A DOUBLE-BLIND CLINICAL COMPARISON BETWEEN
BUDESONIDE AND PLACEBO IN ALLERGIC RHINITIS

J. Suonpää, ENT-Dept., University of Turku,
Finland

N. Lindqvist, Medical Dept., AB Draco, Lund,
Sweden

J. Suonpää, M.D.

N. Lindqvist, M.Pharm.Sci

791217
SUMMARY

25 patients with seasonal rhinitis entered a double-blind study comparing nasal sprays of budesonide 200 µg b.i.d. with placebo. Patients were allocated randomly to two parallel groups. Symptoms were assessed over a treatment period of 3 weeks. Nasal peak expiratory flow rate (PEFR) was also daily measured at 8 a.m., 5 p.m. and 10 p.m.

There were statistically significant differences in favour of budesonide on nasal PEFR at 8 a.m. and 10 p.m. Symptom scores were also lower in patients on budesonide, but the difference against placebo was not statistically significant. There was no effect on adrenocortical function. Side effects were mild and the incidence was negligible.
A DOUBLE-BLIND CLINICAL COMPARISON BETWEEN BUDESONIDE AND PLACEBO IN ALLERGIC RHINITIS

Purpose

To compare clinical effect and side effects of budesonide 200 μg b.i.d. with placebo in patients suffering from hay fever.

Patients

25 out-patients, 8 males and 17 females, and their ages ranged from 14 to 53 years (mean age 29.5 years). All patients had a history of hay fever with two or more of the symptoms blocked nose, running nose and sneezing for at least 2 years. All patients had been tested by skin-prick with various common allergens and shown a positive reaction to at least one, all demonstrated a positive reaction to birch. The trial was carried out during the birch pollen season, May 11th - June 11th, 1979.

Patient exclusion criteria

Pregnancy. Patients less than 14 years of age.

Informed consent

Before including a patient the investigator gave a full information about the trial and also about his right to withdraw at any time. All patients gave their consent to the trial.

Dosage, administration and duration of treatment

The test preparations were given as pressurized aerosols with one puff into each nostril morning and afternoon, e.g. 8 a.m. and 8 p.m. For patients using the active spray this provided a total daily dose of 400 μg.

The trial was a double-blind comparison between budesonide spray and an identical placebo spray, being conducted over three weeks. Patients were allocated randomly to two groups, one receiving placebo and one budesonide.
Concomitant therapy

All patients were allowed to take Lunerin™ mite tablets containing 6 mg brompheniramine and 25 mg phenylpropanolamine when the symptoms became too severe. Other medications for rhinitis treatment were withdrawn.

Registration

1. The patients recorded daily symptom scores for nasal blockage, nasal discharge and sneezing bouts according to the following scale:

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No</td>
</tr>
<tr>
<td>1</td>
<td>Mild</td>
</tr>
<tr>
<td>2</td>
<td>Moderate</td>
</tr>
<tr>
<td>3</td>
<td>Severe</td>
</tr>
</tbody>
</table>

Maximal total symptom scores were 9.

2. Nasal peak expiratory flow rate (PEFR) manoeuvres were daily recorded at 8 a.m., 5 p.m. and 10 p.m. The highest value of three readings was used for statistical evaluation. A mini-Wright peak flow meter adapted to a face mask was used by the patients.

3. Consumption of Lunerin™ mite tablets was daily recorded.

4. Side effects were daily recorded.

The patient saw the investigator before and after the treatment period, when a general ENT-examination was performed. During these visits always at the same hour in the morning (7-9 a.m.) blood for serum cortisol determination was drawn.

Statistical analysis

Two-sided Student's t-test was used for statistical analysis of the diary cards and serum cortisol.

Drop outs

One patient (placebo) did not return to the clinic after the first visit and one patient (budesonide) stopped the treatment after some days due to lack of symptoms.
Results

11 patients were treated with budesonide and 12 patients with placebo.

A. Mean symptom scores and nasal PEFR values

The trial started on May 11th and ended on June 11th, 1979. Birch pollen count in the air was daily registered and reached over 40/m$^3$ during May 18th - 25th. During this period 20 patients, 10 in each treatment group, were involved in the study. These days as well as the whole treatment period have been evaluated statistically.

1. Total nasal symptoms (May 18th - 25th).

Symptom scores were lower in the budesonide group, but the difference against placebo was not statistically significant (Table 1 and Table 2).

2. Nasal PEFR (May 18th - 25th) 8 a.m.

There was a statistically significant difference in favour of budesonide treated patients (Table 1 and Table 2).

