TOOLS FOR PRACTICE #371 | August 6, 2024

TOOLS FOR PRACTICE

PEER PATIENTS EXPERIENCE EVIDENCE RESEARCH

It’s time to challenge penicillin allergy labels!

CLINICAL QUESTION

Can low-risk patients with beta-lactam allergy receive an oral beta-lactam challenge safely?

BOTTOM LINE

In adults with a history of non-severe cutaneous reaction to a beta-lactam over 5-10 years ago, the penicillin allergy label can be removed 87-98% of the time. Direct oral challenge with a beta-lactam is likely as safe and effective as doing a skin test first. Risk of severe adverse reactions <1%.

EVIDENCE

- Oral challenge alone versus skin testing followed (if negative) by oral challenge:
    - Two randomized controlled trials (RCTs) in patients recruited from allergy outpatient clinics, with non-severe cutaneous reaction to beta-lactam >1 year ago (children)[1] or >10 years ago (adults).[1,2]
        - First RCT (382 adults), amoxicillin 250-500mg:[2]
            - No serious adverse effects, hospitalizations or emergency room visits.
            - Penicillin allergy label removed: >98% (both groups).
            - Immune mediated reaction <1 hour after test: One in each group (cutaneous, mild).

        - Delayed rash/urticaria: 3.2% versus 1.6% (skin test first), no statistical difference.
    - Second RCT (159 adults/children), amoxicillin 20-40mg then 200-400mg 30 minutes later based on age/weight:[1]
        - Reaction <30 minutes after test: 4% (cutaneous, mild) versus 0% (skin test first), no statistical difference (PEER calculation).
        - Penicillin allergy label removed: 96% versus 87% (skin test), no statistical difference.
- Oral challenges with no prior skin testing: Six systematic reviews of cohort studies, children/adults, mostly outpatients (2-31 cohorts, 595-6,980 oral challenges):[3-8]
    - Immediate/delayed hypersensitivity reactions: 2.7-8.8%.[3-7]
    - Severe reactions (examples: anaphylaxis needing epinephrine, serum-like illness, interstitial nephritis): 0-0.04%.[6-8] Additional systematic review: Inconsistent reporting.[3]
- Limitations: Various definitions of "low-risk patients" or harms (example: anaphylaxis), limited data in primary care.

CONTEXT

- Penicillin "allergy": Reported in ~10% of the general population.[9]
- Amoxicillin associated with non-IgE (delayed onset) rash in ≤7% children; associated with concurrent viral infection.[10]
- Guidelines recommend:[10]
    - Direct amoxicillin challenge (with no preceding skin test): Adults with remote (>5 years ago) and benign cutaneous history.
    - Skin test: Patients with history of anaphylaxis/recent IgE-mediated reaction (example: immediate onset urticaria).
    - Avoid testing: Patients with severe cutaneous reactions to beta-lactams (examples: DRESS, Stevens-Johnson syndrome).
    - Single-step or 2-step challenge (10% of therapeutic dose then remaining dose after 30-60 minutes), with 60-minute observation.

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