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Review Article

Predictors of Long-Term Withdrawal to Mandibular Advancement Device Treatment in Obstructive Sleep Apnea Syndrome

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ABSTRACT

The mandibular advancement device (MAD) is an important part of the treatment of obstructive sleep apnea syndrome (OSA). The objective of our study was to evaluate the compliance of MAD in the short, medium and long term and the predictive factors of withdrawal. Among the 78 patients using MAD for OSA treatment, we successfully contacted by phone 64 patients (73% men, age 53 ± 10 years old, body mass index 25,6 kg/m^2 ± 2,86) 3,9 years (1,9-4,9) after MAD placement. Among the 64 patients, 35 of them (55%) were still carriers of their MAD. The higher risk of withdrawal in the 29 patients (45%) who abandoned their MAD was observed during the first eight months of treatment and was mainly due for 8 patients (28%) to pain in the temporomandibular joint. Maxillomandibular dysmorphosis appears as the only predictor of abandonment.

In conclusion, the MAD provides an effective and sustained solution in the treatment of mild to moderate OSA with good long-term compliance, except in case of maxillo-mandibular dysmorphosis. A close follow up during the first months could improve treatment compliance.

Keywords: Mandibular advancement device; Obstructive sleep apnea syndrome; Predictive factors; Withdrawal; Long term; Maxillomandibular dysmorphosis

INTRODUCTION

Obstructive sleep apnea (OSA) is a chronic condition characterized by repeated interruptions of breathing during sleep due to a complete or partial obstruction of the upper airway despite an inspiratory effort [1]. This syndrome affects around 13% of men and 6% of women between 30-70 years [2-6]. Its incidence is higher in obese patients, in men and increases with age and with the consumption of alcohol and tobacco. Craniofacial anomalies such as retromandibulia or retromaxillia are also risk factors [2,3,5,6]. OSA is mainly associated with cardiovascular risks, arterial hypertension, cognitive impairment and road or work accidents [3,4,7,8].

Obstructive apnea is caused by decreased activity of the dilating muscles during sleep causing collapse of the upper airway [5,6,9]. Obstructive sites are located between the nasopharynx and the larynx, most often between the base of the tongue or the soft palate and the posterior wall of the pharynx [5,10].

The management of OSA consists of a decrease in the factors favoring the disease (decrease of alcohol and tobacco consumption, weight loss), associated with conservative or surgical treatment [7,8]. Non-surgical options include mainly the prescription of Continuous Positive Airway Pressure (CPAP) or the placement of a mandibular advancement device (MAD) to maintain the mandible in the anterior position during sleep [7,8]. The MAD is mainly proposed in mild to moderate severity of OSA (AHI<30 E/h), for which MAD and CPAP show similar results in decreasing daytime sleepiness and improving quality of life [10-12]. The MAD can also be proposed in severe OSA, in case of failure or intolerance of the CPAP, or refusal/contraindication of surgery [13]. Although CPAP treatment provides a better reduction in AHI, the MAD is better tolerated [11,12,14,15]. Several types of MAD exist on the market; those custom made, composed of 2 pieces, with a modified propulsion offer the best results [11,14].

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The main causes of discontinuation of the device are the pain in the temporomandibular joint, sensations of oppression, hypersalivation, gingival and dental discomfort [16].

The aims of our study were to evaluate the tolerance and complication of the MAD treatment for OSA in short, medium and long term and to identify the risk factors of MAD withdrawal.

MATERIALS AND METHODS

This retrospective study was carried out in the department of Oral and maxillo-facial surgery department of the CHU Saint-Pierre in Brussels. The protocol of the study was approved by the ethics committee of the hospital. All adult patient (≥ 18 years) presenting an OSA treated by the maxilla-facial surgeon E.B. at the CHU Saint-Pierre between 2009 and 2015, by a custom made device (type Silensor), for at least one night were included in the study. The characteristics of the patients were extracted from the medical files of the patients. Patients were excluded only when not enough data could be recovered from these files. The data were collected by 2 authors (T.B. and X.V.E.) and analyzed by T.B.

The study consisted of a phone survey which was conducted by T.B. and approved by M.B. All patients were contacted by phone and invited to respond to a standard questionnaire, assessing compliance, tolerance and efficacy of treatment on daytime sleepiness by using the Epworth sleepiness scale (ESS) [17] made by M.B. In the event of discontinuation of treatment, the delay and, principal causes of withdrawal and alternative treatments were recorded.

