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J DENT RES 2008 87: 882
DOI: 10.1177/154405910808700917

RESEARCH REPORTS
Clinical

Obstructive Sleep Apnea Therapy

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J Dent Res 87(9):882-887, 2008

ABSTRACT

In clinical practice, oral appliances are used primarily for obstructive sleep apnea patients who do not respond to continuous positive airway pressure (CPAP) therapy. We hypothesized that an oral appliance is not inferior to CPAP in treating obstructive sleep apnea effectively. We randomly assigned 103 individuals to oral-appliance or CPAP therapy. Polysomnography after 8-12 weeks indicated that treatment was effective for 39 of 51 persons using the oral appliance (76.5%) and for 43 of 52 persons using CPAP (82.7%). For the difference in effectiveness, a 95% two-sided confidence interval was calculated. Non-inferiority of oral-appliance therapy was considered to be established when the lower boundary of this interval exceeded -25%. The lower boundary of the confidence interval was -21.7%, indicating that oral-appliance therapy was not inferior to CPAP for effective treatment of obstructive sleep apnea. However, subgroup analysis revealed that oral-appliance therapy was less effective in individuals with severe disease (apnea-hypopnea index > 30). Since these people could be at particular cardiovascular risk, primary oral-appliance therapy appears to be supported only for those with non-severe apnea. *Abbreviations:* CI = confidence interval, CPAP = continuous positive airway pressure.

KEY WORDS: sleep apnea syndromes, orthodontic appliances, positive-pressure ventilation, treatment outcome, CPAP therapy.

Received June 8, 2007; Last revision February 25, 2008; Accepted May 15, 2008

A supplemental appendix to this article is published electronically only at http://jdr.iadrjournals.org/cgi/ content/ full/87/8/882/DC1.

INTRODUCTION

Obstructive sleep apnea is characterized by disrupted snoring and repetitive upper-airway collapse (Malhotra and White, 2002). Its neurobehavioral consequences include excessive sleepiness, an increased risk of accidents, and an impaired quality of life (Malhotra and White, 2002; Giles *et al.*, 2006). Cardiovascular consequences include hypertension and increased risk of ischemic heart disease, congestive heart failure, and stroke (Marin *et al.*, 2005; Yaggi *et al.*, 2005). Continuous positive airway pressure (CPAP), the standard treatment (Giles *et al.*, 2006), improves blood pressure (Pepperell *et al.*, 2002) and neurobehavioral outcomes (Giles *et al.*, 2006), but since it requires the wearing of an obtrusive device, individuals may abandon or adhere poorly to therapy (Barbe *et al.*, 2001; Barnes *et al.*, 2002).

Oral-appliance therapy is an alternative to CPAP that relieves upper-airway collapse during sleep by modifying the position of the mandible, tongue, and pharyngeal structures (Cistulli *et al.*, 2004). Although effective, it is generally considered less effective than CPAP (Barnes *et al.*, 2004; Hoekema *et al.*, 2004; Lim *et al.*, 2006). Nevertheless, many people prefer an oral appliance to CPAP, and physiological and neurobehavioral outcomes are not substantially different between the therapies (Barnes *et al.*, 2004; Hoekema *et al.*, 2004).

Specific indications for oral-appliance therapy are indeterminate (Cistulli *et al.*, 2004; Hoekema *et al.*, 2004; Lim *et al.*, 2006). It is prescribed primarily for persons unwilling or unable to tolerate CPAP (Lim *et al.*, 2006). Moreover, insurance regulations, as in The Netherlands, usually dictate that oral appliances be used as a secondary intervention in case CPAP fails. We hypothesized that an oral appliance is not inferior to CPAP in treating obstructive sleep apnea effectively. Because of indications that effectiveness of oral-appliance therapy is related to disease severity, we designed a randomized parallel trial to evaluate the treatment in individuals representing the entire spectrum of the disorder.

METHODS

Participant Selection

Participants were recruited through the Department of Home Mechanical Ventilation of the University Medical Center Groningen, The Netherlands. Individuals over age 20 yrs who underwent polysomnography and were diagnosed as having obstructive sleep apnea were eligible. Participants were selected based on medical, psychological, and dental criteria. The trial was approved by the Groningen University Medical Center's ethics committee. Written informed consent was obtained from participants before enrollment. Details of the trial are provided in Appendix 1.

