Effect of nasal valve dilation on effective CPAP level in obstructive sleep apnea

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Summary Nasal problems are frequent at high continuous positive airway pressure (CPAP). We hypothesized that a reduction of the nasal resistance reduces CPAP and investigated the effect of a nasal valve dilator (Nozovent®) on CPAP in patients with obstructive sleep apnea. In a randomized cross-over design Nozovent® was inserted in 38 patients during one of two nights using AutoSet T®. CPAP differences > 1 cm H2O were considered as clinically relevant. With Nozovent® the median CPAP pressure was reduced from 8.6 cm H2O to 8.0 H2O (P = 0.023) in all patients, but the number of patients with a reduction of CPAP by 1 cm H2O was not significant. The median CPAP level among 20 patients requiring a CPAP level of above 9 cm H2O was reduced from 10.3 to 9.1 cm H2O, P < 0.05. A clinical improvement with Nozovent® was seen in 10 of 20 patients requiring a pressure of above 9 cm H2O compared with 4 of 18 patients who needed lower pressures, P = 0.025. Nozovent® reduces the CPAP level 1 cm H2O in 50% of patients requiring a high pressure (> 9 cm H2O). Future studies should identify possible patients benefiting from a nasal dilator during CPAP therapy.

KEYWORDS
Sleep apnea syndromes; Continuous positive airway pressure; Nasal resistance; Nasal obstruction; Nasal dilation; Auto-CPAP

Introduction

Nasal dryness, nasal congestion and drippy nose occur in about 50% of patients treated with continuous positive airway pressure (CPAP) because of obstructive sleep apnea (OSA).1–3 These nasal problems are a main side effect of CPAP and also a main reason for discontinuing CPAP therapy.4 Mesiler et al.3 observed that a dry mouth and a drippy nose were more frequent at pressure levels of above 12 cm H2O than below 8 cm H2O. Disturbances from a noisy blower was another main complaint.2,3

Several nasal dilating devices, including the nasal valve dilator (Nozovent®), reduce nasal resistance and improve nasal breathing.5,6 The Nozovent® consists of a plastic bar that dilates the anterior part of the nose, the valve region, in order to increase airflow. Nozovent® lacks effect on snoring and sleep apnea,6,7 but it reduces nasal resistance and increases airflow. A consequent treatment of nasal obstruction might reduce nasal side effects during CPAP therapy and hence improve compliance with CPAP. In this study we aimed to investigate whether Nozovent® would lower the CPAP level required to abolish sleep apneas. We therefore investigated the effect of a plastic nasal valve dilator (Nozovent®) during CPAP treatment. We
applied a validated CPAP autotitration device (AutoSet T\textsuperscript{R}),\textsuperscript{8} in order to provide a more reproducible procedure to find the adequate CPAP level compared to traditional CPAP titration.

**Materials and methods**

**Patients**

The population consisted of subjects referred to the Krankenhaus Kloster Grafschaft for assessment of possible sleep disordered breathing. Thirty-eight consecutive patients with respiratory disturbances index over 20 events/h, according to simplified ambulatory sleep apnea recordings and a history of snoring were included. They were 31 men and 7 women with a mean age of 55.4 ± 11.4 years old. All subjects were tired during the daytime with an Epworth sleepiness scale score over 10. An informed consent was obtained from each participating subject.

**The nasal dilator**

The nasal dilator (Nozovent\textsuperscript{R}, Prevancure AB, Sweden, Fig. 1) consists of a plastic bar with two tabs on each end. It is designed to fit inside the nostril and dilate the nasal valves by means of its elasticity and thus decrease nasal resistance and improve airflow. Each patient was given the optimal size of the device (i.e. small, medium or large). Patients with reduced tolerance were instructed to apply the device at least two times a day in order to familiarize with the treatment.

**Study design**

The nasal dilators (Nozovent\textsuperscript{R}) were inserted with a randomized cross-over design during one of two CPAP titration nights. Median, 95% percentile and maximum of CPAP pressure during the CPAP titration nights were analyzed using AutoSet T\textsuperscript{R} automatic CPAP system (ResMed, Mönchengladbach, Germany) which eliminates detected airflow limitations by increasing CPAP pressure. In all patients the upper and lower limits of CPAP pressure levels were kept stable for both nights at a minimum of 4 cm H\textsubscript{2}O and at a maximum of 16 cm H\textsubscript{2}O. The stabilization time for reacting on detected events by increasing CPAP pressure was set to 1 min. Pressure differences of 1 cm H\textsubscript{2}O or more were considered clinical relevant.

All patients were given the following question after each study night: “Did an intranasal irritation caused by Nozovent disturb your sleep quality during the past night?” They were asked to answer “yes” and “no” and also to make additional comments.

**Polygraphic recordings**

Standard polygraphic recordings were made using PolyMESAM (MAP, Martinsried, Germany) and standard polysomnographic recordings were done with the MAP-LAB\textsuperscript{R} system (MAP, Martinsried, Germany). Respiration was monitored using oro-nasal thermistors and thoracic and abdominal movements by piezo belts. Body position and oxygen saturation (\textit{SaO}_2) using finger oximetry were also recorded. A microphone was placed immediately below the larynx. Breathing sounds were analyzed based on the MESAM 4 algorithm.

