An Individually Adjustable Oral Appliance vs Continuous Positive Airway Pressure in Mild-to-Moderate Obstructive Sleep Apnea Syndrome*

Winfried J. Randerath, MD, FCCP; Markus Heise, DSD; Rolf Hinz, DSD; and Karl-Heinz Ruehle, MD

**Background:** For the treatment of nonsevere obstructive sleep apnea syndrome (OSAS), mandibular advancement devices (MADs) are employed as an alternative to nasal continuous positive airway pressure (CPAP) therapy. However, very few specific data on the effectiveness of MADs in this group of patients are available. We therefore compared an individually adjustable intraoral sleep apnea device (ISAD) that permits movements of the lower jaw in three dimensions, with CPAP in the treatment of patients with an apnea/hypopnea index (AHI) < 30/h.

**Methods:** In a randomized crossover study, 16 men and 4 women (mean ± SD age, 56.5 ± 10.2 years; body mass index, 31.2 ± 6.4; AHI, 17.5 ± 7.7/h) were treated for 6 weeks with each modality.

**Results:** In the initial phase, a significant improvement in AHI (baseline, 17.5 ± 7.7/h; ISAD, 10.5 ± 7.5/h [p < 0.05]; CPAP, 3.5 ± 2.9/h [p < 0.01]) and in breathing-related arousals (baseline, 8.9 ± 6.1/h; ISAD, 3.7 ± 3.3/h [p < 0.01]; CPAP, 1.4 ± 1.6/h [p < 0.01]) was achieved with both modalities. Considering all 20 subjects, after 6 weeks of treatment, normalization of the respiratory parameters was seen only with CPAP. However, 30% of the patients had a lasting reduction in AHI to < 10/h with the ISAD also. The patients considered the ISAD to be easier to use (scale of 1 to 6: ISAD, 1.8 ± 1.1; CPAP, 3.1 ± 1.5 [p < 0.05]), and indicated greater utilization of the device in comparison with CPAP.

**Conclusion:** Even in patients with mild-to-moderate OSAS, CPAP is the more effective long-term treatment modality. In the individual case, the better compliance seen with the ISAD may be advantageous.

*CHEST 2002; 122:569–575*

**Key words:** continuous positive airway pressure; mandibular advancement device; orthodontic appliances; positive pressure ventilation; sleep apnea, obstructive

**Abbreviations:** AHI = apnea/hypopnea index; ASDA = American Sleep Disorders Association; BMI = body mass index; CPAP = nasal continuous positive airway pressure; ISAD = intraoral sleep apnea device; MAD = mandibular advancement device; NS = not significant; OSAS = obstructive sleep apnea syndrome; SaO₂ min = minimal oxygen saturation in relation to respiratory disturbances during total sleep time; TST = total sleep time

---

Despite its effectiveness in the treatment of the obstructive sleep apnea syndrome (OSAS), nasal continuous positive airway pressure (CPAP) is not fully accepted by all patients. Therefore, attempts have been made to employ oral appliances alternatively. The aim of such treatment is to enlarge the anteroposterior diameter of the retroglossal space, and thus reduce pharyngeal collapse. Of particular interest in this context are mandibular advancement devices (MADs), which are orthodontic appliances capable of advancing the lower jaw. In contrast to tongue-retaining appliances, MADs are more readily accepted by the patient. Schmidt-Nowara et al investigated 68 patients treated with a dental orthosis for an average of 7 months. An improvement in snoring and sleep quality on the basis of subjective parameters was found, together with a reduction in the apnea/hypopnea index (AHI) that, however, did not go to < 20/h with treatment. Eveloff et al, studying a “Herbst MAD,” found a decrease in AHI from 34.7 ± 5.3 to 12.9 ± 2.4/h. Bloch et al, using...
two different MADs (a single-piece and a two-piece appliance), found a reduction in AHI to < 10/h in 88% of the patients, at least with one device. In contrast, Millman et al found only 10 responders to treatment with an “adjustable mandibular advancement Herbst appliance” in 24 patients who had previously undergone uvulopalatopharyngoplasty. Recently, Mehta et al, in a placebo-controlled study, reported that 62.5% of the patients treated with a “mandibular advancement splint” showed at least a “partial response.”

