A randomized crossover study comparing two mandibular repositioning appliances for treatment of obstructive sleep apnea

Bradley M. Bishop BMSc, DDS, MS, FRCD(C)
Private Practice
#203, 1890 Cooper Rd
Kelowna, BC, V1Y 8B7
bbishop@legatocentre.com
Tel. (250) 860-5253
Fax (250) 860-5259

Ronald G. Verrett DDS, MS
University of Texas Health Science Center at San Antonio
Graduate Prosthodontics (Mail Code 7912)
7703 Floyd Curl Drive
San Antonio, TX 78229-3900
verrett@uthscsa.edu
Tel. (210) 567-6377
Fax (210) 567-6376

Thomas B. Girvan, DMD
Audie L Murphy Memorial VA Hospital
7400 Merton Minter Blvd
San Antonio, Texas
thomas.girvan@va.gov
Tel. (210) 949-8911
Fax (210) 949-8901

Conflicts of Interest

We declare that we have no conflict of interest related to the Remmers Sleep Recorder, nor the mandibular repositioning appliances used in this investigation.

Abstract

Purpose The purpose of this study was to determine whether treatment outcomes vary according to the design of the mandibular repositioning appliance (MRA). Two titratable MRA`s were compared. The designs differ in advancement hardware and configuration of acrylic both in bulk and interocclusal contact.

Materials and Methods The primary treatment outcome was the Respiratory Disturbance Index (RDI). Other outcomes that were compared included Sleep Apnea Quality of Life Index (SAQLI), Epworth Sleepiness Scale, oxygen saturation and subjective feedback regarding experiences with the appliances. Twenty-four subjects were recruited from consecutive referrals for MRA therapy following diagnosis of OSA by polysomnography. Subjects were randomly assigned to a treatment arm of the crossover study. Each subject underwent an initial sleep study with a type III home monitor to establish a baseline RDI. Subjects were then treated with one of the two MRAs determined by random assignment. The MRA self-titration phase was monitored until a treatment position was determined, and the home sleep study was repeated. After a two-week period without any OSA treatment, subjects received the second MRA and the self-titration treatment protocol was repeated. At completion of treatment with each appliance, subjects answered questionnaires and underwent a sleep study with the type III monitor. The outcome data for each appliance were compared using analysis of variance.

Results Eighteen subjects completed the treatment protocol. There were no significant statistical differences in treatment outcomes between the two appliances. There was a statistically significant ($p \leq 0.05$) preference for a MRA design with minimal coverage of teeth and palate. The subjects' appliance selection was consistent with a corresponding reduction in SAQLI score for the selected appliance.

Conclusion Although no statistically significant difference was observed between the two appliances in the outcomes measured; there was a trend toward greater improvement with the appliance with less acrylic resin bulk and less interocclusal contact. MRA selection should favor titratable, unobtrusive designs with appropriate construction to promote acceptance and adherence to MRA therapy.

Keywords Obstructive sleep apnea, mandibular repositioning appliance, crossover study, design, RDI,

Introduction

Obstructive sleep apnea (OSA) results from repetitive collapse of the upper airway during sleep and is a disorder of significant public health concern. Undiagnosed sleep disordered breathing is prevalent among middle-aged adults with a wide range of severity [1].There are several negative physiologic consequences including oxygen desaturation and arousal from sleep [2]. OSA is an important risk factor for cardiovascular and cerebrovascular disease. OSA also contributes to excessive daytime sleepiness (EDS), impaired cognitive function, and reduced quality of life[3, 4, 5, 6, 7].

The rationale of a MRA is to displace oropharyngeal tissues by repositioning the mandible which results in a patent airway [8, 9, 10]. Mandibular position can be manipulated in two basic fashions: rotation and translation. Rotation increases the vertical space between the maxilla and mandible. Translation positions the mandible anteriorly (protrusion). The effect of both types of movement must be considered in the treatment of OSA.

