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RESEARCH

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The utility of various predictive equations in patients with severe Obstructive Sleep Apnea: a clinical practice viewpoint in settings with limited resources

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Abstract

Background The continuous positive airway pressure (CPAP) needed for the treatment of obstructive sleep apnea (OSA) can be determined after a manual titration study which is often expensive and time consuming. Hence, different predictive equations were suggested to simplify the treatment of OSA. The purpose of this work was to compare the CPAP identified with manual titration with that calculated using various equations in a cohort of patients with severe OSA.

Methods This work was conducted on patients diagnosed with severe OSA. Data collected included full medical history, demographic and anthropometric measures, polysomnography results, and the CPAP pressure obtained after manual titration which was further compared to 15 predictive equations retrieved from the literature.

Results A total of 166 patients [137 (82.5%) males and 29 (17.5%) females] with severe OSA were recruited in the study. Their mean age was 55.91 ± 12.64, and their baseline diagnostic apnea hypopnea index was 71.75 ± 23.70. The mean CPAP manual titration pressure was 11.31 ± 2.9 cmH_2O. Non-significant statistical difference was found ($p > 0.05$) when the mean titration pressure was calculated by Eqs. 2 (11.36 ± 2), 3 (11.55 ± 1.68), 10 (11.51 ± 2.29), 11 (11.14 ± 2.04), and 14 (11.71 ± 2.06), whereas the mean titration pressure calculated by Eqs. 1, 4, 5, 6, 7, 8, 9, 12, 13, and 15 differed significantly from the manual titration pressure ($p < 0.05$).

Conclusion Predictive equations suggested to calculate CPAP pressure, albeit simple and easy to apply, yielded variable results and should be investigated carefully before their use into clinical practice.

Keywords OSA, CPAP, Manual titration, Predictive equations

Introduction

Phenotypic approach for the treatment of obstructive sleep apnea (OSA) has gained considerable interest in recent years [1], yet continuous positive airway pressure (CPAP) remains the cardinal treatment measure to reverse the side effects and the complications of the moderate to severe OSA [2].

The current standard method and recommended guidelines to determine the optimal therapeutic CPAP is to perform manual titration of positive airway pressure during attended polysomnography [3]. However, these

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titration studies are often time-consuming and expensive, thus contributing to delays in the treatment of OSA, and may not be readily available in many health care facilities particularly in developing countries, where recent studies have shown an increased prevalence of OSA [4, 5].

Hence, different CPAP predictive equations, commonly derived from demographic, anthropometric and polysomnographic parameters, were suggested and validated in different populations in order to simplify the treatment of OSA, but their application showed varying degrees of success [6].

In the present work, we aimed to compare the optimal CPAP level determined after manual titration studies with that calculated from various published predictive equations in a cohort of Egyptian patients diagnosed with severe OSA.

Subjects and methods

Study design

This cross-sectional study was conducted on patients visiting or referred to the outpatient clinics of chest diseases and Complementary medicine, Medical and Scientific Centre of Excellence, National Research Centre, and the outpatient clinic of chest diseases department at the faculty of medicine of Ain Shams university, complaining from any of these symptoms: snoring, difficulty breathing, and/or choking sensation during sleep with or without daytime sleepiness.

Subjects

Patients included in this study were older than 18 years old and meeting the diagnostic criteria of severe OSA defined as the total apnea hypopnea index/hour calculated as the total number of apneas and hypopneas events divided by the total hours of sleep time (AHI/TST) to be greater than 30/h according to the third edition of the international classification of sleep disorders [7], whereas patients known to have comorbid chronic cardiac diseases, chronic obstructive pulmonary disease, obesity hypoventilation syndrome and chronic neurological diseases or present with a history of current alcohol, or drug abuse were excluded.

Methods

In the present work, medical files were reviewed, and data collected included full medical history, demographics, measurements of weight and height, body mass index (BMI) in kg/m^2, neck circumference (NC), and waist to hip circumference ratio (WHR). The diagnosis of OSA was concluded after a polysomnography study (Philips Respironics Inc., Murrysville, PA, USA) was conducted and further interpreted manually and validated by a certified sleep specialist [8] and involved the recording of electroencephalography with two frontal derivations, two central derivations and two occipital derivations, right and left eye derivations, nasal pressure, nasal-oral airflow (thermal device), snore sensor, respiratory effort (abdominal and thoracic effort), oxygen saturation with pulse oximetry, and submental EMG. For manual CPAP titration, an attended polysomnography as described above was performed on a subsequent night, and after orientation to the function of CPAP, the subjects were fitted with an appropriately sized nasal or oronasal CPAP mask according to the need and comfort of each patient. CPAP was manually titrated following the clinical guidelines of the American Academy of Sleep Medicine [3]. The optimal CPAP level retrieved by manual titration was compared with that calculated from 15 predictive equations numbered and summarized in Table 1.

