Research Article

Effects of Different Types of Titration Procedures and Home Technical Assistance on Compliance to CPAP Therapy

Valentina Francese, Alessandra Giordano, Elisa Fattori, Antonella Iadarola, Francesca Aglì, Maria Falbo, Fabio Cavallo, and Alessandro Cicolin*

Department of Neuroscience, University of Torino, Italy

Abstract

Objectives: The aim of the study was to clarify the relationships between titration procedures and home technical assistance with compliance and adherence to continuous positive air pressure (CPAP) therapy in patients with obstructive sleep apnea syndrome (OSAS), evaluating the effectiveness of equation-based titrations and differences with standard titration procedures.

Methods: The titration pressures as predicted by different equations (Stradling, Series and Hoffstein) were compared to the pressure assessed through auto-continuous positive airway procedure (APAP)(sub-study a) in 204 patients with OSAS. Secondary, efficacy, compliance and adherence to therapy, and satisfaction for technical assistance during the first 3 months of CPAP therapy were evaluated comparing different titration methods (sub-study b) in 289 patients.

Results: We found a significant positive correlation between APAP titration and pressures predicted through three different equations(sub-study a), but(sub-study b) patients who underwent equation-based titration had significantly less satisfaction for the therapy, they used CPAP for less hours and showed more daytime somnolence than APAP titrated patients. Moreover a positive correlation was found between the overall satisfaction level with the home technical assistance and the hours of use of the CPAP per night in controls.

Conclusion: Equation-based titrations, even if reliable at least in intermediate pressure regimens, seem actually less effective than APAP titration in terms of compliance and daytime residual sleepiness.

ABBREVIATIONS

PAP: Positive Airway Pressure; OSAS: Obstructive Sleep Apnea Syndrome; CPAP: Continuous Positive Airway Pressure; APAP: Auto-continuous Positive Airway Pressure; BMI: Body Mass Index; NC: Neck Circumference; AHI: Apnea-Hypopnea Index; ODI: Oxygen Desaturation Index; ESS: Epworth Sleepiness Scale

INTRODUCTION

Obstructive Sleep Apnea Syndrome (OSAS) interests more than 4% of the male and 2% of the female population in Western countries. Although the positive airway pressure (PAP) therapy represents the treatment of choice for this pathology it is estimated that about 20% of patients initially refuse PAP therapy, up to 25% interrupt it within three years and a percentage that varies between 21 and 46% uses the therapy in a sub-optimal way [1]. Studies that considered predictive factors of treatment adherence pointed out that problem with therapy often occur within the earliest weeks of treatment and that they are related to the side effects. In the light of the above, it appears relevant to support patients during the more critical stages of therapy: during the initial acceptance of therapy, during the earliest nights of use, when titration difficulties arise, and after 3-4 months of use in reason of the possible side effects [2]. Different modalities of home technical assistance and clinical procedures could therefore play a relevant role in reduce the impact of the therapy on patients. The continuous positive airway pressure

Cicolin et al. (2016)
Email: alessandro.cicolin@unito.it

⊘SciMed Central

(CPAP) device titration represents a crucial phase of the clinical practice. Although the titration during assisted overnight polysomnography remains the gold standard, in clinical practice it is frequently used a home titration procedure through an auto-continuous positive airway pressure (APAP) device [3].

Nevertheless, both in laboratory and at home titrations represent time and resources consuming procedures. During last year, different procedures based on equations considering anthropometric and clinical features of patients have been proposed. Previous studies evaluated the effectiveness of these equations and their differences with standard titration procedures [4-6], with only partial agreement between authors.

The aims of the study were to clarify the relationship of titration procedure and home technical assistance with compliance and adherence to CPAP therapy in patients with OSAS.

MATERIALS AND METHODS

The study was performed through 2 sub-studies:

a) The titration pressures as predicted by different equations and assessed according to standard procedures (through APAP device) were compared;

b) Efficacy, compliance and adherence to therapy, and satisfaction for technical assistance were evaluated during the first 3 months of CPAP therapy comparing two different titration methods (equation and APAP).

The study was approved by the local hospital ethics committee.