Study Design

We used block randomization to allocate participants to groups treated with

an oral appliance or CPAP (Altman, 1991). At baseline, each person underwent a physical and neurobehavioral examination. Severity of disease was assessed based on the apnea-hypopnea index: the mean number of apneas and hypopneas *per* hr of sleep. Participants were classified as having non-severe (apnea-hypopnea index 5-30) or severe (apnea-hypopnea index > 30) obstructive sleep apnea.

After participants used an oral appliance or CPAP for 8 wks, the effect was assessed with a second polysomnographic study. For those whose apnea-hypopnea index was still ≥ 5, treatment was adjusted, if possible, to improve effectiveness, and the follow-up period was extended another 4 wks. The effect was then assessed with a third polysomnographic study. This adjustment sequence continued until the apnea-hypopnea index was < 5 or until adjustments became uncomfortable for the individual. Follow-up review ended with a person's final polysomnographic evaluation or when a participant discontinued treatment because of poor tolerance or another reason. At their final follow-up review, participants again underwent the physical and neurobehavioral examinations performed at baseline.

Treatment was considered effective when the apnea-hypopnea index either was < 5 or showed "substantial reduction", defined as reduction in the index of at least 50% from the baseline value to a value of < 20 in a person who had no symptoms while using therapy (Hoekema *et al.*, 2004). Persons not meeting these criteria at their final review were considered "non-responsive" to treatment. Those who discontinued treatment for any reason were considered "non-adherent" to treatment.

Interventions

The oral appliance (Thornton Adjustable Positioner type-1, Airway Management, Inc., Dallas, TX, USA) positioned the individual's mandible in a forward and downward position. By turning a propulsion screw incorporated anteriorly into the appliance, participants could adjust mandibular advancement in 0.2 mm increments. They advanced the mandible until symptoms abated or until further advancement caused discomfort. CPAP titration aimed at abolishing all signs of apnea, hypopneas, and snoring was performed during an afternoon nap (Hoekema *et al.*, 2006).

Polysomnography

Polysomnography (Embla® A10 digital recorder, Medcare, Reykjavik, Iceland) for baseline and follow-up evaluations was conducted while participants slept at home and was evaluated according to standardized criteria (Appendix 1).

Physical and Neurobehavioral Examination

Physical examination included documentation of height, weight, neck circumference, alcohol consumption, tobacco use, and current medications. For the neurobehavioral examination, participants completed questionnaires addressing sleep apnea-related symptoms (Johns, 1991; Weaver *et al.*, 1997), health perceptions (Ware and Sherbourne, 1992), and presence of anxiety or depression (Zigmond and Snaith, 1983). At final follow-up review, participants completed a questionnaire assessing treatment usage and grading their satisfaction with treatment on a 10 point scale.

Statistical Analysis

In the assessment of non-inferiority of oral-appliance to CPAP therapy, non-inferiority was defined as a difference between the proportions of treatment effectiveness of less than 25%. With a one-sided significance level of 5%, a power of 90%, and an assumed proportion of treatment effectiveness of 90%, a minimum of 46 participants would be required in each treatment group.

