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Comparison of titrable thermoplastic *versus* custom-made mandibular advancement device for the treatment of obstructive sleep apnoea

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ABSTRACT

Backgound and objectives: The disadvantages of custom-made mandibular advancement devices (MAD) for obstructive sleep apnoea (OSA) therapy are the cost and delay required to manufacture the device. This study aimed to evaluate the efficacy of a titrable, thermoplastic MAD compared to a custom-made MAD for OSA therapy.

Methods: In this prospective nonrandomized study, 158 patients with OSA from two French sleep centers were treated for 6 months with a titrable thermoplastic MAD (n = 86) or a custom-made MAD (n = 72). The primary outcome was the change in sleep-disordered breathing (SDB) severity.

Results: After adjustment for baseline values, age, body mass index and study site, no significant inter-group differences were observed between thermoplastic and custom-made MAD for the outcome of apnoea, hypopnoea and oxygen desaturation indices. No between treatment differences were observed for the outcome of subjective sleepiness, symptoms of snoring and fatigue, depressive symptoms, and quality of life. Thermoplastic MAD therapy was associated with higher side effects scores for tooth pain ($p < 0.0001$) and self-reported occlusal changes ($p = 0.0069$). Mean (SD) reported compliance was lower in the thermoplastic MAD group than in the custom-made MAD group (6.4 [0.2] *vs* 7.1 [0.1] h/night; $p = 0.035$).

Conclusions: This study demonstrates the efficacy of a titrable thermoplastic MAD in reducing SDB and related symptoms in patients with mild to severe OSA. Reported compliance at 6 months was high despite more dental discomfort than with custom-made MAD.

1. Introduction

Obstructive sleep apnoea (OSA) is a highly prevalent disease [1] characterized by recurrent episodes of partial or complete obstruction of the upper airway during sleep. Continuous positive airway pressure (CPAP), being the first line therapy for moderate to severe OSA, improves daytime alertness, health-related quality of life (HRQL) and reduces blood pressure [2,3]. Observational prospective cohort studies indicate that regular CPAP therapy is also associated with a lower risk of driving-related accidents and cardiovascular events [4,5]. However, among OSA patients in whom

Abbreviations: AHI, apnoea-hypopnoea index; AI, apnoea index; BMI, body mass index; CPAP, continuous positive airway pressure; ESS, Epworth Sleepiness Scale; MAD, mandibular advancement device; ODI, oxygen desaturation index; SF36, Outcomes Study 36-item Short-Form; SDB, sleep-disordered breathing; T90, sleep time with SaO2 <90%; VAS, visual analogue scale (VAS).

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CPAP is recommended, approximately 40% are at risk of non-adherence especially if they have mild to moderate OSA [6]. Mandibular advancement devices (MAD) have emerged as the main therapeutic alternative for OSA. Despite the superior efficacy of CPAP in reducing sleep-disordered breathing (SDB), most randomized trials comparing MAD and CPAP in OSA have reported similar heath outcomes in terms of sleepiness, neurobehavioral functioning, quality of life and blood pressure [3,7–10]. When MAD therapy is prescribed, practice guidelines also suggest with a low quality of evidence to use a custom, titratable MAD over non-custom devices [11]. However, potential disadvantages of these custom-made MAD are the cost and delay required to manufacture the device. In addition, not all patients benefit from MAD, and presently no method exists to predict the outcome prior to fabrication of the device [12]. Thus, a trial with an inexpensive thermoplastic titrable MAD would be of great interest. A previous randomized cross-over trial found that a monobloc nonadjustable thermoplastic MAD with insufficient overnight retention was less effective that a custom-made MAD [13]. The main requirement for a MAD to be effective is the adequate retention on the teeth while the patient is asleep [14,15]. The aim of this study was to evaluate the efficacy of a titrable, thermoplastic MAD compared to a custom-made MAD for mild to severe OSA therapy.

2. Methods

This prospective nonrandomized study was conducted on the *Institut de Recherche en Santé Respiratoire des Pays de la Loire [IRSR] sleep cohort* [6]. Approval was obtained from the University of Angers ethics committee and the "Comité Consultative sur le Traitement de l'Information en matière de Recherche dans le domaine de la Santé [C.C.T.I.R.S.] (07.207bis)". The database is anonymous and complies with the restrictive requirements of the "Commission Nationale Informatique et Liberté [C.N.I.L.]", the French information technology, and personal data protection authority. All patients included in the *IRSR sleep cohort* have given their written informed consent.