Translation of the mandible will also position the soft tissues attached to the mandible anteriorly, thus increasing the patency of the oronasopharynx. A protrusive mandibular repositioning appliance has been shown radiographically to increase pharyngeal dimensions [11]. Mandibular protrusion has been repeatedly demonstrated as a critical component of MRA therapy. Several investigators have investigated the ideal amount of protrusion [12, 13, 14]. These studies treated patients at either 50% or 75% of maximum mandibular protrusion. The primary treatment outcome measured was Apnea-Hypopnea Index (AHI). Secondarily, they measured subjective evaluation of treatment. They concluded with regard to both variables that there is no difference in the treatment outcome between 50% and 75% mandibular protrusion. These studies did not reveal a minimum amount of mandibular protrusion required for reduction of OSA.

The vertical component of mandibular positioning (rotation) has been evaluated using a similar appliance at 4mm and 14mm [15]. Both appliances produced identical mandibular protrusion. It was concluded that increased occlusal vertical dimension (OVD) does significantly reduce AHI, but that the 4mm and 14mm appliances produce the same treatment effects. Hans and coworkers compared the effects of increased OVD and protrusion separately and in combination [16]. They concluded that increased OVD and protrusion in combination provided the greatest treatment effect.

A MRA that covers all of the maxillary and mandibular teeth by its nature must increase the occlusal vertical dimension at least a few millimeters. Therefore the degree of protrusion becomes the more important spatial dimension to consider in the design of an MRA.

Several authors have recommended the MRA comparisons for the purpose of determining key features [17, 18, 19, 20]. The following features have been manipulated and studied: OVD, mandibular protrusion, titratability, materials and appliance bulk [12, 13, 15, 16, 21, 22, 23, 24, 25].

There are many mandibular repositioning appliances on the market for treating OSA and very little literature to guide clinicians in selection. To date, a limited number of clinical studies have compared oral appliances. A recent cross-over study reported on initial and long term treatment efficacy and subjective evaluation of two widely used oral appliances, the Klearway and Silencer [26, 27]. The research presented herein is the first cross-over design that compares the Klearway and TAP 3 oral appliance, two commonly utilized MRAs which differ appreciably in construction.

Methods

Subjects

Twenty-four subjects were recruited from the Audie L. Murphy Veteran Affairs Hospital Dental Service in San Antonio, Texas. All participants had previously been diagnosed with obstructive sleep apnea by polysomnography and had rejected treatment with CPAP. Exclusion criteria included inadequate tooth support to retain a MRA, severe cardiovascular, neurological, or respiratory disease, severe nasal obstruction, TMJ dysfunction, concurrent OSA treatment, previous surgical treatment for OSA and previous MRA therapy.

The study was reviewed and approved by the University of Texas Health Science Center at San Antonio Institutional Review Board (HSC20070681H). Subjects gave written and oral consent to participate.

Appliances

The two titratable appliances selected were the Klearway and the TAP3. The Klearway (K) appliance allows 44 incremental mandibular protrusive adjustments of 0.25mm which allows for very fine adjustment to treatment needs and patient comfort. The K appliance is made of thermoactive acrylic resin which is warmed in water prior to insertion. Additional retention is obtained from Adam's clasps placed on first or second molars. A screw mechanism for advancing the mandible is positioned in the palatal vault. The upper member is connected to the lower member using a tube and large diameter wire which allows lateral and vertical jaw movement.

The TAP3 (T) appliance is a titratable MRA made with thermoplastic acrylic that fits firmly over the maxillary and mandibular teeth. The upper member and the lower member can be separated for insertion and removal. The T appliance is also advanced 0.25mm per full turn using a removable Allen wrench. The mechanism for advancing the mandible is a small metal hook and base assembly placed on the anterior maxillary and mandibular members of the appliance. This connection also permits limited lateral movement.

Two commercial laboratories fabricated the appliances: the K group was made by Great Lakes Orthodontics (Tonawanda, NY) and the T group was made by the same certified dental technician at The Prosthodontic Lab Inc., (San Antonio, Texas).

