Pollen immunotherapy reduces the development of asthma in children with allergic rhinoconjunctivitis (The PAT-Study)

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Aim

To study the influence of allergy vaccinations (specific immunotherapy) with birch and/or grass pollen allergen extracts in children suffering from allergic rhinoconjunctivitis on the onset of bronchial hyperresponsiveness and the development of asthma.
**Materials and methods I**

- **Patients**
  
  Children (aged 6-15 yr.) with allergic rhinitis caused by grass (*Phleum pratense*) and/or birch (*Betula verrucosa*)

- **Criteria of inclusion**
  
  - Clinical history of pollinosis
  - Skin Prick Test (D+d)/2 > 3 mm (Soluprick SQ)
  - Conj. challenge test < 100,000 SQ-U (Aguagen SQ)
  - Positive specific IgE test

- **Criteria of exclusion**
  
  - Allergic clinical symptoms caused by perennial allergy
  - Any diagnose of asthma

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**Materials and methods II**

- **Metacholine challenge test**
  
  0.5, 1, 2, 4, 8, 16 mg/ml, Pari Provocation Test (PARI 346 nebulizer)

- **Allocation**
  
  Based on age, sex, bronchial hypersensitivity to metacholine and the duration of allergy

- **Treatment**
  
  - **Control group:** Optimal symptomatic medication
  - **SIT group:** Vaccines (Alutard SQ) for three years and optimal symptomatic medication

- **Maintenance dose**
  
  - Grass (20 µg Phl p5)
  - Birch (13 µg Bet v1)
Demographic data

<table>
<thead>
<tr>
<th></th>
<th>All included</th>
<th>No asthma</th>
<th>Asthma ***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>208 (205)*</td>
<td>163</td>
<td>42</td>
</tr>
<tr>
<td>Mean age (range)</td>
<td>10.7 (6-15)</td>
<td>10.7 (6-15)</td>
<td>10.6 (6-14)</td>
</tr>
<tr>
<td>Sex M/F</td>
<td>138/70 (137/68)*</td>
<td>108/55</td>
<td>29/13</td>
</tr>
<tr>
<td>Mean years with hay fever (range)</td>
<td>4.7(1-15)** N=171</td>
<td>4.6(1-15)** N=137</td>
<td>4.9(1-9)** N=34</td>
</tr>
<tr>
<td>Methacholine PC20 Mean (range)</td>
<td>10.8 (0.03-16)</td>
<td>12.2 (0.16-16)</td>
<td>5.1 (0.03-16)</td>
</tr>
<tr>
<td>Control/SIT for 3 years</td>
<td>94/87</td>
<td>72/79</td>
<td>22/18</td>
</tr>
</tbody>
</table>

*   Three patients dropped out of before baseline monitoring season (0-season)
**  Only patients with reliable information’s included
*** Mild seasonal asthma during first season before randomization

Patient specifications

- **Sensitisation**
  - Birch allergic 43
  - Grass allergic 124
  - Birch and Grass allergic 41

- **Patients without other sensitivities** 56 (27%)
  - Average other sensitivities 1.6
  - Few patients with more than 3 sensitivities

- **Non diagnosed asthma at inclusion** 40 (20%)
Bronchial hyperresponsiveness at inclusion
(percentage of patients in each of three classes)

<table>
<thead>
<tr>
<th>Season</th>
<th>&lt; 2</th>
<th>≥ 2 - &lt;8</th>
<th>≥ 8</th>
</tr>
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<tbody>
<tr>
<td>Birch</td>
<td>48.2</td>
<td>20.5</td>
<td>31.3</td>
</tr>
<tr>
<td>Grass</td>
<td>36.5</td>
<td>26.3</td>
<td>37.2</td>
</tr>
<tr>
<td>Winter</td>
<td>33.2</td>
<td>24.5</td>
<td>42.3</td>
</tr>
</tbody>
</table>

PC20 (mg/ml metacholine)

MBPT- During season
Relative change from baseline

Mean PC20

-1 -0.5 0 0.5 1
Control Active

1st year 2nd year 3rd year
MBPT- Out of season (Winter)
Relative change from baseline

<table>
<thead>
<tr>
<th>Mean PC20</th>
<th>1st year</th>
<th>2nd year</th>
<th>3rd year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active</td>
<td></td>
<td></td>
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</tbody>
</table>

* 1st year
** 2nd year
*** 3rd year

Definition of clinical asthma

- Two out of the following symptoms (repeated):
  - Coughing
  - Wheezing
  - Shortness of breath

- Not triggered by infections
- Effect of beta2-agonist
Development of asthma at 3 years
N=151 (patients without asthma in season one)

Odds-ratio = 2.52
(1.3 – 5.1)

Conclusion

- In allergic children suffering from hay fever caused by allergy to grass and/or birch pollen and no diagnosed asthma, there is a high frequency of bronchial hyperresponsiveness and undiagnosed asthma.

- Allergy vaccinations reduces the risk for development of asthma in children suffering from hay fever.