Sub-study A

Two hundred and fifty consecutive patients with diagnosis of OSAS undergoing CPAP titration referred to Sleep Medicine Center were evaluated.

All patients underwent an out of center sleep testing (OCST) through a portable monitoring device (Embletta X100, Natus Medical Inc, Pleasanton, CA, USA), monitoring anterior tibialis electromyogram, airflow (nasal-cannula), respiratory effort (thoracic and abdominal), oxygen saturation and cardiac frequency, body position, and snoring. Respiratory and motor events were scored by a sleep technician and interpreted by a sleep medicine–certified physician by using standard scoring procedures [3]. OSAS were diagnosed according to ICSD III criteria [7]. All patients underwent standard instrumental examinations (hematological tests, electrocardiogram, chest X-ray, ENT visit with endoscopy and pulmonary clinic visit with spirometry test and arterial blood gas analysis).

After giving written informed consent, all subjects were interviewed by a psychologist trained in sleep medicine and a board-certified sleep medicine physician and demographic data were collected (age, gender, education). Exclusion criteria for all subjects enrolled were major not stabilized medical illnesses other than sleep breathing disorders, known or suspected history of alcoholism, drug dependence or abuse, neurological disorders, mental disorders according to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-V) [8], Mini Mental

State Examination (MMSE) score <26.

All patients were required information to verify the homogeneity of the examined groups and to check the presence of elements potentially influencing the treatment compliance [9]:

- Personal data: age, gender

- Clinical data: BMI (Body Mass Index), NC (Neck Circumference), systolic and diastolic pressure levels, presence of other pathologies, AHI (Apnea-Hypopnea Index), ODI (Oxygen Desaturation Index), ESS (Epworth Sleepiness Scale) [10]

- Ventilation therapy data: CPAP titration pressure levels, mask model and size, humidification level, ramp starting pressure, habitual position during sleep.

All recruited patients underwent CPAP titration using APAP at home and optimal pressure defined as suggested by Callahan et al. [11], Anthropometric and clinical data, (BMI, NC, ODI, AHI) were collected in order to calculate the following most used titration equations[6]:

$$0.048*ODI+0.128*NC+2.1 \text{ [12]}$$

$$0.193*BMI+0.077*NC+0.02*AHI-0.611 \text{ [13]}$$

$$0.16*BMI+0.13*NC+0.04*AHI-5.12 \text{ [14]}$$

Results were finally compared with the therapeutic pressure obtained through at home APAP titration, and the best fitting equation identified.

Sub-study B

Three hundred and fifty consecutive patients with OSAS were evaluated and recruited as in sub-study a, and they were subsequently randomly assigned to standard at home APAP titration following a 2 hours training (Group 1) or experimental equation titration (previously identified through sub-study a) (Group 2) according to a ratio 6:1. Physical parameters as well as adherence and compliance to treatment, by direct measures (such as hours and days of actual use of CPAP and presence of side effects) and indirect measures (such as the quality of sleep and the daytime sleepiness) and technical assistance satisfaction were evaluated during follow up visits after 3 months, in order to check the presence of elements influencing the treatment compliance [7]. Subjective treatment adherence and compliance were examined through a face-to-face questionnaire administration evaluating:

- the mean use of CPAP: total hours of use, hours/night and nights/week

- perception of symptoms improvement: daytime sleepiness (Epworth Sleepiness Scale – ESS) [8], quality and quantity of sleep (sleep latency, total sleep time)

- patients' judgment (poor, adequate, good) about mask comfort, air pressure, humidity and temperature, and frequency of side effects such as noise of the exhalation from the device or the mask, moisture on the face, watery eyes, redness of the conjunctiva, feeling of cold air on the face, feeling of pressure in the chest, nasal obstruction or dryness, running nose, nosebleeds, dry mouth or throat, air leaks from the mask, tightness around the nose, stomach bloating, feelings of suffocation or claustrophobia,

difficulty falling asleep due to the variation of the usual position (never, 1-2 times a months, 1-2 times a week, always) [15].

Treatment objective compliance was acquired from the device hour meter.

