Manually Defined Continuous Positive Airway Pressure versus Mathematically Calculated for Obstructive Sleep Apnea

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Received: September 30, 2017 **Accepted: October 25, 2018**

Published: June 30, 2019

Abstract: *The determination of therapeutic pressure in patients with Obstructive sleep apnea (OSA) is crucial. Manual adjustment of Continuous positive airway pressure (CPAP) under polysomnography (PSG) is considered the better practice. Recently, different formulas were presented for predicting CPAP using body mass index (BMI), neck circumference (NC) and apnea/hypopnea index (AHI).*

The aim of the study was to assess the correlation between the values of pressure calculated by two formulas as well as manual obtained pressure values.

Forty patients (33 male, 7 female) with suspected OSA were examined by PSG. Manual titration was applied using standard protocol. For predicting CPAP were used two equations hereinafter referred to as Eq. (1) and Eq. (2). For men the determined pressure was higher when using the Eq. (1) whereas with the Eq. (2) the pressure was lower than predicted. For women the differences were larger.

The pressures calculated with the Eq. (1) and the Eq. (2) for both genders were lower and higher, respectively, than those experimentally obtained. From a practical point of view, when it is not possible to determine pressure experimentally, the Eq. (2) should be preferred because higher pressure prescription is better for OSA therapy.

Keywords: *Obstructive sleep apnea, Continuous positive airway pressure, Titration, Prediction.*

Introduction

In recent years, there has been a growing awareness that obstructive sleep apnea (OSA) is one of diseases with highest social importance. Its main manifestation is the periodical cessation of breathing during sleep, with subsequent episodes of sharp decrease in oxygen saturation in the blood. The condition is permanent – it appears in every sleep, albeit with varying severity. Spontaneous cure of sleep apnea is impossible and at this stage, there is no drug response. If the patient is left untreated, the long-term consequences for his physical and mental health (of the affected person) are disastrous [7, 10].

At present, the only treatment is physical and its idea is to create an airway prosthesis of the upper respiratory tract by means of specialized compressors, designed for home use and called continuous positive airway pressure (CPAP) [2, 3]. Applied properly and persistently such treatment has a very good and distinct effect, dramatically improving the quality of life of patients. A major difficulty in the application of this treatment remains the precise determination of the pressure parameters delivered to the respiratory tract. The gold standard is the manual titration of this pressure by a qualified medical practitioner under the conditions of a full-time laboratory examination – commonly known as full-night polisomnography (PSG). All of this makes the methodology a little clumsy, but most importantly expensive. In countries with limited financial resources for social security, this is a major obstacle to the widespread coverage of patients with OSA and their proper treatment. Even where there is complete or partial reimbursement of OSA treatment, a CPAP with fixed pressure is usually reimbursed (purchased), which however requires annual control by titration and correction of therapy parameters. The paradox is that for the period of treatment of one patient, this certainly leads to even higher costs than their expected reduction.

An attempt to deal with this problem is the effort of many authors to find a link between some easily measurable parameters and the therapeutic pressure in OSA treatment. Thus, in recent years, a number of formulas have been presented for which the authors claim that they accurately predict the therapeutic pressure for OSA treatment. The first and most commonly used formula is that of Hoffstein et al. [4]. However, a number of authors report that racial or ethnic differences may be essential in determining the parameters involved in the formula and hence influencing its accuracy [5, 9, 11].

At this stage formulas are not used to predict CPAP pressure in Bulgaria. Therefore, the goal we have set in the present study is to investigate the practical use of ready-to-use formulas for the determination of therapeutic pressure in the duration of the treatment of Bulgarian patients with sleep apnea.

Materials and methods

Subjects

The study involved 40 adult patients, aged 18 and above – 33 men and 7 women. All of them had sleep apnea of obstructive type with varying severity, defined as an apnea-hypopnea index (AHI) > 5 events/h.

Equipment

The study was carried out in ESleep, Ltd. Sleep Laboratory. The local ethics committee approved the study and all subjects gave written informed consent. The examination began with a detailed measurement of the anthropometric variables of the patient – weight, height, neck circumference, body mass index, etc., using a body composition apparatus "Tanita" type. The presence of OSA was evidenced by an overnight diagnostic PSG by means of Miniscreen Pro. The PSG recordings performed according to established standards by the American Academy of Sleep Medicine which consisted of electroencephalogram, electrooculogram, electromyogram, electrocardiogram, chest wall movement, nasal and oral air flow and oxygen saturation.