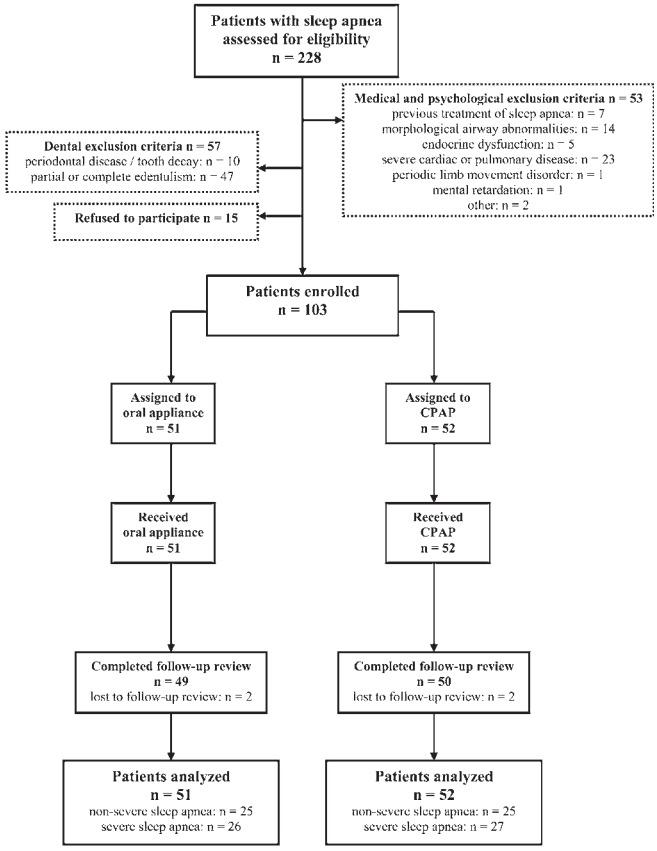

Figure. Flow diagram of participants through each stage of the trial. Of the 103 persons included, two in the oral-appliance group and in the CPAP group did not return for the follow-up polysomnography and neurobehavioral examinations (lost to follow-up review). Abbreviation: CPAP = continuous positive airway pressure.

The primary outcome measure was the proportion of participants whose oral-appliance or CPAP therapy was effective (intention-to-treat analysis). Participants lost to follow-up review were considered "non-adherent" to treatment (worst-case scenario). Secondary outcome measures were polysomnographic and neurobehavioral outcomes at final follow-up review. To determine the relative effectiveness of oral-appliance therapy, we compared primary and secondary outcomes with those of CPAP. Comparison of the proportions of effectiveness between the groups was also performed as a function of disease severity to provide insight into the major indications for oral-appliance therapy (pre-specified subgroup analyses).

Means and standard deviations, and medians and interquartile ranges in skewed distributions, are reported. For the difference between the proportions of effectiveness of the therapies (oral-appliance minus CPAP therapy), a 95% two-sided confidence interval was calculated. Non inferiority of oral-appliance therapy was considered established when the lower boundary of this confidence interval was less then 25 percentage points (*e.g.*, 55% is 25 percentage points lower than 80%). We compared secondary outcomes by calculating effect sizes with two-sided 95%

Table 1. Polysomnographic Outcomes for 103 Individuals Treated with an Oral Appliance or CPAP

Variable	Baseline[a] Oral Appliance (n = 51)	Baseline[a] CPAP (n = 52)	Follow-up Review[a] Oral Appliance (n = 47)[b]	Follow-up Review[a] CPAP (n = 47)[b]	Difference in Effect at Follow-up Review: Effect Size (95% CI) or *p*-value[c]
Total sleep time (min)	408.0 ± 69.0	389.7 ± 79.9	425.0 ± 63.7	404.5 ± 68.4	0.31 (-0.10 to 0.71)
Sleep efficiency (%)[d]	88.3 ± 9.7	85.5 ± 15.5	86.1 ± 8.1	86.2 ± 10.0	0.00 (-0.40 to 0.40)
Apnea-hypopnea index[e]	39.4 ± 30.8	40.3 ± 27.6	7.8 ± 14.4	2.4 ± 4.2	$p = 0.006$
			2.2 (0.0–9.5)	0.0 (0.0–3.0)	
Lowest oxyhemoglobin saturation (%)	78.0 ± 8.5	77.9 ± 9.9	87.7 ± 6.3	89.7 ± 5.8	-0.33 (-0.73 to 0.08)
Non-rapid-eye-movement sleep stages 1 & 2 (%)[f]	65.3 ± 13.1	67.8 ± 14.7	53.2 ± 10.1	54.0 ± 10.0	-0.08 (-0.48 to 0.33)
Non-rapid-eye-movement sleep stages 3 & 4 (%)[f]	13.7 ± 9.0	13.0 ± 11.5	20.4 ± 7.7	21.8 ± 8.0	-0.18 (-0.58 to 0.23)
Rapid-eye-movement sleep (%)[f]	21.0 ± 7.8	19.2 ± 7.4	26.5 ± 6.7	24.1 ± 5.7	0.39 (-0.03 to 0.79)

