Therapeutics Bulletin

Management of adverse reactions to N-acetylcysteine (NAC)

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Paracetamol overdose is common and can lead to severe hepatotoxicity if inadequately treated. N-acetylcysteine (NAC) is the antidote of choice in paracetamol toxicity due to demonstrated efficacy and good tolerability.[1] The 3-bag NAC regimen is most commonly used (Figure 1).

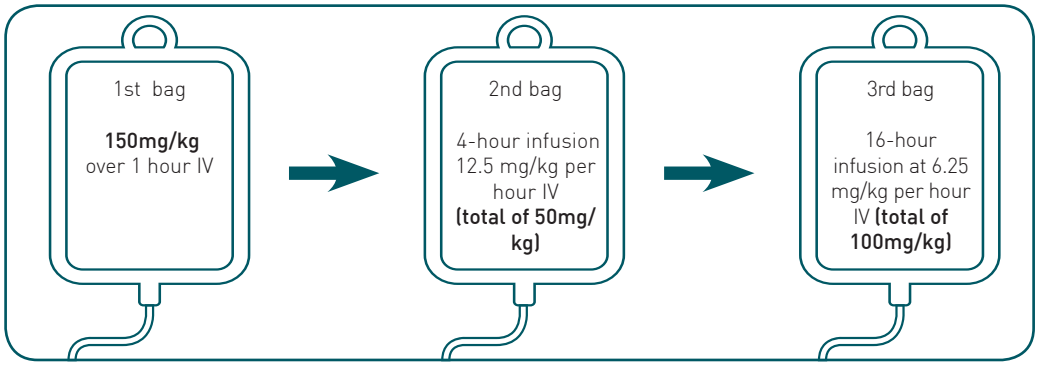


Figure 1: 3-bag NAC regimen

Intravenous NAC results in 14% to 18% non-allergic anaphylactic reactions (NAARs) or non-immunologic anaphylaxis, formerly known as anaphylactoid reactions.[2,3] Unlike immunologic anaphylaxis, it is not IgE mediated and does not require prior sensitization.[4] NAARs are dose related and are mostly seen during the initial phase of NAC administration since half the dose is given in the 1st hour. To overcome this a 2-bag regimen is proposed (Figure 2).

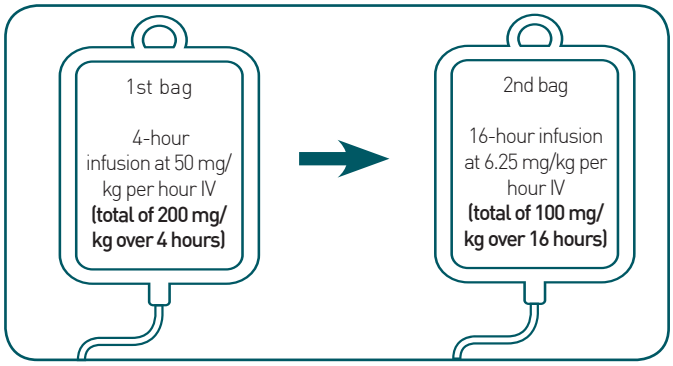


Figure 2: 2-bag NAC regimen

Example of how to administer the 2-bag NAC regimen in a 70-kg patient:

- 1st bag at 200mg/kg over 4 hours = 14 g of NAC over 4 hours
  1 ampoule of NAC = 2 g / 10 mL (200 mg / mL) therefore 7 ampoules will be needed, which adds up to 70 mL NAC.

  If using 5% dextrose solution 500 mL bag, remove 70 mL solution and inject 70 mL NAC into the 5% dextrose. Run the infusion at 125mL/hr (3.5g NAC/hr).

  If using 0.9% normal saline solution 1L bag, remove 70 mL solution and inject 70 mL NAC into the 0.9% solution. Run infusion at 250 mL/hr (3.5g NAC/hr).

- 2nd bag at 100 mg/kg over 16 hours = 7 g of NAC over 16 hours
  From a 1 L 5% dextrose solution **OR** 1 L 0.9% normal saline, remove 35 mL solution and add 35 mL NAC (3.5 ampoules) into the 1 L 5% dextrose **OR** 0.9% normal saline bag. Run infusion at 62.5mL/hr (0.4 g NAC/hr).

A comparison of the simplified 2-bag to the conventional 3-bag regimen has been studied and demonstrates lower incidence of NAARs in the 2-bag regimen versus the 3-bag regimen.[5–7]

Since NAARs are dose related, the reaction can be treated by reducing the rate of the infusion. In selected patient groups the administration of antihistamines may be warranted (table 1).

Table 1: Management of non-allergic anaphylactic reactions (anaphylactoid reactions)

Presentation	Management recommendation
Flushing	• Reassess need for NAC • Continue NAC if needed at a reduced infusion rate ❖ Restart infusion at 25% of the dose and titrate to normal dose rate over 1 hour. E.g. in a 70-kg patient, restart 1st bag infusion at 32 mL/hr and titrate up to 125 mL/hr over the next hour)
Urticaria	• Reassess need for NAC • Promethazine 0.25-0.5 mg/kg/dose intravenously • Continue NAC if needed at a reduced infusion rate ❖ Restart infusion at 25% of the dose and titrate to normal dose rate over 1 hour. E.g. in a 70-kg patient, restart 1st bag infusion at 32 mL/hr and titrate up to 125 mL/hr over the next hour)
Angioedema	• Stop NAC • Promethazine 0.25-0.5 mg/kg/dose intravenously • Reassess need for NAC • If no symptoms after 1 hour, restart NAC • Restart infusion at 25% of the dose and titrate to normal dose rate over 1 hour. ❖ E.g. in a 70-kg patient, restart 1st bag infusion at 32 mL/hr and titrate up to 125 mL/hr over the next hour)
Respiratory symptoms or hypotension	• Stop NAC infusion • Assess airway, breathing and circulation: Treat symptomatically • Promethazine 0.25-0.5 mg/kg/dose intravenously • Reassess need for NAC • If no symptoms after 1 hour, restart NAC • Restart infusion at 25% of the dose and titrate to normal dose rate over 1 hour. ❖ E.g. in a 70-kg patient, restart 1st bag infusion at 32 mL/hr and titrate up to 125 mL/hr over the next hour)

Adapted from Bailey et al., 1998.[8]

Key points:

- 2-bag NAC regimen is associated with reduced NAARs
- NAARs can be overcome by reducing the rate of the NAC infusion
- 2-bag regimen allows for easier administration in a setting with limited staff
- If NAARs are persistent, consult Clinical Pharmacologist on call



References:

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