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THE IMPORTANCE OF SYMPTOMATOLOGY IN NON-ADHERENCE OF PATIENTS WITH OBSTRUCTIVE SLEEP APNOEA SYNDROME TO CONTINUOUS POSITIVE AIRWAY PRESSURE THERAPY

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Abstract

Obstructive sleep apnoea syndrome (OSAS) is a lesser-known pathology in Romania. Continuous positive airway pressure therapy (CPAP) is the gold standard for treating OSAS. The study's main objective was to investigate how adherence to therapy influences the evolution of OSAS. We conducted a prospective, observational, non-randomized study on an essay of 380 observations with 95 observational units (95 patients who were diagnosed with OSA, part of the tracked variables being measured at 4-time points: I-moment of diagnosis, II-1 month, III-6 months, IV-12 months). There are differences in statistical significance for Epworth scores measured at different points in time. Associated with the Epworth score, the following predictive factors had influences with statistical significance: the presence of air humidifier, systolic blood pressure, diastolic blood pressure, heart rate, Mallampati score, type of CPAP, type of CPAP mask, level of CPAP pressure. Many factors can influence the adherence of patients with OSAS to CPAP therapy. The level of daytime sleepiness can be an important predictor of adherence to therapy.

Rezumat

Sindromul de apnee obstructivă în somn (SASO) este o patologie mai puțin cunoscută în România. Terapia cu presiune pozitivă continuă a căilor respiratorii (CPAP) este standardul de aur pentru tratamentul OSAS. Obiectivul principal al studiului a fost de a investiga modul în care aderența la terapie influențează evoluția SASO. Am efectuat un studiu prospectiv, observațional, nerandomizat, pe un eșantion de 380 de observații cu 95 de unități observaționale (95 de pacienți, care au fost diagnosticați cu SASO, o parte din variabilele urmărite fiind măsurate la 4 momente de timp: momentul I al diagnosticului, II-1 lună, III-6 luni, IV-12 luni). Există diferențe în ceea ce privește semnificația statistică pentru scorurile Epworth măsurate în diferite momente în timp. Asociat cu scorul Epworth, următorii factori predictivi au avut influențe cu semnificație statistică: prezența umidificatorului de aer, tensiunii arteriale sistolice, tensiunii arteriale diastolice, frecvenței cardiace, scorului Mallampati, tipului de CPAP, tipul de mască CPAP, nivelul presiunii CPAP. Aderența pacienților cu SASO la terapia CPAP poate fi influențată de mulți factori. Nivelul de somnolență din timpul zilei poate fi un predictor important al aderenței la terapie.

Keywords: sleep apnoea, adherence, Epworth score, sleepiness

Introduction

Sleep is a natural, physiological, reversible state which involves a temporary abolition of consciousness, being, from birth, necessary for normal physical development [1]. Among the potential functions of sleep, the role in neurogenesis (especially REM sleep), in the maintenance of synaptic plasticity, the maintenance of mental health (some sleep disorders are also accompanied by psychiatric disorders), the consolidation of memory, the regulation of metabolic functions, the role in immunity, in the maintenance of general well-being, in ensuring an appropriate physical status to achieve performance [2]. In general, short-term sleep deprivation has an important effect on many cognitive domains, including attention, activity memory, work speed, short-term memory and reasoning - with few effects observed in highly complex activities [3]. Major global changes in the proportion of obese patients, both adults and children, as well as the ageing of the population, make OSAS one of the important contributors to the quality of the population's health in the future [4]. Obstructive sleep apnoea syndrome is a lesser-known pathology in Romania. Although it often has polymorphous aspects, the detection in our country in severe stages and in the phase when the disease has become visceralized demonstrates once again the lack of information in this field both among family doctors and in terms of the organ specialist. OSAS is characterised by recurrent episodes of airway obstruction (occurring during sleep), leading to marked reductions in airflow (hypopnoea) or its absence (apnoea) in the nose or mouth. The appearance of