[a] Plus-minus values are means ± standard deviations; values with additives in parentheses are medians with interquartile ranges.
[b] The mean treatment period from baseline until final follow-up review was 78.3 ± 26.5 (median, 68.0; interquartile range, 60.0–96.0) days in the oral-appliance group and 85.5 ± 55.0 (median, 63.0; interquartile range, 60.0–88.0) days in the CPAP group ($p > 0.05$).
[c] We compared polysomnographic outcomes at follow-up review by calculating effect sizes with two-sided 95% confidence intervals (effect size reported with confidence interval in parentheses). For comparing outcomes with skewed distributions, Mann-Whitney U tests were used (*p*-values reported).
[d] Sleep efficiency is the total sleep time expressed as a percentage of the total time in bed.
[e] The apnea-hypopnea index is the mean number of apneas and hypopneas *per* hr of sleep.
[f] Sleep stages are expressed as a percentage of total sleep time. Abbreviations: CI = confidence interval, CPAP = continuous positive airway pressure.

Table 2. Neurobehavioral Outcomes for 103 Individuals Treated with an Oral Appliance or CPAP

Variable	Range	Direction of Improvement	Baseline[a] Oral Appliance (n = 51)	Baseline[a] CPAP (n = 52)	Follow-up Review[a] Oral Appliance (n = 49)[b]	Follow-up Review[a] CPAP (n = 50)[b]	Difference in Effect at Follow-up Review: Effect Size (95% CI) or *p*-value[c]
Epworth sleepiness scale	0–24	-	12.9 ± 5.6	14.2 ± 5.6	6.9 ± 5.5	5.9 ± 4.8	$p = 0.53$
					7.0 (2.0–9.5)	6.0 (3.8–12.0)	
Functional outcomes of sleep questionnaire							
- general productivity	1–4	+	3.0 ± 0.7	3.0 ± 0.8	3.5 ± 0.6	3.5 ± 0.7	0.10 (-0.30 to 0.49)
- social outcome	1–4	+	2.9 ± 0.9	3.0 ± 1.0	3.6 ± 0.7	3.6 ± 0.7	0.01 (-0.38 to 0.41)
- activity level	1–4	+	2.6 ± 0.8	2.7 ± 0.8	3.3 ± 0.6	3.3 ± 0.7	-0.12 (-0.52 to 0.27)
- vigilance	1–4	+	2.6 ± 0.8	2.4 ± 0.9	3.2 ± 0.8	3.3 ± 0.8	-0.08 (-0.47 to 0.32)
- intimate relationships & sexual activity[d]	1–4	+	2.6 ± 1.0	2.9 ± 1.0	2.9 ± 1.1	3.1 ± 1.1	-0.21 (-0.61 to 0.20)
- total score	5–20	+	13.7 ± 3.1	13.9 ± 3.7	16.6 ± 2.8	16.7 ± 3.1	-0.05 (-0.44 to 0.34)
Medical outcomes study, 36-item short-form health survey							
- physical functioning	0–100	+	71.8 ± 23.3	68.9 ± 24.2	78.8 ± 21.5	80.6 ± 18.5	-0.09 (-0.48 to 0.31)
- social functioning	0–100	+	66.4 ± 22.9	68.6 ± 23.6	79.7 ± 21.4	78.6 ± 21.1	0.05 (-0.34 to 0.45)
- role physical	0–100	+	40.7 ± 40.3	42.6 ± 41.3	67.3 ± 42.5	71.5 ± 40.4	$p = 0.60$
			25.0 (0.0–75.0)	25.0 (0.0–100.0)	100.0 (25.0–100.0)	100.0 (43.7–100.0)	$p = 0.60$
- role emotional	0–100	+	70.6 ± 41.5	70.0 ± 38.9	78.9 ± 37.1	77.2 ± 38.0	$p = 0.86$
			100.0 (33.0–100.0)	100.0 (33.0–100.0)	100.0 (66.8–100.0)	100.0 (58.5–100.0)	
- mental health	0–100	+	70.9 ± 17.8	68.2 ± 17.6	77.5 ± 16.5	75.0 ± 16.2	0.15 (-0.24 to 0.55)
- vitality	0–100	+	39.0 ± 18.6	39.2 ± 21.8	63.8 ± 21.2	61.3 ± 19.9	0.12 (-0.27 to 0.52)
- bodily pain	0–100	+	75.4 ± 26.6	77.6 ± 25.9	79.9 ± 26.5	82.3 ± 23.9	-0.10 (-0.49 to 0.30)
- general health perception	0–100	+	57.6 ± 21.3	54.8 ± 22.7	65.5 ± 20.6	60.9 ± 23.4	0.21 (-0.19 to 0.60)
- health change	0–100	+	39.7 ± 24.6	38.2 ± 25.2	74.0 ± 27.5	73.5 ± 26.4	0.02 (-0.38 to 0.41)
Hospital anxiety and depression scale							
- anxiety	0–21	-	5.6 ± 3.8	5.4 ± 3.6	4.5 ± 3.5	4.3 ± 3.4	$p = 0.81$
			4.0 (3.0–8.0)	5.0 (3.0–8.0)	3.0 (2.0–6.5)	3.5 (1.8–7.0)	
- depression	0–21	-	5.8 ± 3.8	7.1 ± 4.3	3.8 ± 3.7	4.8 ± 4.5	$p = 0.25$
			5.0 (3.0–8.0)	7.0 (4.0–10.0)	2.0 (1.0–7.0)	3.0 (1.0–8.5)	

