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CHAPTER 29:

PREVALENCE AND EFFECT OF SUPINE-DEPENDENT OBSTRUCTIVE SLEEP APNEA ON ORAL APPLIANCE THERAPY

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Summary

Oral appliance (OA) therapy is a non-invasive treatment option for patients with obstructive sleep apnea (OSA). The most common type of OA therapy prescribed for the treatment of OSA is an oral appliance worn intraorally at night in order to reduce upper airway collapse by protruding the mandible (OA_m). In this chapter, we will focus on the effect of supine-dependent OSA (sdOSA) on treatment outcome during OA_m therapy, the prevalence of sdOSA before and under OA_m therapy and the effect of combination of an OA_m and positional therapy. Retrospective analyses of clinical, physiological and polysomnographic variables were performed in literature in order to identify predictors of treatment success with OA therapy. Six studies assessed a significant association between the efficacy of OA_m therapy and the presence of sdOSA, whereas the results of two other studies couldn't confirm this finding. In order to evaluate the treatment effect of OA_m therapy among patients with or without sdOSA, it can be important to determine the prevalence of sdOSA in the patient population starting OA_m therapy. In this restricted patient group, the prevalence of sdOSA at baseline ranged from 27 to 80 %. In addition, up to one third of patients undergoing OA_m therapy have sdOSA under OA_m therapy. Those patients could probably benefit from additional therapy with a supine-avoidance device. Two studies assessed the efficacy of OA therapy combined with positional therapy showing promising results for this specific combination therapy.

Keywords: oral appliance therapy, supine-dependent, prevalence

Introduction

Oral appliance (OA) therapy is increasingly prescribed as a non-invasive treatment option for patients with snoring and mild to moderate OSA and as an alternative for patients who do not comply with or refuse CPAP [1]. Oral appliances are designed to prevent upper airway collapse and can be divided into 2 major classes: 1) a tongue retaining device (TRD) holding the tongue in a forward position due to a negative pressure and resulting suction in a flexible bulb [2] and 2) an oral appliance protruding the mandible during the night (OA_m). It is reported that the TRD appliances have lower tolerance, preference and compliance when compared to OA_m therapy [3]. Therefore, nowadays, OA_m is the most common type of OA therapy prescribed for the treatment of OSA [4]. Within this group, the custom-made OA_m (Figure 1) are reported to give a better overall clinical outcome than prefabricated ‘boil and bite’ devices made out of thermoplastic material [5]. Furthermore, OA_m with an integrated titratable mechanism allowing for gradual mandibular protrusion [6] are superior in their ability to reduce the apnea severity as compared to the monobloc types where upper and lower parts are rigidly interconnected [7]. Different titratable oral appliances with unique design features are currently available (Figure 2).

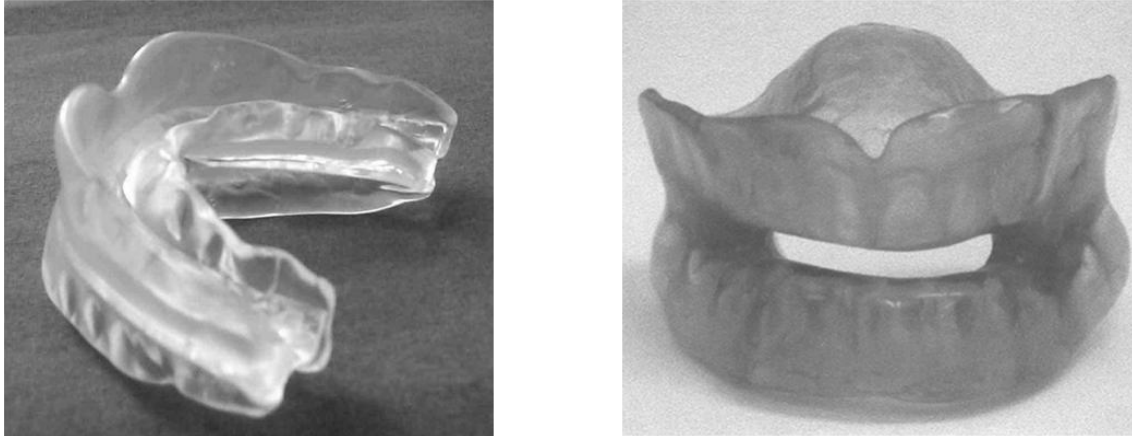


Figure 1: Two types of oral appliances used for the treatment of obstructive sleep apnea.