The subjective efficacy of the MAD was evaluated by comparing an ESS performed during the phone call with the ESS performed before treatment.

Predictors of MAD withdrawal were searched among demographic characteristics, comorbidities, severity of OSA, complaints, physical examination and treatment efficacy. All patients who have dropped treatment were included in this assessment and among those who have not given up treatment, due to the high chance of dropping the MAD in the first 6 month, only patients treated for at least 6 months were included.

STATISTICAL ANALYSIS

Statistical analyses were performed using SPSS computer programs (version 23.0.0, SPSS, Inc., Chicago, IL) and Graphpad Prism 6 (GraphPad Software, Inc.). The Kolmogorov-Smirnov test was used to evaluate the normality of a distribution. The data are presented as mean ± standard deviation (SD) for values with Gaussian distribution or interquartile space (IQR) 25-75 for values with non-Gaussian distribution. The tests used are: the Wilcoxon signed rank test for paired values, the Wilcoxon-Mann-Whitney test, the Student test for independent and paired values, the Chi2 test, Cronbach's statistic, alpha, was used as a measure of the internal consistency of the items in the questionnaires, the binary and multivariate logistic regression test and the achievement of a cumulative survival curve estimated by Kaplan Meier. For all statistics, p values were considered to be statistically significant of below a threshold of 0.05. An overall assessment of compliance was carried out by the development of a cumulative maintenance curve for the MAD according to Kaplan Meier, based on the data collected during the phone call. For patients who could not be contacted, the information gathered during the last consultation with a specialist of the OSA was retained as the last contact.

RESULTS

From 2009 to 2015, 78 patients were treated with Silensor® MAD. Out of the 78 patients treated with a MAD, we successfully contacted 64 patients by phone and all these patients responded with good collaboration to the questionnaire. Despite repeated calls, 14 patients could not be contacted.

The characteristics of the patients were presented in Table 1. All patients complained of snoring and/or non-restorative sleep before MAD. The ESS score was low (median score of 6 points) witnessing an overall absence of excessive daytime sleepiness. A retromandibulia was found in 37 (58%) of the 64 patients who had physical examination.

Table 1: Characteristics of the patients (n=64).

Parameters	**n** (%)
Demographic data (n=64)	
Age (year)	53 ± 10
Gender (H/F)	46/18 (72%/28%)
BMI (kg/m^2) (n=56)	25,9 (± 2,8)
Life style	
Alcohol consumption (n=64)	16 (25%)

<2 glasses/d	15
>2 glasses/d	1
Tobacco (n=64)	13 (20%)
Comorbidities (n=64)	
Allergy	20 (31%)
Hypertension	20 (31%)
Diabetes mellitus	5 (8%)
Cardiomyopathy	4 (6%)
Asthma	4 (6%)
Gastroesophageal reflux	8 (12%)
Depression/burn out	8 (12%)
Physical examination (n=64)	
Retromandibulia	37 (58%)
Retromandibulia alone	20 (31%)
Retromandibulia with retromaxillia	17 (26%)
ESS (n=62)	
ESS score	6 (5-10)
PSG before MAD (n=62)	
AHI index (E/h)	21,6 (15-27,7)
Control PSG with MAD (n=38)	
AHI index	6,7 (3,8-13,1)
Decrease in AHI (%)	63,5 (46,5-78,25)
Treatment response (number of patient with 50% decrease in AHI)	27/38 (71%)

Note: MAD: Mandibular Advancement Device, BMI: Body Mass Index, ESS: Epworth Sleepiness Scale, PSG: Polysomnography, AHI: Apnea Hypopnea Index; E/h: Event per hour

A previous unsuccessful treatment of OSA was found in 28 patients (43%) among which 15 patients have received CPAP, 12 septoplasties combined with turbinectomies. MAD was the first treatment of 50 (78%) patients with mild to moderate OSA (Table 2) and always after failure or refusal of MAD in patients with severe OSA.

Table 2: Indications of the mandibular advancement device. (N=64 patients).

