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Mandibular advancement appliances and obstructive sleep apnoea: a randomized clinical trial

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SUMMARY This randomized placebo-controlled cross-over trial assessed the effectiveness of a mandibular advancement appliance (MAA) in managing obstructive sleep apnoea (OSA). Twenty-one adults, with confirmed OSA, were provided with a maxillary placebo appliance and a MAA for 4–6 weeks each, in a randomized order. Questionnaires at baseline and after each appliance assessed bed-partners' reports of snoring severity (loudness and number of nights per week), and patients' daytime sleepiness (Epworth Sleepiness Score, ESS). The Apnoea Hypopnoea Index (AHI) and Oxygen Desaturation Index (ODI) were measured at baseline and with each appliance during single night sleep studies.

Seventy-nine per cent of subjects wore their MAA for at least 4 hours at night. Sixty-eight per cent of subjects wore their MAA for 6–7 nights per week. Excessive salivation was the most commonly reported complication. One subject was unable to tolerate the MAA and withdrew from the study. Among the remaining 20 subjects, the MAA produced significantly lower AHI and ODI values than the placebo. However, although the reported frequency and loudness of snoring and the ESS values were lower with the MAA than the placebo, these differences were not statistically significant.

When wearing the MAA, 35 per cent of the OSA subjects had a reduction in the pre-treatment ODI to 10 or less, while 33 per cent had an AHI of 10 or less. The MAA was less effective in the subjects with the most severe OSA (pre-treatment ODI > 50 and/or pre-treatment AHI > 50).

Introduction

Obstructive sleep apnoea (OSA) is a serious disorder that affects up to 4 per cent of middle-aged men and 2 per cent of women over the age of 30 (Young *et al*., 1993). A main symptom of untreated OSA is excessive daytime sleepiness, which can result in significant reductions in the quality of life experienced by patients (Douglas, 1995). The often extreme levels of hypersomnolence are associated with an increased risk of being involved in road traffic accidents (Findley *et al*., 1988; Aldrich, 1989; Haraldsson *et al*., 1990). Although increased cardiovascular mortality and morbidity may occur in association with OSA, a recent systematic review concluded that the severity of these complications may have been overestimated (Wright *et al*., 1997). However, as the authors of that review also reported that many of the reviewed studies were poorly designed, these conclusions should be interpreted with caution.

The pathogenesis of OSA and the associated symptom of snoring involve a combination of reduced pharyngeal muscle tone and unfavourable pharyngeal anatomy (with reductions in airway dimensions). These factors result in repeated pharyngeal obstructions during sleep that reduce the arterial oxygen saturation, and cause repeated arousals and consequent daytime sleepiness. The assessment of OSA severity is usually undertaken using a combination of clinical history, clinical

examination of the upper airway, validated questionnaire measures, such as the Epworth Sleepiness Score (ESS), and overnight sleep monitoring at home or in a hospital setting.

The treatment of OSA is aimed at reducing the frequency and severity of obstructive episodes either by increasing the airway dimensions or by reducing the tendency for collapse. The current gold standard of OSA treatment is nasal Continuous Positive Airway Pressure (nCPAP), which is effective in almost all OSA patients, although compliance is often a problem. Orthodontists have recently begun to play a major role in the management of snoring and OSA with the increasing use of oral mandibular advancement appliances (MAAs; Bonham *et al*., 1988; Cote, 1988; Lowe, 1994). MAAs are inexpensive, well accepted by patients, and any side-effects, such as muscle and temporomandibular joint (TMJ) discomfort, are usually reversible. Although the appliances have a relatively high success rate for patients with non-apnoeic snoring (Johnston *et al*., 2001), their success rate in OSA is thought to be lower. Nevertheless, when MAAs are effective, patients often prefer them to nCPAP (Ferguson *et al*., 1996).

The most commonly used measures for assessing treatment outcome are the ESS, the Apnoea Hypopnoea Index (AHI) and the hourly rate of arterial oxygen desaturations (ODI). Although the evidence for the effectiveness of nCPAP is now based on the results of published randomized controlled trials (Engelman *et al*., 1998, 1999; Jenkinson *et al*., 1999) the level of scientific evidence to support the use of MAAs is not as strong. The effectiveness of MAAs has not been fully assessed by prospective randomized controlled trials (Lowe, 1994) and most previous reports have been at the case series level of evidence. Nevertheless, several studies have compared MAAs with nCPAP (Ferguson *et al*., 1996, 1997), MAAs with a placebo in a parallel-groups trial (Hans *et al*., 1997), and a Herbst-type MAA with a placebo in a small cross-over trial (Sjoholm *et al*., 1994).

