Reproducibility of the Cytokine Response Following Nasal Allergen Challenge

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BACKGROUND

Nasally inhaled allergen provokes increased nasal secretion, cytokine production and nasal symptoms. This induces a biphasic allergic response comprising of an early (0-2 hours) and a late component (4-8 hours). This response can be measured by objective measurement using acoustic rhinometry, nasal symptom questionnaires and nasal secretion sampling using Ivalon® Post-op Sinus Pack K9.1

AIMS

To investigate the reproducibility of late response cytokine levels in secretions post nasal allergen challenge.

METHODS

24 subjects with allergic rhinitis underwent nasal allergen challenge.

Skin prick testing was performed to determine the choice of allergen (which comprised cat, house dust mite and 6 species of grass) utilized to challenge study subjects.

Nasal secretions (collected by Ivalon® Post-op Sinus Pack K9), nasal secretion weight, nasal cross sectional area (measured by acoustic rhinometry) and total nasal symptom score were measured from baseline up to 8 hours post allergen inhalation.

A repeat nasal allergen challenge was performed 7 to 14 days later.

Concentrations of IL-8, IL-5 and Eotaxin in the post allergen challenge nasal secretions were determined using ELISA.

The 8 hour time point was assessed for reproducibility using intraclass correlation (r) and the Fleiss criteria.

RESULTS

Figure 1: IL-8

Figure 2: IL-5

Figure 3: Eotaxin

Figure 4: Visit 2 Maximal IL-5

Table 1: Patient Demographics

Table 2: 8 hr Time Point Reproducibility

Table 3: Summary of Measurement Reproducibility

Table 4: Summary of Measurement Reproducibility

DISCUSSION

Nasal responses to allergen gained using this protocol are similar to the results published in the literature.

Allergic rhinitis subjects undergoing nasal allergen challenge can be divided into non-responders and responders based on their IL-5 response being above the lower limit of detection (23.4 pg/ml) on ELISA.

Ivalon® Post-op Sinus Pack K9 sponges are able to sample the late phase cytokine responses. This is important as they have previously only been used to sample the early phase cytokine response.

This nasal allergen challenge protocol is simple, robust, repeatable and can be utilised for future drug research to treat allergic rhinitis.

CONCLUSION

Nasal allergen challenges using Ivalon® Post-op Sinus Pack K9 sponges can be used to reproducibly detect and study the nasal late phase cytokine response.

REFERENCES


Figure 1: Concentration of IL-8 in nasal secretions over 8 hours following 2 nasal allergen challenges in 24 subjects. Data is presented as mean with 95% CI and analysed using Wilcoxon matched pairs. The dotted vertical line represents nasal allergen administration time in all figures.

- No significant difference between any time points.
- Late phase response present.

Figure 2: Concentration of IL-5 in nasal secretions over 8 hours following 2 nasal allergen challenges in 24 subjects. Data is presented as mean with 95% CI and analysed using Wilcoxon matched pairs. The dotted vertical line represents nasal allergen administration time in all figures.

- Significant differences at 4 hour (p=0.03) and at 8 hour time point (p=0.04).
- Late phase response.

Figure 3: Concentration of Eotaxin in nasal secretions over 8 hours following 2 nasal allergen challenges in 17 subjects (12 producing detectable Eotaxin). Data presented as mean with 95% CI and analysed using Wilcoxon matched pairs.

- No significant difference between each time point.
- Late phase response.

Table 1: Patient Demographics

<table>
<thead>
<tr>
<th>Allergic Rhinitis Subjects (n=24)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>38 (20-53)**</td>
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<tr>
<td>Sex</td>
<td>M:14, F:10</td>
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<tr>
<td>FEV1 (litre)</td>
<td>2.46 ± 1.21</td>
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<tr>
<td>FEV1% Predicted</td>
<td>95.50 ± 12.94</td>
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<tr>
<td>BMI</td>
<td>27.72 ± 5.72</td>
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Table 2: 8 hr Time Point Reproducibility

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Nasal Secretions (pg/ml)</th>
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<th>Nasal Secretions (pg/ml)</th>
<th>Intraclass Correlation coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-8</td>
<td>0.87 ± 0.19, 95% CI: 0.80, 0.95</td>
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<tr>
<td>IL-5</td>
<td>0.87 ± 0.19, 95% CI: 0.80, 0.95</td>
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<tr>
<td>Eotaxin</td>
<td>0.87 ± 0.19, 95% CI: 0.80, 0.95</td>
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Table 3: Summary of Measurement Reproducibility

- Acoustic rhinometry demonstrates excellent reproducibility.
- Nasal secretion weight demonstrates good reproducibility.
- Total nasal symptom score demonstrates good reproducibility.