The required optimal therapeutic pressure was determined in a follow-up full-night PSG study, however, with Continuous positive airway pressure (CPAP-ICON, Fisher&Paykel) – associated device, and a manual titration module (LabSmart, Fisher&Paykel). The latter was carried out on a standard protocol – manual titration of CPAP starting from 4 cm H_2O and increasing with 0.5 cm H_2O within an interval of 2 min. The lowest effective pressure was found when all sleep breathing events disappeared, including snoring.

Pressure calculation formulas

We have selected two of presumably the most cited formulas in the available literature [4, 8]:

$$P_{t(1)} = 0.16\,BMI + 0.13\,NC + 0.04\,AHI - 5.12, \tag{1}$$

$$P_{t(2)} = 0.193\,BMI + 0.077\,NC + 0.02\,AHI - 0.611, \tag{2}$$

where

$P_{t(1)}$ is the therapeutic pressure that eliminates breathing disturbances during sleep, theoretically calculated by the Eq. (1);
$P_{t(2)}$ – therapeutic pressure that eliminates breathing disturbances during sleep, theoretically calculated by the Eq. (2);
BMI – body mass index;
NC – neck circumference, [cm];
AHI – apnea-hypopnea index.

Measured parameters

As seen from above, the anthropometric measurement gives us some of the parameters that are used in the formulas for theoretical calculation of therapeutical pressure. Neck circumference is a directly measurable parameter, ready for substitution in the formulas. The *BMI* is a parameter that the "Tanita" provides us, but it can also be calculated as the ratio of the weight (in kilograms) of the examined person to the square of their height (in meters). The third measurement in the Eqs. (1) and (2) – the *AHI* index – shows the number of breathing pauses per hour of sleep, averaged over the time of whole night's sleep. This index is one of the most important features of existing sleep disorder during sleep. It is obtained after manual or automatic processing of the polysomnographic record. For the purpose of our study, the records of all surveyed people were verified manually by the same researcher, following a standard protocol. During the second night of the study, for each patient the therapeutic pressure that eliminates all sleep breathing events, including snoring, was determined – P_{exp}. For all subjects the determination of this pressure was done by one researcher on a standard protocol.

Object of the study

Object of the present study is the therapeutic pressure within the duration of sleep apnea treatment with a CPAP device. Using the above measurements and calculations for each of the patients we had three therapeutic pressure values:

P_{exp} – experimentally established;
$P_{t(1)}$ – theoretically determined by the Eq. (1);
$P_{t(2)}$ – theoretically determined by the Eq. (2).

Subject of the study

As a subject of our study we can point out the difference between the manually determined therapeutic P_{exp} pressure and the theoretically calculated by both proposed formulas $P_{t(1)}$, $P_{t(2)}$.

Statistical methods to minimize the error

To determine the ability of the proposed formulas to predict the required therapeutic pressure we need to assess the differences between theoretically calculated and experimentally established pressure.

 doi: 10.7546/ijba.2019.23.2.000523

Accuracy was assessed by two methods:

1. Mean Square Error (*MSE*)

$$MSE = \frac{1}{n}\sum_{i=1}^{n}\left(Y_i - \hat{Y}_i\right)^2,$$

where n is the number of observations, Y_i are the observed values and $\hat{Y}_i$ are the values predicted by the model.

2. Akaike Information Criterion (*AIC*) [1]

$$AIC = 2k - 2\log(L),$$

where k is the number of parameters in the model and L is the model's likelihood function estimated at the standardized residuals of the model, which are the quotients between the model's error terms and their corresponding standard deviations.

The use of the *MSE* is more traditional, but it has good informativeness for a narrow area of relatively small samples. Further division of subjects by gender is still a narrower part of the sample because women are much less represented as carriers of OSA, both in the data we present and in the general population as a whole. This made it necessary to use the *AIC* where these examples are, in principle, part of a much larger group and therefore assess not so much the difference in specific values as the difference of trends.

Results and discussion

Table 1 shows the mean and standard deviations of all parameters included in the formulas discussed, broken down by gender. It is noticeable that the mean *AHI* is almost the same for both samples, although with a much higher standard deviation for men. The standard deviation of this indicator is quite large because it is used to determine the severity of sleep apnea. *AHI* of more than 30 #/hr is considered to be a severe state for the disease and patients with such condition are included in the sample. However, there are patients with *AHI* of 140 #/hr as well, who also have a severe degree of sleep apnea.