The current paper reports the results of a prospective clinical trial of a custom-made MAA in the treatment of OSA. The investigation used a randomized placebo-controlled cross-over experimental design to evaluate the effectiveness of MAAs in managing OSA.

Subjects and methods

Subjects

All subjects were recruited from a dedicated sleep disorders clinic. Each patient underwent initial overnight oximetry monitoring, which was conducted at home, and those with an hourly rate of 10 or more desaturations (4 per cent or greater fall in SaO_2) were invited to participate in the clinical trial. Patients with any concurrent serious illness including pulmonary disease were excluded. Edentulous patients and those with an inadequate number of sound teeth to support a MAA were also excluded. Based on these selection criteria, a total of 21 subjects (17 males and four females) were included in the study after informed consent was obtained. Ethical approval for the study was obtained from the local Research Ethics Committee.

Study design and sample size calculation

The study used a placebo-controlled cross-over design with each subject completing consecutive trial periods with a MAA and a placebo appliance. The subjects were randomized to decide which appliance they received first. Sample size calculation was based on the two main outcome measures from the sleep studies, the ODI and the AHI. On the basis of data from previous studies, the standard deviations of ODI and AHI were estimated as 15 events per hour (Ferguson *et al*., 1996) for the purposes of sample size calculation. It was decided that a clinically relevant difference between the MAA and placebo for AHI and ODI would be regarded as 10 events per hour. For a study with 80 per cent power and a significance level of 5 per cent, a sample size of 18 subjects was required for a within-patient controlled design.

Two previously published studies have used a cross-over design to compare the effectiveness of mandibular appliances with nCPAP in the management of OSA (Ferguson *et al*., 1996, 1997). As neither of these studies identified the

presence of any carry-over effects following treatment with MAAs, a washout period was not used in the current study, thus simplifying the experimental design.

Appliance design

The MAA was constructed from a bilaminate acrylic material with a soft fitting surface ('Proform Dual Laminate', Dental Resources, Delano, MN, USA). The appliance was fabricated by a specialist orthodontic technician on stone models that were articulated using a wax occlusal record. The occlusal record was obtained using softened pink wax and a Projet bite fork (Orthocare, Bradford, UK) with the mandible protruded by 75 per cent of maximum protrusion (mean 5.7 mm, range 4–9 mm), with a 4-mm inter-incisal vertical clearance (Figure 1). The placebo appliance was a single arch upper anterior bite plane design on a dual laminate base constructed to produce approximately 1.5 mm of separation between the upper and lower posterior teeth.

Data collection

Anthropometric data included age, gender, weight, height, and body mass index (BMI). Each subject was asked to complete three sleep questionnaires: at baseline and after 4–6 weeks with each appliance. Subjects' bed-partners (when applicable) were asked to rate the severity of the snoring using 5-point scales to describe the loudness of snoring and the number of nights per week that the subject snored. Subjects rated how refreshed they felt when waking each morning using a 5-point scale. These questions are detailed in Appendix 1. The sleep questionnaire also included a standard ESS, which estimated the degree of daytime sleepiness with a minimum score of 0 and a maximum score of 24 (Johns, 1993). Additional questions also investigated the typical pattern of appliance wear (number of nights per week and hours per night) and the incidence of complications (occlusal and TMJ discomfort, dryness of the mouth, and excessive salivation).

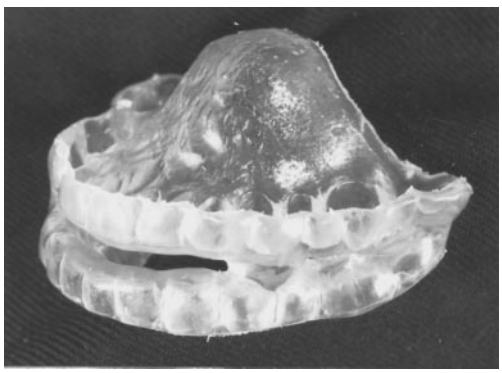

Figure 1 The mandibular advancement appliance used in the study.

