

Management of Non-Allergic ("Anaphylactoid") Reactions to Acetylcysteine (NAC)

Background

- IV NAC can cause non-allergic (anaphylactoid) reactions.
- Most reactions are cutaneous (flushing, pruritic, urticaria).
- Severe reactions (hypotension, bronchospasm) are rare.
- These reactions are not true IgE-mediated anaphylaxis. Likely mechanisms include non-IgE histamine release or complement activation.
- Risk factors include asthma, atopy or prior NAC reactions, lower serum acetaminophen concentrations and rapid or high-rate NAC infusion.
- A prior non-allergic reaction to NAC is *not* a contraindication to using NAC again if indicated.
- Management follows principles from anaphylaxis care. A toxicologist consultation is available at any time.

Suggested Management

Flushing

- Confirm indication for NAC.
- Continue NAC if indicated. No specific treatment needed.

Urticaria

- Confirm indication for NAC.
- Diphenhydramine 1mg/kg (max 50mg) IV/IM x 1 dose OR cetirizine 10-20 mg.
- Continue NAC if indicated.

Angioedema, Stridor, Wheeze, Hypotension

- Stop NAC infusion.
- Confirm indication for NAC.
- Epinephrine 0.15 mg IM (child < 30 kg), OR 0.3mg IM (weight > 30 kg). May repeat in 5-10 min.
- Fluids 10mL/kg bolus NS or Ringers' Lactate.
- Oxygen as needed.
- **Stridor:** nebulized epinephrine 1 mg in 4 mL NS (in addition to IM dose).
- **Wheeze:** nebulized β agonist.
- Once symptoms resolve and if NAC is still indicated, restart after 1 hour at maintenance infusion rate. If reaction occurred during the maintenance infusion phase, call the Poison Centre.
- If reaction recurs or is severe, consider switching to oral NAC.

NOTE: Antihistamines are primarily effective for cutaneous symptoms; they do not treat airway or hypotensive reactions. Routine use of corticosteroids for NAC-related anaphylactoid reactions is not well supported and is not routinely recommended.

Muraro A, Worm M, Alviani C, et al; European Academy of Allergy and Clinical Immunology, Food Allergy, Anaphylaxis Guidelines Group. EAACI guidelines: Anaphylaxis (2021 update). *Allergy*. 2022; 77: 357–377. doi.org/10.1111/all.15032

Yarema, M., Chopra, P., Sivilotti, M.L.A. et al. Anaphylactoid Reactions to Intravenous *N*-Acetylcysteine during Treatment for Acetaminophen Poisoning. *J. Med. Toxicol.* **14**, 120–127 (2018). doi.org/10.1007/s13181-018-0653-9.



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