Protocol

At the initial appointment the subjects completed a Medical and Dental History, Epworth Sleepiness Scale (ESS) [28], and Sleep Apnea Quality of Life Index (SAQLI) [29, 30, 31]. Subjects were randomized into one of two treatment arms by selecting from a large envelope one small piece of folded paper from a collection of papers with the same dimensions with an equal number of K's and T's printed on them. Group K was initially treated with Appliance K, while Group T was initially treated with the Appliance T. Maxillary and mandibular alginate impressions were made along with an interocclusal record made at two-thirds of maximum protrusion using a George gauge [32]. Subjects were instructed on the use of the Remmers Sleep Recorder (RSR), a level III sleep recorder [33, 34]. The RSR has been validated as an alternative to PSG in two large clinical studies [35,36]. Written and verbal instructions included how to apply the probes and how to properly validate each signal using the visual-analogue scale on the front of the recorder. Subjects were instructed to use the RSR for one night of sleep and then to return the RSR within 24 hours. The sleep data was then downloaded onto a dedicated computer where the data was analyzed by the Remmers Insight Software using an algorithm to determine the respiratory disturbance index (RDI) [37]. According to The American Academy of Sleep Medicine guidelines, the term RDI for a portable monitor (PM) has been defined as the number of apneas + hypopneas/ total recording time rather than total sleep time [38].

Three probes were used to acquire five signals. The pulse oximeter finger probe was used to acquire a signal for oxygen saturation and heart rate. The tracheal transducer was placed on the skin above the sternal notch to record snoring sounds and sleep position. The nasal cannula was used to measure respiratory airflow. All

recordings were assessed by the Primary Investigator to assure complete signal reception on all channels and the resulting data was reviewed by a Diplomate of the American Board of Sleep Medicine.

The appliances were inserted two to three weeks after the initial appointment. The appliance was initially fitted at the protrusive position correlating with the interocclusal record. The subject was instructed to begin advancing the appliance by turning the screw one turn per night until snoring ceases, the subject experiences optimal reduction in sleepiness (as determined by the subject) or cannot advance the mandible further. The subject used these parameters to determine the end point of treatment.

Three to four weeks after beginning titration the subject was again evaluated. If the subject had experienced adequate reduction in snoring, optimal reduction in sleepiness or could not advance the mandible further he or she completed ESS and SAQLI and Follow-up Questionnaires. If the appliance was not adequately titrated the subject was appointed for an additional evaluation two to four weeks later. Repeated evaluations continued until a satisfactory endpoint was achieved. At that time the subject underwent an additional ambulatory sleep study. When the subject returned the RSR within 24 hours of completing the sleep-study they surrendered their first treatment appliance. Subjects were reminded that they must not participate in any other treatment of OSA and that they would receive the second MRA at the beginning of the second phase of the study in two weeks.

Treatment Phase Two followed the same protocol as treatment phase one except that Group K was treated with Appliance T and Group T was treated with the Appliance K. At the completion of Treatment Phase two (i.e. the end of the patient's research participation) the subject was instructed to select either the Appliance K or Appliance T for ongoing OSA therapy – their choice was recorded. Subjective feedback on the MRAs was recorded throughout all appointments. These experiences included symptoms, side effects and recommendations for a better appliance.

Statistics

Objective physiologic data and subjective questionnaire data were analyzed to determine if appliance design affects appliance efficacy and patient preference. The sample size of 18 was determined for the primary treatment outcome, RDI, based on values from literature [21] using the nQuery 6.0 software. When n= 18, a paired t-test with a 0.025 one-sided significance level (0.05 two-sided significance level) had 80% power to detect clinically relevant difference between the two appliances, assuming the SD of difference =7.0. The SD was calculated assuming a correlation of 0.6 for observations on the same patient and a SD of 7.8 for a single set of observations [21]. A 10% dropout rate was assumed. This analysis indicated a sample size of 20 would permit demonstration of equivalence or non-equivalence between appliances. Contrary to initial expectations for a 10% dropout it was necessary to recruit twenty-four subjects to obtain complete results from eighteen.

Results

Of the twenty-four subjects recruited to participate six did not complete the protocol leaving eighteen subjects. This satisfied the power analysis completed prior to beginning the study. There was no significant difference ($p \leq 0.05$) in outcome variable between those who did and did not complete the study protocol.