Apnea was defined as a complete cessation of oro-nasal airflow for at least 10s. Apneas were classified as obstructive when thoracic or abdominal movements were present. A central apnea was
scored if a complete cessation of oro-nasal airflow lasting at least 10 s occurred in the absence of thoraco-abdominal movements. A hypopnea was defined as a 50% or larger reduction in the amplitude of the airflow waveform from a preceding stable baseline, associated with a decrease in oxygen saturation of 4% or more. Apnea index (Al) was defined as the number of apneas divided by hours of sleep and respiratory disturbance index (RDI) as the mean number of apneas and hypopneas per hour of sleep. Finally, the mean and nadir oxygen saturation (SaO2) associated with an abnormal respiratory event during sleep were determined.

Statistical analysis

Results were expressed as the mean ± standard deviation (SD). For comparison of pressures, RDI, Al, SaO2 mean and SaO2 nadir with and without Nozovent®, t-tests for dependent samples were used. For identification of responder-subgroups t-tests for independent samples (gender) and Pearson product-moment correlations (age) were used. Chi-square test was used to test whether the number of patients with clinical improvement or deterioration differed. A two-tailed P-value < 0.05 was considered significant.

Results

Thirty-eight patients (31 males, 7 females) with a mean body mass index of 35.3 ± 5.6 kg/m², a mean age of 55.4 ± 11.4 years, a mean RDI of 47.2 ± 22.9/h and a mean Al of 17.1 ± 18.3/h were included in the study. Using Nozovent®, the median CPAP pressure in the whole population was reduced from a mean (SD) of 8.6 (±2.2) to 8.0 (±2.2) cm H₂O (P = 0.023). Mean 95% percentile of CPAP pressure and maximum CPAP pressure during the night were unaffected by the use of Nozovent® (Table 1). The median CPAP pressure with Nozovent® remained within ±1 cm H₂O in 18 patients compared to CPAP Pressure without Nozovent®. We found no difference in the number of patients with clinical improvement (i.e. CPAP pressure decreased in 14 patients) or deterioration (i.e. CPAP pressure increased in six patients) (P > 0.05).

Taking 9 cm H₂O as a threshold value 20 of 38 patients required a median pressure of above 9 cm H₂O without Nozovent (Group 1). They had a mean median pressure of 6.7 (±1.4) without Nozovent® and 6.8 (±2.1) cm H₂O with Nozovent® (P > 0.05).

A clinical improvement, i.e. with a reduction of CPAP pressure more than 1 cm H₂O, using Nozovent® was seen more often in group 1 than compared group 2 (P = 0.025). The median pressure was reduced by >1 cm H₂O in 50% (10 of 20 patients) in group 1, in nine patients the resulting difference was <1 cm H₂O and in one patient it increased by exactly 1 cm H₂O using Nozovent®. In contrast to that, in group 2 only 4 of 18 patients reduced the pressure more than 1 cm H₂O, seven patients increased the pressure >1 cm H₂O and seven patients had a difference of <1 cm H₂O between the two recordings.

There were no gender differences regarding the effect of Nozovent® on CPAP level or polygraphic data and no correlation with age was observed. The responder group (>1 cm H₂O decrease of median CPAP level) did not differ from non-responders regarding BMI, RDI or Al (P > 0.3).

RDI and Al decreased and SaO2 values increased significantly during CPAP therapy (P < 0.001) but

Table 1. CPAP pressure with and without nasal dilator.

<table>
<thead>
<tr>
<th>Pressure (cm H₂O)</th>
<th>Without Nozovent</th>
<th>With Nozovent</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>8.6 ± 2.2</td>
<td>8.0 ± 2.2</td>
<td>0.0231</td>
</tr>
<tr>
<td>95%-Percentile</td>
<td>10.8 ± 2.0</td>
<td>10.6 ± 2.3</td>
<td>0.4637</td>
</tr>
<tr>
<td>Maximum</td>
<td>12.0 ± 2.1</td>
<td>11.9 ± 2.4</td>
<td>0.5281</td>
</tr>
</tbody>
</table>

Fig. 2 Median CPAP without and with Nozovent® in the two groups with CPAP < or >9 cm H₂O without Nozovent®.
these indices were not influenced from the nasal dilator \((P>0.05; \text{ Table 2})\). Polygraphic data at baseline and during CPAP titration with and without Nozovent\(^\mathbb{R}\) are given in Fig. 3.

Finally, no patient indicated sleep disturbance caused by local side effects of Nozovent\(^\mathbb{R}\).

**Discussion**

Using Nozovent\(^\mathbb{R}\), the required CPAP level was reduced for the whole group of 38 patients studied, but the reduction was below 1 cm H\(_2\)O and therefore not regarded as clinically relevant. The reduction was, however, more prominent among subjects who required a CPAP of above 9 cm H\(_2\)O and 50\% of these patients had a clinical relevant reduction of the median CPAP level of 1 cm H\(_2\)O or more using Nozovent\(^\mathbb{R}\). We can however not exclude that high initial CPAP pressures reduce more than lower pressures after intervention, i.e. a “regression towards the mean” phenomenon.