	N	%
Mild or moderate OSA (AHI<30 E/h)	50	78%

1st treatment	38	76%
Failure/intolerance of previous treatments	12	24%
CPAP	7	58%
other treatment	5	42%
Severe OSA (AHI≥30 E/h)	14	22%
Intolerance to CPAP	7	50%
Refusal of CPAP	7	50%

Note: PSG: Polysomnography, AHI: Apnea Hypopnea Index, E/h: Event per hour, CPAP: Continuous Positive Airway Pressure

EVALUATION OF THE MAD DURING PHONE CONTACT

For the 64 patients contacted by phone, MAD has been placed for a median of 3.9 years (range: 1.9 to 4.9 years) before the phone call. All had at least one complain about MAD (Figure 1), the main ones being MAD break (42%), temporomandibular joint (TMJ) pain (38%), gingival and/or dental pain (34%), hypersalivation (30%), masseter muscle pain (28%), and sensation of dental mobility (27%).

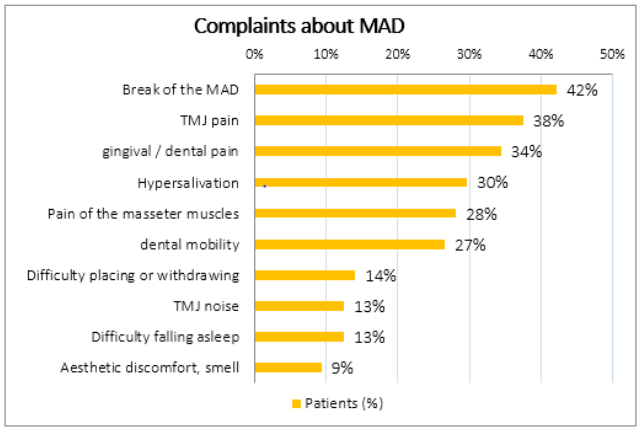

Figure 1: Patients complains regarding MAD (64 patients). MAD: Mandibular Advencement Device; TMJ: Temporo-mandibular Joint.

At the time of the phone contact, 35 patients (55%) still wore their MAD: among them, 25 patients (71%) wear them the entire night and 29 (83%) more than 4 nights a week.

When comparing ESS performed before MAD placement and at phone contact in the 35 patients still wearing their MAD, we found a significant decrease in ESS from 7 (5-10) to 5 (3-8) points (p<0,05) (Figure 2) signifying a subjective improvement of their sleepiness. However, despite clinical improvement, all of them had at least on complain, the main one being persistent discomfort (22 (63%) patients), hypersalivation (12 patients, 34%), and impression of maladaptation of the MAD (6 patients 18%). They also reported frequent break of the MAD, with at least one break in 22 (63%) of them.

Twenty-nine patients (45%) of the 64 patients had abandoned their MAD after a median delay of 122 days (7-915). The reasons for withdrawal were pain, especially at the level of the TMJ (28%) and gum (17%), the impression of inefficiency (24%) and the feeling of choking (14%).

In this group of patients, 41% of withdrawals (12 patients) occurred during the first month of treatment.

The cumulative maintenance curve of the MAD showed a median use of 45 months (33-57 months) (Figure 3). The curve showed a significant decrease during the first 8 months of 30% and after the second year of treatment.

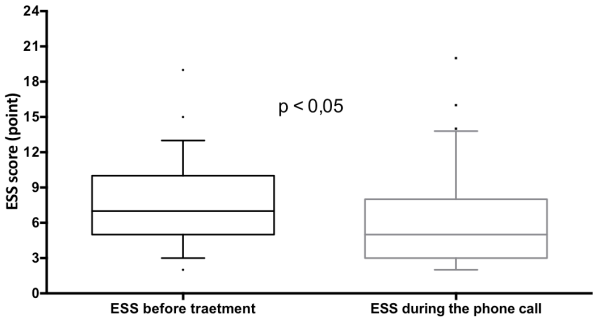

Figure 2: Comparison of the ESS before treatment by MAD and during phone call with patients still wearing their MAD. The ESS score of 7 (5-10) decreases to 5 (3-8) points. ESS: Epworth sleepiness scale.

