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Assessment of interfering factors in non-adherence to oral appliance therapy in severe sleep apnea

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Abstract

Objective: Oral appliances (OA) are recommended for patients with severe obstructive sleep apnea who fail to comply with continuous positive airway pressure (CPAP) therapy. This mixed methods study aimed to quantify adherence to OA therapy and evaluate subjective reasons associated with non-adherence.

Materials and Methods: The medical records of 52 patients with an apnea-hypopnea index (AHI) ≥ 40, treated with OA after discontinuation of CPAP treatment, were examined for OA adherence. Patients were divided according to usage at the time of a phone interview. The USER group included all forms of usage whereas those who completely ceased using the OA were in the NUSE group. The timing of the phone interview was from five months to six years (average 44.63±17.17 months) after OA delivery.

Results: The overall adherence rate was 57.7% (30/52 patients). The mean usage times were 10.07±8.96 and 44.30±17.3 months in the NUSE and NUSE groups respectively. The main factors associated with non-adherence were concerns about the effects of the OA on teeth (22%) and insufficient efficacy (22%). Other factors were discomfort (15%) or improved wellbeing following weight loss (15%). The overall number of interfering and discontinuity factors was significantly higher in the NUSE group than in the USER group (p=0.041). Nine out of 52 (17.3%) patients resumed CPAP use. Subjective and objective outcomes, determined by using a second sleep test with OA in 69.2% of patients, were related to the continuation of treatment.

Conclusions: Non-adherence to OA is strongly associated with patient reservations regarding the effects of the device on teeth, possible lack of efficacy and discomfort. Clinicians should

closely monitor adherence patterns and assess potential interfering factors during their diagnostic work up. Patients should be reassured regarding device safety, particularly following dental work that may interfere with the insertion of the OA.

Key words: Adherence, Obstructive sleep apnea, Oral appliance, Snoring

Introduction

Obstructive sleep apnea (OSA) is characterized by repetitive full or partial cessations of airflow during sleep, followed by a reduction in blood oxygen saturation (Remmers, deGroot, Sauerland, & Anch, 1978). Diagnosis of OSA is established by polysomnography (Iber, Ancoli-Israel, Chesson, & Quan, 2007). The results are used to calculate the apnea-hypopnea index (AHI) which is the sum of the average number of apnea (full airflow cessation) and hypopnea (partial airflow cessation) events per hour of sleep. An AHI score of ≥ 30 indicates severe OSA ("Sleep-related breathing disorders in adults: Recommendations for syndrome definition and measurement techniques in clinical research. The report of an american academy of sleep medicine task force," 1999).

Risks of OSA:

Severe OSA has long-term consequences such as cardiovascular disease (Marin, Carrizo, Vicente, & Agusti, 2005) e.g. myocardial infarction (Zhang et al., 2012); metabolic syndrome (Fusetti et al., 2012); hypertension (Young, Peppard, & Gottlieb, 2002); cerebrovascular complications (Gibson, 2004), neuro-cognitive impairment (Lal, Strange, & Bachman, 2012) and general daily sleepiness and decrease quality of life (Giles et al., 2006).

Treatment:

Treatment recommendations are based on the severity of OSA, patient habits and upper airway anatomy. It incorporates behavioral measures, surgical approaches and noninvasive therapeutic options.

Behavioral modifications include: weight loss (Strobel & Rosen, 1996) (Peppard, Young, Palta, Dempsey, & Skatrud, 2000), avoiding sleep in the supine position (Oksenberg, Khamaysi, Silverberg, & Tarasiuk, 2000), avoiding alcohol before going to bed, proper treatment of lung diseases if any and minimizing the use of sleeping pills (Berry, Kouchi, Bower, Prosise, & Light, 1995). The accepted surgical procedures for OSA vary in complexity and postoperative complications. Uvulopalatopharyngoplasty (UPPP) aims to remove soft tissue in the throat and palate in order to widen the upper airway (Khan et al., 2009). More complex surgeries with higher chances of success for the treatment of severe OSA include bi-maxillary and orthognathic procedures that change facial and upper airway proportions by permanent advancement of one or both jaws (Foltan et al., 2011).