Only few data obtained from prospective randomized studies comparing MADs with CPAP are currently available. Clark et al found a reduction in respiratory disturbances of 39% with an “anterior mandibular positioning device,” and 50% with CPAP. However, the AHI with CPAP was reduced only to 11.15 ± 3.93/h. Moreover, comparison of the two treatment modes in this study was not done in randomized fashion. Ferguson et al performed a randomized crossover study with a nonadjustable oral appliance. Respiratory disturbances and daytime symptoms showed significantly greater improvement with CPAP than with an MAD. After 4 months of treatment using an adjustable anterior mandibular positioner, the same authors recorded a decrease in AHI from 25.3 ± 15.0 to 14.2 ± 14.7/h, corresponding to 44% of the baseline value. In seven patients, the AHI remained > 10/h. Although a clearly greater improvement in the respiratory disturbances was seen with CPAP, no relevant differences were observed between the two modalities in terms of sleep profile, and there was no improvement vs baseline in sleep profile. With regard to compliance, the oral appliance also proved to be clearly superior to CPAP treatment.

In contrast to uncontrolled studies, which report large reductions in AHI, the above-mentioned controlled studies failed to find such a positive effect of an MAD on sleep-related disturbances. On the basis of these data, the use of MADs was recommended only in patients with nonobstructive snoring or mild sleep apnea. In severe OSAS, MADs should only be used if the patients refuse CPAP. Against this background, we therefore carried out a randomized crossover study to compare—for the first time, as far as we are aware—an MAD with CPAP applied over the long term exclusively in patients with an AHI ≤ 30/h in accordance with the recommendations of the American Sleep Disorders Association (ASDA). Our aim was to investigate the effectiveness and acceptance of an adjustable orthodontic device permitting jaw movements in three dimensions (an intraoral sleep apnea device [ISAD]), in comparison with CPAP.

**Materials and Methods**

**Patients**

Twenty patients (16 men and 4 women; mean ± SD age, 56.5 ± 10.2 years; body mass index [BMI], 31.2 ± 6.4), who had been referred to a university sleep laboratory for the diagnosis and treatment of OSAS were investigated between January 1999 and December 1999. Inclusion criteria were an AHI of 5/h minimum and 30/h maximum (mean, 17.5 ± 7.7/h) measured in two diagnostic polysomnographies, and clinical symptoms of OSAS. The patients were submitted to two diagnostic measurements to ensure that, in the event of appreciable night-to-night variability, only patients with an AHI ≤ 30/h were admitted. Exclusion criteria were an AHI > 30/h, temporomandibular joint disorders, bruxism, and patients with gaps in their dentition precluding fitting of the device. We studied only patients with mild-to-moderate OSAS, so as to comply with ASDA recommendations. Patients with more severe OSAS were not included since MADs are recommended in this group only if CPAP is not accepted. Since the diagnosis of OSAS and the need for treatment were established for the first time in all participants, refusal of CPAP could not legitimately be used as an inclusion criterion. All patients gave their informed consent. The study was approved by the ethics committee of the University Witten/Herdecke.

**Devices**

The ISAD (IST; Hinz; Herne, Germany) is an oral appliance for the noninvasive treatment of sleep-disordered breathing. Two thin thermoplastic parts, worn on the upper and lower jaws, are connected by two adjustable telescopic guide rods (Scheidental; Iserlohn, Germany) in the vestibule. The ISAD works by advancing and slightly depressing the mandible and tongue while imparting a slight vertical clockwise rotation. Prior to customizing the device, any pathology of the temporomandibular joints was excluded by a manual functional examination, with particular attention being paid to excursive movements. After obtaining an impression of the upper and lower teeth, the dentist determined the amount of mandibular advancement and the size of the bite opening with a construction bite obtained with the George Gauge instrument. The maximum forward protrusion of the mandible was measured, and this amount reduced to about two thirds before mounting the casts in the articulator (Fig 1).

**CPAP Devices**

Patients were treated with commercially available CPAP devices (Max II, MAP, Martinsried, Germany; Somnotron, Weinmann, Hamburg, Germany; and Vector, Hoffrichter, Schwerin, Germany). The treatment pressure was increased in incremental steps of 1 cm H2O until respiratory disturbances were minimized and respiration related arousals were reduced to ≤ 5/h. The mean CPAP treatment pressure was 7.4 ± 0.9 cm H2O.