Our results support that Nozovent\(^\mathbb{R}\) might be of value in selected patients requiring high CPAP. It is possible that the nostrils are diminished in size because of the external pressure on the alae nasi during high CPAP levels. Subjects with floppy alae nasi are probably more vulnerable to external pressures. As the analysis included consecutive patients referred to the clinic, an even higher potential benefit of Nozovent\(^\mathbb{R}\) in selected patients may have been masked.

In this context it is a limitation of the study that no elaborated examination of the nasal anatomy (e.g. rhinomanometry or the investigation of the alar status) by an ear–nose–throat specialist was done. The later possibly delivers deeper pathophysiologic insight and predictors of a successful intervention with Nozovent\(^\mathbb{R}\).

Only a few studies investigate the effect of reduced constant CPAP levels on treatment compliance. However, recently a long-term follow up was published investigating patients with OSA and moderate nasal obstruction \((n=39)\) who underwent functional rhinosurgery before CPAP therapy.\(^6\)

Mean nasal flow increased by 70\% (i.e. from 398 to 711 ml/s) in the intervention group. Compared to the control group, after 3 years the mean CPAP pressure was 1.5 cm H\(_2\)O lower and the daily use increased by 0.8 h/day in the interventional group. These results indicate that a reduced CPAP level improves compliance, since a negative correlation between the CPAP level and the daily CPAP use was observed in both groups.

Recent studies,\(^10\)–\(^12\) report that nasal resistance has no impact on the pathogenesis of OSA. Thus, both snoring and sleep apnea are probably caused by other factors, such as restrictive processes in the pharyngeal area, rather than increased nasal resistance at the nasal valves. Metes et al.\(^6\) did not find any effect on snoring, apneas, hypopneas or oxygen saturation in a small sample of patients, despite a reduction in nasal resistance. Moreover, in a recent study we did not find any effect of Nozovent\(^\mathbb{R}\) on OSA.\(^7\)

Although nasal resistance and Nozovent\(^\mathbb{R}\) do not seem to affect OSA, it is still possible that the degree of nasal resistance may affect the CPAP level to abolish apneas. We did not measure the nasal resistance or the anatomy of the alae nasi, which are limitations of the present study. It is therefore not possible from this study to predict which patients in particular may benefit from nasal dilator during CPAP therapy.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Diagnosis</th>
<th>Without Nozovent</th>
<th>With Nozovent</th>
<th>P-value (Nozovent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RDI (/h)</td>
<td>47.2 ± 22.9</td>
<td>11.9 ± 8.5</td>
<td>12.4 ± 8.7</td>
<td>0.7673</td>
</tr>
<tr>
<td>AI (/h)</td>
<td>17.1 ± 18.3</td>
<td>2.8 ± 2.7</td>
<td>3.4 ± 3.5</td>
<td>0.2100</td>
</tr>
<tr>
<td>SaO(_2) mean (%)</td>
<td>92.2 ± 3.1</td>
<td>94.4 ± 2.3</td>
<td>93.8 ± 2.8</td>
<td>0.0791</td>
</tr>
<tr>
<td>SaO(_2) nadir (%)</td>
<td>72.9 ± 11.6</td>
<td>84.4 ± 4.9</td>
<td>80.6 ± 9.3</td>
<td>0.0632</td>
</tr>
</tbody>
</table>

**Table 2** Polygraphic data at baseline, CPAP1 (without Nozovent\(^\mathbb{R}\)) and CPAP2 (with Nozovent\(^\mathbb{R}\)).
In a recent publication, Wiest et al. reported that manual CPAP titration results in a difference of up to 3.0 cm H2O between two consecutive CPAP titrations despite the use of a standardized protocol.13 We applied an autotitration system (AutoSet® automatic CPAP system) to determine the effective minimum pressure required to abolish sleep apneas. AutoSet® is based on an automated, objective method to eliminate inspiratory flow limitation. Its algorithm yields a significant improvement of sleep-disordered breathing and sleep architecture considering the titration period14 and maintained at 3 and 8 months.8 This method is based on a consistent algorithm and therefore reduces the potential influence of subjectivity during manual CPAP titrations.

We intended to measure whether a nasal dilator could lower the CPAP level or not in an unselected group of patients. Clinical issues, which need a longer observation period, were not the aim of this physiologic study. Thus we did not investigate whether patients experienced a beneficial effect from Nozovent® regarding sleep quality, improved nasal ventilation, mask leakage and compliance to CPAP therapy. In the future we suggest studies using Nozovent in combination with CPAP on patients with problems from the nose during CPAP therapy.

One could speculate that the addition of a second device to the CPAP nasal mask would irritate the patient and disturb sleep. We cannot exclude such a negative side from our data, since we did not investigate whether patients experienced a beneficial effect from Nozovent® regarding sleep quality, improved nasal ventilation, mask leakage and compliance to CPAP therapy. In the future we suggest studies using Nozovent in combination with CPAP on patients with problems from the nose during CPAP therapy.

References