Ethical consideration

This study was conducted in respect to the guidelines laid down in the declaration of Helsinki and was reviewed and approved by the Ethical Committee of the National Research Centre, Cairo, Egypt. A written informed consent was provided by each participant prior to their inclusion in the study.

Statistical methods

Statistical analyses were performed using Statistical Package for Social Sciences software (SPSS for Windows, version 17.0; SPSS Inc., Chicago, Illinois, USA). Kolmogorov–Smirnov test of normality for continuous data was done. Descriptive statistics were presented as minimum, maximum, median, and mean ± SD. Categorical statistics were presented as number and percentage. Comparison between the normally distributed mean values was done using the Paired t test, whereas comparison between the non-normally distributed mean values was done using the Wilcoxon Signed Ranks test. Statistical significance was set at P value less than 0.05.

Results

A total of 166 patients diagnosed with severe OSA and successfully completed their manual positive airway titration, during attended polysomnography, were enrolled in this study [137 (82.5%) males and 29 (17.5%) females]. Their demographic and their anthropometric data are listed in Table 2.

Data representing their polysomnographic findings of both the diagnostic and the manual titration studies are shown in Table 3 exhibiting a significant statistical difference between both studies regarding the latency to stage REM, percentage of stages N1, N2, N3 and stage REM, obstructive apneas, mixed apneas, hypopneas, AHI, NREM-AHI, REM-AHI, average and minimum oxygen

Table 1 The predictive equations used to calculate the optimal CPAP in patients with OSA

Equation number	Mathematical formula	Authors
1	0.16(BMI) + 0.13 (NC) + 0.04 (AHI)—5.12	Hoffstein et al. [9]
2	30.8 + RDI × 0.03—nadir saturation × 0.05—mean saturation × 0.2	Loredo et al. [10]
3	0.048 (ODI) + 0.128 (NC) + 2.1	Stradling et al. [11]
4	0.148 × NC + 0.038 × ODI	Basoglu and Tasbakan [12]
5	6.2 × [BMI × 0.11]	Skomro et al. [13]
6	4.95 + (0.18 × AHI) – (0.133 × DI)	Panagou et al. [14]
7	(0.07 × NC) + (0.02 × BMI) + (0.03 × AHI) + 3.2	Hoheisel and Teschler [15]
8	0.05 × AHI + 0.15 × BMI + 0.066 × NC – 1.712	Luo et al. [16]
9	6.380 + 0.033 × AHI – 0.068 × SaO_2 nadir + 0.171 × BMI	Wu et al. [17]
10	0.681 + (0.205 × BMI) + (0.040 × AHI)	Choi et al. [18]
11	1.98 + 0.184 × BMI + 0.01 × AHI + 0.016 × DI	Chuang et al. [19]
12	0.52 + 0.174 × BMI + 0.042 × AHI	Lin et al. [20]
13	4.740 + 68.575 × (N/H) – 0.153 × (Minimal SpO2)	Wahab and Ahmed [21]
14	0.193(BMI) + 0.077 (NC) + 0.02 (AHI)—0.611	Sériès [22]
15	19.27 + 0.05 (ODI) + 0.06 (total arousal index) – 0.13 (min O_2 Sat.)	Bamagoos et al. [23]

AHI apnea hypopnea index, *BMI* body mass index, *DI* desaturation index, *NC* neck circumference, *N/H* neck to height ration, *ODI* oxygen desaturation index, *RDI* respiratory disturbance index

Table 2 Demographic and anthropometric data of patients enrolled in the study

Age (years)	55.91 ± 12.64
Weight (Kg)	109.85 ± 23.14
Height (cm)	168.92 ± 10.23
Body mass index (Kg/m^2)	38.84 ± 9.07
Neck circumference (cm)	43.96 ± 3.43
Waist to hip ratio	1.04 ± 0.06

Data are expressed as mean ± SD

saturation, desaturation index, arousal index, and snoring index ($p < 0.05$).