Subjects in arms K and T were compared with respect to the variables measured at baseline. The subjects in arm T had a significantly greater weight, BMI and neck circumference. No other differences were significant between the baseline measurements of arm K and arm T. Thus, the distributions of variables in the two arms were similar as expected because of random assignment.

OSA is classified as mild (AHI 5-14.9), moderate (AHI 15-29.9) or severe (AHI≥30). To examine the effects of treatment for patients of differing severity, we grouped the patients according to this classification. The patients were distributed as follows: five mild, six moderate and two severe. The results of the analyses indicated that there was no significant statistical difference in any of the response variables between the two appliances (Table 1). We note that even though the individual differences were not statistically significant, for all five variables, the means for Appliance T were lower than the means for Appliance K. This suggested that overall there might be a difference in the two appliances that was not detectable using any single variable alone. When these five variables were analyzed using multivariate analysis, the two appliances were still not significantly different (P=0.3316).

Although there was no difference in the two appliances, it was also necessary to determine whether the treatment of the patients with these appliances was effective. In order to determine this, the baseline measurements were compared to the measurements at the end of treatment. For both appliances the ESS and SAQLI were significantly ($p \leq 0.05$) lower than the baseline, but the RDI and percentage of time that SaO_2<90% were not (Table 2).

We also analyzed the data to determine if either appliance had a different effect within the AHI classifications (Table 3). Neither appliance proved to be more effective than the other in any AHI classification for any variable recorded. There was no observed significant interaction of AHI and other treatment outcome measures. This finding supports using the difference in treatment group means, in association with AHI, as the preferred indicators of treatment effect.

One of the goals of this study was to consider subjective perception of the appliances. At the end of the treatment protocol we asked the subjects which appliance they preferred for ongoing therapy. Table 4 displays the selection made for the definitive appliance. Thirteen of 18 subjects completing the study selected Appliance T as their preferred appliance (13/18=72.2%) while 5 of 18 subjects (5/18=27.8%) selected Appliance K as their preferred appliance (P=0.0963 for testing a null hypothesis that one-half of the subjects would choose each appliance). Based on the number selecting appliance T, it would seem that there is a preference for appliance T. However it is also critical to consider the subject's affinity to the first appliance they used. There was no significant association (P=1.000, Fisher's Exact Test) of preferred choice with the order that an appliance was tested (Table 4). Seven of the 13 subjects that selected appliance T received that MRA first (7/13=53.9%) and 3 of the 5 subjects that selected appliance K received it first (3/5=60.0%).

Subjects were asked why they made their selection. All subjects who selected Appliance T referred to the minimal bulk as a determinant in their decision. The second most common reason for selecting Appliance T related to the lack of hardware against the palate. There was no consensus for choosing Appliance K. The subjects' appliance selection was associated with the SAQLI score with the appliance selected. Those who selected appliance T had a significantly lower SAQLI score ($p \leq 0.05$) for Appliance T than these subjects had for Appliance K. Likewise, those who selected Appliance K had a significantly lower SAQLI score ($p \leq 0.05$) for Appliance K than for the subjects who preferred Appliance T had with Appliance K. Additionally those who selected Appliance K had a significantly lower ESS score ($p \leq 0.05$) with Appliance K than the subjects who preferred with Appliance T had with Appliance K.

Discussion

Previous research delineated the importance of several characteristics of MRAs – titratable protrusion and increased vertical dimension. This study compares two commonly used MRAs that include these characteristics. The results describe both quantitative and qualitative outcomes of MRA therapy. This direct comparison provides direction in both appliance design and appliance selection.

The objective of the study was to determine if two different appliance designs result in different treatment outcomes. The crossover design allowed both appliances to be tested with a closely monitored clinical treatment protocol and effectively compared using a relatively small number of subjects. The crossover design permitted the evaluation of twice as many appliances while removing the inter-patient variability – all comparisons were made relative to the within-subject variation (intra-patient variation).

