

# CPAP Pressure Prediction Calculation. An Alternative to the Difficulty of Performing a Titration Within the Context of the COVID19 Pandemic

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## Abstract

**Introduction:** The treatment of choice for the obstructive sleep apnea-hypopnea syndrome (OSAHS) is continuous positive air pressure in the airway (CPAP), titrating the effective pressure that eliminates obstructive events through validated methods. From the beginning of the COVID 19 pandemic, it has been recommended that conventional titration should be postponed, replacing it with self-adjusting equipment. In our population, access to these devices is difficult.

**Objective:** To show whether there is a difference between the CPAP pressure level calculated through a prediction formula and the pressure determined by titration under polysomnography.

**Materials and Methods:** We included patients with OSAHS who underwent effective CPAP titration and compared it with the calculated CPAP by the Miljeteig and Hoffstein formula.

**Results:** We included medical records of 583 patients, (56%) men, 51 years (41-61), apnea-hypopnea index (AHI) of 51.3 (29.2-84.4), calculated CPAP, 9.3 cm H<sub>2</sub>O vs. effective CPAP, 8 cm H<sub>2</sub>O ( $p < 0.0001$ ). Comparing according to the degree of severity of the OSAHS, the average difference between calculated CPAP and effective CPAP was 0.24, 0.21, and 0.41 (non-significant differences) for mild, moderate and severe, up to an AHI < 40; in patients with an AHI  $\geq 40$  this difference was 1.10 ( $p < 0.01$ ). We found an acceptable correlation between the calculated CPAP and the effective CPAP, with an intraclass correlation coefficient of 0.621,  $p < 0.01$ .

**Conclusion:** We could use CPAP pressure prediction calculations to start treatment in patients with OSAHS who don't have access to self-adjusting therapies within the context of the pandemic, until standard calibration measures can be taken.

**Key words:** Continuous positive pressure in the airway; Prediction, Titration, Sleep apneas

## Introduction

The apnea-hypopnea syndrome (OSAHS) is a clinical entity characterized by the presence of recurrent episodes of apneas and hypopneas secondary to the collapse of the pharynx during sleep, and is associated with arterial hypertension, stroke, deterioration in quality of life, car accidents and higher risk of death by cardiovascular events<sup>1</sup>. A 2015 review of epidemiological studies showed a mean prevalence of 22% in men and 17% in women<sup>2</sup>. The use of continuous positive air pressure in the airway (CPAP) during sleep is the treatment of choice for OSAHS<sup>3-6</sup>. For the purpose of starting treatment with CPAP in a patient with OSAHS, the effective pressure that removes obstructive events should be previously

titrated. The method of manual titration under polysomnography (PSG) is considered the gold standard in the measurement of the CPAP effective pressure level, but comparable results can be obtained using different validated methods such as self-adjusting devices and split-night PSG<sup>7-11</sup>.

The literature includes various prediction equations that try to calculate the CPAP effective pressures<sup>12</sup> through the use of different variables. The equations were subsequently used to estimate the initial pressures or during the assessment studies of the positive airway pressure (PAP) at the laboratory as reference pressure, without replacing the validated methods. Thus, this obtained value may be applied provisionally, though it should not be considered the definite value. Miljeteig, H. and Hoffstein, V. proposed the CPAP prediction using a formula that includes the apnea-hypopnea index (AHI) and two anthropometric parameters such as the body mass index (BMI) and the neck circumference (NC), validating their use in subsequent studies<sup>13-15</sup>.

At the end of 2019, a new coronavirus was identified as the cause of a group of pneumonia cases in Wuhan, a city in the province of Hubei, China. This virus spread quickly, resulting in an epidemic throughout China, followed by an increasing number of cases in other countries of the world, and finally declared a pandemic by the World Health Organization (WHO) in March, 2020. The entity was named COVID-19, which means coronavirus disease 2019, and the virus producing it is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)<sup>16</sup>. PAP therapies are considered aerosol-generating procedures, one of the main SARS-CoV-2 routes of transmission. As a consequence, within the context of the pandemic and given the high degree of transmission and virulence of this virus, the Center for Disease Control and Prevention (CDC) of the United States and the main World Associations of Sleep Medicine recommended to postpone and reschedule, the PAP titration studies, due to the risk of aerosolization<sup>17-19</sup>.