[a] Plus-minus values are means ± standard deviations; values with additives in parentheses are medians with interquartile ranges.
[b] The mean treatment period from baseline until final follow-up review was 78.3 ± 26.5 (median, 68.0; interquartile range, 60.0–96.0) days in the oral-appliance group and 85.5 ± 55.0 (median, 63.0; interquartile range, 60.0–88.0) days in the CPAP group ($p > 0.05$).
[c] We compared neurobehavioral outcomes at follow-up review by calculating effect sizes with two-sided 95% confidence intervals (effect size reported with confidence interval in parentheses). For comparing outcomes with skewed distributions, Mann-Whitney U tests were used (*p*-values reported).
[d] At baseline, this item was completed by 48 individuals in the oral-appliance group and 47 in the CPAP group. At follow-up review, this item was completed by 47 persons in the oral-appliance group and 46 in the CPAP group. Abbreviations: CI = confidence interval, CPAP = continuous positive airway pressure.

confidence intervals. For comparing outcomes with skewed distributions, Mann-Whitney U tests were used. All tests were two-sided, and p-values < 0.05 indicated significance.

RESULTS

Between September 2002 and May 2005, 103 people were enrolled (Appendix 2). Randomization yielded an oral-appliance group of 51 and a CPAP group of 52 (Fig.). Of the oral-appliance group, 47 completed polysomnographic evaluation; seven required adjustment of their appliance after 8 wks of treatment. At final follow-up review, mean advancement of the mandible was 81.0 ± 18.7% of maximum advancement. Of those using CPAP, 47 completed polysomnographic evaluation; seven required pressure adjustment after 8 wks of treatment. At final review, mean pressure was 8.1 ± 1.9 cm H_2O.

Table 3. Proportions of Effective Treatments with an Oral Appliance or with CPAP.

	Oral Appliance[a]	CPAP[a]	Difference (95% CI)[b]
Effective treatment[c]			
Total population (n = 103)	39 / 51 (76.5%)	43 / 52 (82.7%)	-6.2% (-21.7 to 9.4)
Non-severe sleep apnea (n = 50)	21 / 25 (84.0%)	20 / 25 (80.0%)	4.0% (-17.7 to 25.4)
Severe sleep apnea (n = 53)	18 / 26 (69.2%)	23 / 27 (85.2%)	-16.0% (-37.1 to 6.8)

[a] Values are the number of effective treatments divided by the total number of persons in the treatment group. Values in parentheses are the percentages of effective treatments.

[b] Differences in effectiveness between oral-appliance and CPAP therapy (oral-appliance minus CPAP therapy) are reported as percentages with two-sided 95% confidence intervals in parentheses.