The study protocol used the subject's and clinician's best judgment with respect to improvement of symptoms to determine the protrusive endpoint with oral appliance therapy. It was at this position that the final sleep study was performed with each appliance. Two subjective measures (SAQLI and ESS) and two objective measures (RDI and SaO2) were measured. Both subjective measures had statistically significant improvement ($p \leq 0.05$) after treatment with both appliances. Both objective measures did not have statistically significant improvement ($p \leq 0.05$). However, the improvement in RDI achieved by appliance T is very near the level of statistical significance and may be clinically significant as indicated by the subjective measures. A larger sample size may have demonstrated a statistically significant difference in the change in RDI. The inconsistency between subjective and objective measures also highlights the importance of using objective measures for determining the treatment endpoint. The protocol used herein to determine endpoint, although flawed, simulates typical clinical conditions. Clinicians should use subjective data to determine when to acquire objective measurements that can then be used to identify an appropriate therapeutic endpoint [39].

This research protocol was conducted in a VA facility, which provided ready access and recruitment of subjects. Most patients in the VA system are male so this patient source provided only one female for the study. Additionally many VA patients suffer from multiple ailments that complicated availability and ability to participate. The male to female ratio was much greater than the usual population referred for MRA therapy. The effect of this is unknown, but it is an important consideration for the application of the results.

The subject dropout rate was higher than anticipated. The dropouts were not related to one appliance or the other. They were however related to age, the dropout patients having an average age of 59.4 and the completing subjects having an average age of 47.4 years. This data indicate that age negatively influences a patient's ability or willingness to adapt to an intraoral appliance. The number of dropouts was too small to determine the effects, if any, of appliance construction on the dropout rate.

Although there was a significant difference for weight, BMI and neck circumference between treatment arms, these differences had no influence on our estimates of treatment differences. Because each subject in the study received both appliances, the comparisons of appliances are within subject. The body weight, BMI, and neck circumference were measured once and thus the same values of these "covariates" would be used to adjust the responses to each of the two appliances. The adjustment due to the covariates would affect only between-subjects comparisons - the within-subject comparison will all have adjustments that are numerically equal to zero [40].

The relationship between SAQLI score and appliance selection is important because it indicated that subjects preferred the appliance associated with a greater improvement in quality of life. It also may indicate that both appliances affect a different improvement in quality of life and that it is appropriate to select a different appliance for certain patients. It is important to determine the patient variables that might dictate selection of a treatment appliance.

Several variables were evaluated to determine success with the appliances. None of the variables showed any difference in treatment success between the two appliances. Both appliances induced mandibular protrusion, increased vertical dimension and were titratable. Despite differences in construction and materials, no significant differences were observed in measured objective treatment outcomes.

Difference in final protrusive position was evaluated and compared between the two appliances. We were able to do this because the first and second appliance for each patient was fabricated using the same interocclusal record. The data in Table 1 suggest that patients choose a less protrusive position, but the difference was not statistically significant ($p \leq 0.05$) between the two appliances.

In summary, no statistically significant difference was found between the two appliances of different design and construction based on ESS, SAQLI, RDI and SaO_2. Despite similar physiologic improvements the clear majority of subjects preferred an appliance that is less bulky and covers fewer surfaces of the mouth. Subjective measures approximate endpoint, but objective measures should determine therapeutic endpoint when possible. When selecting or designing an appliance bulk should be minimized, particularly adjacent to the palate and tongue. The appliance should allow titratable protrusion and should provide some increase in the vertical space between the maxillary and mandibular teeth.