3. Nasal PEFR (May 18th - 25th) 5 p.m.

PEFR values were higher in the budesonide group but the difference against placebo was not statistically significant. (Table 1 and Table 2.)

4. Nasal PEFR (May 18th - 25th) 10 p.m.

There was a statistically significant difference in favour of budesonide treated patients (Table 1 and Table 2).

Comments

The birch-pollen season in Turku this year was mild and this can be seen in the very low total nasal symptom scores recorded by the patients. Maximal total symptom scores were 9. Mean values over all days are just about the same as during the selected period with highest pollen count.
B. **Consumption of Lunerin mite tablets**

Four tablets were taken during budesonide treatment by one patient and 30 tablets by four patients during placebo treatment.

C. **Serum cortisol**

Serum cortisol levels did not change significantly from baseline values after three weeks of treatment in either the active or the placebo groups, confirming the lack of suppressive effect of budesonide 400 ug/day on adreno-cortisol function (Table 3).

**Side effects**

**Placebo:**
- itching in the eyes, tiredness
- sneezing occurring immediately after use of the spray
- mild itching in the nose
- itching in the eyes

1 patient

**Budesonide:**
- headache, day 2
- itching, sneezing occurring immediately after use of the spray
- nausea after spray

1 patient
TABLE 1. Mean values ± SEM of total nasal symptom scores and nasal PEFR during the period May 18th – 25th, 1979

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>n</th>
<th>Budesonide</th>
<th>n</th>
<th>Diff. Budesonide-Placebo</th>
<th>mean</th>
<th>t-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total nasal symptom</td>
<td>2,30±0,43</td>
<td>10</td>
<td>1,88±0,35</td>
<td>10</td>
<td>-0,42</td>
<td>-0,74 NS</td>
<td></td>
</tr>
<tr>
<td>scores</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEFR 1/min. 8 a.m.</td>
<td>160,3±14,3</td>
<td>9</td>
<td>232,6±21,1</td>
<td>8</td>
<td>72,3</td>
<td>2,83 x</td>
<td></td>
</tr>
<tr>
<td>PEFR 1/min. 5 p.m.</td>
<td>173,2±14,0</td>
<td>9</td>
<td>226,1±25,1</td>
<td>8</td>
<td>52,9</td>
<td>1,84 NS</td>
<td></td>
</tr>
<tr>
<td>PEFR 1/min. 10 p.m.</td>
<td>165,8±12,4</td>
<td>9</td>
<td>233,7±23,7</td>
<td>8</td>
<td>67,9</td>
<td>2,40 x</td>
<td></td>
</tr>
</tbody>
</table>

x = p<0,05

TABLE 2. Mean values ± SEM of total nasal symptom scores and nasal PEFR during 3 weeks of treatment

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>n</th>
<th>Budesonide</th>
<th>n</th>
<th>Diff. Budesonide-Placebo</th>
<th>mean</th>
<th>t-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total nasal symptom</td>
<td>2,27±0,28</td>
<td>11</td>
<td>1,85±0,31</td>
<td>12</td>
<td>-0,42</td>
<td>-0,97 NS</td>
<td></td>
</tr>
<tr>
<td>scores</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEFR 1/min. 8 a.m.</td>
<td>179,6±13,2</td>
<td>7</td>
<td>241,6±22,2</td>
<td>7</td>
<td>42,0</td>
<td>2,47 x</td>
<td></td>
</tr>
<tr>
<td>PEFR 1/min. 5 p.m.</td>
<td>193,5±12,9</td>
<td>7</td>
<td>244,4±22,3</td>
<td>7</td>
<td>50,9</td>
<td>2,03 NS</td>
<td></td>
</tr>
<tr>
<td>PEFR 1/min. 10 p.m.</td>
<td>185,6±10,9</td>
<td>6</td>
<td>242,1±24,3</td>
<td>7</td>
<td>56,5</td>
<td>2,21 x</td>
<td></td>
</tr>
</tbody>
</table>

x = p<0,05
### TABLE 3. Mean serum cortisol levels ± SEM at baseline and after three weeks of treatment

<table>
<thead>
<tr>
<th></th>
<th>Baseline cortisol/s mg/ml ± SEM</th>
<th>Final cortisol/s mg/ml ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Budesonide group n = 11</td>
<td>17.3 ± 1.89</td>
<td>15.6 ± 2.00</td>
</tr>
<tr>
<td>Placebo group n = 12</td>
<td>12.2 ± 1.49</td>
<td>12.6 ± 0.80</td>
</tr>
</tbody>
</table>