Objective measurements of OSA severity were obtained at baseline and with each appliance at the end of each treatment arm using an Edentrace II multi-channel recording system (Nellcor, Puritan and Bennett Inc., Eden Prairie, MN, USA). The system used a finger probe to measure arterial oxygen saturation (SaO_2) and a thermistor to measure oronasal airflow. A desaturation event was defined as a reduction in SaO_2 of 4 per cent or more. An apnoea was defined as a complete cessation of oronasal airflow for at least 10 seconds, while a hypopnoea was defined as a decrease in oronasal airflow of at least 50 per cent combined with a desaturation event. The AHI was calculated as the hourly rate of apnoeas and hypopnoeas and the ODI as the hourly rate of desaturation events.

Statistical analysis

The sleep questionnaire data, AHI, and ODI values in the cross-over data were analysed using the method described by Altman (1991). Independent sample *t*-tests were used to assess the possible influence of a period effect (using the differences in outcome measures between the MAA and placebo appliances) and for any treatment period interactions (using the average outcome scores for each appliance). Finally, paired samples *t*-tests were used to evaluate the clinical effectiveness of the MAA compared with the placebo appliance.

Subjects were classified as treatment successes or failures based on the change in the objective outcome measures AHI and ODI with the MAA relative to the corresponding baseline measures.

There is currently no universally agreed definition of treatment success for OSA (Cohen, 1998). Therefore, in order to allow comparison with previously published reports of MAA treatment, success was defined according to two different definitions based on reduction of AHI to 10 or less per hour (Schmidt-Nowara *et al*., 1995), and ODI to 10 or less per hour (Lojander *et al*., 1996). Cohen's kappa statistic was used to examine the level of agreement between AHI and ODI when used to define treatment success.

To further investigate the clinical effects of the appliances, the subjective questionnaire scores were compared with baseline scores for each subject to evaluate whether the appliance provided an improvement in reported snoring loudness and frequency and the frequency of waking unrefreshed. Using the method of Lojander *et al*. (1996), a 2-point or greater reduction in a rating scale response was classified as 'Improved'.

Results

Twenty-one subjects agreed to participate in the study. One subject was unable to tolerate the MAA and withdrew. This subject had been randomized to receive the MAA first and was excluded from further analysis. Thus, a total of 20 subjects (16 males and four females) completed the trial period with both appliances. The baseline data are summarized in Table 1. All subjects completed three sleep studies (baseline, MAA, and placebo). One subject failed to return their placebo questionnaire and a further four subjects failed to fully complete some questionnaire responses. Two subjects were unable to obtain bed-partner reports of snoring severity as they lived alone, having originally presented complaining of daytime sleepiness rather than disruptive snoring. Therefore, the comparison of the questionnaire responses for frequency and loudness of snoring in the cross-over data was restricted to 15 subjects for frequency and 16 subjects for loudness.

Randomization resulted in eight subjects receiving the placebo first (treatment sequence A), while the remaining 12 received the MAA first (treatment sequence B). Comparison of the baseline data between these two groups revealed no statistically significant differences.

The individual AHI and ODI results for each treatment sequence are shown in Figures 2–5.

Statistical analysis showed that there was no evidence of either period effect or a treatment–period interaction for any of the questionnaire or sleep study outcome measures. This allowed pooling of all the MAA scores and all placebo scores for each outcome measure.

Cross-over analysis: MAA versus placebo

The pooled scores for the MAA were significantly lower than those for the placebo appliances for AHI and ODI. This indicated that the MAA was significantly more effective than the placebo in improving these outcome measures (Table 2).

Although the mean pooled scores of the questionnaire responses were lower for the MAA

Table 1 Baseline data for all subjects completing the trial (n = 20).