Long term adherence to noninvasive therapeutic options

Noninvasive therapies for OSA include Continuous Positive Airway Pressure devices (CPAP) and Dental / Oral appliance (OA). Both types of device need to be used indefinitely, and therefore adherence to treatment is of paramount importance. The overall global adherence rate estimates that only 50% of patients with chronic diseases in developed countries follow treatment recommendations (*Adherence to long-term therapies: Evidence for action*, 2003). A recent study by McEvoy (McEvoy et al., 2016) evaluated CPAP use in patients with OSA and cardiac conditions and found that patients only used the CPAP device for an average of 3.3 hours per night. Interestingly, patient characteristics were not found to

be predictive of adherence to long term therapy (*Adherence to long-term therapies: Evidence for action*, 2003).

Continuous Positive Airway Pressure (CPAP):

The CPAP device uses a pump and face mask to continuously increase air pressure in the upper airways thereby preventing their collapse during sleep. CPAP has a very high efficacy and is considered to be the best treatment available (Giles et al., 2006) since 1981 (Sullivan, Issa, Berthon-Jones, & Eves, 1981).

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The lack of long term studies regarding CPAP makes it difficult to determine adherence rates. Some 4-5 year studies determined 64.4% to 81% adherence, whereas others noted 51.8% to 54% (Campos-Rodriguez, Martinez-Alonso, Sanchez-de-la-Torre, & Barbe, 2016). Lower rates, from 29% to 46% have also been reported (Kribbs et al., 1993; Lindberg, Berne, Elmasry, Hedner, & Janson, 2006; Weaver & Grunstein, 2008). Some of these studies used questionnaires sent in the mail, which may introduce bias and cause the reporting of higher rates of adherence (McColl et al., 2001).

Usually patients with severe OSA not adhering to CPAP are referred for other treatments such as oral appliance (OA).

Dental / Oral appliance (OA)

According to the guidelines for treatment of the American Academy of Sleep Medicine (Kushida et al., 2006) OA are indicated for snoring patients (with no OSA), as well as for patients with a minor to medium degree of sleep apnea syndrome or patients with severe OSA who cannot adapt to CPAP therapy**.** These were updadated in 2015 (Ramar et al., 2015), to 6 main points guidelines. According to the new guidelines OA are indicated for primary

snoring or for adult with OSA who are intolerant of CPAP therapy or prefer alternate therapy regardless severity degrees.

OA are intraoral removable devices worn during sleep to treat snoring and OSA (Deane et al., 2009). The most commonly used appliance, with the highest adherence rate, is a mandibular advancement appliance. This device fits onto the teeth and pushes the mandible forward (Deane et al., 2009). Consequently, the base of the tongue moves forward, widening the upper respiratory tract and creating a free air passage (Lim, Lasserson, Fleetham, & Wright, 2006).

OA seem to be easier to adjust to than the CPAP device (Aarab, Lobbezoo, Heymans, Hamburger, & Naeije, 2011; Ferguson, Ono, Lowe, Keenan, & Fleetham, 1996). The efficacy of OA has been reported regarding mild to moderate OSA (Chan, Lee, & Cistulli, 2007; Ferguson, Cartwright, Rogers, & Schmidt-Nowara, 2006). Short term success of OA in cases of severe OSA varies from 14% to 61% (Lowe et al., 2000) (Lam et al., 2011) (Barthlen et al., 2000), partly because of differences in the definition of success. To the best of our knowledge, long term efficacy of OA in severe OSA has not been documented**.**

Recently we reported that OA, like CPAP, reduces AHI scores in severe cases of OSA, but we did not investigate patient adherence rates (Haviv et al., 2014). Clearly the device can be rendered ineffective by poor adherence and needs to be used for many years.

Long term adherence to treatments for chronic conditions with high morbidity rates such as OSA is vital (Gibson, 2004; Marin et al., 2005; Robichaud-Halle, Beaudry, & Fortin, 2012).. Both OA and CPAP are considered permanent treatment modalities and adherence has high prognostic value. There are only a few studies with short follow-up times for OA (Grunstein, 1995; Kribbs et al., 1993; Weaver & Grunstein, 2008).

Considering the paucity of data regarding long term adherence among severe OSA patients to OA therapy, we conducted a retrospective chart review study of severe OSA patients to

examine long-term adherence to OA and contacted patients to determine the reasons for non-adherence.