The purpose of our study was to show whether there is concordance between the level of CPAP calculated with the Miljeteig and Hoffstein formula and the pressure determined by means of manual titration under polysomnography. If there weren't any significant differences it would be possible to start CPAP treatment and wait until titration of a definite pressure can be done by means of currently validated methods.

## Materials and Methods

**Concordance of methods study.** We analyzed the information obtained from the patients' database used in the Pulmonary Function/ Sleep Laboratory of the Hospital Posadas for statistical purposes between January, 2016 and December, 2019. We included all the patients with complete medical records with an OSAHS diagnosis who had undergone effective CPAP titration.

We evaluated the AHI recorded in the basal PSG and the anthropometric parameters such as BMI and NC obtained from the medical records. In all the cases we carried out CPAP titration during a second PSG night or else during the same night the diagnosis was established (split-night study). In all the cases the titration was done manually under PSG supervision. Leak control was performed according to the criteria established by the clinical guidelines of the American Academy of Sleep Medicine for full-night and split-night titration. The effective pressure titration was the one that fulfilled the established criteria as optimum, good and acceptable, where respiratory events are eliminated or partially corrected (AHI of less than 10/hour)<sup>1, 19</sup>.

We used the Miljeteig and Hoffstein formula (effective pressure =  $0.16 \times \text{BMI} + 0.13 \times \text{NC}$  in centimeters +  $0.04 \times \text{basal AHI} - 5.12$ ) for calculating the prediction value of the CPAP pressure.

We compared the data of the effective pressure (effective CPAP) in the global group and according to the AHI severity degrees with the pressure predicted by the Miljeteig and Hoffstein formula (calc. CPAP).

## Statistical Analysis

The results are expressed as percentages in the categorical variables or as median and interquartile range in the continuous variables, according to the distribution of the population. For the comparison of differences of continuous data, we used Wilcoxon. We compared both methods by means of the intraclass correlation coefficient. We also used plot representation with Bland Altman for the graphical analysis of the relationship between measurement types. A two-tailed value of  $p < 0.05$  was considered to be significant.

## Results

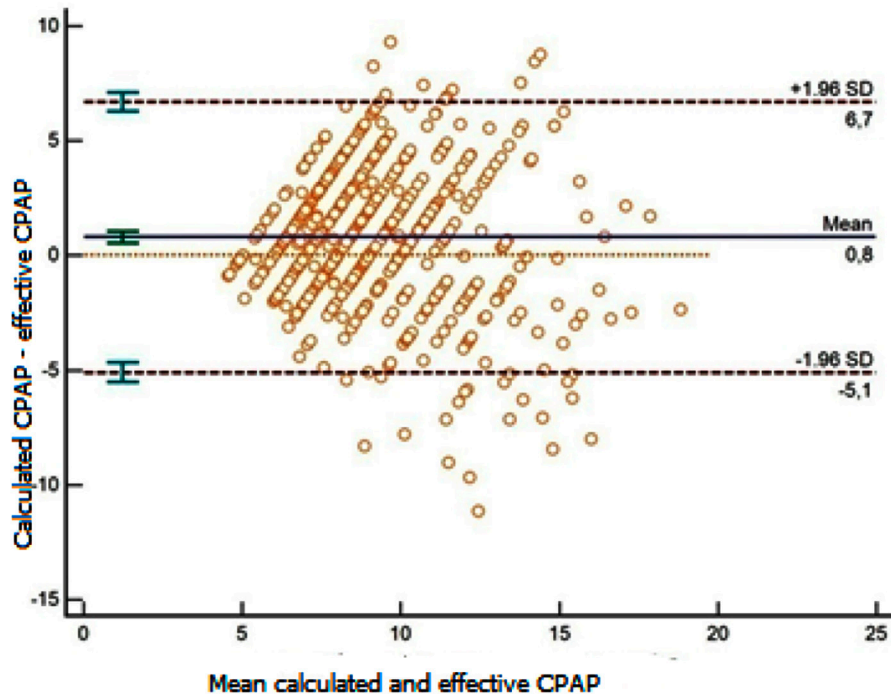
We included the medical records of 583 patients, median age 51 years (41-61), 329 (56%) men. Table 1 shows the anthropometric and polysomnographic variables and the CPAPs obtained by both methods. Patient distribution according to the OSAHS degree of severity defined by the AHI: mild OSAHS 32 (5.5%), moderate OSAHS 121 (20.7%), severe OSAHS 430 (73.8%). The median of calc. CPAP for all the patients was 9.3 cm H<sub>2</sub>O vs. effect. CPAP 8 cm H<sub>2</sub>O  $p < 0.01$ . Whereas the difference is statistically significant, the difference in absolute values was 1.3 cm H<sub>2</sub>O with an average value of 0.79 cm H<sub>2</sub>O.