	Mean	Minimum	Maximum	SD
Age (years)	55.10	35.49	64.36	6.87
Weight (kg)	91.80	54.00	126.50	17.04
Height (m)	1.70	1.52	1.83	0.09
BMI (kg/m^2)	31.63	21.09	43.77	5.94
AHI	31.93	3.90	69.20	21.18
ODI	30.69	12.80	76.89	18.82
ESS	13.90	2	24	6.39
Reported frequency of snoring	3.80	2	4	0.52
Reported loudness of snoring	3.20	1	4	1.01
Frequency of waking unrefreshed	3.45	0	4	1.15

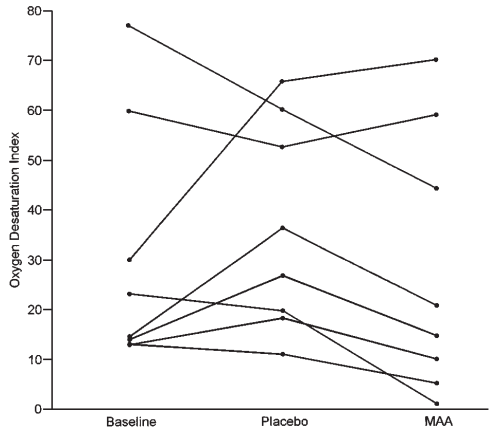

Figure 2 Individual ODI values for treatment sequence A, placebo first (n = 8).

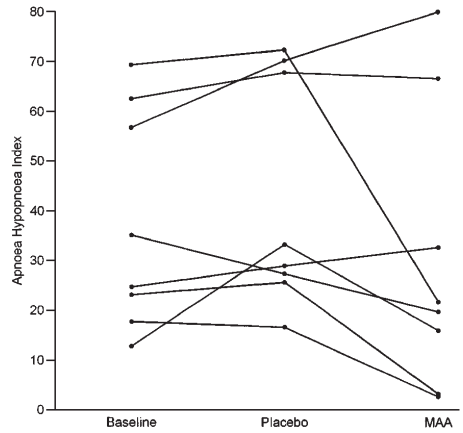

Figure 4 Individual AHI values for treatment sequence A, placebo first (n = 8).

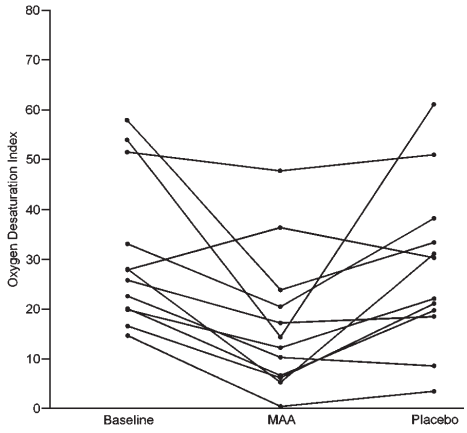

Figure 3 Individual ODI values for treatment sequence B, MAA first (n = 12).

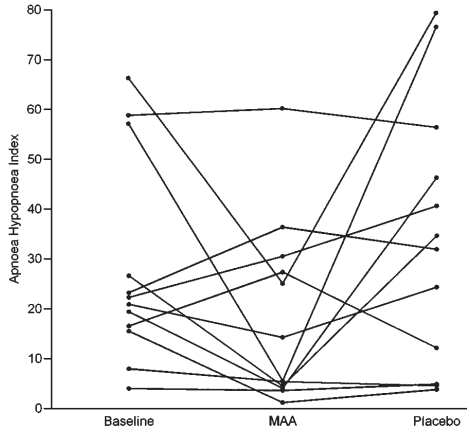

Figure 5 Individual AHI values for treatment sequence B, MAA first (n = 12).

than placebo appliances, the differences did not reach statistical significance (Table 2).

Comparison of MAA with baseline and treatment success rate

Twenty subjects had a baseline ODI of 10 or more. Seven (35 per cent) were defined as successful on the basis of an ODI of 10 or less with the MAA. Six of the 18 patients with a baseline AHI of 10 or more (33.3 per cent) had an AHI of 10 or less with the MAA.

Of the six subjects who had pre-treatment AHI values above 50, only one had a reduction to less than 10 events per hour. Furthermore, nine subjects still had AHI values above 20 when wearing the MAA. None of the six subjects with a pre-treatment ODI of more than 50 had a reduction to less than 10 with the MAA.

The kappa value for agreement between the two definitions of treatment success with the MAA was 0.75 (P = 0.001). This indicated substantial agreement between the use of AHI and ODI for defining treatment success.

Table 2 Comparison of pooled outcome scores between MAA and placebo.