We hypothesize that adherence rates of OA in severe OSA will not differ from reported adherence rates in other chronic diseases (*Adherence to long-term therapies: Evidence for action*, 2003). Additionally, we wished to determine if there was evidence in our population that "sleepier patients" with a higher AHI have higher adherence rates (Bizieux-Thaminy et al., 2005; Campos-Rodriguez et al., 2016; Waldhorn et al., 1990) and if patient characteristics were predictive of adherence rates (*Adherence to long-term therapies: Evidence for action*, 2003).

Materials and Methods:

The data from a Dental Sleep Medicine Center were examined from January 2006 to June 2012. Data for patients with very severe OSA (AHI $\geq$ 40) who did not tolerate CPAP and were referred for treatment with an OA were collected. AHI score of $\geq$ 30 indicates severe OSA ("Sleep-related breathing disorders in adults: Recommendations for syndrome definition and measurement techniques in clinical research. The report of an american academy of sleep medicine task force," 1999). We used a stricter inclusion criterion of AHI $\geq$ 40 as most of the patients (64) were of that severity and the majority performed a second sleep test. While generalizing to other populations may not be fully warranted, we assumed that if this method is appropriate for patients with a more severe situation there are good chances that it will work for patients of less severe AHI.

Of the 64 eligible patients, 52 were available for the phone interview. Institutional Review Board approval was attained (Barzilai Medical Center (No. BRZ-0111-13)).

All patients were treated with a custom-made, two-piece mandibular repositioning OA (Herbst device) with a latero-lateral plunger mechanism (Lawton, Battagel, & Kotecha, 2005;

Schiavoni, 2011). A raised 0.6 – 1 cm protrusive bite registration was taken for each patient by a single experienced dentist (YH). The appliance was titrated from 50% to 75% of maximum protrusion, and patients were not able to alter this. A second sleep test with the OA was performed in 36 (69.2%) of the patients who responded to the survey. Patients were asked to schedule appointments; 1 month, 3 months and once a year for follow up. They also were advised to contact their ENT or family physicians.

All patients were interviewed by phone using a combination of open ended questions regarding interfering factors and forced choice questions (regarding adherence and efficacy). Interfering factors (IF) were evaluated and quantified from the answers. In order to evaluate efficacy, the patients were asked about reductions in snoring and in daily tiredness (Ghazal, Sorichter, Jonas, & Rose, 2009). They were also asked about resumption of CPAP after trying OA.

Outcome variables included: gender, age, body mass index (BMI) and primary AHI; all recorded at intake, secondary AHI with the OA, date of OA delivery and follow up time-span.

Patients were divided into 2 groups according to adherence: The USER group included patients using the OA at the time of the interview, they were divided into sub-groups: i. more than 5 nights a week, ii. patients that use the appliance 1 to 5 nights per week and iii. patients who used OA when not sleeping at home. The 'non user' (NUSE) group included patients who stopped using the OA before the phone interview (Figure 1). Follow up duration was between five months and six years (average 44.63±17.17 months) after OA delivery.

Statistical analysis:

The dependent variable was defined as oral appliance adherence; while all other possible predictors were considered as independent variables. Continuous variables were descriptively presented by means and standard deviations, and categorical variables by frequencies. A univariate analysis was performed regarding age, BMI, initial AHI, follow-up period (months), and number of interfering factors (IF) between oral appliance adherence groups using an independent t-test. BMI was subdivided, above 30 was defined as 'obese' ("Global database on body mass index," 2006) and less than or equal to 30 as 'non obese'. The univariate analysis for categorical variables was by Chi Square Test. In order to identify multivariate independent influences of confounders or mediators on the results, a multiple logistic regression analysis was applied. Only independent variables that reached a significance level of $p<0.2$ were entered into the equation. SPSS 21.0. software was used and statistical significance was considered as $p<0.05$.

Results

Thirty patients out of 52 (57.7%) used the appliance at the time of the interview (USER) and the remaining 22 had stopped using it (NUSE). In the USER group 23 individuals (77.0%) reported regular use, 4 (13.0%) used it 1 to 5 nights per week, and 3 (10.0%) used it when not sleeping at home.

The mean time from OA delivery to the phone call was 44.63±17.17 months (range 5 months to 76 months), with no significant differences between the groups (44.30±17.3 and 45.09±17.38 months, for USER and NUSE respectively, $p=0.872$).