Left panel: prefabricated ‘boil and bite’ oral appliance after direct fitting in the patient

Right panel: custom-made monobloc oral appliance made on casts of the tooth arcs

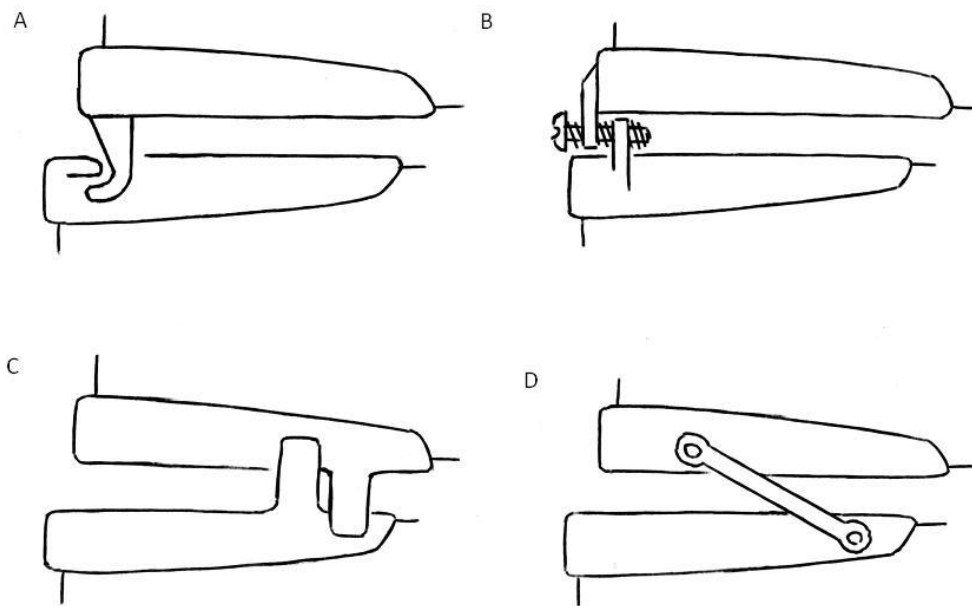


Fig. 2 (taken from [6]): Schematic overview of titratable, duo-bloc MRA designs used in current clinical practice: *(Nico toestemming vragen aan de oorspronkelijke Publisher)*

- (A) OA_m with an anteriorly articulating component
- (B) OA_m with attachments for adjustment of mandibular protrusion in the frontal teeth area;
- (C) OA_m with two lateral positioning attachments for incremental protrusion of the mandible;
- (D) OA_m with lateral telescopic rods that force the mandible into an anterior position.

When compared to CPAP therapy, OA_m therapy has been proven to reduce the severity of sleep apnea to a lesser or similar extent than CPAP [8-11], although OA_m therapy seems to have a higher acceptance rate and patient preference compared to CPAP [12, 13].

Recently, an objective compliance monitor for OA_m therapy became available, allowing for calculation of the mean disease alleviation as a measure of therapeutic effectiveness [14]. This calculation showed that comparable therapeutic effectiveness between OA_m therapy and the gold standard treatment for patients with OSA, being CPAP, has been reported because the superior efficacy of CPAP in alleviating OSA is offset by inferior acceptance and patient preference relative to OA_m therapy [8, 14, 15].

Efficacy of oral appliance therapy

OA_m therapy is effective in reducing the apnea severity in some but not in all patients. In general 65 % of patients respond to the treatment with a ≥ 50 % reduction in apnea-hypopnea index (AHI) with the OA_m in situ compared to baseline. On average 52 % of patients achieve

an AHI < 10 events/hour with the OA_m in situ [12]. In the past, retrospective analyses of clinical, physiological and polysomnographic variables were performed in order to identify predictors of treatment success with OA_m therapy. There is evidence to support the findings that OA_m therapy is more likely to be successful in younger female patients [16], with lower body mass index [17], a smaller neck circumference [11] and less severe sleep apnea [16, 18, 19].

In this chapter, we will focus on studies evaluating the effect of sleep position or the presence of sdOSA on OA_m efficacy. Eight [16, 20-26] studies evaluated the effect of sdOSA on the outcome of OA therapy. Six studies [16, 20-24] reported that the efficacy of OA therapy is influenced by sleep position in a way that patients with sdOSA have better treatment outcomes, where two other studies did not find a difference in success rates between non-sdOSA and sdOSA patients [25, 26].