**Design**

Following the diagnostic polysomnographies, manual CPAP titration, and customized fitting of the ISAD, the patients underwent, in randomized crossover fashion, 1 night of polysomnography with CPAP (CPAP, first night) and 1 night with the ISAD (ISAD, first night), which was then followed by 6 weeks of home treatment with CPAP and 6 weeks with the ISAD or vice versa. During the initial 6 weeks of treatment with the ISAD, patients need to adapt to the device, so the amount of protrusion was not adjusted during this period. Eight patients began treat-
A hypopnea was defined as a reduction of flow or effort of 50% in comparison with baseline for at least 10 s or any reduction of flow and effort and a decrease in oxygen saturation of at least 4%. To quantify snoring, the number of epochs (30 s per page) with evidence of microphone signals for at least 2 s outside of movement artifacts were counted as previously described.26–28

Also calculated was the minimal oxygen saturation in relation to respiratory disturbances during the total sleep time (TST) \([\text{Sa}_2 \text{O}_2 \text{ min}]\).

Statistics

The statistical calculations for significant differences between baseline and the treatment modes, with rejection of the null hypothesis at a \(p < 0.05\), were carried out with the analysis of variance with Bonferroni correction. Comparisons between responders and nonresponders to ISAD treatment were effected with the Mann-Whitney test.

RESULTS

With CPAP, a significant improvement in the respiratory parameters (AHI, snoring, \(\text{Sa}_2 \text{O}_2 \text{ min}\)) and sleep quality (total number of arousals and respiration-induced arousals) was achieved at both measuring time points (first night and 6 weeks; Table 1). The AHI decreased from 17.5/h ± 7.7 to 3.5 ± 2.9/h (first night) and 3.2 ± 2.9/h (6 weeks) \([p < 0.01\text{ in each case};\] the arousal index decreased from 21.8 ± 9.9 to 15.7 ± 5.1/h (first night) and 14.1 ± 5.1/h (6 weeks) \([p < 0.05\text{ in each case};\] and the respiration-induced arousals decreased from 8.9 ± 6.1 to 1.4 ± 1.6/h (first night) and 2.3 ± 4.3/h (6 weeks) \([p < 0.01\text{ in each case};\ Table 1].

With ISAD also, a significant decrease in AHI from 17.5 ± 7.7 to 10.5 ± 7.5/h \((p < 0.05)\) and in respiration-induced arousals from 8.9 ± 6.1 to 3.7 ± 3.3/h \((p < 0.01)\) was observed on the first night. For the overall group, long-term treatment