The mean OA usage time in the NUSE group, was 10.07±8.96 months (n=22, range 1 day to 2 years). Mean total cohort time of use was 24 months. Three patients (13.6%) stopped using the OA before the end of the first month, eight (36.4%) stopped 1 to 6 months after delivery,

six (27.2%) stopped between 6 and 12 months and a further five stopped 1-2 years (22.7%) after delivery. Four (7.7%) females and 48 (92.3%) males were included in the study. Female number was too small to assess if gender was associated with OA usage and adherence. There was no significant difference in age, BMI and initial AHI between the USER and the NUSE groups (Table 1)

Thirty-six out of 52 (69.23%) patients, underwent a second sleep test, 23 (63.9%) kept using the OA, and 13 (36.1%) stopped using it. Mean initial AHIs of these groups were 57.22±11.86 Vs 51.77±7.83 P=0.148; respectively. The second sleep test revealed that the USER group had a lower AHI: 14.86±9.24 Vs 22.85±12.34, respectively (P=0.034); table 2. BMI was not associated with adherence rate. Fifty seven percent of patients were obese with BMI > 30; of those, 20 patients were USER (66.7%) and 10 NUSE (33.3%), (p =0.126) ,(Table 3).

Twenty-seven patients (90%) in the USER group reported a significant improvement while using the device (p =0.002) with a reduction in both snoring and daily tiredness. In the NUSE group, 11 patients (50%) reported a significant improvement, 6 (27.3%) reported no change and 5 (22.7%) were unsure. Overall, 38 (73.1%) of all patients reported a reduction in both snoring and daily tiredness, 6 (11.5%) reported no change and 8 (15.4%) were uncertain. Subjective efficacy significantly correlated with OA use (p = 0.002; Table 3).

In the NUSE group the two main interfering factors that ultimately led OA cessation were: insufficient subjective efficacy and dental treatments performed after OA insertion; in particular insertion of dental implants and fear that the appliance will harm the teeth or the new dental restorations. Other reasons for cessation were loss of weight causing an improvement in subjective snoring and daily tiredness and inconvenience of the appliance (15%). Some patients gave one than more reason (Figure 2).

Overall, the mean number of side effects and factors that interfered with the treatment (Interfering factors, IF) (Stange, 2003) according to patient reports was 1.33±1.3 for each patient. The mean IF for the USER group was 0.67±1.18 and for the NUSE group was 2.22±0.81, and was significantly associated with non-adherence to the OA (p= 0.041). Interestingly, 9 out of 52 (17.3%) patients resumed CPAP use. Of these, three patients continued using the OA when not sleeping at home while six completely returned to CPAP use. A backward stepwise multiple logistic regression model by odds ratio was applied for all variables predicting oral appliance adherence (Table 4). According to the model, the variables which reached statistical significance as predictors of adherence in either group were IF (p=0.004) and objective efficacy (p=0.042).

Discussion

There are few publications regarding the long-term adherence rate for OA therapy in severe OSA, (Ahrens, McGrath, & Hagg, 2010). Furthermore, most adherence studies involved questionnaires sent via mail with a response rate of around 40% (Bachour et al., 2016; de Almeida et al., 2005; Jauhar, Lyons, Banham, Cameron, & Orchardson, 2008). Mail questionnaires introduce bias and inaccuracy, since patients not using the device will be less likely to reply to this form of questionnaire (Jauhar et al., 2008).

In the current study, we had a response rate of 81% to our phone survey. The patients we were unable to contact may have changed phone number, or address or simply did not answer our calls. All patients that did answer the phone fully participated in the survey. This method of telephoning has an advantage over the mailing methods used in previous studies. A telephone survey, when subjects are actively approached, achieves a more even handed sampling and has a higher response rate (McColl et al., 2001). Our present study demonstrates an OA adherence rate of 57.6% in patients with severe sleep apnea syndrome

with a marked difference between groups. These findings are congruent with the 50-65% adherence rates found in studies that examined mild to moderate OSA (Clark, Sohn, & Hong, 2000; Doff et al., 2013; Ingman, Arte, Bachour, Back, & Makitie, 2013; McGown et al., 2001). This rate is also in keeping with the overall global adherence rate that estimates that only 50% of patients with chronic diseases in developed countries follow treatment recommendations (*Adherence to long-term therapies: Evidence for action*, 2003). We find these results encouraging since all our patients had stopped using their CPAP device and one would have expected that their rate of adherence to a different device would be even lower than the 50% adherence rate reported.

