ARTICLE:
- USA
- Funding: Not stated

PURPOSE:
- Purpose: To determine the efficacy of cimetidine, an H2-receptor antagonist, compared with that of diphenhydramine, an H1-receptor antagonist, alone and in combination, for mild-to-moderate anaphylactic reactions.
- Hypothesis:

DESIGN/Inclusion/Exclusion/Methods:
- **Study Design:** Prospective, randomized, double-blind trial with three groups
  1. 50mg Diphenhydramine iv + placebo
  2. 300mg cimetidine iv + placebo
  3. 50mg DPN iv + 300mg cimetidine iv
- **Setting:** Carolina Medical Center (777 bed hospital) and U. of Utah (375 bed)
- **Inclusion:** All patients between 18-50 y/o with <12 hours pruritus, urticaria, throat tightness, or facial swelling
- **Exclusion:** >12 hours, allergy to drug class, CAD/CHF, pregnancy, lactation, AMS, asthma, COPD, patients w/o telephone, unstable vitals (HR >120, SBP <100), respiratory distress (air hunger, dyspnea, tachypnea, or bronchospasm), or other experimental medication.
- **Enrollment:** 39 patients enrolled, all completed study
  1. DPN only: 14 patients
  2. Cimetidine only: 12 patients
  3. DPN + Cimetidine: 13 patients
- **Evaluation:** 110mm horizontal visual analog scale to assess degree of each symptoms (no findings to worst findings possible)
  1. Physician + self-evaluation (hour 0)
  2. Physician + self-evaluation (hour 0.5)

METHODS:
- Consent was signed and a physical exam followed
- Items: 110mm horizontal visual=analog scale to grade severity
  - (No findings to worst possible findings)
- Intervention: IV injection over 5-10 minutes for each medication
  - HR, pulse, and BP at 5, 10, and 15 minutes
**Reassessment:** Performed by both physician and patient self-reporting
- If “significant” improvement (i.e., a change of 25mm or more on the visual analog scale) – clinically significant relief they were discharged
- If “not significant” patients were withdrawn from the study and physician could treat at their discretion, breaking the blind if requested
- Discharged patients were sent home with PO study meds for 6, 12, 18, 24 hours post discharge self-dosing.

*Clinically significant symptoms were defined as ones at least 30mm from the left bar on the visual-analog scale. If not >30mm, symptoms were not included for analysis.*

**DATA ANALYSIS:**
- Statistical analysis:
  - Analysis of relief scores used one-way analysis of variance for overall differences
  - A student’s t-test was used between groups.
  - Contingency testing was performed to compare presence or absence of clinically significant relief among the three groups using a two-tailed fisher’s exact test.
  - P=.05 for statically significant findings.

**RESULTS:**
- Authors conclusions:
  - **Pruritus:** DPN exceeds CTD alone in treating pruritus (P=0.029)
    - DPN mean relief 80.3
    - CTD mean relief 48.8
    - DPN+CTD mean relief 68.5
  - **Urticaria:** DPN+CTD or CTD alone exceeds DPN alone (p=0.027)
    - DPN mean relief 30 (started @ 51)
    - CTD mean relief 55.3 (started @73)
    - DPN+CTD mean relief 42.9 (started @74)
  - *Pretreatment scores had significant variability P=0.004*

- Additional findings:
  - Adverse effects were minimal and required no significant intervention for resolution
  - **H1 blockers:** Great at treating pruritus and vasodilation
  - **H2 blockers:** Great at Urticaria, good at angioedema and hypotension
  - Failed to detect difference between DPN vs CTD alone in Urticaria

- **Limitations:**
  1. Small study size, 39 patients
  2. Good generalization, but applicability in pediatrics is not studied
  3. Duration of study is short (30 minutes), with unblinding following
  4. Unable to study efficacy of treatment on:
     a. Throat tightness, facial swelling, pharyngeal edema, and facial edema
  5. Follow-up limited due to inability to contact patients – treatment failures?
IMPLICATIONS FOR PRACTICE:

- *Applicable to this clinical practice:*
  - Very applicable. Easy to administer, safe, and combination does not appear to have significant downsides

- *Feasible (cost, resources, etc):*
  - Very easy to provide this care. Cost is minimal. Fast acting.

- *Clinically Relevant: Absolutely*
  - Faster relief of symptoms
  - Decrease need for additional medications/doses
  - Possibility of discharge at 30 minute post-administration with PO taper

LEVEL OF EVIDENCE / DECISION FOR USE:

- *X Ready for use*
- *Level of Evidence: 1B – Adds to previously reported literature.*