Data illustrated in Table 4 describes the comparison between the titration PAP pressure and the predictive equations: The mean optimal CPAP recorded by manual titration was 11.31 ± 2.9 cm H_2O. Non-significant statistical difference ($p > 0.05$) was observed when the mean titration pressure was calculated by Eqs. 2 (11.36 ± 2), 3 (11.55 ± 1.68), 10 (11.51 ± 2.29), 11 (11.14 ± 2.04), and 14 (11.71 ± 2.06). In contrast, the mean titration pressure calculated by Eqs. 1 (9.68 ± 2.17), 4 (9.54 ± 1.42), 5 (16.49 ± 6.19), 6 (7.27 ± 2.64), 7 (9.21 ± 0.89), 8 (10.6 ± 2.13), 9 (10.82 ± 2.42), 12 (10.29 ± 2.07), 13 (12.36 ± 3.25), and 15 (17.91 ± 4.05) differed significantly from the manual titration pressure ($p < 0.05$).

Discussion

Fundamentally, the mean pressure calculated by manual CPAP titration (11.31 ± 2.9) revealed no statistically significant difference when compared with the mean pressure calculated by the predictive Eqs. 2 (11.36 ± 2); 3 (11.55 ± 1.68); 10 (11.51 ± 2.29); 11 (11.14 ± 2.04), and 14 (11.71 ± 2.06) which were developed and validated by Loredo et al., Stradling et al., Choi et al., Chuang et al., and Sériès respectively [11, 18, 19, 22, 24].

In agreement with the comparison results of the present study, Elshahaat et al. [25] performed manual titration on 48 Egyptian patients diagnosed with OSA and yielded equivalent findings when testing the equations developed by Hoffstein et al. [9], Loredo et al. [24], Stradling et al., and Sériès [22] (Eqs. 1, 2, 3, and 14 respectively). Further comparison of the above formulas with manual titration revealed similar results in in different ethnic groups of patients [26–28].

In the current work, the equations developed by Choi et al. [18] and Chuang et al. [19] (Eqs. 10 and 11, respectively) also yielded positive results with the manually titrated CPAP pressure. Although these formulas were derived in Asian populations, one might argue that since ethnic populations have different characteristics, they should not be applied to other ethnicities. However, Basoglu and Tasbakan [12] developed a new predictive formula in a Turkish population and found no statistical difference neither with the one suggested by Hoffstein et al. [9] that was validated in Caucasians [29] and in a large sample of Greek patients [30] nor with the equation derived by Lin et al. in the Asian population [20], leading to the assumption that the mathematical algorithm itself rather than race may be the determining factor in predicting CPAP levels.

Table 3 Baseline diagnostic and manual titration polysomnography descriptive results

	Diagnostic PSG	Titration PSG	*P* value#
Total recording time	375.77 ± 78.63	373.23 ± 79.7	0.806
Time in bed	359.16 ± 79.93	354.16 ± 80.32	0.460
Total sleep time	287.23 ± 86.15	291.5 ± 87.43	0.520
Stage N1 latency	14.40 ± 17.70	16.96 ± 21.91	0.363
Stage N2 latency	20.62 ± 21.85	20.81 ± 20.21	0.427
Stage N3 latency	96.86 ± 60.76	63.46 ± 50.65	0.096
Stage REM latency	186.68 ± 87.58	122.88 ± 84.98	0.000
Sleep efficiency	79.11 ± 15.03	79.8 ± 16.8	0.598
% REM stage/TST	4.15 ± 4.81	15.52 ± 11.08	0.000
% N1 stage/TST	20.87 ± 13.12	12.46 ± 11.42	0.000
% N2 stage/TST	70.96 ± 13.72	51.16 ± 14.03	0.000
% N3 stage/TST	4 ± 6.34	20.85 ± 12.34	0.000
Central apneas	3.77 ± 17.22	2.13 ± 4.09	0.707
Obstructive apneas	295.13 ± 167.22	19.75 ± 33.32	0.000
Mixed apneas	8.48 ± 20.25	0.92 ± 2.65	0.000
Hypopneas	38.32 ± 47.96	17.36 ± 25.12	0.000
Apnea hypopnea index	71.75 ± 23.70	8.93 ± 11.64	0.000
NREM AHI	71.68 ± 23.66	9.84 ± 13.03	0.000
REM AHI	60.60 ± 25.59	2.91 ± 5.4	0.000
Average heart rate	69.11 ± 15.87	69.79 ± 15.41	0.236
Average O_2	91.11 ± 5.09	94.12 ± 3.82	0.000
Minimum O_2	67.17 ± 16.55	81.64 ± 10.75	0.000
Desaturation index	79.60 ± 31.26	20.65 ± 22.9	0.000
Arousal index	58.14 ± 27.99	16.49 ± 12.07	0.000
Snoring index	32.02 ± 24.47	11.42 ± 14.26	0.000