The satisfaction for the CPAP treatment has been evaluated through a multiple choice questionnaire [16] assessing:

- the global satisfaction for the basic care: information completeness, improvement of health status, CPAP treatment satisfaction, importance of technical assistance, need to request additional assistance

- the quality of the telephonic and/or domiciliary service on demand: ease of access, prompt intervention, kindness, clarity, expertise and problem solving ability of the technicians

All statistical tests were two-tailed and conducted at a 5% significance level. Tests for normality were conducted on all continuous data, which were transformed if appropriate. The objective parameters were submitted to Spearman's or Pearson's correlation, U Mann-Whitney test or Student's T test for independent samples, chi square test. The data analysis software system SPSS version 22.0 (IBM SPSS Statistics, US) was used for statistical analysis.

RESULTS

Sub-study A

Out of 250 consecutive patients evaluated, 204 were recruited (mean age: 59.9 ± 10.4 yrs; AHI: 45.6 ± 22.4; 151 males, 54 females, respectively 73.7% and 26.3%). The results of APAP titration and the pressure values predicted by the equations (Stradling, Sériès and Hoffstein) [6] are shown in Table (1a). Values are quite similar without statistically differences between procedures, except for the Hoffstein's equation that predicted lower pressures than APAP titration Table (1b). All equation titration pressures result significantly related with APAP titration pressure even if the Stradling's equation seems to be characterized by the highest correlation index Table (1b).

Sub-study B

Out of 350 consecutive patients evaluated, 289 were recruited (mean age: 62.6 ± 11.2 yrs; AHI: 44.1 ± 20.6; 198 males, 91 females, respectively 68.5% and 31.5%). Two hundred and forty-nine patients were assigned to the standard APAP titration (Group 1) and 40 to the experimental equation titration (Group 2). In reason of the highest correlation index the Stradling's equation was chosen (see results of sub-study a). Demographic and clinical data collected before CPAP therapies are shown in Table (2a).

There are no significant differences in the mean age and in gender frequency between the groups of patients, and the sample could be considered representative of population affected by OSAS in term of sex and age distribution [9]. Clinical data are the same between the groups. Body mass index values show the presence of class I obesity, within a wide range of values (normal to severe overweight).The mean blood pressure values are within normal limits. The average values of AHI and ODI indicate the presence of severe obstructive sleep apnea

Table 1a: Mean values of APAP (H_2O cm) and equations-based titrations.

	titration pressure (H_2O cm) (mean ± SD)
Straddling	9.8 ± 1.5
Series	9.9 ± 1.7
Hoffstein	7.5 ± 2.0
APAP	9.7 ± 1.9

Abbreviation: APAP: Auto-Continuous Positive Pressure

Table 1b: Statistical differences and correlations between APAP titration and equation titrations.

	p*	r^2∞
APAP vs Stradling	ns	.343
APAP vs Series	ns	.302
APAP vs Hoffstein	≤ .001	.339

Abbreviation: APAP: Auto-Continuous Positive Pressure
*: Student's paired samples t test
∞: Pearson's significant correlations

Table 2a: Patient's Clinical Data.

	Group 1 (mean ± SD)	Group 2 (mean ± SD)	P
Age (yrs)	62.75 ± 10.90	61.83 ± 12.8	ns **
BMI (kg/m²)	31.42 ± 6.60	31.39 ± 6.83	ns **
systolic blood pressure (mmHg)	129.97 ± 12.47	128.39 ± 9.84	ns **
diastolic blood pressure (mmHg)	81.01 ± 8.10	78.87 ± 5.75	ns **
AHI (#/h)	44.73 ± 20.19	41.41 ± 22.75	ns **
ODI (#/h)	43.33 ± 21.28	39.07 ± 23.70	ns **
ESS (score)	13.20 ± 3.08	13.60 ± 2.20	ns **

Abbreviations: BMI: Body Mass Index; AHI: Apnoea–Hypopnoea Index; ODI: Oxygen Desaturation Index; ESS: Epworth Sleepiness Scale
**: Student's independent samples t test

Table 2b: CPAP pressure, humidification use and mask type in Group 1 and 2.