obstructive sleep apnoea is a consequence of the breakdown of the fragile balance that exists between the anatomical arrangement, the pharyngeal intraluminal pressure, muscle activity and central control [5]. During sleep, snoring is the most common symptom in patients with OSAS. The most common daily symptoms include excessive sleepiness and fatigue [6]. Excessive daytime sleepiness is the most common daytime symptom. It can be measured using the Epworth test that determines the risk of falling asleep [7, 8]. Car and workplace accidents can occur in patients with OSAS. Neurocognitive studies have shown that driving performance correlates with the severity of hypoxemia and the degree of sleep fragmentation due to respiratory events [9]. The most used and studied method of polygraphic outpatient monitoring includes at least four channels. As a rule, they measure respiratory flow, respiratory effort, peripheral arterial oxygen saturation and pulse [10]. The management of OSAS includes behavioural changes, weight loss, exercise, drug treatment, CPAP therapy, oral application devices (tongue, orthodontic or spinal cord advancement devices), surgical procedures (tracheostomy, uvulo-palato-pharyngoplasty, laser uvuloplasty, maxillary advancement operations, maxillo-mandibular advancement, hypoglossal nerve stimulation [11]. Continuous positive airway pressure therapy (CPAP) is the gold standard for OSAS treatment, and when it is effective, it decreases AHI and hypoxemia [12]. It is used to rectify the collapse of the upper airways, functioning as a pneumatic splint [13]. A minimum of 3 - 4 hours *per* night of therapy use is necessary to obtain long-term benefits [14, 15]. Thus, the benefit of symptomatology is obtained depending on the time of use of the therapy. Given that CPAP is a chronic therapy and that, in most cases, it must be used for life, good adherence to treatment is essential for the patient to feel its benefits [16].

The main objective of the study was to investigate how adherence to therapy influences the evolution of OSAS. The secondary objectives of the study were to examine the existence of other predictors, the clinical/demographic/paraclinical parameters for the evolution of OSA and the statistical-descriptive characterisation of patients.

Materials and Methods

Study design

We conducted a prospective, observational, non-randomized study on an essay of 380 observations with 95 observational units (95 patients who were diagnosed with OSA, a part of the tracked variables being measured at 4-time points: I-moment of diagnosis, II-1 month, III-6 months, IV-12 months). The study design was with correlated measurements (parameters that were measured at 4 different times in the same patient).

Patients were considered adherent if they used therapy for at least 4 hours *per* night for at least 70% of the recommended number of days. The patients were divided into two groups: the first group, consisting of 50 patients considered adherent to the instituted therapy, and the second group, consisting of 45 patients considered non-adherent to the instituted therapy.

The inclusion criteria were as follows: written informed consent, patients over 18 years old recently diagnosed with OSAS for whom CPAP therapy was indicated, who had not previously used CPAP, and for whom no other therapeutic methods were indicated. The exclusion criteria were patients younger than 18 years old, central sleep apnoea, patients who had used CPAP in the past, patients who lacked access to a telephone network, and those unable to complete the questionnaire for objective reasons, severe associated comorbidities (decompensated cardiac failure, hypercapnic respiratory failure, cancer), absence of the written informed consent.

Ethical considerations

The study was carried out with the Helsinki Declaration; informed consent was obtained from each patient, and the approval of the Ethical Council of Rosiori de Vede Pneumology Hospital was given for the study. Informed consent has been obtained from all individuals included in this study

Data collection

The patients were evaluated over a period of one year by filling out a questionnaire and analysing the data from the CPAP machine compliance cards. These data were analysed at one month, six months, and twelve months of therapy.

The cardio-respiratory polygraphy was done with the Miniscreen or Lowenstein portable polygraph and the CPAP titration with the Miniscreen or Lowenstein portable polygraph and Auto-CPAP Lowenstein. The severity of OSAS was determined by the Apnea-Hypopnea Index (AHI). Apnoea and hypopnoea were analysed according to the American Academy of Sleep Medicine guidelines, with apnoea being defined as the absence of airflow for at least 10 seconds and hypopnea as a reduction in airflow by 30% associated with a desaturation of at least 3%. The prescription recommended CPAP in fixed pressure or Auto-CPAP.

The Epworth questionnaire identifies the level of sleepiness during the day. It includes 8 questions regarding various daily situations and establishing the possibility of falling asleep in these situations. The situations analysed are the following: sitting and reading a book or newspaper, watching a TV show, sitting idle in a public place, being a passenger in a car for an hour-long trip, sitting in bed after lunch, sitting and talking to someone, sitting after a non-

alcoholic meal, driving a car during a traffic stop of a few minutes. A score above 10 implies excessive sleepiness during the day, which may be related to a sleep disorder [7, 8].