[c] Treatment was considered effective when the apnea-hypopnea index (*i.e.*, mean number of apneas and hypopneas *per* hr of sleep) either was < 5 or showed "substantial reduction", defined as reduction in the index of at least 50% from the baseline value to a value of < 20 in a person who had no symptoms while using therapy. Abbreviations: CI = confidence interval, CPAP = continuous positive airway pressure.

Treatment Effectiveness

Polysomnographic outcomes were available for 47 people in each group. At final review, the CPAP group had a significantly lower apnea-hypopnea index than the oral-appliance group (Table 1). Two participants using oral-appliance therapy had an increase in their apnea-hypopnea index, from 15 to 17 and from 9 to 19, respectively. No other adverse events occurred. There were no significant differences in other polysomnographic outcomes at final review (Table 1).

Neurobehavioral outcomes were available for 49 people in the oral-appliance group and 50 in the CPAP group; none was available for two persons lost to follow-up review in each group. There were no significant differences between groups at final review (Table 2).

Oral-appliance therapy was effective for 39 participants (76.5%); of the other 12, eight were "non-responsive", two were "non-adherent", and two were lost to follow-up review. In the CPAP group, treatment was effective for 43 participants (82.7%); of the other nine, two were "non-responsive", five were "non-adherent", and two were lost to follow-up review. The difference in effectiveness was -6.2%, and the lower boundary of the confidence interval was 21.7%, indicating that oral-appliance therapy met the criterion for non-inferiority (Table 3).

Satisfaction and Treatment Usage

In each group, 41 participants were "satisfied" or "very satisfied" with treatment. On the 10 point scale, participants graded their satisfaction as a mean 7.6 ± 1.9 points in the oral-appliance group and 7.4 ± 2.1 points in the CPAP group ($p > 0.05$). There were no significant differences in reported treatment usage. Of the 49 participants completing follow-up review of oral-appliance therapy, 42 reported wearing the appliance 7 nights each wk (mean for all participants, 6.7 ± 1.0 days); 46 wore it ≥ 5 hrs each night (mean for all participants, 6.9 ± 1.0 hrs). Of the 50 participants completing follow-up review of CPAP therapy, 42 reported using CPAP for 7 nights each wk (mean for all participants, 6.7 ± 0.8 days); 44 used CPAP ≥ 5 hrs each night (mean for all participants, 6.5 ± 1.6 hrs).

Treatment Effectiveness in Relation to Severity of Sleep Apnea

For non-severe obstructive sleep apnea, treatment was effective for 21 of the 25 individuals using oral-appliance therapy (84.0%) and 20 of the 25 individuals using CPAP (80.0%). Within this subgroup, oral-appliance therapy met the criterion for non-inferiority (Table 3). For severe obstructive sleep apnea, oral-appliance therapy did not meet the criterion for non-inferiority; oral appliance therapy was effective for 18 of 26 individuals (69.2%) and CPAP for 23 of 27 individuals (85.2%) (Table 3).

DISCUSSION

Our results showed a relatively more positive effect of oral-appliance therapy than those in previous studies. Variables correlating with increased effectiveness of oral appliances have included being female, being young, being non-obese, and having non-severe disease (Liu *et al.*, 2001; Mehta *et al.*, 2001; Marklund *et al.*, 2004). However, our patients, while demographically comparable with those in most of these studies (Barnes *et al.*, 2004; Hoekema *et al.*, 2004), were generally more obese and had more severe disease. Two other factors may explain the difference. First, effectiveness of oral appliances usually increases with greater advancement of the mandible, and mean mandibular advancement in our study was generally more extended than in most previous studies (Hoekema *et al.*, 2004). Second, our definition of "effective treatment" consisted of criteria based on polysomnographic and clinical outcomes. If the rigid criterion of an index < 5 defines effective treatment, analysis of our data suggests non-inferiority of oral-appliance therapy only in those with non-severe obstructive sleep apnea (see Appendix 3). However, all previous studies comparing oral-appliance and CPAP therapy used an index < 10 as the criterion for effective treatment (Barnes *et al.*, 2004; Hoekema *et al.*, 2004). Had we used that criterion for our patients with a baseline index ≥ 10, we would have obtained similar results in terms of effectiveness of oral-appliance therapy. Finally, since polysomnographic measurements that formed the basis for

inclusion were also used as baseline values, a regression to the mean-effect may also have affected the outcomes in this study. However, we propose that the relatively more positive effect of oral-appliance therapy we observed is best explained by greater mandibular advancement.