### Table 1—Study Data*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Baseline</th>
<th>CPAP Night 1</th>
<th>CPAP 6 wk</th>
<th>ISAD Night 1</th>
<th>ISAD 6 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHI, per h of TST</td>
<td>17.5 ± 7.7</td>
<td>3.5 ± 2.9(\dagger)</td>
<td>3.2 ± 2.9(\dagger)</td>
<td>10.5 ± 7.5(\dagger)</td>
<td>13.8 ± 11.1(\dagger)</td>
</tr>
<tr>
<td>Snoring, epochs/h</td>
<td>54.5 ± 25.9</td>
<td>13.9 ± 8.0(\dagger)</td>
<td>10.3 ± 5.0(\dagger)</td>
<td>28.8 ± 11.1(\dagger)</td>
<td>36.4 ± 17.7(\dagger)</td>
</tr>
<tr>
<td>(\text{Sa}_2 \text{O}_2), min, %</td>
<td>83.6 ± 4.6</td>
<td>88.7 ± 2.7(\dagger)</td>
<td>89 ± 3.4(\dagger)</td>
<td>85 ± 3.9</td>
<td>85.3 ± 3.1(\dagger)</td>
</tr>
<tr>
<td>TST, min</td>
<td>333.8 ± 44.2</td>
<td>291.1 ± 85.6(\dagger)</td>
<td>324.8 ± 48.9</td>
<td>337.2 ± 34.9</td>
<td>327 ± 45.4</td>
</tr>
<tr>
<td>Wake after sleep onset, min</td>
<td>35.9 ± 26.4</td>
<td>45.3 ± 32.8</td>
<td>39.4 ± 24.9</td>
<td>19.7 ± 9.6</td>
<td>39.9 ± 31</td>
</tr>
<tr>
<td>Sleep stage 1, % TST</td>
<td>15.2 ± 9.5</td>
<td>13.6 ± 12.1</td>
<td>12 ± 7.2</td>
<td>11.5 ± 7.3</td>
<td>15 ± 7.9</td>
</tr>
<tr>
<td>Sleep stage 2, % TST</td>
<td>53.6 ± 9.9</td>
<td>50.1 ± 12.3</td>
<td>55 ± 6.8</td>
<td>52.1 ± 8</td>
<td>54.4 ± 10</td>
</tr>
<tr>
<td>Sleep stages 3 and 4, % TST</td>
<td>14.2 ± 10.6</td>
<td>18.6 ± 14.6</td>
<td>16.2 ± 9.1</td>
<td>16.5 ± 8.9</td>
<td>14.1 ± 10.8</td>
</tr>
<tr>
<td>Rapid eye movement, % TST</td>
<td>15.1 ± 5.9</td>
<td>13.3 ± 8.2</td>
<td>15.3 ± 6.8</td>
<td>18.5 ± 18.5</td>
<td>14.8 ± 7.3</td>
</tr>
<tr>
<td>Arousals, per h of TST</td>
<td>21.8 ± 9.9</td>
<td>15 ± 7.5(\dagger)</td>
<td>14.1 ± 5.1(\dagger)</td>
<td>16.3 ± 6.4</td>
<td>17 ± 5.1</td>
</tr>
<tr>
<td>Respiration-induced arousals, per h of TST</td>
<td>8.9 ± 6.1</td>
<td>1.4 ± 1.6(\dagger)</td>
<td>2.3 ± 4.3(\dagger)</td>
<td>3.7 ± 3.3(\dagger)</td>
<td>6 ± 5.6</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD.
\(\dagger\)Significantly different from baseline \((p < 0.05)\).
\(\dagger\)Significantly different from baseline \((p < 0.01)\).
\(\dagger\)Significantly different from CPAP at the corresponding measurement \((p < 0.05)\).
\(\dagger\)Significantly different from CPAP at the corresponding measurement \((p < 0.01)\).
with the ISAD showed a small improvement in AHI that, however, did not reach the level of significance (Table 1). Treatment with the ISAD significantly reduced snoring both in the first night and after 6 weeks (baseline, $54.5 \pm 25.9$ epochs per hour; first night, $28.8 \pm 11.1$ epochs per hour [$p < 0.01$]; six weeks, $36.4 \pm 17.7$ epochs per hour [$p < 0.01$]). After 6 weeks, AHI with CPAP was significantly lower than with the ISAD (CPAP, $3.2 \pm 2.9$/h; ISAD, $13.8 \pm 11.1$/h [$p < 0.01$]). At both measuring points, snoring was significantly lower with CPAP as compared with the ISAD (Table 1).

The study population was classified into three subgroups by baseline AHI ($< 10$/h, 10 to $< 20$/h, and $\geq 20$/h). In the two more seriously affected groups, AHI and snoring improved significantly after the first night and after 6 weeks with CPAP. In patients with AHI $< 10$/h, the reduction in respiratory disturbances did not reach the level of significance. There were no significant differences in AHI between baseline and treatment with the ISAD in either of the subgroups (Fig 2). However, with the ISAD, snoring significantly improved in the two more seriously affected groups in the first night: the subgroup with AHI of 10 to $< 20$/h snoring baseline, $44.4 \pm 13.8$ epochs per hour; first night, $26.4 \pm 8.2$ epochs per hour [$p < 0.01$]; 6 weeks, $33.8 \pm 12.8$ epochs per hour (not significant [NS]); and the subgroup with AHI $\geq 20$/h snoring baseline, $67.1 \pm 26.5$ epochs per hour; first night, $28.1 \pm 2.7$ epochs per hour ($p < 0.01$); 6 weeks, $41.7 \pm 13.5$ epochs per hour (NS).