	Placebo		MAA		Difference	Paired *t*-test
	Mean	SD	Mean	SD	Mean difference (95% CI)	*P*
AHI	37.68	24.86	22.86	22.84	14.82 (3.87–25.77)	0.011
ODI	31.21	18.22	21.08	19.82	10.12 (4.35–15.89)	0.002
ESS (n = 18)	12.56	6.29	11.61	6.73	0.94 (–1.43–3.32)	0.414
Reported frequency of snoring (n = 15)	3.13	0.99	2.60	1.30	0.53 (–0.05–1.12)	0.072
Reported loudness of snoring (n = 16)	2.25	1.00	1.56	1.09	0.69 (–0.06–1.43)	0.068
Frequency of waking unrefreshed (n = 19)	3.16	1.38	2.58	1.26	0.58 (–0.11–1.27)	0.094

Nine out of 19 subjects (45 per cent) had a post-treatment ESS of 10 or less. However, in six of these nine subjects, the ESS was also 10 or less at baseline.

Reported snoring loudness and frequency

Data for MAA snoring loudness and frequency were available for 17 subjects. Loudness of snoring with the placebo was available for 17 subjects and frequency results were available for 16 subjects. Fifty-three per cent of the subjects reported a reduction in the loudness of snoring when using the MAA, while 29 per cent reported a reduction with the placebo. With the MAA, 41 per cent of subjects reported snoring on fewer nights per week, while with the placebo 19 per cent reported a reduction.

Compliance and complications with the MAA

These findings are reported for the MAA only. Sixty-eight per cent of subjects wore their appliances every or almost every night, while one subject wore the MAA for only one night per week. Seventy-nine per cent of subjects wore their appliances for 4 or more hours per night and 84 per cent reported that the MAA came out of their mouth when asleep on two nights per week or less. The most commonly reported complication was excessive salivation when wearing the appliance (68 per cent). Forty-four per cent of subjects reported temporary occlusal changes in the morning although only 10 per cent reported that this sometimes persisted during the day. Temporary TMJ discomfort on waking was common (42 per cent), although only one subject reported persistent TMJ discomfort during the day.

Discussion

Decisions about healthcare interventions should ideally be guided by evidence from randomized controlled trials (Cochrane, 1972; Richards and Lawrence, 1995). Although oral appliance therapy is now a common treatment for OSA, there are still few well-controlled scientific studies to support their use. While randomized controlled clinical trials are regarded as the most rigorous and desirable method of evaluating treatment regimens (Cochrane, 1972; O'Brien and Craven, 1995; Richards and Lawrence, 1995), this level of evidence is currently lacking to support the use of MAAs in managing OSA.

Study design

In order to obtain the same precision of estimation, a cross-over trial requires fewer subjects than a parallel-group trial. The effects of between-patient variation are reduced with a cross-over study, which is particularly useful in OSA trials in which matching of controls would otherwise be very difficult due to the wide variation in demographic factors and severity. Lowe (1993) stated that cross-over trials are most suitable for disorders of a chronic nature with a low likelihood of spontaneous deterioration or improvement during the period of study. Cross-over trials are also suited to conditions in which discontinuation of successful treatment results

in the reappearance of signs and symptoms (i.e. treatment is reversible). Ideally, there should be previous evidence to indicate the lack of carry-over effects and there should also be a relevant quantifiable short-term response to treatment. Two previously published studies have used a cross-over design to compare the effectiveness of mandibular appliances with nCPAP in the management of OSA (Ferguson *et al*., 1996, 1997). The first of these studies used a non-adjustable appliance ('Snore-Guard'), while in the second a custom-made adjustable MAA was used. Both of these investigations showed that neither a carry-over or period effect occurred with either MAAs or with nCPAP. These findings, in conjunction with the reversible nature of MAA treatment of OSA and the ability to easily measure OSA severity using overnight monitoring mean that a placebo-controlled cross-over study design is ideally suited for investigating OSA treatment with MAAs. It is surprising therefore that this cross-over study design has been so infrequently used for OSA clinical trials, and only one previous study (of only six subjects using a Herbst-type appliance) has used a placebo as a control (Sjolholm *et al*., 1994). One of the shortcomings of using a cross-over trial is that patients are required to undergo two treatment regimens and compliance can therefore be a problem. In the current study, the subjects were generally highly motivated and only one subject out of 21 did not complete the trial.