	Group 1	Group 2	P
Titration pressure (H_2O cm)	9.4 ± 1.98	9.5 ± 1.29	ns*
Humidification use	88.1%	84%	ns§
Nasal mask use	96.6%	97.5%	ns§

*: independent samples t test
§: χ^2 test

syndrome (OSAS) within a wide range of AHI values (between 15 and 100). Mean pressure CPAP values are similar in Group 1 and Group 2 (respectively 9.4 ± 1.98 vs 8.8 ± 1.35 H_2Ocm; ns). ESS basal values are over the cut off score in both groups (13.20 ± 3.08 in Group 1 vs 13.60 ± 2.20 in Group 2; ns), indicating the presence of excessive daytime sleepiness. A nasal mask was mainly prescribed in both group (Group 1: 96.6%, Group 2: 97.5%) and the most used mask model was Philips Respironics Comfort Gel Blue. Titration parameters are shown in Table (2b). The clinical and therapeutics parameters at the follow up visit (3

Cicolin et al. (2016)
Email: alessandro.cicolin@unito.it

⊘SciMedCentral

months) are shown in Table (3).

The comparison of direct and indirect measures of compliance between the groups shows that Group 2 patients are significantly less satisfied for therapy. Moreover, these patients use CPAP for fewer hours per night, have more daytime somnolence, and feel more air temperature discomfort than Group 1 patients.

The analysis of relationships between the satisfaction for home technical assistance, the treatment adherence and clinical variables in Group 1 Table (4) shows:

- A significant positive correlation between the overall satisfaction level and the CPAP hours of use (as reported by the patient as well as by the device counter) a significant negative correlation between the overall satisfaction and the amount of side effects

- a significant positive correlation between the overall satisfaction for the therapy of the patients and BMI, AHI, ODI; and a significant negative correlation with age and ESS

- no significant correlation between the CPAP hours of use per night (both subjective and objective) and the amount of side effects.

The same analysis in Group 2 Table (4) shows:

- no significant correlations between satisfaction for the therapy and compliance measurements

- a significant negative correlation between the mean use of the CPAP per night and side effects and ESS.

Particularly, the only factor that significantly affects the compliance to therapy in terms of hours of use of CPAP in Group 2 is the comfort with the pressure as evaluated by patients, while in Group 1the compliance is also affected by the masks comfort.

Finally, the request of additional home technical assistance is not significantly different between groups (Group 1: 32.1% vs Group 2: 20.0%).

DISCUSSION

In an attempt to reduce costs and waiting lists, many researchers analyzed the efficacy of equation-based titration procedures which have the advantage of being faster and cheaper. Many studies reported cheering results [4,17,18], other ones

Table 3: Satisfaction, compliance, efficacy, side effects of CPAP treatment.

	Group 1 (mean ± SD)	Group 2 (mean ± SD)	P
Satisfaction for therapy	11.68 ± 3.18	10.16 ± 3.06	≤.001 ††
CPAP use per night (h)	5.06 ± 2.11	4.04 ± 2.45	≤ .05 ††
ESS	4.93 ± 4.34	6.28 ± 3.57	≤ .01 ††
Side effects	4.16 ± 5.46	4.17 ± 3.8	ns††
Air pressure discomfort	8.3%	21.2%	≤ .05 §

Abbreviations: CPAP: Continuous Positive Airway Pressure; ESS: Epworth Sleepiness Scale; º: Independent Samples U Mann-Whitney §: χ² test

Table 4: Correlations between satisfaction for the assistance service, measure of compliance and clinical data.

		p †
Group 1		
Global satisfaction vs	CPAP hours of use (subjective)	< .01
	CPAP hours of use (objective)	< .01
	amount of side effects	< .01
	ESS	< .01
	BMI	< .01
	AHI	< .01
	ODI	< .01
	Age	< .01
Group 2		
CPAP hours of use (subjective) vs	amount of side effects	< .01
	ESS	< .01
CPAP hours of use (objective) vs	amount of side effects	< .01

†: Spearman's significant correlations
Abbreviations: BMI: Body Mass Index; AHI: Apnoea–Hypopnoea Index; ODI: Oxygen Desaturation Index; ESS: Epworth Sleepiness Scale

recommended caution [5,6]. A previous study [6] found indeed a positive correlation between pressures values as predicted by equations and assessed through standard procedures (both APAP and manual), but it considered this result insufficient to demonstrate the ability of predictive formulas to identify the optimal therapeutic pressure in each patient, since the equations correctly predicted only pressures within a range of 8 to 11 cm H_2O, but not those lower than 8 or higher than 11.