**TABLE 1.** Anthropometric, clinical and polysomnographic variables and data of measured and calculated CPAP of all the patients

Variables	n = 583
Age (years)	51 (41-61)
Sex (m/f)	329/254
BMI (kg/m <sup>2</sup> )	39.13 (33.3-48.3)
NC (cm)	45 (41-48)
Epworth scale	10 (6-16)
AHI (events/hour)	51.3 (29.2-84.4)
Basal SaO <sub>2</sub> (%)	94 (92.8-95.3)
Mean SaO <sub>2</sub> (%)	91.5 (88.7-93.3)
Min. SaO <sub>2</sub> (%)	75 (66-82)
ODI	29.15 (14.8-57.3)
Effec. CPAP (cmH <sub>2</sub> O)	8 (7-10)
Calc. CPAP (cmH <sub>2</sub> O)	9.3 (7.7-11.3)
CPAP diff. (cmH <sub>2</sub> O)	1 (-1-3)

Values expressed in median and interquartile range; BMI: body mass index; NC: neck circumference; AHI: apnea-hypopnea index; SaO<sub>2</sub>: pulse oximetry; ODI: desaturation index; effec. CPAP: effective positive airway pressure; calc. CPAP: calculated positive airway pressure; CPAP diff.: difference between calculated and effective positive airway pressure.

We found that with the Miljeteig and Hoffstein formula we were getting closer to a successful pressure (calculated CPAP pressure within  $\pm 3$  cm H<sub>2</sub>O in comparison with the effective CPAP pressure obtained during titration) in 430 patients (74%), observing an acceptable correlation between both methods, with an intraclass correlation coefficient of 0.621 (95% CI 0.555-0.679)  $p < 0.01$ , **Figure 1**.



**Figure 1.** Distribution of calculated CPAP pressures in relation to effective CPAP pressures. We can observe the mean differences between both methods and their dispersion.

In the comparison of CPAP pressures obtained through every method according to the degree of severity of the OSAHS, we observed that there isn't any significant difference between the calculated CPAP and the effective CPAP in patients with mild and moderate OSAHS. The difference between both pressures in patients with severe OSAHS is statistically significant, but in absolute values that difference was only 1 cm H<sub>2</sub>O (**Table 2**).

**TABLE 2.** Difference between calculated and effective CPAP according to the AHI

Severity (AHI)	n	Median effect. CPAP	Median calc. CPAP	Mean CPAP diff.	SD of CPAP diff.	p value
Mild (5-15)	32	7.00	7.55	0.24	1.86	0.47
Moderate (15-30)	121	7.00	7.77	0.21	2.46	0.34
Severe (> 30)	430	9.30	10.30	0.99	3.19	< 0.0001

AHI: apnea-hypopnea index; effect. CPAP: effective positive airway pressure; calc. CPAP: calculated positive airway pressure; CPAP diff.: difference between calculated and effective positive airway pressure; SD CPAP diff.: standard deviation of the difference between calculated and effective positive airway pressure.