In a study of Cartwright et al. [20], the association between the efficacy of a TRD and the factors obesity, age, supine sleep posture and severity of sleep apnea was investigated in 16 male patients. The authors concluded that an increase in sleep apnea severity in the supine sleep position was the strongest predictor of success with a TRD.

Marklund et al. [16, 23] evaluated the effect of sdOSA on therapy outcome with success defined as AHI < 10 events/hour in both the supine and non-supine sleeping positions with the OA_m in situ. They reported that sdOSA was a strong predictor of successful apnea reduction with OA_m therapy. In addition, it was suggested that a low AHI in the lateral position is important in predicting a successful apnea reduction with OA_m therapy [23]. After subdividing the patient population according to gender, sdOSA remained the strongest predictor of OA_m therapy success in men but did not relate to a successful apnea reduction in female patients [16].

Yoshida [24] assessed a significant decrease in both supine AHI and AHI in prone position under OA_m therapy. The AHI increased in the lateral position, although not significantly. A successful apnea reduction under OA_m therapy (AHI < 10 events/hour) was achieved in 61.4 %, 84.6 % and 0 % of patients with respiratory disturbances most frequently observed in supine, prone and lateral position, respectively. Yoshida [24] concluded that the efficacy of OA_m therapy is influenced by sleep posture.

In a study of Chung et al. [22] using Cartwright's definition [27], the decrease in both total AHI as well as supine AHI under OA_m therapy was significantly higher in sdOSA patients when compared to non-sdOSA patients. The decrease in non-supine AHI did not differ between the two groups. The complete response rate with AHI < 5 events/hour under

OA_m therapy was higher in sdOSA patients when compared to non-sdOSA patients. Applying a multiple linear regression model, the presence of sdOSA turned out to be the only factor associated with a decrease in overall AHI or with a complete response.

Lee et al.[21] evaluated the efficacy of OA_m therapy in 100 Korean patients in terms of supine dependency. The success rate, defined as a reduction in AHI of 50 % or more and an AHI under OA_m of < 10 events/hour, was significantly higher in sdOSA compared to the non-sdOSA group.

Fransson et al. [25] subdivided their total patient population in supine-dependent ODI patients if 50 % or more of the estimated sleeping time was in supine position when desaturations were registered. In contrast with the previously described results that suggests that sdOSA is associated with a better treatment response, Fransson et al.[25] did not find a supine dependent difference in responder rate, defined as patients with a reduction in ODI of at least 50 % or with an ODI value under OA_m therapy of < 5 events/hour.

Sutherland et al. [26] assessed differences in treatment response among 386 patients with and without sdOSA. In this study, no difference in complete response (AHI < 5 events/hour) was noted between sdOSA and non-sdOSA patients.

Several confounders must be taken into account when comparing the studies evaluating the effect of sdOSA on the outcome of OA therapy.

A first confounder is the presence of different criteria for sdOSA in the literature (table 1). The application of three different criteria for sdOSA makes it hard to compare the prevalence of sdOSA and the effect of sdOSA among the different studies.

A second confounder is the lack of a consensus in literature regarding the definition of successful treatment outcome. Some studies defined success as a reduction in AHI under therapy of $\geq 50\%$ compared to baseline, where other studies used a post-treatment AHI of less than 5, 10 or 20 events/hour as a successful treatment outcome. In addition, some studies used a combination of a reduction in AHI of $\geq 50\%$ compared to baseline combined with a post-treatment AHI of less than 5, 10 or 20 events/hour as criteria for success. One study uses the ODI as the main outcome parameter with success defined as a reduction in ODI of at least 50 % or with an ODI value under OA_m therapy of < 5 events/hour [25].

A third confounder is the use of different types of oral appliances in the discussed studies: one study used a TRD [20] where the other studies used an OA_m [16, 21-26]. Furthermore, a monobloc OA_m was used [16, 21, 23-25], whereas only in two studies a titratable OA_m was used [22, 26]. In the studies using a monobloc OA_m, 4 out of 5 studies

(80%) did find an association between the efficacy of OA_m therapy and the presence of sdOSA, whereas only 1 out of 2 studies (50 %) using a titratable OA_m could confirm these results.

