A potentially fatal prescribing error in the treatment of paracetamol poisoning

Clinical records

Patient 1

An intubated and ventilated 73-year-old woman was transferred to a tertiary referral hospital intensive care unit for investigation and management of coma after suspected drug overdose, complicated by pulmonary aspiration. Her initial 12-lead electrocardiogram showed acute changes consistent with tricyclic antidepressant-induced cardiotoxicity. She had normal international normalised ratio (INR; 1.0) and serum alanine aminotransferase (ALT) level (25 IU/L; reference range, ≤ 40 IU/L) at presentation.

Her serum paracetamol concentration at 6 hours after ingestion was 2713 μmol/L (410 mg/L) (treatment level, 150 mg/L at 6 hours after ingestion) and intravenous *N*-acetylcysteine (NAC) was ordered. However, only 10% of the recommended intravenous NAC doses were ordered for each of the infusion bags (ie, 1200 mg loading dose instead of 12 000 mg, followed by 400 mg instead of 4000 mg in the first infusion, followed by 800 mg instead of 8000 mg in the second infusion).

This error was not detected until 40 hours after presentation, by which time her serum ALT level was 4940 IU/L and INR was 2.2. The correct dose was commenced. The serum ALT level peaked at 5360 IU/L 52 hours after ingestion, and then decreased rapidly. The patient recovered fully after a prolonged stay in the intensive care unit complicated by aspiration pneumonia and sepsis.

Patient 2

A 28-year-old woman presented to a regional hospital within 30 minutes of ingesting 35 g of paracetamol and 400 mL of rum, and was given activated charcoal.

Her 4-hour serum paracetamol level was 2395 μmol/L (362 mg/L) (treatment level, 200 mg/L at 4 hours after ingestion) and intravenous NAC was commenced 5 hours after ingestion. Her INR (1.0) and serum ALT level (30 IU/L) were normal at presentation. The NAC infusion was ceased after the standard 20 hours. However, by 48 hours after ingestion her INR was 3.4 and serum ALT level was 9450 IU/L. She was transferred to a teaching hospital for further management.

Review of the medical records on arrival 72 hours after the overdose revealed that only 10% of the recommended intravenous NAC dose had been given in each of the infusion bags (ie, 900 mg instead of 9000 mg, followed by 300 mg instead of 3000 mg, followed by 600 mg instead of 6000 mg). Intravenous NAC was recommenced at standard doses. Eighty hours after ingestion, her INR and ALT peaked at 3.5 and 11 500 IU/L, respectively, before normalising. She recovered well and was discharged to the regional hospital. ◆

Paracetamol is one of the most common agents involved in deliberate self-poisoning in Australia.[1,2] *N*-Acetylcysteine (NAC; Parvolex, Mayne Pharma Pty Ltd, Parkville, Vic) is the specific antidote,[3,4] and its administration is recommended to all patients judged to be at risk of developing hepatotoxicity following paracetamol overdose. The standard administration regimen in Australia is a dose of 300 mg/kg given by staged intravenous infusion in 5% dextrose solution (150 mg/kg over 15–60 minutes, followed by 50 mg/kg over 4 hours, followed by 100 mg/kg over 16 hours). This is how staff in Australia routinely calculate doses of NAC for infusion.

For these two patients, intravenous NAC was commenced but, because of either a miscalculation or transcription error, the final order involved a 10-fold underdosing error. In both cases, intravenous NAC was ordered and commenced by staff who rarely initiate this therapy.

N-Acetylcysteine for intravenous use is packaged as a liquid preparation in 10-mL ampoules, each containing 2000 mg. If NAC is prescribed in *milligrams*, the prescriber must calculate the correct dose based on the patient's known or estimated weight. The person making up the infusion must then derive the volume of NAC required to add to the 5% dextrose solution. For an adult patient, multiple ampoules of NAC are typically required for each of the staged infusions. If a 10-fold error is made, then it is not surprising that the person preparing the infusion may not realise the volume is inappropriate. However, the Parvolex package insert and eMIMS contain a useful table that shows the *volume in millilitres* of NAC required for ranges of body weight (Box). This removes the need for calculations based on patient weight and conversion of milligrams to millilitres; use of this table should greatly reduce the potential for error.

Parvolex intravenous infusion dosage guide

Patient's body weight (kg)	Initial: 150 mg/kg in 200 mL of 5% glucose in 15–60 min	Second: 50 mg/kg in 500 mL of 5% glucose in 4 hours	Third: 100 mg/kg in 1 L of 5% glucose in 16 hours	Total
	Parvolex (mL)	Parvolex (mL)	Parvolex (mL)	Parvolex (mL)
50	37.5	12.5	25	75
60	**45.0**	**15.0**	**30**	**90**
70	52.5	17.5	35	105
80	60.0	20.0	40	120
90	67.5	22.5	45	135
x	0.75*x*	0.25*x*	0.5*x*	1.5*x*

Consider a 60 kg patient requiring *N*-acetylcysteine (NAC; Parvolex). Conventionally, the first dose is calculated by: 60 kg × 150 mg/kg = 9000 mg NAC. The staff drawing up the NAC then have to ascertain what volume of NAC this is [9000 mg/200 mg/mL NAC = 45 mL, which is 4.5 ampoules of NAC].

Using this table, one can immediately see that a 60 kg person's first dose will be 45 mL NAC, and subsequent doses are 15 mL and 30 mL.

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Lessons from practice

- *N*-Acetylcysteine (NAC; Parvolex) is an effective antidote in the treatment of paracetamol poisoning.
- Prescription errors can occur when calculating the dose of NAC using the recommended milligram per kilogram dose.
- Using the supplied "Parvolex intravenous infusion dosage guide" allows prescribing a "dose in millilitres" of NAC to be administered and greatly reduces the potential for error. ◆

In our clinical toxicology service, all NAC infusion orders are prescribed in terms of NAC volumes directly derived from the package insert table. We strongly recommend that this practice be adopted elsewhere, particularly by inexperienced prescribers of NAC.

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