For the purpose of maximizing the performance of the formula for most severe patients (severe OSAHS), they were divided in 2 groups. In the first group, patients with AHI  $\geq 30$  and  $< 40$ , and in the second group, patients with AHI  $\geq 40$ . Thus, we can observe that there isn't a significant difference between the calc. CPAP and the effect. CPAP in the group of severe patients with an AHI  $< 40$  (**Table 3**).

**TABLE 3.** Difference between calculated and effective CPAP according to the AHI dividing severe patients in 2 categories

Severity (AHI)	n	Median effect. CPAP	Median calc. CPAP	Mean CPAP diff	SD of CPAP diff	p value
Mild (5-15)	32	7.00	7.55	0.24	1.86	0.47
Moderate (15-30)	121	7.00	7.77	0.21	2.46	0.34
Severe (30-40)	71	8.00	7.87	0.41	2.49	0.06
Severe (> 40)	359	9.00	10.45	1.10	3.31	< 0.01

AHI: apnea-hypopnea index; effect. CPAP: effective positive airway pressure; calc. CPAP: calculated positive airway pressure; CPAP diff.: difference between calculated and effective positive airway pressure; SD of CPAP diff.: standard deviation of the difference between calculated and effective positive airway pressure

## Discussion

In this study, we found that the level of CPAP obtained by means of standard calibration in patients with sleep apneas does not differ significantly from that obtained by means of the prediction formula of Miljeteig and Hoffstein, up to values of AHI < 40.

The treatment of choice for OSAHS is the use of PAP. The effective pressure that corrects the respiratory events must be determined individually in each patient regardless of the method that is used. Manual titration during a second night under PSG is the gold standard method for measuring the level of effective CPAP pressure; however, comparable results can be obtained during the same night of the basal study (split night) or using an auto-adjusting CPAP device (APAP) under supervision or at the patient's home for several nights<sup>7-11, 20</sup>.

Since the beginning of the pandemic, in Wuhan, China, produced by the SARS CoV-2 virus, we were forced to establish strategies, from the different areas and specialties of medicine, for the prevention of infection, diagnosis and treatment not only in COVID-19 patients, the general population, and healthcare staff, but also regarding the way we approach the diseases seen daily in the practice of our profession. For that reason, renowned professionals of different disciplines have created guidelines and recommendations to be followed in each case. COVID-19 is highly contagious; it is transmitted through respiratory drops from carriers which are spread until they reach the mouth, nose or eyes of people who are less than 2 meters apart<sup>16</sup>.

The CDC of the United States and the main world and national associations of sleep medicine recommended to postpone and reschedule the administration of PAP therapy in sleep laboratories due to the risk of aerosolization, one of the main SARS-CoV-2 routes of transmission. It is recommended that outpatient studies should be prioritized with APAP in selected patients that need to be treated due to the severe clinical impact of OSAHS and with high probabilities that they won't start treatment<sup>17, 18, 20</sup>.

Our laboratory is located in the west area of the outskirts of Buenos Aires, and it is included in the category of Self-Management Public Hospitals. It has an influence area of approximately 6,000,000 inhabitants and referrals from all the country, since it is a National Reference Center for the treatment of diseases that require complex treatment.

In our area, patients can obtain the equipment they need for their treatment (CPAP) through 3 different types of health coverage: prepaid medical care, health insurance obtained through trade unions and the state public system. Most patients don't have prepaid medical care or health insurance, and the PAP equipment is provided to them through state social support, with a delay of 60-120 days. Patients who require a second study night for the titration also have to wait between 60-90 days. Both situations definitely generate a late therapeutic response in patients with OSAHS and, consequently, a risk in their morbidity and mortality, mainly in the case of patients with severe OSAHS.