Prevalence of supine-dependent sleep apnea under oral appliance therapy

The prevalence of sdOSA in a general population ranges from 20 to 60 %, depending on the definition used (table 1). This prevalence was also studied in a more restricted population of patients starting OA_m therapy. In order to do so, Marklund et al. [23] defined sdOSA as a supine AHI ≥ 10 events/hour with a lateral AHI < 10 events/hour. According to this definition, 46 % of patients were diagnosed as having sdOSA. Applying the same definition, Dieltjens et al. [28] found a comparable prevalence of 46 % prior to the start of the OA_m therapy. In three studies, the prevalence of sdOSA as defined by Cartwright's criteria was assessed before starting OA_m therapy and ranged from 58 to 80 % [21, 22, 28]. In a study of Yoshida, 61 % of patients starting OA_m therapy exhibited the respiratory events most frequently in supine sleeping position [24]. Overall, the prevalence of sdOSA found in patients starting OA_m therapy ranged from 27 to 80 % and was comparable to the prevalence of sdOSA in the general population (table 1). These results however do not reveal the evolution of sdOSA once OA_m has started and until recently, the prevalence of sdOSA under OA_m therapy was unknown. In a recent study 183 patients with polysomnographic data before and under OA_m therapy were evaluated showing a prevalence under OA_m therapy ranging from 18 to 34 %, depending on the definition used. In addition, it was shown that up to one third of patients shift from non-sdOSA at baseline to sdOSA under OA_m therapy [28].

Positional therapy in combination with oral appliance therapy

Patients with sdOSA under OA_m therapy could probably benefit from additional therapy with a supine-avoidance method. Up to this date, there are only 2 studies comparing the efficacy of positional therapy and OA therapy and assessing whether there is any additional benefit combining positional therapy and OA therapy [29, 30].

In the study of Cartwright et al. [29], the efficacy of a TRD and a posture alarm giving an auditory beep when in supine position were compared, as well as the efficacy of combination therapy of the posture alarm and the TRD. Patients were assigned to either therapy with the posture alarm, the TRD or combination therapy of the posture alarm and the TRD. Nine out of 15 patients (60 %) and 8 out of 15 patients (53 %) achieved a complete

response ($AHI < 5$ events/hour) with the tongue retaining device and the posture alarm, respectively. The group with combination therapy showed the highest success rate with 11 of 15 patients (73 %) reaching a complete response.

In an ongoing prospective randomized controlled trial [30], the additional effect of a chest-worn sleep position trainer (SPT) (NightbalanceTM, Delft, The Netherlands) [31] is assessed in patients with sdOSA under OA_m therapy. After a baseline PSG and PSG with OA_m , patients who were unsuccessfully treated ($AHI < 5/h$ under OA_m therapy) due to the presence of sdOSA under therapy following both Cartwright's and Marklund's criteria under OA_m therapy, were invited for 2 PSGs in a randomized order: one PSG with SPT alone and one with combination therapy of SPT and OA_m . The SPT used in this study continuously monitors sleep position, vibrating when in supine position. If the patient shifts to non-supine position, vibration of the SPT stops. The results of this randomized controlled trial suggest that combination of a SPT and OA_m therapy in patients with sdOSA under OA_m therapy is effective with a significant and additional reduction in apnea severity as compared to baseline and the individual treatment modalities. The preliminary results of this research seem promising.

Conclusions

Retrospective analyses of clinical, physiological and polysomnographic variables at baseline were reported in literature, identifying predictors of treatment success with oral appliance therapy.

Six studies observed an association between the efficacy of OA therapy and the presence of supine-dependent OSA (sdOSA), whereas the results of two other studies couldn't confirm this finding. The divergence of defining sdOSA, outcome definitions and type of oral appliances makes it hard to compare the results with respect to predictive value of sdOSA for a successful OA therapy outcome with a need for larger clinical studies on this topic.

The prevalence of sdOSA in a patient population starting OA_m therapy ranged from 27 to 80 %. In addition, up to 34 % of patients have sdOSA under OA_m therapy and one third of patients shift from non-sdOSA to sdOSA under OA_m therapy.

Combination of an oral appliance with positional therapy show promising results for this specific combination therapy.

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Table 1: Definitions supine-dependent obstructive sleep apnea

Definitions of supine-dependent OSA		Prevalence general population	Prevalence population starting OA_m therapy
Cartwright et al. [27]	Supine AHI at least twice as high as non-supine AHI	50 - 60 %	58 – 80 %
Mador et al. [32]	Supine AHI at least twice as high as non-supine AHI AHI < 5 events/hour 15 min threshold for sleep in both postures	20 - 35 %	27 %
Marklund et al. [16, 23]	Supine AHI ≥ 10 events/hour together with non- supine AHI < 10 events/hour	/	46 %