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Nasal allergen challenge with Blomia tropicalis in children and adolescents

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Abstract
Background: Local allergic rhinitis (LAR) is a well-defined phenotype in adults, but still there is little data available on children. This scarcity of data can be partly attributed to the lack of standardized protocols for Nasal Allergen Challenges (NAC) in this demographic.
Methods: 20 controls (control group) and 24 patients (rhinitis group) with allergic rhinitis diagnosis sensitized to Blomia tropicalis (Bt) underwent the NAC with Bt. The acoustic rhinometry was performed after instillation of increasing concentrations of Bt (5,000 BU/mL).
Results: The median reduction in the volume of the nasal cavity in its first five centimeters (V5) by the conclusion of the NAC in the rhinitis group was markedly higher than that observed in the control group, at −22.9% (range: −21.1% to −26.2%) compared to −7.7% (ranging: −4.8% to +12.8%).
Conclusions: Our research demonstrates the efficacy and safety of the NAC protocol utilizing Bt in distinguishing allergic from non-allergic children.

Introduction

Local allergic rhinitis (LAR) is a localized nasal allergic response in the absence of systemic atopy characterized by the local production of specific IgE (sIgE) antibodies.1 While LAR is a well-defined phenotype in adults, however, there is little data available on children. This scarcity of data can be partly attributed to the lack of standardized protocols for Nasal Allergen Challenges (NACs) in this demographic.

Blomia tropicalis (Bt) is a mite commonly linked with early sensitization and ongoing symptoms of asthma and allergic rhinoconjunctivitis in countries with tropical and subtropical climates, where high humidity and temperature promote its proliferation.[2] Molecular analysis reveals that

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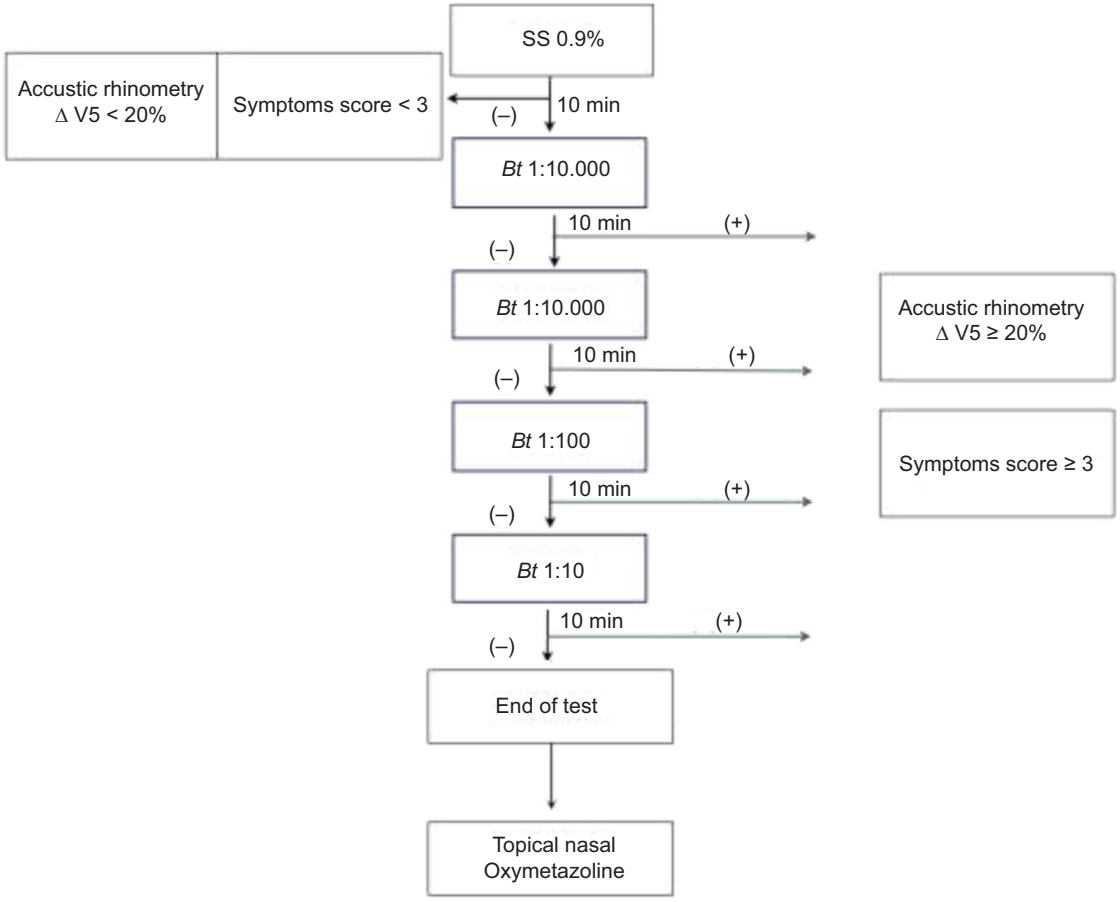