2.1. Study population

According to French clinical guidelines, MAD therapy is recommended as an appropriate first-line treatment option for mild to moderate OSA in patients without severe cardiovascular comorbidity or as a second line option in patients intolerant to CPAP [16]. Between Jun 01, 2015 and January 25, 2017, consecutive OSA patients in whom MAD therapy was considered in two French sleep centers (University Hospital of Angers and Saint-Antoine Hospital of Paris, France) participating to the *IRSR sleep cohort* were offered the choice of being treated immediately with a custom-made MAD or starting with a trial of thermoplastic MAD.

A flow diagram is presented in Fig. 1. Two hundred and twenty patients in whom MAD had been prescribed for at least 6 months were eligible for the study. None of these patients were on CPAP therapy during the study period. One hundred and twenty five patients had been treated with thermoplastic MAD and 95 had been treated by custome-made MAD. One hundred and fifty-eight patients were included in the analysis, 86 in the thermoplastic MAD group and 72 in the custom-made MAD group. The baseline characteristics of study participants are summarized in Table 1. Significant intergroup differences were observed for age, body mass index (BMI) and OSA severity. Patients treated with thermoplastic MAD were younger ($p = 0.0039$), had lower BMI ($p = 0.0079$) and had less severe OSA ($p = 0.0022$ for AHI and 0.0445 for sleep time with SaO2 <90%).

2.2. Device fitting and titration

A customizable, titratable, thermoplastic MAD (BluePro®; BlueSom, France), with sufficient retention forces to resist mouth opening forces [15], was evaluated in the present study (Fig. 2A). Two titrable custom-made MADs with proven clinical efficacy in treating OSA [9,17] were used in the study: 63 patients were treated with the AMO® device (SomnoMed, France) and 9 with the Somnodent® device (SomnoMed, France) (see Fig. 2B and C). All patients were fitted with the chosen MAD by a qualified dentist. The same MAD titration procedure was used for thermoplastic and custom-made MADs. As previously described, once fitted with the device, patients underwent an acclimatization period during which the mandible was incrementally advanced by 1-mm steps every 1 or 2 weeks until symptom relief or the maximum comfortable limit of advancement was achieved [17].

2.3. Outcomes and follow-up

All outcomes were assessed at baseline and after 6 months of MAD therapy. Outcome assessors were unaware of the device assignment. The primary outcome was the change in SDB severity as assessed by the apnoea-hypopnoea index (AHI), the apnoea index (AI), the 3% oxygen desaturation index (ODI) and the sleep time with SaO2 <90% (T90) between baseline and after 6 months of thermoplastic or custom-made MAD. Secondary outcome measures included changes in daytime sleepiness, depressive symptoms, HRQL, clinical symptoms of OSA, treatment side effects and compliance. Daytime sleepiness was evaluated by the Epworth Sleepiness Scale (ESS) [18]. Symptoms of depression were assessed with the Pichot QD2A depression score [19]. HRQL was evaluated with a validated French-language version of the Medical Outcomes Study 36-item short-form (SF36) [20]. Outcome of OSA symptoms, global treatment satisfaction, and reported side effects were assessed at 6-month follow-up using previously described specific questionnaires [10,17]. Reported compliance was assessed through a diary during the 6 months of treatment with thermoplastic or custom-made MAD. Each night, patients recorded the number of hours that the device was used. A mean reported daily use over the study period was then calculated.

2.4. Sleep recordings

At baseline all patients underwent type III overnight respiratory recordings (CID 102 LX, Cidelec, Sainte-Gemmes sur Loire, France) with continuous recording of arterial oxygen saturation, nasal-oral airflow, chest and abdominal wall motion, and body position [19]. Respiratory events were scored manually using recommended criteria [21]. At 6 months, SDB severity was evaluated under thermoplastic or custom-made MAD with either type III overnight respiratory recording ($n = 120$) or overnight pulse oximetry ($n = 38$) using Nonin 8500 M (Nonin Medical Inc. Plymouth, MN, USA) with calculation of the ODI and T90 [22].

2.5. Statistical analysis

Continuous variables were described as mean (standard deviation [SD]) or mean (95% confidence interval, [CI]) for variables with a normal distribution and as median (interquartile range [IQR]) for variables with a non-normal distribution. Normality of distribution was assessed using the Kolmogorov–Smirnov test. Normal variables were analyzed using an unpaired *t*-test for intergroup difference and a paired *t*-test for intragroup difference. Linear regression analysis was used to adjust for baseline values and potential covariates. Non-normal variables were analyzed using the