Medical instructions can be completely ignored or partially followed by those with chronic conditions. In our study 7 patients used the OA 1 to 5 nights per week or only while traveling. This partial following of instructions is not rare. A recent study (McEvoy et al., 2016) based its conclusion on CPAP efficacy for improving cardiac conditions on 3.3 hours of CPAP use per night, which differs from the accepted recommendation (>5 hours). Clearly partial compliance is better than not using the device at all. Furthermore, the use of the OA device while traveling, in patients that resumed CPAP treatment, is an elegant solution of combining several treatment modalities to increase convenience. Combination therapies, especially for patients struggling with CPAP should be investigated.

Approximately half of the patients in the NUSE group stopped using the appliance within six months of getting it, while the rest stopped within 2 years. These findings are similar to those of de Almeida et al., who reported that most withdrawals occurred within the first year (de Almeida et al., 2005). Our findings coincide with those regarding CPAP adherence; that the first six-months are critical for long term adherence (Aloia, Arnedt, Stepnowsky, Hecht, & Borrelli, 2005; McArdle et al., 1999; Meurice, 2006).

We found three main parameters which negatively impact long-term adherence: low subjective efficacy, smaller objective success rate, measured in sequential sleep test, and a high number of interfering factors and non-continuity reasons.

Objective efficacy using second sleep test was measured in 69% of patients and revealed mean significant lower AHI with the OA of users when compared to non-users. Even though, there were patients who discontinued the treatment with the OA despite efficacy.

The decision to stop using the OA device was significantly associated with the number of interfering factors and subjective side effects (IF). The most frequent reason for discontinuation was dental treatments, especially the insertion of implants. The changes in the dentition meant that the appliance did not fit correctly, or the patients became concerned that the appliance could harm the teeth or the new dental restorations. These issues should be discussed with the patient prior to fitting the appliance (de Almeida et al., 2005). Moreover, routine dental therapy should be monitored by a clinician familiar with OA therapy.

Fifteen percent of the NUSE group complained that the device was generally uncomfortable to sleep with, this was not due to masticatory muscle or temporomandibular joint discomfort reported by others (Hammond et al., 2007; Marklund & Franklin, 2007; Petit et al., 2002; Spencer et al., 2013). Nine patients (17.3%) resumed CPAP due to its better efficacy, even though they rejected it initially. It seems that the failure of the OA made the patients more willing to use CPAP. This observation is in agreement with Almeida *et al*. who demonstrated that 23% of non-users with moderate to severe OSA switched back to CPAP (de Almeida et al., 2005). This motivating factor is an additional reason to try OA in severe OSA.

Furthermore, three subjects who resumed CPAP use reported that they used OA when travelling.

Initial AHI, age and gender did not predict long-term adherence, nor did disease severity and baseline sleepiness, and therefore patient characteristics did not predict adherence to OA. Similarly, studies on CPAP adherence have not found any predictive patient characteristics, thereby refuting the current hypothesis that sleepier patients with a higher AHI have higher adherence rates (Bizieux-Thaminy et al., 2005; Campos-Rodriguez et al., 2016; Waldhorn et al., 1990). The inability to predict non-adherence based on patient characteristics has also been reported regarding treatments for other chronic diseases (*Adherence to long-term therapies: Evidence for action*, 2003).

The present study has several limitations: The possibility of the medical conditions of the patients being motivating factors was not explored. The phone questionnaire was not performed at a set time post appliance delivery; thus a wide range of follow-up time points were included. Our patients' population was restricted to those with AHI>40, a severe form of OSA. We are unable to say to what extent their AHI degree affected their rate of adherence. Further studies concerning less severe cases should be performed to validate this statement.

Author contribution:

YH made substantial contributions to the study's conception and design, acquisition of data, and analysis and interpretation of data; drafted the submitted article and provided final approval of the version to be published. AZ conducted the statistics.GA, NK and YS wrote, revised and approved the manuscript. DJA analyzed the data and revised and approved the manuscript.

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Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all participants in the study.

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Table 1

The mean and standard deviation (mean±SD) of age, BMI, initial AHI and IF by group (USER-user group; NUSE– non user group).

