

BRIEF COMMUNICATION

Thermographic imaging during nasal peanut challenge may be useful in the diagnosis of peanut allergy

A. Clark¹, J. Mangat², Y. King¹, S. Islam¹, K. Anagnostou¹, L. Foley¹, J. Deighton¹ & P. Ewan¹

¹Department of Allergy, Cambridge University Hospitals, Cambridge, UK; ²Department of Clinical Engineering/Medical Physics, Cambridge University Hospitals, Cambridge, UK

To cite this article: Clark A, Mangat J, King Y, Islam S, Anagnostou K, Foley L, Deighton J, Ewan P. Thermographic imaging during nasal peanut challenge may be useful in the diagnosis of peanut allergy. *Allergy* 2012; DOI:10.1111/j.1398-9995.2012.02788.x

Keywords

food allergy; food challenge; peanut allergy; pediatrics; thermography.

Correspondence

Andrew Clark, Department of Allergy,
Cambridge University Hospitals,
Cambridge, UK.
Tel.: 00 44 1223 245151
Fax: 00 44 1223 216953
E-mail: atclark@doctors.org.uk

Accepted for publication 28 December 2011

DOI:10.1111/j.1398-9995.2012.02788.x

Edited by: Wytske Fokkens

Abstract

Background: Double-blinded challenges are widely used for diagnosing food allergy but are time-consuming and cause severe reactions. Outcome relies on subjective interpretation of symptoms, which leads to variations in outcome between observers. Facial thermography combined with nasal peanut challenge was evaluated as a novel objective indicator of clinical allergy.

Methods: Sixteen children with positive blinded peanut challenge underwent nasal challenge with 10 µg peanut protein or placebo. Mean skin temperatures were recorded from the mouth and nose using infrared thermography over 18 min.

Results: The area under curve of nasal skin temperature was significantly elevated after peanut vs placebo (18.2 vs 4.8°Cmin). The maximum increase in temperature was also significantly greater after peanut: mean difference +0.9°C.

Conclusion: This feasibility study shows thermography can detect inflammation caused by nasal challenges whilst employing one thousand-fold less peanut than an oral challenge. This novel technique could be developed to provide a rapid, safe and objective clinical allergy test.

Development of accurate methods for diagnosing food allergy is essential. In clinical practice, the presence of allergen-specific IgE combined with a typical clinical history is sufficient to diagnose allergy in most circumstances (1). Open challenges are used routinely in clinical practice to exclude food allergy, or confirm resolution, where a lack of symptoms after a meal-sized portion is a sufficiently robust outcome to rule out allergy.

In research, we are more interested in confirming that allergy is present. As we move into a new era of studying disease-modifying treatments, it is more important than ever that we are able to tightly define a homogenous population with the disease of interest. Here, the presence of history or allergen-specific IgE alone is insufficient, and the double-blind placebo-controlled food challenge (DBPCFC) is the accepted diagnostic standard (1, 2). However useful, oral DBPCFCs have significant drawbacks, being time-consuming and carrying a significant risk of severe reactions (3, 4). There is large variation between centres with regard to allergen preparation, blinding, dose range/intervals and stopping/adjudication rules. Most importantly, the robustness of the

challenge outcome relies on the subjective opinion of a third-party observer (4). Here, there is room for error; for example, two clinicians may disagree about the severity of abdominal pain required to trigger stopping a challenge. What is required to improve diagnosis for research is a single binary objective measure of a positive challenge, but no major advances have been made in this area for nearly two decades.

Infrared thermography can reliably detect the tiny (<1°C) increases in surface temperature associated with positive skin prick tests and allergen-induced rhinitis (5). Using this method, we previously showed that nasal temperatures were elevated during positive oral egg challenges (6). Facial skin temperatures were compared between children who had positive compared to negative oral egg challenges. We found that mean skin temperature was significantly higher in defined facial areas (mouth and nose) during positive oral challenges. The most striking difference was found in the nasal area. A cut-off of +0.8°C for the maximum increase in nasal skin temperature predicted the challenge outcome with high sensitivity (91%) and specificity (93%) (6). We therefore hypothesized that measurement of nasal skin temperature after direct

nasal instillation of allergen could provide a safe, rapid and objective measure for diagnosis of clinical allergy. This feasibility study is the first utility of thermography combined with direct nasal food challenges.

Method

Sixteen children with a positive DBPCFC to peanut were studied. Antihistamines were withheld prior to nasal challenge. One hundred microlitres of buffered saline placebo was administered to each nostril by fine aerosol. This was followed 30 min later by aerosol administration of 10 µg peanut protein (50% protein flour – used in DBPCFC; dose determined by pilot) in 100 µl buffered saline. Allocation was blinded, and symptoms were recorded.

Thermographic images were analysed by a single blinded operator independent of the study team. A temperature-controlled room (23°C) was used. The camera (FLIR systems Thermocam 500, West Malling, Kent, UK) had 24° optics, resolution 320 × 240, sensitivity 0.07°C and accuracy ±2°C. Thermographic imaging software (FLIR Researcher 2001) was used to determine mean surface temperature within a defined area of nose (a circle with diameter from the top of the philtrum to the bridge of the nose) at defined time points. The baseline temperature was the mean stable temperature prior to the first challenge dose. Nasal temperatures were recorded using facial thermography at predefined time points for 18 min after each nasal challenge. Temperature changes in relation to baseline (ΔT) were calculated for each time point. The difference between baseline and mean nasal temperature at each time point (ΔT), maximum positive ΔT achieved during the nasal challenge ($\Delta T_{\max}$) and area under curve of ΔT against time (ΔT_{AUC}) were calculated.