Statistical analysis

All statistical analyses were performed using R software (version 4.4.0; R Core Team, 2024), a language and environment for statistical computing developed by the R Foundation for Statistical Computing (Vienna, Austria). The following R packages were utilized to support data analysis: gtsummary, lme4, lmerTest, and sjPlot. A two-tailed alpha level of 0.05 was set as the threshold for statistical significance, with p values less than 0.05 considered statistically significant.

Results and Discussion

Patients were divided into two groups according to their adherence to therapy: group 1, with 50 patients considered adherent, and group 2, with 45 patients considered non-adherent. Regarding the age of patients, there were no patients in the age group 18 - 29 years. Most patients were in the 50 - 69 age group. There was also a predominance of male sex in both groups of patients. Regarding the origin (rural or urban), most of the adherent patients were from rural areas. In the non-adherent patient group, there was no predominant origin. As a level of education, most patients in both groups finished high school. Also, most patients in both groups lived with someone in the house (Table I).

Table I

The distribution of patients according to age, gender, the residential environment, level of education, family status

Demographic characteristic	Total number	The number of adherent patients	The percentage of adherent patients	The number of non-adherent patients	The percentage of non-adherent patients
18 - 29 years old	0	0	0%	0	0%
30 - 39 years old	5	4	80%	1	20%
40 - 49 years old	10	2	20%	8	80%
50 - 69 years old	68	36	52.94%	32	47.05%
> 70 years old	12	8	66.66%	4	33.33%
Male	60	32	53.33%	28	46.66%
Female	35	18	51.42%	17	48.57%
Urban	40	19	47.5%	21	52.5%
Rural	55	31	56. 36%	24	43.63%
Middle school degree and below	5	1	20%	4	80%
High school degree	73	40	54.79%	33	45.20%
Bachelor's degree and above	17	9	52.94%	8	47.05%
Lives alone	20	6	30%	14	70%
Lives with someone	75	44	58.66%	31	41.33%

The percentage of patients using CPAP in fixed pressure compared to those using Auto-CPAP was not significantly different between the two groups. Most patients in both groups did not use an air humidifier. However, the percentage of patients using an air humidifier was higher in the adherent patient group. The majority of patients in both groups used an oro-nasal mask. However, the percentage was lower in the adherent patient group (Table II).

Table II

The distribution of patients according to the type of CPAP used, the use of an air humidifier, the type of mask used

CPAP	The number of adherent patients	The percentage of adherent patients	The number of non-adherent patients	The percentage of non-adherent patients
Auto-CPAP	22	44%	24	53.33%
CPAP in fixed pressure	28	56%	21	46.66%
With air humidifier	11	22%	4	8.88%
Without air humidifier	39	78%	41	91.11%
Nasal mask	9	18%	3	6.66%
Oro-nasal mask	41	82%	42	93.33%

The adherence of patients in group 1 was high during the first period (first night and first week) of therapy use (98% and 100%). In group 2, adherence to therapy was very low during this period (26.66 % and 8.88%) (Table III).

Table III

The distribution of patients according to adherence in the first night and first week of therapy

Adherence to therapy	The number of adherent patients	The percentage of adherent patients	The number of non-adherent patients	The percentage of non-adherent patients
First night with good adherence	49	98%	12	26.66%
First night with low adherence	1	2%	33	73.33%
First week with good adherence	50	100%	4	8.88%
First week with low adherence	0	0 %	41	91.11%

We noted that there are differences in statistical significance for Epworth scores measured at different points in time, GES indicated that 65% of the variability in the Epworth score was due to the timing of the measurement, so because of the evolution in time (Table IV).

Table IV

Statistical differences between Epworth scores at different moments of time

Effect	GL numerator	GL denominator	F	p value	GES
Moment of time	1.52	143.07	268.157	< 0.0001	0.652

The variant was analysed using repeated measurements (Repeated Measures ANOVA-RM ANOVA), where GL is degrees of freedom and GES is generalized effect size.

A posthoc procedure RM ANOVA was used to identify the moments between which there were differences with statistical significance, using paired T-test adjusted for multiple comparisons, using the Bonferroni procedure (I-time of diagnosis, II-1 month, III-6 months, IV-12 months. The only moments between which there were no differences with statistical significance were III *versus* IV (6 months *versus* 12 months) (Table V).

We noticed that the evolution of patients was favourable, with a decrease in the average Epworth score (Table VI).