Table 1. Mean values and standard deviations of all parameters involved in the Eqs. (1) and (2), broken down by gender

Gender	***AHI*, [#/h]**		***BMI***		***NC*, [cm]**		**Pressure, [cm H_2O]**	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Female	72.3	23.5	41.2	2.6	38.1	5.9	11.8	2.6
Male	74.8	30.6	36.2	6.7	45.0	4.1	10.5	2.9

At the same time, the mean *BMI* is significantly higher for women, with a standard deviation less than that for men. This shows a greater uniformity of the female sample and at the same time indicates that they reach the same *AHI* as men, although with significantly higher weight gain.

It is also evident that the much higher average *BMI* for women goes with a significantly lower average cervical circumference. This fact alone, compared to the mean values of *AHI*, indicates that the neck circumference could not be critical for the severity of the disease and could not serve as the only criterion for determining the therapeutic pressure.

This is also evidenced by the fact that the mean values of therapeutic pressure in both genders are practically the same, taking into account its mean values and the magnitude of the standard deviations for both samples.

The results of the applied calculations are presented in Tables 2 and 3. Table 2 shows the accuracy of prediction of the therapeutic pressure by Eqs. (1) and (2) as measured by the method of the *MSE* for three models: for all tested individuals – male and female, only for men and only for women. The smaller the figure of the metric – the better the formula's ability to predict the actual therapeutic pressure.

Table 2. Results from the application of *MSE* method

Model	**Gender**	**Indicator Eq. (1)**	**Indicator Eq. (2)**
MSE	male and female	6.9739947	6.267339139
MSE male	male	6.111322424	6.64633126
MSE female	female	11.04087829	4.480661996

From the presented results it is evident that Eq. (1) provides better therapeutic pressure for men. In contrast, Eq. (2) provides much more accurate pressure for women as well as for the whole sample. Especially for women the accuracy is much higher. Here is the place to make the provision that men are much more than women in terms of percentage of the general population with this disease. That is why the above data may appear paradoxical at first glance.

Table 3 presents the results for the accuracy of predicted therapeutic pressure in Eqs. (1) and (2) as assessed by the *AIC* for three models: for all subjects – male and female, only male and only female. The smaller the figure of the metric – the better the formula's ability to predict the actual therapeutic pressure.

Table 3. Results from the application of *AIC* method

Model	**Gender**	**Indicator Eq. (1)**	**Indicator Eq. (2)**
AIC	male and female	110.7125092	102.7058358
AIC male	male	89.71080192	87.46272205
AIC female	female	43.32354638	37.56495279

From the table above it can be seen that if we take into account the trends for a larger group, the predictive power of Eq. (2) is definitely higher. This applies to both men and women, as well as to the whole population. Again, the prognostic power for women is much higher than for men.

Conclusion

Eq. (1) gives better results for male studies, whereas Eq. (2) provides better results for the study of only women and for the entire population. For the population that is examined, Eq. (2) is more appropriate.

The power of prediction of Eq. (2) in women is so great that it gives rise to even more interesting assumptions. Probably the presence of sleep apnea in women leads to much more uniform changes in the studied parameters. On the other hand, similar changes in the described parameters lead to a greater and more difficult to make prediction of the variation in the required therapeutic pressure in men. The pathogenesis of sleep apnea in women and men is noticeably different.

Up to date, there is no reimbursement in Bulgaria for either the diagnosis or the therapy of OSA. At a certain point, however, this will happen. In accordance with the current regulatory framework, the cheapest solutions will be preferred. With regard to CPAP therapy, this means – an apparatus operating at a fixed therapeutic pressure. In the absence of a pre-titration of this pressure (examination in lab) for each patient approximation of the formula will be used.

An additional complication is the need to periodically conduct control titration on patients who are on therapy with a fixed CPAP. However, measured anthropometric parameters of patients change during treatment and this change may be synchronic with a change in the therapeutic pressure.

Our recommendation is to use Eq. (2) in both new and follow-on Bulgarian patients, giving a result closer to the actual population. This in the long term would have a positive effect on both patients and the health system. Moreover, Rawley et al. [6] says that the use of a predicted CPAP equation may improve CPAP titration success.

Acknowledgements

We thank our colleagues and investigated persons for their assistance.

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