To study the influence of weight on the efficacy of the appliances, the population was classified according to BMI ($< 27$, 27 to $< 30.5$, and $\geq 30.5$). The AHI showed a tendency to improve in the subgroup with BMI $< 27$ with both modalities, and significant improvements were seen in the other groups receiving CPAP. Moreover, the ISAD brought about a significant reduction in AHI in patients with a BMI $\geq 30.5$ both on the first night and after 6 weeks of treatment (Fig 3).

In 6 of the 20 patients investigated (30%), long-term treatment with the ISAD resulted in a reduction in AHI to $< 10$/h, which was interpreted as signifying efficacy, and was statistically significant.
The patients in whom effectiveness was demonstrated in the first ISAD application differed from nonresponders by their significantly younger age and heavier weight (mean age, 48.3 ± 10.3 years vs 60.6 ± 6.5 years [p < 0.05] and weight, 105.6 ± 23.8 kg vs 82 ± 9.8 kg [p < 0.05], respectively). Also, the ISAD responders to long-term application were significantly younger than the nonresponders (51.3 ± 5.3 years vs 57.5 ± 11.4 years, respectively; p < 0.05). Otherwise, there were no significant differences between responders and nonresponders.

Patient self-assessment revealed no significant differences between the two modalities in terms of improvement in daytime sleepiness, snoring, and concentration. The patients identified the ISAD as being easier to use (score of 1 to 6: ISAD, 1.8 ± 1.1; CPAP, 3.1 ± 1.5 [p < 0.05]).

In the questionnaire, the patients reported greater compliance for the ISAD as compared with CPAP. This applied both to the number of nights during which treatment was applied, and also to the hours of use per night (at > 8 h/d: CPAP, 9%; ISAD, 33% [NS]; at 6 to 7 h/d: CPAP, 27%; ISAD, 53% [NS]; at 4 to 5 h/d: CPAP, 64%; ISAD, 7% [p < 0.01]; and at 2 to 3 h/d: CPAP, 0%; IST, 7% [NS]). All patients used both devices on at least 5 nights per week (7 days: CPAP, 54%; ISAD, 62%; and 5 to 6 days: CPAP, 46%; ISAD, 38% [NS]).

With CPAP treatment, eight patients noted a sensation of pressure on the face (with the ISAD, two patients [p < 0.05]). With the ISAD, two patients noted a feeling of pressure in the mouth (with CPAP, 0 patients [NS]). With the ISAD, eight patients complained of early morning, nonpersisting discomfort in the mouth and temporomandibular joint (with CPAP, 0 patients [p < 0.01]). With regard to other side effects, no relevant differences were found. There were no significant differences between the genders in terms of polysomnographic or compliance parameters.

**Discussion**

The ASDA recognizes intraoral appliances as an alternative to CPAP treatment of nonobstructive snoring and mild OSAS. These ASDA guidelines are grade C recommendations supported by level V evidence. Numerous devices are presently avail-
able that differ widely in terms of material, freedom of mandibular movement, amount and rigidity of dental coverage, amount of mandibular advancement, and bite opening.6–20,22,28 Despite the predominantly positive results, only a few randomized controlled studies have so far been performed to compare MADs with the standard treatment of OSAS applied over the long term.19,20 Stradling et al20 presented data on snoring in the absence of OSAS, showing an improvement also in respiratory effort and autonomous parameters. Ferguson et al19 investigated a nonadjustable device, while our study looked at a device (the ISAD), that is individually adjustable and permits three dimensional movements of the lower jaw. In the study by Ferguson et al,19 patients showed a wide range in the severity of their conditions on diagnostic polysomnography (AHI, 5 to 55/h), although the mean value was not substantially higher than that in our own study. On the basis of the ASDA recommendations,21 our study dealt exclusively with the group of patients with nonsevere OSAS (AHI ≤ 30/h), which was confirmed by two diagnostic polysomnographies. This was done both to exclude patients with severe OSAS erroneously diagnosed as mild on the first night in the sleep laboratory due to intraindividual variability, and also to ensure, on the basis of the symptoms and AHI, that the patients investigated really did have OSAS.