Treatment outcome

The main findings from analysis of the cross-over data in the current study were that the objective measures of OSA severity (AHI and ODI) were significantly lower with the MAA than with the placebo in the sample of 20 OSA subjects. However, although there were lower scores for the mean severity of snoring and daytime sleepiness (including ESS) with the MAA as reported by bed-partner questionnaires, the differences between the MAA and placebo were not statistically significant. The placebo used in the current study was a similar design to that used in a parallel-groups controlled study of a commercially produced appliance reported by Hans *et al*. (1997). In that investigation, the placebo was also shown to be ineffective in reducing the ESS and AHI in OSA subjects.

Most authorities agree that the complete resolution of symptoms, in particular the reduction in daytime sleepiness, should be an important aim of treatment. Daytime sleepiness is difficult to measure objectively, although the ESS is commonly used. The originator of the ESS reported that the normal range of ESS is between 2 and 10 (Johns, 1993), and so a successful treatment result should also be associated with a reduction of the ESS to this level. In the present study, the differences in ESS between the MAA and placebo were not significant. Nine out of 19 subjects in the current study (45 per cent) had a post-treatment ESS of 10 or less, although it should be recognized that in six of these the ESS was also 10 or less at baseline. Therefore, the effectiveness of the MAA in improving the ESS outcome measure in the present sample of OSA subjects is questionable. The low magnitude of improvement in ESS with the MAA is surprising when viewed in the context of the significant differences observed between the MAA and placebo with regard to the objective severity measurements (AHI and ODI). One possible explanation may be that daytime sleepiness has other contributory factors apart from OSA. These might include the continuation of repeated arousals from sleep, resulting from mild discomfort or restriction of oral breathing when wearing the MAA, particularly in subjects with nasal insufficiency. Furthermore, any clinical improvement in successful OSA treatment may not have presented as reduced sleepiness during the short time period of the current trial.

The problems with adequately defining and measuring treatment outcome in terms of symptomatic improvement have resulted in previous reports of MAAs using the objective definitions of treatment success. The most commonly used definitions of success have been reduction of the AHI to less than 10 events per hour and/or by at least 50 per cent. Some clinicians have, however, regarded a more modest reduction in AHI to less than 20 as successful (Waite, 1998). The current study defined treatment success in two different ways, based on reduction of AHI and ODI. The

success rate, based on AHI reduction to 10 or less was 33 per cent in the present trial. This is at the lower end of the range of success reported in published case series. Schmidt-Nowara *et al*. (1995) reviewed the treatment of OSA with oral appliances and reported that the success rate for AHI reduction to 10 or less varied between 25 and 73 per cent, with a mean of 51 per cent. However, it should be recognized that these conclusions were based entirely on case series studies, rather than controlled trials. Furthermore, the authors also drew attention to the possibility of a positive publication bias in the literature.

The most recent studies to compare MAAs with nCPAP have reported MAA success rates in reducing the AHI to 10 or less of 48 and 55 per cent, respectively (Ferguson *et al*., 1996, 1997). While the success rate in the current study (33 per cent) may initially appear disappointing in comparison with these results, it should be noted that only one of 25 and one of 20 of the subjects in the 1996 and 1997 studies by Ferguson's group had baseline AHIs over 50. The inclusion criteria for the current study were such that there was no maximum value of AHI or ODI specified for recruitment to the trial. Six of the 20 subjects had pre-treatment AHI values above 50, indicating that the sample contained relatively more subjects with severe OSA than the studies by Ferguson *et al*. (1996, 1997). Closer examination of the current results shows that among these six subjects, only one had a reduction in AHI to 10 or less. If these six subjects with the most severe OSA (AHI > 50) are excluded from the current results, then among the remaining 12 subjects with a pre-treatment AHI of more than 10, five would be classified as MAA treatment successes (post-treatment AHI of 10 or less) giving a success rate of 42 per cent. Other investigators have also concluded that the effectiveness of MAAs is limited in subjects with severe OSA. Schmidt-Nowara *et al*. (1991) reported that successful MAA treatment was unlikely with high initial AHI values and O'Sullivan *et al*. (1995) observed that in nine subjects with an initial AHI of more than 60 only two had their AHI reduced to 10 or less with a MAA. The current results support these findings and indicate that the generic MAA used in the study is unlikely to reduce the AHI to normal levels in those subjects with the most severe OSA (baseline AHIs of greater than 50 events per hour).