Figure 1 Flowchart used to perform the NAC with Bt (5,000 UBE/mL) in children and adolescents.

approximately 64% of the allergens found in Bt are unique,[3] and this distinctiveness complicates the use of standardized testing protocols designed for other mites and underscores the need for a tailored approach. Bt has been tested in NAC[4,5] in adults, but there are no validated protocols in pediatric population.

Methods

We developed a standardized NAC protocol with Bt for patients aged between 7 and 18 years. Participants were categorized into two groups: a) a control group without symptoms and/or diagnosis of allergic respiratory conditions and a negative immediate hypersensitivity skin test for a panel of aeroallergens (*D. pteronyssinus*, *D. farinae*, Bt, cockroach, dog, cat, and fungi); b) a group consisting of patients with rhinitis (according to the ARIA initiative)[6] who had a positive skin test for Bt (mean papule diameter of ≥ 3 mm). The study was approved by the Institutional Research Ethics Committee. Written informed consent was obtained from all legal guardians and individual participants included in the study.

During the NAC, Bt extracts (FDA ALLERGENIC® - Brazil, 5,000 UBE/ml, 0.15 mcg/mL Blo t 5) were diluted at different levels in 0.9% saline solution. Objective monitoring was conducted using acoustic rhinometry (AcR) (A1, GM Instruments, Scotland - UK) alongside subjective evaluations through a symptom questionnaire. These assessments were consistently performed in triplicate by the same observer, adhering to international recommendations.[7] Baseline metrics were established following the administration of 0.15 mL of saline solution. Subsequently,

Table 1 Symptom questionnaire registered during specific NPT with *Blomia tropicalis*.

Symptom		Points
Nasal secretion at anterior rhinoscopy (examiner's judgment)	As before/normal	0
	Slight increase/minor amounts visible	1
	Pronounced	2
Irritation	0–2 sneezes	0
	3–5 sneezes	1
	> 5 sneezes	2
Distant symptoms	None	0
	Watery eyes and/or Palatal itching and/or Deep aural itching	1
	Conjunctivitis and/or Chemosis and/or Urticaria and/or Cough and/or Dyspnea	2

Table 2 Demographic and clinical characteristics observed in rhinitis and control groups.

	Rhinitis group (N = 24)	Control group (N = 20)	P
Age (months)*	144 (124-188)	120 (86-149)	0.02
Male gender (%)	66.7	35.0	0.04
Asthma (%)	45.8	0	<0.001
Atopic dermatitis (%)	25.0	15.0	0.33
TNSS*	6 (5-8)	2 (0-3)	<0.001
MCA1 (cm^2)*	1.03 (0.78-1.32)	1.19 (0.88-1.28)	0.65
MCA2 (cm^2)*	1.91 (1.03-2.18)	2.23 (1.73-2.59)	0.04
V5 (cm^3)*	9.18 (7.19-11.59)	9.51 (7.99-10.66)	0.62

*averages and interquartile ranges.
MCA1 and MCA2: The two smaller cross-sectional areas; TNSS: total nasal symptom score; V5: Volume of the first 5 cm of the nasal cavity.

