The Allergic Rhinitis Clinical Investigator Collaborative (AR-CIC) - Nasal Allergen Induced Eosinophilia -

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Abstract

BACKGROUND: The Allergic Rhinitis Clinical Investigator Collaborative (AR-CIC) is a Canadian multi-centre initiative with the primary goal of performing standardized nasal allergen challenge (NAC) to study the anti-allergic effects of novel therapeutic agents for allergic rhinitis (AR). The model further allows identification of potential mechanisms of allergic disease and biomarkers. In this study we examined differential counts, more specifically eosinophil numbers, in nasal lavage samples before, 1, 2, 3, and 6 hours after direct nasal allergen challenge.

METHODOLOGY: Thirty-three atopic and five non-atopic participants were enrolled at four study centers. All atopic participants had AR symptoms following exposure to environmental allergens and a supportive skin test response. Using the Pfeiffer Bidose Nasal Delivery Device 10μg allergen solution was delivered to each nostril. Atopic pilot study participants were challenged with a threshold dose of allergen determined via titration 1 week prior to NAC, non-atopic participants were challenged with a 1/2 allergen dose. The allergens used included either ragweed, grass, D furari, D pteronyssinus and cat hair. Nasal Lavage samples were also collected at 1 and 6 hours after challenge.

OBJECTIVE OUTCOMES: Total cell counts (TCC) were determined on unstained samples prior to cytospin. Cytospin slides were prepared and differentially stained (i.e. DiffQuick). Eosinophil counts were recorded in relation to total white blood cells.

Results

Table 1: Thirty-three atopic and 5 non-atopic healthy, male and female volunteers with a history of AR to relevant allergens were enrolled at 4 Canadian study centers. All participants gave written informed consent. Individual ethics approval were sought from each study site.

Methods

RECRUITMENT: Thirty-three atopic and five non-atopic participants healthy, male and female volunteers (18-65 years of age) with a history of AR to relevant allergens (see NAC description) were enrolled during an initial screening visit (visit 1) at McMaster University (Queen’s University, Université Laval and University of Alberta. All participants gave written informed consent.

Key exclusion criteria - History of developing AR symptoms on exposure to a common allergen + positive skin prick test (SPT)

Key exclusion criteria - signs/symptoms of acute perennial or seasonal AR - experienced an upper or lower respiratory infection within 2 weeks prior to the screening or challenge visit - current smoker or has a history of smoking within the previous 3 months - reports a Total Nasal Symptom Score (TNS) of greater than 4 at screening or immediately prior to allergen challenge - history of allergy

Figure 1: Study workflow

Figure 2: (a) Cytospin aerosolising and dosing (b) used for NAC dosing across all study sites. The type and dose of allergens were selected with challenge were determined by SPT and titration during screening (visit 1), 1-2 days prior to the NAC (visit 2). All participants gave written informed consent. Each study center obtained ethics approval individually.

Figure 3: The number of eosinophils (A) in nasal lavages of allergic participants was significantly upregulated 1 hour after NAC. Nasal lavage total cell counts (B) were elevated in allergic participants, however not significantly. Shown are the total cell counts (TCC) determined on unstained samples prior to cytospin. Eosinophil counts were performed on fixed, differentially stained slides, and recorded as percentage of total white blood cells. Each bar indicates the median of each group and their standard deviation. Statistical significance was determined with Wilcoxon test using GraphPad Prism.

Conclusions

In this study we examined differential counts, more specifically eosinophil numbers, in nasal lavage samples before, 1 and 6 hours after direct nasal allergen challenge. For this purpose we enrolled 33 atopic and 5 non-atopic healthy, male and female volunteers with a history of AR to relevant allergens at 4 Canadian study centers. Common allergens used for NAC included either ragweed, grass, D furari, D pteronyssinus and cat hair at a dose range of 1/2 to 1/2048.

The number of eosinophils in nasal lavages of atopic participants was significantly upregulated 1 hour after NAC (p=0.0147, Wilcoxon test). Nasal lavage total cell counts were elevated in atopic participants, however not significantly.

Nasal lavage collection for differential count analysis is a robust assay that can be integrated into clinical trials conducted using the AR-CIC.

References

(3) Grossberg H et al, Allergy (1993) 48: 87-93

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