

Acetylcysteine for the treatment of paracetamol overdose and toxicity – new 2-bag dosing guidance

The National Poisons Centre has issued new dosing guidance for acetylcysteine for the treatment of paracetamol overdose and toxicity.

A 2-bag dosing regimen is now recommended:

	<u>Dose acetylcysteine</u>
1. First bag	200 mg/kg IV over 4 hours
2. Second bag	100 mg/kg IV over 16 hours

Current evidence suggests a modified two-bag dosing regimen is associated with a reduction in adverse effects associated with acetylcysteine administration. As the new dosing recommendations are simpler than the traditional ones, there is a reduced risk of administration errors.

Background

Acetylcysteine is approved for the treatment of paracetamol overdose and is highly effective for the mitigation or prevention of paracetamol hepatotoxicity, particularly when administered within 8 hours of overdose. The MEDSAFE approved dosing regimen provides a total of 300 mg/kg given intravenously over a period of 21 hours by 3 different infusions:

- First bag: 150 mg/kg over 1 hour.
- Second bag: 50 mg/kg over 4 hours.
- Third bag: 100 mg/kg over 16 hours.

Clinical experience with this standard dosing regimen has demonstrated a moderate risk of adverse reactions, particularly anaphylactoid reactions. Various studies report rates of adverse effects associated with administration of acetylcysteine ranging from 8.5–77 percent.⁴ Anecdotal experience also indicates that administration errors occur due to the complexity of having 3 different infusions to give the patient (wrong dose, wrong duration, or gaps between bags during which time no acetylcysteine is administered).

New recommended regimen

Growing evidence shows that a 2-bag dosing regimen is associated with lower rates of adverse effects from acetylcysteine, as well as lower rates of administration error. The 2-bag regimen gives the same total dose of 300 mg/kg over a period of 20 hours:

- First bag: 200 mg/kg IV over 4 hours.
- Second bag: 100 mg/kg IV over 16 hours.

The lower rate of adverse effects is thought to be primarily related to the peak serum acetylcysteine concentration being lower using the 2-bag regimen compared to the 3-bag regimen which gives an acetylcysteine bolus of 150 mg/kg over 1 hour.

For these reasons the National Poisons Centre is now recommending the 2-bag dosing regimen for treatment of paracetamol toxicity. The recommended acetylcysteine dose is the same for patients of all ages. However, caution must be taken when treating young children

(particularly those weighing less than 20 kg) to choose an appropriate type and volume of fluid to avoid iatrogenic complications like volume overload and hyponatraemia.

Further advice from a clinical toxicologist is available 24/7 by calling the National Poisons Centre at 0800 764 766 (0800 POISON) for questions related to this, or any other clinical poisoning scenario.

Adam Pomerleau
Director, National Poisons Centre
30 January 2019

Useful references:

1. Wong A, Graudins A. Simplification of the standard three-bag intravenous acetylcysteine regimen for paracetamol poisoning results in a lower incidence of adverse drug reactions. *Clin Toxicol (Phila)*. 2016; 54(2): 115-9.
2. McNulty R, Lim JME, Chandru P, Gunja N. Fewer adverse effects with a modified two-bag acetylcysteine protocol in paracetamol overdose. *Clin Toxicol (Phila)*. 2018; 56(7): 618-621.
3. Schmidt LE, Rasmussen DN, Petersen TS, et al. Fewer adverse effects associated with a modified two-bag intravenous acetylcysteine protocol compared to traditional three-bag regimen in paracetamol overdose. *Clin Toxicol (Phila)*. 2018; 56(11): 1128-1134.
4. Chiew AL, Isbister GK, Duffull SB, Buckley NA. Evidence for the changing regimens of acetylcysteine. *Br J Clin Pharmacol*. 2016; 81(3): 471-81.