20 hours divided into two bags that follow on immediately from one another and have different concentrations.

Infusion 1: 200mg/kg NAC in 500ml of 5% dextrose given IV over 4 hours.

Infusion 2: 100mg/kg NAC in 1000ml 5% dextrose given IV over 16 hours.

DOSAGE CALCULATOR

* NAC dose is calculated on measured body weight rounded up to the nearest 10kg.
* Patients weighing over 110kg should be dosed based on a bodyweight of 110kg.

	Infusion 1 200mg/kg NAC Added to 500ml 5% Dextrose Given over 4 hours		**Infusion 2 100mg/kg NAC Added to 1000ml 5% Dextrose Given over 16 hours**	
Patient's weight (kg)*	**Dose of NAC** (grams)	**Volume of NAC** (ml of 200mg/ml NAC solution)	**Dose of NAC** (grams)	**Volume of NAC** (ml of 200mg/ml NAC solution)
40 kg	8g	40 ml	4g	20 ml
50 kg	10g	50 ml	5g	25 ml
60 kg	12g	60 ml	6g	30 ml
70 kg	14g	70 ml	7g	35 ml
80 kg	16g	80 ml	8g	40 ml
90 kg	18g	90 ml	9g	45 ml
100 kg	20g	100 ml	10g	50 ml
110 kg	22g	110 ml	11g	55ml

ADMINISTRATION AND PREPARATION

- Standard infusion pump and IV giving set required.
- Add required volume of NAC 200mg/ml to 5% dextrose bag (500ml for first infusion, 1000ml for second infusion.)
- Invert bag 10 times to mix solution thoroughly prior to infusing.
- Resuscitation equipment should be accessible at all times.
- Once an acetylcysteine vial has been punctured the contents may turn from colourless to slightly pink or purple. This does not affect drug potency.
- NAC can be safely administered in normal saline if there are concerns regarding the use of 5% dextrose for example in hyponatraemia, traumatic brain injury and cerebral oedema.

MONITORING

- Observations should be performed before initial infusion and every 15 minutes for the first hour.
- After the first hour, and once any reaction has settled, observations can revert to routine practice.
- For patients presenting after a single ingestion of immediate-release paracetamol < 500 mg/kg, where NAC is started within 8 hours of ingestion, further blood testing is not required - unless the initial

paracetamol level is more than twice the nomogram line OR the patient has symptoms or signs of hepatotoxicity at the end of the NAC infusion. Seek Toxicology advice in these situations.

PRACTICAL POINTS

Drug Interactions

- Nil known.

Adverse Effects

- **Nausea & vomiting**
  - Common.
  - Due to NAC or paracetamol ingestion itself.
  - Give standard antiemetic therapy.
- **Non-allergic anaphylactoid reactions (NAAR)**
  - Modified 2 bag protocol results in less incidence of NAAR compared with the 3 bag protocol[2].
  - May occur during first bag indicated by the following symptoms:
    - Flushing, urticarial rash, itch, tachycardia.
    - Bronchospasm, angioedema, dyspnoea, hypotension, shock (rare). Respiratory symptoms more common in asthmatics.
  - Management:
    - Stop NAC infusion temporarily and seek medical review.
    - Antihistamines may reduce reaction severity.
    - Once symptoms settle recommence infusion at ½ rate and increase to normal rate after 30 minutes.

Compatible fluids

- Glucose 5% and sodium chloride 0.9%

Incompatible drugs

- Cefepime and ceftazidime
- No information on Y site compatibility

Storage

- Ampoule and vial: store below 25 °C. Protect from light[5].
- Product is for single use in one patient only. Discard any residue.

Use in Pregnancy

- Category B2. NAC should be administered to pregnant patients if indicated following overdose.

Use in Breastfeeding

- Safe to use

ACKNOWLEDGMENTS

- Acetylcysteine (NAC) intravenous infusion protocol for paracetamol poisoning, Hoggett *et al,* Royal Perth Hospital Guideline, May 2018.

REFERENCES

1. Chiew AL, et al. Guidelines for the management of paracetamol poisoning in Australia and New Zealand. MJA. 2015; 203: 215-218.
2. McNulty R, et al. Fewer adverse effects with a modified two-bag acetylcysteine protocol in paracetamol overdose. Clinical Toxicology. 2018; 18: 618-621.
3. Wong A, et al. Simplification of the standard three-bag intravenous acetylcysteine regimen for paracetamol poisoning results in a lower incidence of adverse drug reactions. Clinical Toxicology. 2016;54:115-119.
4. Chiew AL, et al. Massive paracetamol overdose: an observational study of the effect of activated charcoal and increased acetylcysteine dose (ATOM-2). Clinical Toxicology. 2017;55:1055-1065.
5. Acetylcysteine. Seventh ed. Collingwood 3066, Australia: The Society of Hospital Pharmacists of Australia; 2019

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