The results of our sub-study a confirm the significant positive correlation between the pressure values as predicted by different equations [12-14] and that one assessed through APAP titration, in agreement with the previous studies [4,17,18]. Even if statistically significant (p < 0.000), the correlation seems to be weak (r^2 < 0.343)suggesting caution in the extreme range of values of pressure (below 8 and over 11 H_2Ocm) as recommended by Marrone et al. [5], and Lacedonia et al. [6].

The results of the sub-study b highlight that the type of titration slightly modify the compliance to therapy in terms of hours/night (1 hour/night more in patients with APAP titration) and the efficacy in terms of daytime sleepiness (1.3 point less at ESS score in patients with APAP titration). These results disagree with other studies that demonstrated no differences in effectiveness and daytime sleepiness between equation-based and standard titration procedures [4,12]. These discrepancies could be explained considering the differences in number of patients recruited and, consequently, in statistical power of studies (Stradling et al. [17], : 75+75 patients; Noseda et al. [4], : 33+36 patients; our sub-study b: 40+249 patients). Nevertheless, it should be noted that at follow up visit the differences in compliance were minimal and that ESS scores fell within normal range between groups in all the studies.

The sub-study b shows that Group 2 patients (equation titrated) have significantly less satisfaction for the therapy as

Cicolin et al. (2016)
Email: alessandro.cicolin@unito.it

◉SciMed Central

evaluated through the Holmdahl's questionnaire [16]: it could be explained considering that these patients skipped the training with technicians that we usually perform before starting the home APAP titration. These data seem to be confirmed by the relevance of pressure comfort feeling on potential difficulties related to CPAP use (i.e. mask, air humidity and temperature discomfort). The CPAP therapy satisfaction following equation titration was poorly evaluated before, even if it could heavily worse the long term compliance and discontinuation rate. In fact, these patients consider information's about the therapy less complete, health status less improved, CPAP treatment less satisfying, home technical assistance less important and then they require additional home technical assistance more rarely than controls, even when necessary. Finally, as regards to the relationship between satisfaction for home technical assistance service, clinical parameters and treatment compliance, we found a positive correlation between patients overall satisfaction and BMI, AHI, ODI and use of the CPAP per night, suggesting that more severe patients are also more compliant probably due to the greatest clinical improvement. Age is inversely correlated with satisfaction, probably because younger patients have better comprehension, problem solving strategies, coping and learning ability, education and easier access to information sources. In agreement with our results, previous studies report that BMI, AHI, age and other clinical variable seems to be effective predictors of adherence, even if the relation between OSAS severity and adherence is still controversial [2]. As regards the effect of home technical assistance service satisfaction and compliance to CPAP therapy, in Group 1 the compliance is directly related to the overall satisfaction level. The main problems affecting satisfaction are related to the use of humidification(34.6%), masks (37.6%), soft start system (17.1%), delays or errors in the supply of masks (13.3%), CPAP general information (23.2%). In this group, side effects and the difficulties in using the CPAP seem to depend on the lack of information about the mask or on a wrong prescription/supply (model and size), as well as on a reduced use of humidification and soft start system; nevertheless these side effects do not impact on compliance.

In Group 2, the amount of side effects, although not significantly higher than in Group 1, negatively affect the compliance and, consequently, the daytime sleepiness, probably in reason of the unfamiliar use of the instrument due to the lack of a technical training before titration procedure. These data seems to confirm that a good level of home technical assistance is crucial during the early period of CPAP therapy.