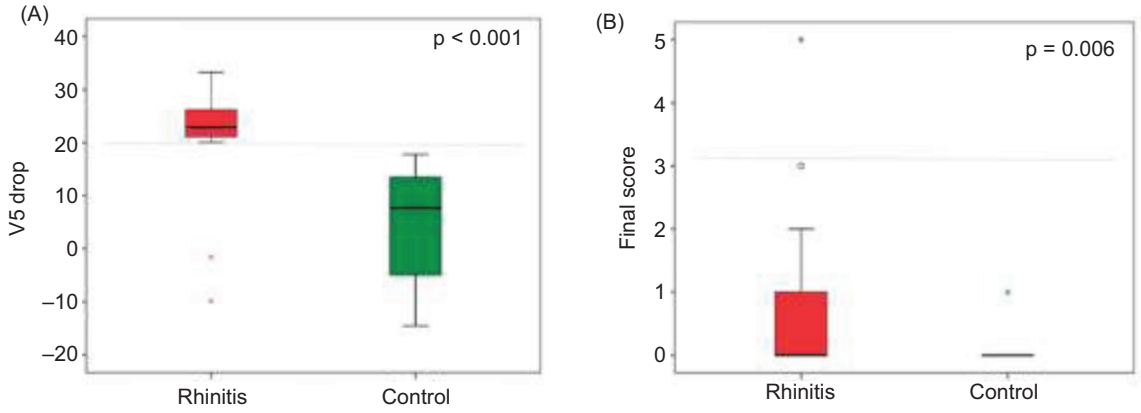

Figure 2 (A) The percentage reduction in the volume of the first 5 cm of the nasal cavity (V5) at the conclusion of the NAC with Bt for both the allergic rhinitis group (in red) and the control group (in green). (B) Final questionnaire symptom score values at the conclusion of the NAC with Bt in the allergic rhinitis group (red) and the control group (green).

0.15 mL of Bt solution, at progressively increasing concentrations, was sprayed into each nostril at 10-min intervals (Figure 1). After each administration, new AcR measurements and symptom questionnaire (Table 1) assessments were taken.

The NAC was concluded upon administering the highest concentration of Bt, on observing a reduction in the volume of the nasal cavity in its first 5 cm (V5 cm^3) by ≥20%, or when a score of >3 was recorded on the symptom questionnaire, with parameters previously used in standardizations in children and adolescents.[8,9] Additionally, the two smallest cross-sectional areas (MCA1 and MCA2 cm^2) in each nostril were measured.

The clinical and demographic profiles of the participating children are detailed in Table 2.

Results

In the rhinitis group, 22 out of 24 patients (91.7%) showed positive results to NAC, all registering significant changes in AcR parameters. Only one patient showed a concurrent shift in their symptom score. We observed a higher incidence of positive NAC outcomes until the 1:100 dilution concentration in 18 out of the 22 positive cases, while a smaller fraction, 4 out of 22, demonstrated positive reactions at the 1:10 dilution.

The median drop in V5 by the end of the NAC in the rhinitis group was markedly higher than that observed in the control group at −22.9% (range: −21.1−−26.2%) compared to −7.7% (range: −4.8−+12.8%), depicted in Figure 2A ($P < 0.001$). This was also observed in the questionnaire, depicted in Figure 2B ($P = 0.006$).

No individual in the control group registered a positive NAC outcome, and no participants experienced late reactions, and adverse nasal or extranasal effects during or after NAC.

Discussion

This study has some limitations such as the small number of participants and the lack of data on the collection of nasal-specific IgE or other cytokines that could further

substantiate the detection of a localized allergic response. However, recently published documentation for standardizing the NAC in adults[10,11] does not require such analyses.

NAC is a relatively simple and safe procedure that has been used for many years as a research tool to investigate the pathophysiology of rhinitis. It has clinical utility in certain clinical settings and is suitable as an office-based setup to diagnose LAR. NAC can be standardized to a good extent, but the results (as a subjective nasal symptom score and/or an objective nasal air flow rate) are sometimes difficult to interpret, especially in the pediatric age group.[12] Despite that, NAC continues to be the gold standard for diagnosing LAR.

In conclusion, our research demonstrates the efficacy and safety of the NAC protocol utilizing Bt in distinguishing allergic children from nonallergic. This protocol not only holds the potential for broadening the spectrum of allergens used in nasal provocation tests but also enhances the diagnostic precision of LAR in pediatric patients.

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