AHI apnea hypopnea index, *NREM* non-rapid eye movements, *PSG* polysomnography, *REM* rapid eye movement, *TST* total sleep time

Data are expressed as mean ± SD

P values less than 0.05 were considered statistically significant

Indeed, and in support of this assumption, manual titration's mean pressure was significantly different when compared to equation derived after studying a group of Saudi patients [23] despite their similar ethnic characteristics or the equation (Eq. 13) elaborated from the data analyzed on other Egyptian patients [21]. However, the discrepancy with the latter mathematical formula could be also explained by the fact that it was derived from a very small number of patients (30 patients), among them only 18 patients were diagnosed with severe OSA [21].

Furthermore, all other mathematical formulas used in this study, including those proposed by Hoffstein et al. [9], Basoglu and Tasbakan [12], Lin et al. [20], Bamagoos et al. [23] or Wahab and Ahmed [21], exhibited a mean pressure which differed significantly ($P < 0.05$) from the manually titrated pressure, and to our knowledge, none of them was previously examined in the Egyptian population except and, as stated before, the 5 predictive equations that were tested on a small sample of Egyptian patients in the work done by Elshahat et al. [25].

Table 4 Comparison between the manual titration pressure and the pressure calculated by predictive equations

Equation pressure		Manual titration pressure	*P* value#
Equation 1	9.68 ± 2.17	11.31 ± 2.9	0.000
Equation 2	11.36 ± 2		0.716
Equation 3	11.55 ± 1.68		1.171
Equation 4	9.54 ± 1.42		0.000
Equation 5	26.49 ± 6.19		0.000
Equation 6	7.27 ± 2.64		0.000
Equation 7	9.21 ± 0.89		0.000
Equation 8	10.6 ± 2.13		0.006
Equation 9	10.82 ± 2.42		0.032
Equation 10	11.51 ± 2.29		0.289
Equation 11	11.14 ± 2.04		0.593
Equation 12	10.29 ± 2.07		0.000
Equation 13	12.36 ± 3.25		0.001
Equation 14	11.71 ± 2.06		0.061
Equation 15	17.91 ± 4.05		0.000

Data are expressed as mean ± SD

P values less than 0.05 were considered statistically significant

However, in the current research, we extended our comparison to 15 equations that were retrieved from different groups of patients because in low income and developing countries, it is logical to think of other alternatives and less expensive modalities to determine the optimal PAP for the treatment of patients with OSA, in contrast to the costly procedure of manual titration which requires an attending professional expertise in a highly capacitated sleep laboratory equipped with the proper devices and materials.

Despite the strengths of the present study, the authors recognize certain limitations such as the absence of patients diagnosed with moderate OSA and the limited number of female patients which we explain to be due cultural reasons and/or because the daytime symptoms of female patients are usually correlated to insomnia rather than OSA making their referral for polysomnography more difficult. Further, multicenter research and follow-up of the patients are required to be able to extrapolate these data on the general population and assess treatment outcomes on their quality of life.

Conclusion

The management approaches for OSA have progressed substantially in the recent decade; nevertheless, the treatment of moderate to severe OSA still essentially relies on CPAP. To this effect, guidelines recommended the manual setting in an incremental fashion, of the optimal positive airway pressure, during an attended polysomnography. However, due to the high cost of this latter process, the use of predictive equations, particularly in low income and developing countries, could serve as an alternative and a reliable option, which is simple and easy to apply in clinical practice but only after careful investigation and validation in the corresponding general population.

Abbreviations

AHI	Apneas and hypopneas index
BMI	Body mass index
CPAP	Continuous positive airway pressure
NC	Neck circumference
NREM	Non-rapid eye movements
OSA	Obstructive sleep apnea
REM	Rapid eye movements
TST	Total sleep time
WHR	Waist to hip circumference ratio

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Authors' contributions
A.G.: material preparation, data collection, literature search, manuscript writing and editing.
MS.E.: material preparation, data collection.
I.G.E.: statistical analysis.
All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Competing interests
The authors declare no competing interests.

Ethics approval and consent to participate
This study was conducted in respect to the guidelines laid down in the declaration of Helsinki and was reviewed and approved by the Ethical Committee of the National Research Centre, Cairo, Egypt. A written informed consent was provided by each participant prior to their inclusion in the study.

Conflict of interest
The authors declare that they have no conflict of interest.

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