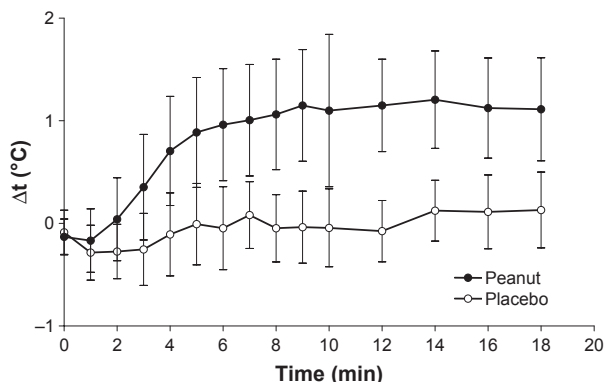


Figure 1 Change in mean nasal temperature from baseline (ΔT) over time (min) for placebo and active peanut nasal challenge arms. Points are mean values from $n = 16$ subjects, with 95% confidence intervals.

Results

No subject reported symptoms after nasal instillation with placebo. All 16 subjects developed rhinitis symptoms within 5 min of nasal peanut instillation (sneezing, congestion and rhinorrhoea). No symptoms arose from other organs. ΔT s for peanut and placebo arms were significantly different (Fig. 1). Median ΔT_{AUC} was significantly greater after peanut compared to placebo (18.2°Cmin (range 4.7–80.8) vs 4.8°Cmin (0–24.7); $P = 0.0006$; Mann–Whitney test). $\Delta T_{\max}$ was also significantly increased after peanut compared to placebo; mean difference = +0.9°C (95% CI = 0.35–1.45°C; paired t -test).

Discussion

With this feasibility study, we have shown that nasal peanut challenge (using one-thousandth of the amount of allergen used in oral challenges) causes a significant rise in nasal temperature compared to placebo. We found a similar magnitude of nasal temperature increase during nasal peanut challenges compared to our previous study of oral egg challenges [$\Delta T_{\max}$ 0.9 vs 0.8°C (6)]. The nose is highly vascular with a large mucosal area, bears large numbers of sensitized mast cells in allergic children and is a shock organ in food allergy (7–9). It is not surprising therefore that direct nasal instillation of small amounts of peanut should cause significant local inflammation in a clinically allergic patient. The key question is whether detection of nasal inflammatory changes can distinguish significant clinical allergy to peanut from sensitization alone. Further development will include a phase II dose-ranging study of both peanut-allergic and non-peanut-allergic peanut-sensitized patients, comparing nasal thermography challenge outcome to the gold standard of oral DBPCFC. From this, we aim to derive a cut-off value for $\Delta T_{\max}$ for which we can construct receiver–operator curves and calculate likelihood ratios for the presence of clinical peanut allergy.

In the current study, we used a tiny amount of peanut protein (10 µg), applied locally to the nose with minimal adverse effects. This has clear safety advantages over oral challenge where one thousand-fold greater amounts of allergen are ingested within a complex bulky matrix, which is digested and absorbed over a prolonged period; as a consequence, severe and late reactions occur (3). This novel technique is rapidly performed, amenable to standardization and low risk to the patient.

Acknowledgements

We would like to thank the Cambridge Biomedical Campus and Wellcome Trust clinical research facility for hosting the research and the Evelyn Trust for funding it.

Conflict of interest

There were no conflicts of interest.

References

1. Ewan PW, Clark AT. IgE-mediated food allergy: when is food challenge needed? *Arch Dis Child* 2005;**90**:551–558.
2. Bindslev-Jensen C, Ballmer-Weber BK, Bengtsson U. Standardization of food challenges in patients with immediate reactions to foods. *Allergy* 2004;**59**:690–697.
3. Hourihane JO, Grimshaw KE, Lewis SA, Briggs RA, Trewin JB, King RM et al. Does severity of low-dose, double-blind, placebo-controlled food challenges reflect severity of allergic reactions to peanut in the community? *Clin Exp Allergy* 2005;**35**:1227–1233.
4. Niggemann B. When is an oral food challenge positive? *Allergy* 2010;**65**:2–6.
5. Seppey M, Hessler C, Bruchez M, Savary M, Pecoud A. Facial thermography during nasal provocation tests with histamine and allergen. *Allergy* 1993;**48**:314–318.
6. Clark AT, Mangat JS, Tay SS, King Y, Monk CJ, White PA et al. Facial thermography is a sensitive and specific method for assessing food challenge outcome. *Allergy* 2007;**62**:744–749.
7. Vinke J, KleinJan A, Severijnen L, Hoeve L, Fokkens W. Differences in nasal cellular infiltrates between allergic children and age-matched controls. *Eur Respir J* 1999;**13**:797–803.
8. Pelikan Z. Nasal response to food ingestion challenge. *Arch Otolaryngol Head Neck Surg* 1998;**114**:525–530.
9. Kajosaari M, Saarinen U. Evaluation of laboratory tests in childhood allergy. Total serum IgE, blood eosinophilia and eosinophil and mast cells in nasal mucosa of 178 children aged 3 years. *Allergy* 1981;**36**:329–335.