Table V

Bonferroni procedure for Epworth scores at different time intervals

Variable	Moment of time	Moment of time	Number of patients	p raw	p adjusted
Epworth	I	II	95	< 0.0001	< 0.0001
Epworth	I	III	95	< 0.0001	< 0.0001
Epworth	II	III	95	0.0001	0.001
Epworth	I	IV	95	< 0.0001	< 0.0001
Epworth	II	IV	95	< 0.0001	< 0.0001
Epworth	III	IV	95	0.147	0.882

Table VI

Statistical marginal averages for different moments of time

Moment of time	Variable	Number of patients	Average	Standard deviation
I	Epworth	95	14.758	4.653
II	Epworth	95	6.589	2.984
III	Epworth	95	4.884	1.792
IV	Epworth	95	4.232	2.131

The following predictive factors had influences with statistical significance (Table VII). Marginally insignificant, BMI (Body Mass Index) was positively associated with the Epworth score; an increase of 1 unit is associated with an increase of 0.09 points (Table VII). Mallampati score is positively associated with the Epworth score; a 1-point increase is associated with an increase of 0.81 points (Table VII).

In patients without auto CPAP, the Epworth score was, on average, 3.2 points higher (Figure 1). In patients without CPAP in fixed pressure, the Epworth score was, on average, 4.3 points higher (Figure 2). In patients without nasal masks, the Epworth score was, on average, 3.3 points higher (Figure 3). In patients without an oro-nasal mask, the Epworth score was, on average, 3.3 points higher (Figure 4). CPAP pressure is negatively associated with the Epworth score; an increase of 1mm Hg is associated with an average drop of 0.82 points in the Epworth score (Figure 5).

Table VII

The association between Epworth score and predictive factors of adherence

Predictive factor	Number of observations	Beta (95% CI)	p value
Air humidifier			
YES	72	-	
NO	308	3.4 (2.1to 4.7)	< 0.001
BMI	380	0.09 (-0.01 to 0.19)	0.067
Systolic blood pressure	380	0.13 (0.10 to 0.17)	< 0.001
Diastolic blood pressure	380	0.10 (0.04 to 0.16)	< 0.001
HR	380	0.14 (0.08 to 0.19)	< 0.001
Mallampati score	380	0.81 (-0.08 to 1.7)	0.076
Acohol			
YES	50		
NO	330	-0.90 (-2.5 to 0.66)	0.255
Smoking			
YES	65		
NO	315	-0.32 (-1.7 to 1.1)	0.659

CI - confidence interval

Table VII

The association between Epworth score and predictive factors of adherence

Predictive factor	Number of observations	Beta (95% CI)	p value
Auto-CPAP			
YES	138	-	
NO	242	3.2 (2.2 to 4.3)	< 0.001
CPAP in fixed pressure			
YES	150	-	
NO	230	4.3 (3.3 to 5.2)	< 0.001
CPAP nasal mask			
YES	36	-	
NO	344	3.3 (1.6 to 5.1)	< 0.001
CPAP oro-nasal mask			
YES	249	-	
NO	131	7.7 (6.9 to 8.6)	< 0.001
CPAP pressure	379	-0.82(-0.88 to -0.75)	< 0.001

CI - confidence interval

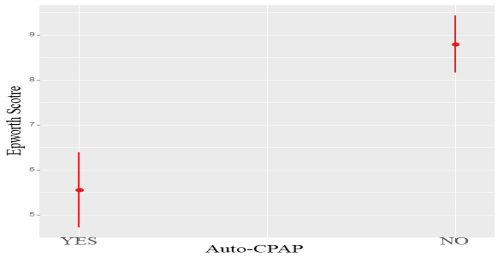

Figure 1.

The association between Epworth score and the use of an Auto-CPAP

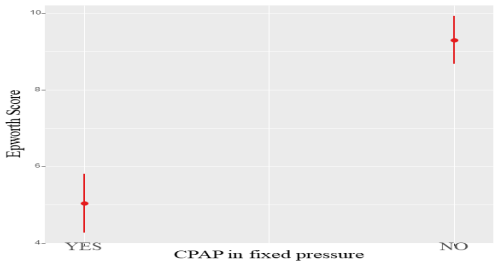

Figure 2.

The association between the Epworth score and the use of a CPAP in fixed-pressure

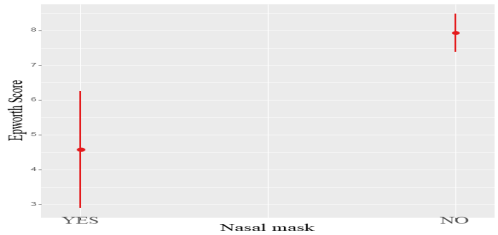

Figure 3.

