



Clinical Pharmacology & Toxicology Pearl of the Week

~ N-acetylcysteine and Anaphylactoid Reactions ~

- ✓ N-acetylcysteine (NAC) is the antidote of choice for treatment of acetaminophen (APAP) toxicity.
- ✓ It has several mechanisms of action when used for APAP toxicity, including: glutathione precursor, glutathione substitute, acting as a substrate for sulfation, and enhancing reduction of NAPQI (toxic metabolite) to acetaminophen.
- ✓ In patients with hepatotoxicity, it increases free radical scavenging, increases ATP production, and improves hepatic oxygen delivery and blood flow.
- ✓ Anaphylactoid reactions to IV NAC are well-described in the literature. The incidence of such reactions is between 2-8% depending on which regimen is used.
- ✓ The mechanism is believed to involve either non-IgE mediated histamine release or direct complement activation.
- ✓ Unlike true anaphylaxis, prior exposure to NAC is not required, nor is continued or future treatment contraindicated.
- ✓ Symptoms include cutaneous features (urticaria, flushing, pruritus, angioedema), respiratory features (cough, wheeze, dyspnea), and in severe cases, hypotension and cardiac arrest.
- ✓ Several factors are associated with an increased risk of anaphylactoid reactions to NAC, including:
 - history of asthma or atopic disease
 - family history of allergy
 - lower acetaminophen concentrations on admission (APAP decreases histamine release from mast cells in a dose-dependent manner)
 - female sex
 - younger age
 - lower alcohol consumption
 - a history of previous reaction to NAC
 - administering the loading dose over less than 60 minutes
 - longer time interval from ingestion to treatment with NAC

- ✓ Suggested management of anaphylactoid reactions to acetylcysteine:
 - Stop the infusion.
 - Review pump programming to ensure it is correct.
 - Contact the Most Responsible Healthcare Provider.
 - Administer one dose of diphenhydramINE (1 mg/kg IV to a maximum of 50 mg) for any cutaneous symptoms (urticaria, pruritus, facial edema).
 - Administer additional medications (beta-2 agonists, corticosteroids, epinephrine) only if the patient develops respiratory symptoms (dyspnea, wheeze, cough) or hypotension.
 - Reassess the patient at one hour after medications given.
 - If the patient's symptoms have improved, the IV infusion can be restarted.
 - If the patient is on the loading dose (150 mg/kg in AB, SK, and NWT), restart with reduced rate as if the load were being given over 90-120 minutes.
 - If the patient is on any portion of the maintenance infusion (15 mg/kg/hr in AB, SK, and NWT), restart at the same rate.
 - If an anaphylactoid reaction re-occurs once the infusion is restarted, switch the patient to oral (PO) acetylcysteine.
 - PO acetylcysteine is the same as the IV acetylcysteine solution but administered orally (mixed with sweet beverage or given via NG to minimize vomiting).
 - If needed, the full dose of PO acetylcysteine is a 140 mg/kg loading dose followed by 70 mg/kg PO Q4H for at least 5 doses (20 hours).
 - If the patient has already received the full IV acetylcysteine loading dose, there is no need to give the PO loading dose if switching to PO.

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral and Specialist Link. You can also find us in the [Alberta Referral Directory](#) (ARD) by searching “Pharmacology” from the ARD home page. Click [HERE](#) for more details about the service.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found in [Alberta Referral Directory](#) (ARD) by searching “Toxicology” from the ARD home page.

More CPT Pearls of the Week can be found [HERE](#).

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