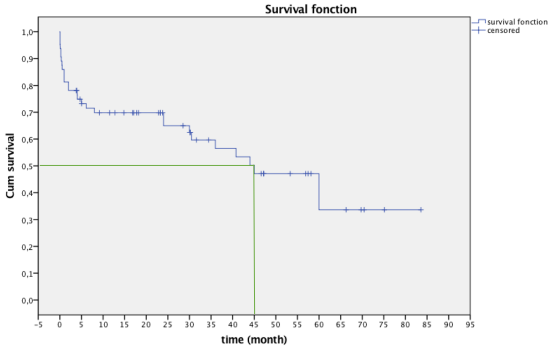

Figure 3: Curve of cumulative maintenance of the Mandibular advancement device (64 patients) Kaplan Meier curve.

PREDICTORS OF MAD WITHDRAWAL

Predictors of MAD withdrawal were searched among demographic characteristics, comorbidities, severity of OSA, complaints, physical examination and treatment efficacy. All patients who have dropped treatment were included in this assessment and among patients still carrying their MAD, only patients treated for at least 6 months were included. For this reason, 3 patients were not considered.

In binary logistic regression, female gender and the presence of maxillo-mandibular dysmorphosis at the clinical examination were statistically associated with withdrawal ($p<0.05$). Only maxillo-mandibular dysmorphosis at physical examination remains predictive in multivariate analysis ($p<0.05$) (Table 3).

Table 3: Predictors of discontinuation of treatment. n=61 (64-3 patients due to drop out before 6 months).

Univariate binary logistic regression test		
Variables	**Odds ratio (OR) (IC 95%)**	**p**
Gender (male=1; female=0) (n=61)	0,262 (0,078-0,877)	0,030
Age, year (n=61)	1,04 (0,994-1,104)	0,082
Tobacco (yes=1; no=0) (n=53)	1,160 (0,303-4,079)	0,817
Alcohol (yes=1; no=0) (n=52)	0,588 (0,168-2,060)	0,407
Allergy (yes=1; no=0) (n=45)	1,144 (0,329-3,974)	0,832
Maxillo-mandibular dysmorphosis (yes=1; no=0) (n=55)	6,691 (1,946-23,0)	0,003
BMI (kg /m^2) (n=52)	0,939 (0,763-1,156)	0,553
Decrease AHI (%) (n=34)	0,592 (0,033-10,475)	0,721
History of CPAP (yes=1; no=0) (n=61)	0,667 (0,204-2,178)	0,502
Pain caused by MAD (yes=1; no=0) (n=60)	1,944 (0,662-5,709)	0,226
TMJ pain Caused by MAD (yes=1; no=0) (n=60)	1,862 (0,724-4,787)	0,197
Multivariate binary logistic regression test		
Sex (male=1; female=0) (n=55)	0,439 (0,177-1,644)	0,221
Maxillo-mandibular dysmorphosis (yes=1; no=0) (n=55)	5,042 (1,441-17,642)	0,011

Note: n: number of patients for which data is available.
ESS: Epworth sleepiness scale; AHI: Apnea/hypopnea Index; SaO2: Oxygen saturation, CPAP: Continuous Airway pressure; TMJ: Temporo-mandibular joint

In order to better characterize the involvement of maxillomandibular dysmorphosis in the risk of discontinuation of MAD treatment, a comparison of treatment efficacy between patients with and without dysmorphosis is performed and does not show a statistically significant difference. Between the 2 groups (Table 4). A comparison of TMJ pain between the 2 groups also showed no significant difference (Table 4).

Table 4: Comparison of patients with and without maxillomandibular dysmorphosis.

	With maxillomandibular dysmorphosis	**Without maxillomandibular dysmorphosis**	**p**
ESS*	6,5 (5,0-9,7) (n=32)	6,0 (3,0-10,0) (n=25)	0,51
AHI (E/h)*	20,4 (15,8-28,5) (n=41)	22,0 (15,1-36,0) (n=27)	0,83

Decrease of AHI (%)*	62,6% (34,4-77,3%) (n=20)	62,9 (48,5-70,1) (n=19)	0,91
TMJ of gum pain (% of patients)**	69% (n=25/36)	64% (n=14/22)	0,64

Note: * Wilcoxon-mann-Whitney test; ** Chi^2 test.
ESS: Epworth Sleepiness Scale; AHI: Apnea Hypopnea Index; TMJ: Temporo-mandibular Joint

Among the 29 patients who abandoned their MAD, 16 patients (55%) had no further treatment; 9 patients (31%) changed for CPAP therapy. Only one patient used maxillo-mandibular advancement surgery. Patients who changed for CPAP had a statistically higher AHI than patients who did not use any subsequent treatment (28.2 (20.3-40.4) and 16.7 (13.0-24.2) E/h respectively, $p<0.05$).