The association between Epworth score and the use of a nasal mask

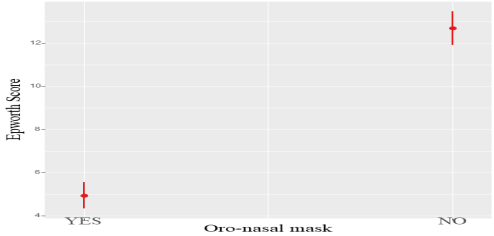

Figure 4.

The association between Epworth score and the use of an oro-nasal mask

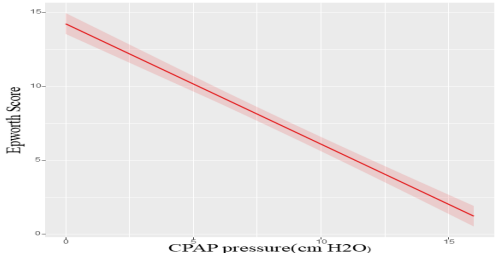

Figure 5.
The association between Epworth score and CPAP pressure

The causes identified and reported by the patient that led to the interruption of CPAP use, the causes of CPAP non-use: side effects of mask or CPAP device, discomfort of the bed partner, misperception of severity disease, disbelief in CPAP therapy, relationship between doctor and patient, low family and entourage involvement, patient education, alternative treatment. High CPAP pressure was not a significant side effect. The number of side effects reported was higher in non-adherent patients. Dry mouth was the main side effect they reported (Table IX).

Table IX
The association between CPAP adherence and side effects of therapy

Predictive factor	Global, N = 380	Adherents, N = 200	Non-Adherents, N = 180	p value
CPAP pressure, mean (SD)	8.11 (4.97)	8.09 (4.98)	8.14 (4.98)	0.92
N/A	1	1	0	
Dry mouth, n (%)				< 0.001
YES	127 (33)	32 (16)	95 (53)	
NO	253 (67)	168 (84)	85 (47)	

Obstructive sleep apnoea syndrome is a common pathology underdiagnosed in Romania, which has many cardiovascular and other complications. Continuous positive airway pressure therapy (CPAP) is the gold standard for OSAS treatment, and when it is effective, it decreases AHI and hypoxemia [12]. It is used to rectify the collapse of the upper airways, functioning as a pneumatic splint [13]. A minimum of 3 - 4 hours/night of therapy use is necessary to obtain long-term benefits [14,15]. Thus, the benefit of symptomatology is obtained depending on the time of use of the therapy. Given that CPAP is a chronic therapy and that, in most cases, it must be used for life, good adherence to treatment is essential for the patient to feel its benefits [16]. Good adherence to therapy can be obtained by avoiding aerial loss in the mask, CPAP pressure should be constant, and the use of the device should be long-lasting and constant [17]. Associated with the Epworth score, the following predictive factors had influences with statistical significance: the presence of air humidifier, systolic blood pressure, diastolic blood pressure, heart rate, Mallampati score, type of CPAP, type of CPAP mask, level of CPAP pressure (Table VII, Table VIII). In the two study groups, the percentage of men was significantly higher than that of women. This is in line with previous studies that have shown a predominance of OSAS in the male sex. There were no significant differences between the two groups of patients in terms of age, origin, or level of education. Most patients in group 1 live with someone; the percentage is higher than in group 2; living with someone may have benefits for adherence to therapy (Table I). This demonstrates that living with someone can be an important predictor of adherence to CPAP therapy. Rapelli *et al*., in the study of 32 patients who participated in an interview, concluded that the barriers to adoption and possible adherence to sleep apnoea treatment (CPAP therapy) depend on the patient's support from the patient's family and entourage, initial experience with therapy and expectations that the patient has from therapy [18]. In another study, the active involvement of the patient's partner in CPAP therapy helped to increase adherence to therapy [19]. Family involvement in CPAP therapy can also help improve adherence [20]. The percentage of patients using CPAP in fixed pressure compared to those using Auto-CPAP was not significantly different between the two groups (Table VIII). Hussain *et al*., in a prospective, randomised trial, have demonstrated that the Auto-CPAP therapy variant is as effective in treating SASO as the fixed pressure CPAP variant but without being associated with fewer side effects, better compliance with therapy, increased patient satisfaction or preference for this type [21]. Most patients in both groups do not use an air humidifier. However, the percentage of patients using an air humidifier is higher in the adherent patient group (Table VII). This may suggest that using an air humidifier in conjunction with the CPAP machine to treat the side effects of dry mouth may be a predictor for adherence. In one study, despite the fact that

patients experienced frequent nasal symptoms, using a humidifier on the night of CPAP titration did not provide any benefit in terms of nasal symptoms, nasal side effects, patient tolerance or attitude towards CPAP therapy [22].