References

1. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S (1993) The occurrence of sleep-disordered breathing among middle-aged adults. New Engl J Med 328(17):1230-1235
2. Kushida CA, Morgenthaler TI, Littner MR, Alessi CA, Bailey D, Coleman J Jr, Friedman L, Hirshkowitz M, Kapen S, Kramer M, Lee-Chiong T, Owens J, Pancer JP (2006) Practice parameters for the treatment of snoring and Obstructive Sleep Apnea with oral appliances: an update for 2005. Sleep, 29:240-243
3. D'Alessandro R, Magelli C, Gamberini G, Bacchelli S, Cristina E, Magnani B, Lugaresi E (1990) Snoring every night as a risk factor for myocardial infarction: a case-control study. BMJ, 300:1557-1558
4. Partinen M, Guilleminault C (1990) Daytime sleepiness and vascular morbidity at seven-year follow-up in obstructive sleep apnea patients. Chest, 97:27-32
5. Shahar E, Whitney CW, Redline S, Lee ET, Newman AB, Javier Nieto F, O'Connor GT, Boland LL, Schwartz JE, Samet JM (2001) Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. Am J Respir Crit Care Med 163:19-25
6. Shamsuzzaman AS, Gersh BJ, Somers VK (2003) Obstructive sleep apnea: implications for cardiac and vascular disease. JAMA, 290:1906-1914
7. Young T, Peppard P (2000) Sleep-disordered breathing and cardiovascular disease: epidemiologic evidence for a relationship. Sleep, 23:S122-6
8. Ferguson KA, Ono T, Lowe AA, al-Majed S, Love LL, Fleetham JA (1997) A short-term controlled trial of an adjustable oral appliance for the treatment of mild to moderate obstructive sleep apnoea. Thorax 52:362-368
9. Hiyama S, Tsuiki S, Ono T, Kuroda T, Ohyama K (2003) Effects of mandibular advancement on supine airway size in normal subjects during sleep. Sleep 26:440-445
10. Skinner MA, Robertson CJ, Kingshott RN, Jones DR, Taylor DR (2002) The efficacy of a mandibular advancement splint in relation to cephalometric variables. Sleep Breath 6:115-124
11. Fransson AM, Svenson BA, Isacsson G (2002) The effect of posture and a mandibular protruding device on pharyngeal dimensions: a cephalometric study. Sleep Breath 6:55-68
12. Tegelberg A, Walker-Engstrom ML, Vestling O, Wilhelmsson B (2003) Two different degrees of mandibular advancement with a dental appliance in treatment of patients with mild to moderate obstructive sleep apnea. Acta Odontol Scand 61:356-362
13. Walker-Engstrom ML, Ringqvist I, Vestling O, Wilhelmsson B, Tegelberg A (2003) A prospective randomized study comparing two different degrees of mandibular advancement with a dental appliance in treatment of severe obstructive sleep apnea. Sleep Breath 7:119-130
14. Pancer J, Al-Faifi S, Al-Faifi M, Hoffstein V (1999) Evaluation of variable mandibular advancement appliance for treatment of snoring and sleep apnea. Chest 116:1511-1518
15. Pitsis AJ, Darendeliler MA, Gotsopoulos H, Petocz P, Cistulli PA (2002) Effect of vertical dimension on efficacy of oral appliance therapy in obstructive sleep apnea. Am J Respir Crit Care Med 166:860-864
16. Hans MG, Nelson S, Luks VG, Lorkovich P, Baek SJ (1997) Comparison of two dental devices for treatment of obstructive sleep apnea syndrome (OSAS). Am J Orthod Dentofacial Orthop 111:562-570
17. Ferguson KA, Cartwright R, Rogers R, Schmidt-Nowara W (2006) Oral appliances for snoring and obstructive sleep apnea: a review. Sleep 29:244-262
18. Kryger MH, Roth T, Dement WC, editors (2005) Principles and practice of sleep medicine. 4th ed. Philadelphia: Elsevier/Saunders
19. Lim J, Lasserson TJ, Fleetham J, Wright J (2006) Oral appliances for obstructive sleep apnoea. Cochrane Database Syst Rev
20. Schmidt-Nowara W, Lowe A, Wiegand L, Cartwright R, Perez-Guerra F, Menn S (1995) Oral appliances for the treatment of snoring and obstructive sleep apnea: a review. Sleep 18:501-510
21. Bloch KE, Iseli A, Zhang JN, Xie X, Kaplan V, Stoeckli PW, Russi EW (2000) A randomized, controlled crossover trial of two oral appliances for sleep apnea treatment. Am J Respir Crit Care Med 162:246-251
22. Eckhart JE (1998) Comparisons of oral devices for snoring. J Calif Dent Assoc 26:611-623
23. Lawton HM, Battagel JM, Kotecha B (2005) A comparison of the Twin Block and Herbst mandibular advancement splints in the treatment of patients with obstructive sleep apnoea: a prospective study. Eur J Orthod 27:82-90
24. Luks V, Lorkovich P, Hans M, Nelson S (1996) Comparing three dental devices for treatment of OSAS. J Dent Res 75 (Special Issue):19
25. Rose E, Staats R, Virchow C, Jonas IE (2002) A comparative study of two mandibular advancement appliances for the treatment of obstructive sleep apnoea. Eur J Orthod 24:191-198