DISCUSSION

Our study aimed to evaluate the global satisfactory of patients treated with MAD in the real life. Unlike studies that focus on short-term risk factors for success, we have focused on both short- and long-term discontinuation factors [11,14,18].

For this, we included all our patients treated with MAD in whom the follow up could be evaluated. However, we found that only one half of them were still wearing their MAD at late follow up. We identified that MAD break is a frequent event (42% of our patients experienced at least one break) and pain was a major complain. We also found that the first 8 months were critical in term of compliance because 30% of the discontinuations occurred during that period.

Our patient population is comparable to that included in most MAD studies with respect to comorbidity factors, the magnitude of daytime sleepiness, and the severity of OSA [13,19-21]. Our indications for wearing MAD were comparable to those conventionally recommended in the literature [7,11-13]. We first confirmed the adequate indications of MAD with 3 quarter of the indications being low of mild OSA and only one quarter with severe OSA but after failure of refusal of CPAP. The ESS scores were low in our patients, without excessive daytime sleepiness. This factor could probably explain the low compliance to the MAD and the absence of further treatment in patients who abandoned their MAD, as found in one half of them. Indeed, if patients were more symptomatic, we could probably observe a better compliance to the MAD treatment. In patients who used another treatment, most choose CPAP and only one patient opted for maxillo-mandibular advancement surgery.

Our study focused on the long-term results of the MAD with a median follow-up of almost 4 years. This monitoring revealed that more than half (55%) of the patients were still carriers of their MAD, and almost daily, which is consistent with the results found in the literature [10,11].

In these patients, we identified that despite the persistence sometimes of discomfort and pain, the improvement of the symptoms outweighed these disadvantages.

Clinical detection of maxillo-mandibular dysmorphosis appears to be the only predictor of discontinuation of MAD therapy. This result cannot be attributed to a subjective or objective sensation of failure since neither ESS nor AHI nor did the relative decrease in AHI differ between patients with or without maxillo-mandibular dysmorphosis. However, even if the difference was not statistically significant, patients with this type of dysmorphosis were more likely to have pain associated with MAD. This point should then be confirmed on the basis of an objective assessment of the dysmorphosis with a latero-lateral teleradiography and a larger population of patients. This could have implications for the follow-up and progressive adaptation of the mandibular propulsion.

To our knowledge, we found only one article showing that MAD as first line of treatment and AHI reduction with complete symptom resolution are strong predictors of long-term of MAD continuation [22].

One critical period seems to be the first 8 months, because 30% of the abandon were during this period. The period of adaptation of MAD represented the main period of abandonment, mostly related to pain of the temporo-mandibular joints and gingival, as well as the impression of inefficiency and choking sensation were the main causes of early withdrawal. During this period we could also see an early dropping of MAD during the first month of treatment and a total of 41% of the dropouts during the first 8 month of therapy. Progressive adaptation of propulsion could probably reduce pain and improve compliance. It can be seen that after this period of adaptation, patients remain long-term carriers of the MAD. Long-term follow-up also showed that the majority of patients, after failure of the MAD, did not use any other treatment.

Our study has several limitations. The first one is the design of the study. The collection of data by phone call includes biases such as loss of information from non-verbal communication, responses given to satisfy or not the evaluator and patients may have incorrect recollection of events leading up to discontinuation therapy. The other limitations are the monocentric side of the study as well as the limited number of patients. The respective aspect of our study did not allow us to assess all the desired criteria such as stress and anxiety witch can impact the quality of sleep.

This study nevertheless provides interesting elements for optimizing compliance with the treatment and can serve as a basis for carrying out prospective studies on a wider scale and offered a long duration of follow-up.

In conclusion, the MAD is a therapeutic option, which in the case of mild and moderate OSA brings an effective and

sustained solution. In the long term, among persistent users, complaints induced by the MAD decrease and are compensated by the improvement of symptoms related to OSA.

However, a decreased compliance is shown in case of maxillo-mandibular dysmorphosis. In these patients, a close follow-up during the period of adaptation could potentially improve compliance.

CONFLICTS OF INTEREST

The authors report no declarations of interest.

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