	Total (N=52)	**USER (n=30)**	**NUSE (n=22)**	**p***
Age (years)	56.75±12.16	56.27±12.57	57.41±84.00	0.741
BMI	29.47± 4.21	28.75± 3.40	30.45± 5.04	0.153
Initial AHI	55.42±11.85	56.87±12.51	53.45±10.84	0.309
IF	1.33± 1.3	0.67± 1.18	2.22±0.81	**0.041**

AHI: apnea-hypopnea index; BMI: Body mass index; IF: interfering factor. *Independent t-test

Table 2

Mean and standard deviation (mean±SD) of AHI of patients who underwent a second sleep test (n=36) by group (USER-user group; NUSE-non user group).

	Total (n=36)	**USER (n=23)**	**NUSE (n=13)**	**p***
Initial AHI	55.25±10.79	57.22±11.86	51.77±7.83	0.148
Second AHI	17.74±11	14.86±9.24	22.85±12.34	**0.034**

AHI: apnea-hypopnea index

Table 3

Distribution of patients by gender, dichotomized BMI, CPAP use, and reported efficacy (N (%)).

		Total	**USER**	**NUSE**	**p***
Gender	M	48 (92.3%)	28 (58.3%)	20 (41.7%)	0.746
	F	4 (7.7%)	2 (50%)	2 (50%)	
BMI	<30	30 (57.7%)	20 (66.7%)	10 (33.3%)	0.126
	>30	22 (42.3%)	10 (45.5%)	12 (54.5%)	
Returned to CPAP use	No	43 (82.7%)	27 (62.8%)	16 (37.2%)	0.104
	Yes	9 (17.3%)	3 (33.3%)	6 (66.7%)	
Reported efficacy	Yes	38 (73.1%)	27 (90%)	11 (50%)	**0.002**
	No	6 (11.5%)	0 (0%)	6 (27.3%)	
	Inconclusive	8 (15.4%)	3 (10%)	5 (22.7%)	

*Chi Square test

Table 4

A backward stepwise multiple logistic regression model by odds ratio for all variables predicting oral appliance adherence (final model)

	B	*P**	OR**	95% CI*** for OR	
				Lower	Upper
BMI	2.715	0.073	15.107	0.780	292.715
IF	-1.830	0.004	0.160	0.045	0.566
Subjective efficacy	4.397	0.042	81.175	1.180	5582.639
Constant	-1.349	0.528	0.259		

BMI: Body mass index; IF: interfering factor.

*two-tailed statistical significance **Odds Ratio ***confidence interval

Figure 1 – Patient groups

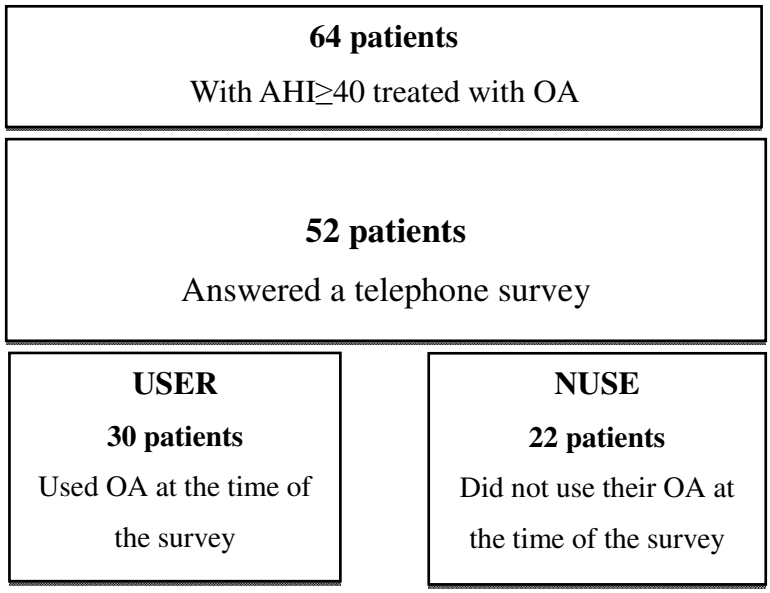

Figure 2

Interfering factors, general difficulties, subjective side effects and reasons given for stopping use of the oral appliance according to patient reports.