26. Gauthier L, Laberge L, Beaudry M, Laforte M, Rompré PH, Lavigne GJ (2009) Efficacy of two mandibular advancement appliances in the management of snoring and mild-moderate sleep apnea; A cross-over randomized study. Sleep Med 10:329-336
27. Gauthier L, Laberge L, Beaudry M, Laforte M, Rompré PH, Lavigne GJ (2011) Mandibular advancement appliances remain effective in lowering respiratory disturbance index for 2.5-4.5 years. Sleep Med 12:844-849
28. Johns MW (1991) A new method for measuring daytime sleepiness: The Epworth Sleepiness Scale. Sleep 14:540-545
29. Flemons WW, Reimer MA (1998) Development of a disease-specific health-related quality of life questionnaire for sleep apnea. Am J Respir Crit Care Med 158:494-503
30. Flemons WW, Reimer MA (2002) Measurement properties of the Calgary sleep apnea quality of life index. Am J Respir Crit Care Med 165:159-164
31. Lacasse Y, Godbout C, Series F (2002) Independent validation of the Sleep Apnoea Quality of Life Index. Thorax 57:483-488
32. Lowe AA (1999) Titratable oral appliances for the treatment of snoring and obstructive sleep apnea. J Can Dent Assoc 65:571-574
33. Ferber R, Millman R, Coppola M, Fleetham J, Murray CF, Iber C, McCall V, Nino-Murcia G, Pressman M, Sanders M, Strohl K, Votteri B, Williams A (1994) Portable recording in the assessment of obstructive sleep apnea. ASDA standards of practice. Sleep 17(4):378-392
34. Flemons WW, Littner MR, Rowley JA, Gay P, Anderson WM, Hudgel DW, McEvoy RD, Loube DI (2003) Home diagnosis of sleep apnea: a systematic review of the literature. An evidence review cosponsored by the American Academy of Sleep Medicine, the American College of Chest Physicians, and the American Thoracic Society. Chest 124:1543-1579
35. Vasquez, J-C, Tsai W, Flemons WW, Masuda A, Brant R, Hajduk E, Whitelaw WA, Remmers JE, (2000) Automated analysis of digital oximetry in the diagnosis of obstructive sleep apnoea. Thorax 55:302-307
36. Issa FG, Morrison D, Hadjuk E, Iyer A, Feroah T, Remmers JE (1993) Digital monitoring of sleep-disordered breathing using snoring sound and arterial oxygen saturation. Am Rev Respir Dis 148:1023-1029
37. Vazquez JC, Tsai WH, Flemons WW, Masuda A, Brant R, Hajduk E, Whitelaw WA, Remmers JE (2000) Automated analysis of digital oximetry in the diagnosis of obstructive sleep apnoea. Thorax 55:302-307
38. Epstein LJ, Kristo D, Strollo PJ, Friedman N, Malhotra A, Patil SP, Ramar K, Rogers R, Schwab RJ, Weaver EM, Weinstein MD (2009) Clinical guidelines for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med 5:263-276
39. McLornan, PM (2009) Evaluation of Obstructive Sleep Apnea Patients' Oral Appliance Titration Protocols [thesis]. [San Antonio, TX]: University of Texas Health Science Center at San Antonio. Pp.117-120
40. Winer BJ (1971) Statistical Principles in Experimental Design. pp. 797. McGraw-Hill, New York

Table 1. Treatment group means.