A further explanation of the relatively low success rate with the MAA in the current investigation may lie in the design of the MAA. The study was designed to examine the clinical effectiveness of the MAA that is routinely used by the authors. This was constructed using a standardized 4 mm inter-incisal opening and 75 per cent of maximum mandibular protrusion. However, it is recognized that the absolute size of the mandibular advancement varies between subjects. This may also be a factor in explaining why the observed differences in reported snoring severity and frequency between the MAA and placebo were not statistically significant. It is possible that the use of a MAA that permits incremental adjustment to titrate the degree of advancement would produce a more favourable clinical response in some subjects.

The other main outcome measure used in the current study was the reduction in the hourly rate of arterial oxygen desaturations ODI to 10 or less. The use of this outcome measure has been less frequently reported in the literature than the AHI. The ODI was evaluated in the current study as it can be assessed using routine overnight oximetry, rather than requiring a more complex and expensive multi-channel recording system. Many clinics managing OSA within the UK health service currently use oximetry for screening and monitoring OSA subjects, and one of the aims of the current study was to evaluate the use of the ODI measure in assessing treatment outcome. In the current study there was a substantial level of agreement between the definitions of success of post-treatment ODI ≤ 10 and AHI ≤ 10, with a kappa value of 0.75. This indicates that the ODI outcome measure may be a useful and cost-effective method of assessing treatment outcome in OSA. The ODI measure has also been used in a previously published clinical trial of surgical uvulopalatopharyngoplasty (UPPP) and nCPAP (Lojander *et al*., 1996). In that trial a reduction in ODI to less than 10 was regarded as a successful outcome, and was observed in 100 per cent of

nCPAP treatments and 39 per cent of surgically treated cases. The range of severity of OSA cases in that study was very similar to that in the current investigation. Using this definition of success of ODI ≤ 10, the current data indicate a success rate of 35 per cent, which compares favourably with that reported by Lojander *et al*. (1996) for UPPP. None of the six subjects in the current study with an ODI of more than 50 had a reduction to 10 or less with the MAA. If these six most severe cases are excluded, then the success rate for mild to moderate OSA was 50 per cent.

Use of questionnaires

A sleep-symptom questionnaire was used in the current clinical trial to obtain bed-partner reporting of the typical severity of snoring symptoms over the entire duration of the trial period with each appliance. Questionnaire outcome measures have been widely used in previous studies of snoring severity and prevalence (Hillerdal *et al*., 1991; Stradling and Crosby, 1991; Davies *et al*., 1992; Ali *et al*., 1994; Kump *et al*., 1994) and for investigating treatment outcome with MAAs (Bonham *et al*., 1988; Ichioka *et al*., 1991; Schmidt-Nowara *et al*., 1991; Clark *et al*., 1993; O'Sullivan *et al*., 1995; Bernhold and Bondemark, 1998; Cameron *et al*., 1998) and UPPP (Vukovic and Hutchings, 1996; Lim and Curry, 1999; Tytherleigh *et al*., 1999). The use of questionnaire outcome measures is, nevertheless, recognized to be subjective, and more objective assessment techniques are available. Measurement of snoring using sound-activated tape recorders has been described in the literature (Stradling, 1993), although this method has the limitation of only providing an estimation of the total length of time spent snoring on the individual night of recording. Furthermore, many subjects do not snore every night and it is also recognized that the duration, timing, and loudness of snoring may vary from night to night in individual snorers. As a consequence, single-night tape recording techniques may poorly assess the true severity of snoring. Several commercially available OSA monitoring systems include the facility to record snoring severity, although these are often limited by having a fixed loudness threshold below which snoring sounds are not registered. It is proposed that the questionnaire technique used in the present study provided a valid assessment of the typical severity of snoring in terms of loudness and number of nights per week. To reduce the influence of between subject variation in reporting, the study utilized a randomized cross-over design in which each subject and bed-partner acted as their own control during statistical analysis. Although the reported frequency and loudness of snoring was lower with the MAA than the placebo for OSA subjects, the differences were not statistically significant. A recent study of non-apnoeic snorers using the same MAA design reported significantly lower scores for loudness and frequency of snoring than with a placebo (Johnston *et al*., 2001). A possible explanation for the differences in outcome between these studies is that there may be more pronounced abnormalities in pharyngeal form and function in OSA subjects compared with non-apnoeic snorers.