Three factors distinguish our study from previous trials comparing these therapies. First, we included individuals with severe obstructive sleep apnea. Although oral appliances tend to decrease in effectiveness with increasingly severe disease (Ferguson *et al.*, 2006), recent studies suggest a future role for oral-appliance therapy of severe sleep apnea (Henke *et al.*, 2000; Mehta *et al.*, 2001). Second, we used a parallel study design rather than a crossover design (Barnes *et al.*, 2004; Hoekema *et al.*, 2004). Crossover studies may not permit derivation of an unbiased estimate of treatment effect (Woods *et al.*, 1989). Moreover, carry-over effects and failure to return to baseline status may be anticipated when oral-appliance and CPAP therapy are compared in crossover studies. Third, we evaluated the effectiveness of treatment with an intention-to-treat analysis. Since only one previous study appropriately used an intention-to-treat analysis (Barnes *et al.*, 2004), most reported trials may have incorporated bias when comparing these therapies (Hoekema *et al.*, 2004).

It could be reasoned that the definition for effectiveness used in this study is not compatible with the goals of CPAP titration. Participants with an apnea-hypopnea index ≥ 5 at follow-up review, and for whom treatment was nonetheless considered effective, had an index in the range of 5 to 20. These individuals may be at risk of a cardiovascular event (Shamsuzzaman *et al.*, 2003). This situation applied to 10 persons in the oral-appliance group and three in the CPAP group, all with severe apnea (see Appendix 3). Evidence that individuals with severe apnea could be at particular cardiovascular risk may support primary oral-appliance therapy only for persons with non-severe apnea (Marin *et al.*, 2005; Yaggi *et al.*, 2005).

We believe that the non-inferiority margin we used met the two major requisite conditions (Gomberg-Maitland *et al.*, 2003): that the smallest expected effect of a control treatment (*i.e.*, CPAP) over placebo should exceed the non-inferiority margin (Giles *et al.*, 2006); and that the non inferiority margin should not exceed the difference between active treatments judged clinically important. Most previous studies comparing these therapies showed differences in effectiveness $\geq$ 25% (Barnes *et al.*, 2004; Hoekema *et al.*, 2004), and all but one concerned only non-severe obstructive sleep apnea (Engleman *et al.*, 2002). We also accounted for the variability in the difference of effectiveness, because we used the lower boundary of the corresponding confidence interval to decide on non-inferiority. Moreover, oral-appliance and CPAP therapy are reversible treatments that can be evaluated by polysomnography and discontinued readily should treatment fail. Considering these factors, we deemed the non inferiority margin of 25% appropriate.

This randomized parallel trial showed that an oral appliance was not inferior to CPAP for effective treatment of obstructive sleep apnea. Non-inferiority of oral-appliance therapy was supported by a lack of significant differences in most polysomnographic and all neurobehavioral outcomes. However, CPAP was more effective in improving the apnea-hypopnea index and was superior to oral-appliance therapy for persons with severe disease. Since these findings suggest that oral-appliance therapy is indicated primarily for those with non severe obstructive sleep apnea, we recommend that it be considered, alongside CPAP therapy, as treatment for persons with mild to moderate disease. Among those with severe disease, oral-appliance therapy should be considered for individuals unwilling or unable to tolerate CPAP.

ACKNOWLEDGMENTS

The authors thank Ms. E.M. Ten Vergert, PhD, from the Medical Technology Assessment Bureau of the University Medical Centre Groningen for her critical appraisal of the manuscript. We are indebted to Ms. S. Eastwood, ELS(D), for her contribution in editing the manuscript. The authors also thank dental laboratory Goedegebuure (Ede, The Netherlands) for their assistance in manufacturing the oral appliances. Financial support for the present study was granted by the Netherlands Organization for Health Research and Development. This paper is based on a thesis submitted to the University Medical Center Groningen, University of Groningen, in partial fulfilment of the requirements for a PhD degree. A preliminary report of the study was presented at the World Congress on Sleep Apnea (Montreal, Canada, September 27-30, 2006).

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