The ISAD reduced snoring at both measuring time points (first night and 6 weeks) but significantly improved the AHI only in the early phase of treatment. In contrast, CPAP normalized AHI, snoring, and arousals throughout the entire treatment period. The remaining number of microphone signals was similar to those of previous studies using the same definition, and may at least partially be artifacts or nonobstructive snores.26–28

This superiority of CPAP may be due to the fact that the ISAD might not have resulted in an enlargement of the upper airways in all patients. Thus, for example, Rodenstein et al30 showed that in patients with OSAS, the long axis of the pharyngeal cross-section may lie in the sagittal plane rather than in the coronary plane. As a result, forward protrusion of the mandible may even diminish the size of the retroglossal space.

Of particular interest would appear to be the fact that the more pronounced effect of the ISAD found initially (first night) subsequently diminished again (6 weeks). Peter et al31 failed to demonstrate an improvement of the success rate of the uvulopalatopharyngoplasty by localizing the site of the stenosis using endoscopy. This was discussed based on the findings that the site of the collapse changes after uvulopalatopharyngoplasty, but an obstruction persists.31 Therefore, our results may also be due to a shift in the location of the obstruction of the upper airways during the course of treatment. In contrast, the effect of CPAP therapy is not influenced by the plane of the long axis of the pharyngeal space, or any shift in the location of the functional narrowing.

Although CPAP therapy is generally more advantageous, adequate treatment (AHI < 10/h) persisting over the longer term was nevertheless also observed in 30% of the patients treated with the ISAD. Responders to treatment with the ISAD were significantly younger than nonresponders. While the mean age of our own patients was 56.5 ± 10.2 years, the patients investigated by Ferguson et al20 had a mean age of 44.0 ± 10.6 years. This might be the explanation for the different percentage of respondents found in the two studies. When the group of 20 patients was classified according to BMI, those with the highest BMI showed a significant improvement in AHI with the ISAD (Fig 3). There were no other differences in the anthropometric or polysonmographic findings between these groups. However, as we did not record body position, the question whether posture might have influenced these results must for the time being remain unanswered.

Another limitation of our study has to be discussed. It is possible that the number of responders might be increased by adjusting the ISAD more specifically. The initial adjustment of the ISAD to 66% of the maximum protrusion was not changed during the treatment period so as to allow the patients to adapt to this form of therapy.

With regard to side effects, mask-related discomfort on the face was frequently observed with CPAP, and morning stiffness in the temporomandibular joint with the ISAD. Evidence of damage in the region of the jaws has not so far been reported,32 although recently published data33 suggest that the use of MADs over 6 to 30 months can cause dental and skeletal changes. The higher percentage of use of the ISAD vs CPAP is in agreement with the results reported by Ferguson et al.20 Moreover, the patients indicated that they found the ISAD easier to use. This might well be the reason why patients applied the ISAD on more days than CPAP. The greater utilization of the ISAD per day might be due to the fact that after waking in the morning, patients no longer reapplied CPAP. The compliance data are largely in accord with the results reported by Weaver et al.,34 who found consistent CPAP use (7 d/wk) in 53% of the patients. However, in that study, intermittent users objectively applied their devices between 2% and 79% of the days, whereas all our patients claimed to use CPAP on at least 5 nights per week. This difference may be due to unreliable self-assessment, in particular by irregular users.
On the basis of the results of effectiveness and compliance taken together, the ISAD cannot be recommended for general use in patients with mild-to-moderate OSAS. An advantage of this modality is its greater acceptance. However, especially the most seriously affected subgroup of our population (AHI ≥ 20/h) failed to show any relevant improvement in AHI. Therefore, also in patients with mild-to-moderate OSAS, CPAP is superior to treatment with the ISAD, in patients who refuse CPAP, the use of mandibular advancement should be considered. The true effectiveness of the ISAD, however, must be assessed on the basis of long-term treatment.

References
3 Cartwright RD, Samelson CF. The effects of a nonsurgical treatment for obstructive sleep apnea. JAMA 1982; 248:705–709
32 Bondermark L. Does 2 years’ nocturnal treatment with a mandibular advancement splint in adult patients with snoring and OSAS cause a change in the posture of the mandible. Am J Orthod Dentofacial Orthop 1999; 116:621–625
33 Robertson BDS. Dental and skeletal changes associated with long-term mandibular advancement. Sleep 2001; 24:531–537
34 Weaver TE, Kribbs NB, Pack AI, et al. Night-to-night variability in CPAP use over the first three months of treatment. Sleep 1997; 20:278–283