Some limits of our study should be highlighted. Mainly the small sample of the Group 2 (40 pts), could have reduced the statistical power of the study as regards some variable with high standard deviation. Moreover, the follow up time (3 months) as well as the lacking of a training procedure in group 2 could have negatively affected the results in term of efficacy and compliance. Finally, we did not evaluate the impact of procedures and therapy on overall quality of life of patients.

CONCLUSION

In conclusion our research highlights that the equation-based titration procedures, even if reliable at least in intermediate pressure regimens, seems actually less effective than APAP titration in terms of compliance and daytime residual sleepiness and that an effective home technical assistance may prevent side effects and increase the compliance to therapy.

ACKNOWLEDGEMENTS

REFERENCES

1. Engleman HM, Wild MR. Improving CPAP use by patients with the sleep apnoea/hypopnoea syndrome (SAHS). Sleep Med Rev. 2003; 7: 81-99.

2. Shapiro GK, Shapiro CM. Factors that influence CPAP adherence: an overview. Sleep Breath. 2010; 14: 323-335.

3. American Academy of Sleep Medicine. Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications, 2nd ed. Westchester, IL: American Academy of Sleep Medicine, 2007.

4. Noseda A, André S, Potmans V, Kentos M, de Maertelaer V, Hoffmann G, et al. CPAP with algorithm-based versus titrated pressure: A randomized study. Sleep Med. 2009; 10: 988-992.

5. Marrone O, Salvaggio A, Romano S, Insalaco G. Automatic titration and calculation by predictive equations for the determination of therapeutic continuous positive airway pressure for obstructive sleep apnea. Chest. 2008; 133: 670-676.

6. Lacedonia D, Sabato R, Carpagnano GE, Carratù P, Falcone A, Gadaleta F, et al. Predictive equations for CPAP titration in OSAS patients. Sleep Breath. 2012; 16: 95-100.

7. American Academy of Sleep Medicine. International classification of sleep disorders, 3rd ed. Darien, IL: American Academy of Sleep Medicine. 2014.

8. Mosquera D, Gonzalez A, Leeds AM. Early experience, structural dissociation, and emotional dysregulation in borderline personality disorder: the role of insecure and disorganized attachment. Borderline Personal Disord Emot Dysregul. 2014; 1: 15.

9. Kim JH, Kwon MS, Song HM, Lee BJ, Jang YJ, Chung YS, et al. Compliance with positive airway pressure treatment for obstructive sleep apnea. Clin Exp Otorhinolaryngol. 2009; 2: 90-96.

10. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991; 14: 540-545.

11. Callahan CY, Norman RG, Taxin Z, Mooney AM, Rapoport DM, Ayappa I, et al. Multinight Recording and Analysis of Continuous Positive Airway Pressure Airflow in the Home for Titration and Management of Sleep Disordered Breathing. SLEEP. 2013; 36: 535-545.

12. Stradling JR, Hardinge M, Paxton J, Smith DM. Relative accuracy of algorithm-based prescription of nasal CPAP in OSA. Respir Med. 2004; 98: 152-154.

13. Sériès F. Accuracy of an unattended home CPAP titration in the treatment of obstructive sleep apnea. Am J Respir Crit Care Med. 2000; 162: 94-97.

14. Hoffstein V, Mateika S. Predicting nasal continuous positive airway pressure. Am J Respir Crit Care Med. 1994; 150: 486-488.

15. Ruhle KH, Franke KJ, Domanski U, Nilius G. Quality of life, compliance, sleep and nasopharyngeal side effects during CPAP therapy with and without controlled heated humidification. Sleep Breath. 2011; 15: 479-485.

16. Stradling JR, Hardinge M, Smith DM. A novel, simplified approach to starting nasal CPAP therapy in OSA. Respir Med. 2004; 98: 155-158.

17. Hertegonne KB, Volna J, Portier S, De Pauw R, Van Maele G, Pevernagie DA, et al. Titration procedures for nasal CPAP: automatic CPAP or prediction formula. Sleep Med. 2008; 9: 732-738.

18. Hertegonne KB, Volna J, Portier S, De Pauw R, Van Maele G, Pevernagie DA, et al. Titration procedures for nasal CPAP: automatic CPAP or prediction formula. Sleep Med. 2008; 9: 732-738.

Cite this article