Variables	Baseline	Appliance K		Appliance T		K vs. T
		Mean ± SE	Significance	Mean ± SE	Significance	
RDI	16.5 ± 3.2	10.3 ± 3.2	P=0.1640	7.7 ± 3.3	P=0.0559	P=0.1359
ESS	12.2 ± 1.1	7.8 ± 1.1	P=0.0017	7.6 ± 1.1	P=0.0012	P=0.9089
SAQLI	60.6 ± 4.7	46.0 ± 4.5	P=0.0091	39.7 ± 4.7	P=0.0004	P=0.3379
SAO_2<90%	7.7 ± 3.1	6.8 ± 3.1	P=0.7224	3.7 ± 3.2	P=0.1156	P=0.1423
Δ Protrusion (mm) (Final-Initial)		3.3 ± 0.4		2.6 ± 0.5		P=0.1612

Table 2. Comparison of baseline variables between per protocol subjects and dropouts.

Variable	Per protocol			Dropout			Significance
	n	Mean	SE	n	Mean	SE	
Age (years)	18	47.4	2.6	6	59.5	3.4	P=0.0218
Weight (kg)	18	100.2	3.7	6	99.8	6.6	P=0.9508
Height (cm)	18	178.5	1.6	6	176.3	2.2	P=0.4874
BMI (kg/m)	18	31.4	1.0	6	32.1	2.1	P=0.7278
Neck Circumference (cm)	18	43.5	0.9	6	45.6	1.2	P=0.2852
AHI	18	19.3	4.6	6	28.5	10.0	P=0.3547
Systolic BP (mmHg)	18	129.3	3.0	6	132.3	7.1	P=0.6550
Diastolic BP (mmHg)	18	77.9	2.3	6	74.3	4.5	P=0.4665
Max Protrusion (mm)	18	11.7	0.5	6	9.8	0.6	P=0.0858
ESS	18	12.2	1.2	6	11.3	2.6	P=0.7427
SAQLI	18	60.6	4.9	6	67.7	5.7	P=0.4490
RDI	18	16.5	5.1	5	15.8	5.0	P=0.9451
SaO2 below 90%	18	7.7	3.4	4	2.5	1.8	P=0.1891

Table 3. Treatment group means by AHI classification.

Variables	AHI classification	Treatment Appliance		Significance of interaction*
		Appliance K	Appliance T	
		Mean ± SE	Mean ± SE	
RDI	Mild	9.5 ± 1.5	5.8 ± 1.5	P=0.2489
	Moderate	8.7 ± 2.0	10.9 ± 2.7	
	Severe	18.6 ± 3.2	11.0 ± 3.2	
ESS	Mild	6.8 ± 1.2	6.7 ± 1.2	P=0.0779
	Moderate	9.0 ± 1.6	5.6 ± 1.6	
	Severe	9.5 ± 2.7	17.5 ± 2.7	
SAQLI	Mild	48.5 ± 5.8	36.7 ± 5.8	P=0.1558
	Moderate	42.7 ± 7.6	33.7 ± 7.6	
	Severe	43.5 ± 12.7	72.5 ± 12.7	
SAO_2<90%	Mild	4.5 ± 1.5	0.9 ± 1.5	P=0.5736
	Moderate	12.5 ± 2.0	13.1± 2.7	
	Severe	1.3 ± 3.2	0.5 ± 3.2	
Δ Protrusion (mm) (Final-Initial)	Mild	2.9 ± 0.4	2.3 ± 0.5	P=0.6462
	Moderate	3.6 ± 0.6	3.5 ± 0.6	
	Severe	3.4 ± 0.9	2.1 ± 0.9	

* The interaction of AHI classification and treatment is a test of difference between K and T by AHI classification. A non-significant test indicates these differences are similar in all AHI classifications.

Table 4. Subjects' preferred appliance.

First treatment arm	Selected appliance		Total
	Appliance T	Appliance K	
T	7	2	9
K	6	3	9
Total	13	5	18