The demographic and resource characteristics in our area make it difficult to use self-adjusting home therapies as methods of calibration or treatment. The need for a different alternative to be able to start

the treatment led us to propose the possibility of using CPAP pressure prediction calculations within the context of this pandemic until a standard calibration can be performed.

Throughout the years, different prediction equations have been described, trying to calculate the effective CPAP<sup>12</sup> pressures by means of the use of different variables. Miljeteig and Hoffstein, who were pioneers in this field, proposed and validated their equation<sup>13-15</sup>. According to these authors, the use of the formula would be to determine an approximate initial pressure in the calibration through conventional methods. The equations have been subsequently used to calculate initial pressures or during the PAP assessment studies at the laboratory as referential pressure, minimizing the time necessary to reach the optimum pressure and achieve a larger amount of sleep in such pressure and thus increase the probability of reaching the REM sleep. It would also be useful in patients with high pretest that could benefit from split-night studies, reducing diagnostic time and cost.

Masa et al compared CPAP levels obtained through titration with self-adjusting home equipment, with CPAP values calculated through the Miljeteig and Hoffstein formula and with CPAP titration supervised under PSG. No significant difference was found between the CPAP level obtained by the standard method and the one adjusted with the mentioned formula, but the latter was different from titration with self-adjusting CPAP:  $8.4 \pm 1$  cm H<sub>2</sub>O vs.  $9.1 \pm 1.9$  cm H<sub>2</sub>O ( $p < 0.05$ ). However, there were no significant differences in the somnolence scale, the AHI or adherence in the three groups. In our group of patients, the calc. CPAP was statistically different from the effect. CPAP,  $9.3$  cm H<sub>2</sub>O vs.  $8$  cm H<sub>2</sub>O  $p < 0.0001$ ; but this absolute difference of  $1.3$  cm H<sub>2</sub>O doesn't seem to be clinically significant, just like the values observed in the Masa group with a similar difference. Also, we found that if we classify patients according to the AHI degree of severity, we can reduce this difference of pressure between both methods to  $0.55$  cm H<sub>2</sub>O for the mild degree and  $0.77$  cm H<sub>2</sub>O for the moderate; whereas in the severe group this difference was stronger:  $1.45$  cm H<sub>2</sub>O. Thus, we look for a cut-off point for the AHI that allows us to predict the CPAP pressure more precisely within the group of severe patients, who benefit the most from the treatment and should access to it as soon as possible, given the higher risk of morbidity and mortality. We found that for an AHI cut-off point of 40, this difference between the calc. CPAP and the effect. CPAP was only  $0.13$  cm H<sub>2</sub>O, not statistically significant.

In their original work, Miljeteig and Hoffstein obtained an optimum subgroup of variables with the maximum regression R<sup>2</sup> coefficient<sup>13</sup> using a statistical procedure of lineal regression. This group of predictor variables (AHI, NC and BMI) resulted in  $R^2 = 0.671$ , that is to say, the model represented 64% of variation in the calculation of the CPAP pressure, evidencing the presence of other variables for determining the pressure that were not considered in this model. In our work, the more severe the OSAHS, the stronger the difference between the calc. CPAP and the effect. CPAP. This loss of accuracy could be caused by the influence of these other variables in the determination of the pressure, not expressed in it.

## Conclusion

In this study we have shown that, in our population, CPAP pressure prediction calculations could be used to start treatment early in patients with OSAHS who don't have access to self-adjusting therapies within the context of the COVID 19 pandemic, until standard calibration measures can be taken. Also, this could be done quite accurately in patients with an AHI of up to 40. In patients with a higher AHI, a closer clinical follow-up should be carried out so as to determine the need to adjust the indicated pressure.

Every center should analyze the characteristics and resources of its population with the aim of evaluating the possibility to start CPAP treatment through this pressure prediction method until the endemic and biosafety conditions of the environment in which they work allow for the performance of conventional techniques.

**Conflict of interest:** The authors of this work declare there is no conflict of interest related to this publication.

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