The majority of patients in both groups use an oro-nasal mask. However, the percentage is lower in the adherent patient group. The percentage of patients who use a nasal mask is higher in the group of adherent patients; this is in line with other studies that have demonstrated better adherence in the case of nasal mask use (Table VIII). A prospective randomised study demonstrated that adherence to CPAP therapy did not differ in the three types of masks (nasal, oro-nasal, and nasal with a chin-supporting mechanism). However, comparing the oro-nasal mask with the nasal one, a lower reporting of side effects and better comfort was observed, as well as better sleep and a more frequent choice of nasal mask [23]. The side effects of the mask and the device were one of the main reasons cited by patients for the low use of CPAP. Among the side effects reported are dry mouth, rhinitis, conjunctivitis, skin lesions, anxiety, chest pain, aerophagia, machine noise, bed partner discomfort, and headache. Of these, the most commonly reported was dry mouth. The second side effect reported was rhinorrhoea. High CPAP pressure was not a major side effect (Table IX). Although CPAP has been used for over 40 years in the treatment of CPAP, research to increase adherence by understanding the mechanisms of side effects in therapy has been few [24]. In the study of Chaidas *et al*., nasal symptoms were common in patients with SASO. Rhinorrhoea was the only nasal symptom associated with decreased adherence to CPAP [25]. In another study, randomised, double-blind, placebo-controlled, the use of fluticasone propionate as a nasal topical agent does not reduce the nasal side effects of CPAP use and does not have a beneficial effect for increasing adherence during the first 4 weeks of treatment in patients with OSAS [26]. We observe that there are differences in statistical significance for Epworth scores measured at different points in time; 65% of the variability in the Epworth score is due to the timing of the measurement because of the evolution in time (Table IV). The only moments between which there were no differences with statistical significance were III *vs*. IV (6 months vs 12 months) (Table V). The evolution of patients under CPAP therapy was favourable, demonstrating the beneficial effect that the therapy has on OSAS symptomatology, especially in adherent patients (Table IV). Li *et al*., in a study involving 7,332 patients, showed that the main factors associated with decreased daytime sleepiness in CPAP patients are age, BMI, initial Epworth score, and adherence to CPAP [27]. In another study, adherence to CPAP was shown to be higher in patients with higher severity of OSAS (a higher AHI) and those with excessive daytime sleepiness (an increased Epworth score) [28]. In one study, symptoms of excessive daytime sleepiness were reported in 30% of patients treated with CPAP at 3 months of evaluation. The main factors that influenced the amplitude of these symptoms were sleepiness before CPAP therapy, CPAP adherence, sleep duration and time elapsed until the first evaluation of CPAP therapy [29]. In another study, when combining the main measurements of sleep by Polysomnography, the level of diurnal drowsiness before PAP therapy can be a predictive element for future adherence to therapy. This may be important in the initial assessment of the patient to determine which patients will be non-adherent and find initial solutions for them [30]. Our study found a positive association between daytime sleepiness levels and systolic and diastolic blood pressure values (Figure 2, Figure 3). A higher degree of daytime sleepiness (a higher Epworth score) may be associated with higher blood pressure values, consistent with previous studies that have found a significant association between OSAS and blood pressure values [31, 32]. There was also a positive association between the Epworth score and heart rate, which aligns with other studies (Figure 4). In one study, individuals with OSA who demonstrate an elevated ΔHR are at increased risk of cardiovascular morbidity and mortality [33]. The study emphasises the importance of addressing individual predictors and providing tailored interventions to optimise adherence and treatment outcomes. However, it is important to mention that two limitations of the present work are the monocentric nature of the study and the relatively small number of patients.

Conclusions

The adherence of patients with OSAS to CPAP therapy can be influenced by many factors. The level of daytime sleepiness can be a significant predictor of adherence to therapy. Future studies are needed to establish its role and other factors in OSAS therapy.

Conflict of interest

The authors declare no conflict of interest.

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