The current study should be regarded as a short-term clinical trial, and therefore the reported compliance and complications should be viewed from this perspective. Most other published studies have also used a short treatment duration before assessing outcome: Hans *et al*. (1997) assessed outcome after two weeks, Clark *et al*. (1993) after three weeks, Sjoholm *et al*. (1994) after two months and Ferguson *et al*. (1996, 1997) after four months. Other studies of MAA effectiveness either have not reported the duration of MAA wear prior to outcome data collection (Mayer and Meier-Ewert, 1995) or have had a wide range of treatment duration, such as O'Sullivan *et al*. (1995) who reported results following 1–9 months of appliance use. In the current study, short-term compliance with the MAA and placebo appliance was good, with only one of the 21 recruited subjects being unable to wear the MAA appliance. That subject refused to persist with the MAA despite reporting that it was relatively comfortable. Hence, the short-term compliance failure rate in the trial was less than 5 per cent. Ferguson *et al*. (1996) reported a compliance failure of 24 per cent, with six out of 25 unable to wear a commercially

produced MAA (Snore-Guard) during a 2-month trial. The good compliance with the generic MAA used in the present trial is therefore an encouraging finding.

Most subjects reported that they wore their appliances on more than five nights per week and for more than four hours per night during the trial period. A review by Schmidt-Nowara *et al*. (1995) noted that previous studies had reported a compliance rate of between 50 and 100 per cent over a maximum period of three years. The frequency of reported side-effects with the MAA in the current trial was low, with the most frequently reported problem being excess salivation while wearing the appliance. This is commonly reported with these types of appliances (O'Sullivan *et al*., 1995; Schmidt-Nowara *et al*., 1995; Ferguson *et al*., 1996, 1997; Bondemark, 1999). Jensen *et al*. (1991) reported stimulation of the salivary reflexes by the presence of a complete denture, and it is probable that the acrylic MAA has a similar effect. The authors' clinical experience indicates that this particular problem is not a persistent one and, although the long-term effects were not examined in the current investigation, previous studies support this view (Ferguson *et al*., 1996, 1997). Occlusal and TMJ symptoms were commonly reported as occurring when waking in the morning, although only two subjects reported that either of these problems sometimes persisted during the day. Nevertheless, the findings emphasize the importance of careful pre-treatment assessment and the need to inform patients of the possible side-effects of appliance wear. As long-term follow-up of these complications was not evaluated in the current study, it is unclear whether these problems may become significant over a longer period of MAA use. As it was found in a recent two-year follow-up of 30 subjects wearing MAAs that no subject experienced a 'permanent sense of altered occlusion' (Bondemark, 1999), it is unlikely that such problems would occur with the MAA used in the present trial.

Conclusions

1. The frequency of respiratory events as measured using the AHI and ODI was significantly lower for the MAA than for the placebo appliance.
2. Based on the reduction of baseline AHI and ODI to 10 or less, the MAA success rate was 33 and 35 per cent respectively.
3. The MAA was less successful in patients with severe OSA (pre-treatment AHI or ODI > 50).
4. Although the MAA was more effective in controlling daytime sleepiness and severity of snoring than the placebo, the differences were not statistically significant.
5. Compliance with the MAA was excellent and reported complications were mild.

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Appendix 1: Questionnaire measures used in the current study

Questionnaire outcome measures

Snoring frequency. Bed-partner reported snoring frequency:

0 Never
1 Less frequently than once a week
2 1 or 2 nights a week
3 3–5 nights a week
4 Every or almost every night

Snoring loudness. Bed-partner reported snoring loudness:

0 Doesn't snore
1 Soft
2 Moderate (sometimes keeps you awake)
3 Loud (often/usually keeps you awake)
4 Very loud and disturbing (disturbs someone sleeping in another room)

Tiredness on waking. Frequency of feeling tired or unrefreshed on waking in the morning:

0 Never
1 Less frequently than once a week
2 1 or 2 mornings a week
3 3–5 mornings a week
4 Every or almost every morning