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Dysfunctional breathing treated with continuous positive airway pressure in newly diagnosed obstructive sleep apnoea: a prospective cohort study

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Abstract

A prospective cohort study investigating patients with obstructive sleep apnoea (OSA) was conducted to determine the prevalence of dysfunctional breathing and if continuous positive airway pressure (CPAP) therapy improves associated symptoms. Almost half of newly diagnosed patients with OSA had dysfunctional breathing and CPAP was not an effective treatment. Dysfunctional breathing is common in patients with OSA.

Obstructive sleep apnoea (OSA) is caused by repetitive pharyngeal collapse during sleep causing intermittent hypoxia, fragmented sleep and excessive daytime sleepiness.[1] A previous study found 22% of patients being investigated for OSA had dysfunctional breathing (DB) as measured by the Nijmegen questionnaire (NQ),[2] a validated tool used to detect symptoms associated with increased work of breathing such as dyspnoea.[3] Obesity is a risk factor for developing OSA[4] and may explain why OSA patients feel breathless as it reduces functional residual capacity (FRC) and expiratory reserve volume (ERV) increasing work of breathing.[5] Also, individuals with severe obesity need to generate higher minute ventilation to maintain eucapnia and work of breathing is increased.[6] Other comorbidities common in OSA that have the potential to contribute to symptoms of breathlessness include cardiovascular disease, smoking and psychiatric conditions such as anxiety and depression.[7–9]

The preferred first line treatment for symptomatic moderate–severe OSA is continuous positive airway pressure (CPAP) therapy which maintains upper airway patency by preventing pharyngeal collapse during sleep.[10] It is an effective treatment that has been shown to reduce apnoea hypopnea index (AHI) in up to 72% of

Abbreviations: AHI, apnoea hypopnea index; BMI, body mass index; CO_2, carbon dioxide; CPAP, continuous positive airway pressure; DB, dysfunctional breathing; ERV, expiratory reserve volume; ESS, Epworth sleepiness score; FRC, functional residual capacity; H_2O, water; NQ, Nijmegen questionnaire; NRD, neural respiratory drive; OSA, obstructive sleep apnoea; RCT, randomised controlled trial

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patients while improving symptoms of excessive daytime sleepiness as measured by the Epworth Sleepiness Score (ESS).[11] In obese patients, CPAP also helps to inflate the chest, increase FRC, decrease airway resistance, offload the respiratory muscles and reduce neural respiratory drive (NRD).[12] These effects may improve symptoms of breathlessness in obese patients with OSA. To the best of our knowledge only one study has investigated CPAP and its impact on symptoms of breathlessness in obese patients with OSA.[13] Xiao *et al*. conducted an observational physiological pilot study of 15 patients who were studied supine and awake on CPAP. The authors found that at low CPAP pressures, breathlessness improved, however as pressures were increased to levels required to abolish upper airway collapse, symptoms of breathlessness increased.[13]

Currently there is a paucity of data about the prevalence of DB in a sleep clinic population and whether symptoms associated with DB such as dyspnoea improve with CPAP. The purpose of this study was to determine if CPAP therapy improves symptoms of DB in patients with OSA after a period of treatment.

Consecutive adult patients with a new diagnosis of OSA (AHI > 5) were asked to participate if they had received a recommendation to proceed to CPAP therapy by a sleep physician and were CPAP treatment naïve. Participants were required to consent to be part of the research project.

Patients who commenced CPAP were included in the treatment group and those who declined or delayed CPAP treatment were included in the control group. The primary outcome was change in DB measured using the NQ.[3] ESS was a secondary outcome measure. The NQ and the ESS questionnaires were administered at baseline and follow up (next attendance at the clinic). Other data collected in the intervention group included mask type, average CPAP pressure and average duration of use per night.

Ethical approval was provided by the Gold Coast University Hospital Human Research Ethics Committee (HREC/17/QGC/56).

Baseline characteristics, ESS and NQ scores were summarised using means (standard deviation) and tested between treatment and control groups using Student's *t*-test if normally distributed and tested between groups using Wilcoxon's rank-sum test otherwise. Categorical variables were tested between groups using Pearson's chi-squared test. Linear regression modelling was used to assess changes in outcome measures between groups after adjusting for baseline values. For ESS, a multivariable linear regression model was built, whereby potential confounders identified *a priori* were entered and then dropped sequentially based on their *P*-values. Variables remained in the model if they were significant at the 5% level or if they influenced the point estimate for the effect of treatment on ESS. A subset analysis was performed on patients who had an elevated NQ score at baseline (>19) indicating patients experiencing DB. Analyses were performed using the Stata statistical software package (Version 13).

Table 1 Characteristics of study participants by treatment status

Variable	Category/units	Control *N* = 43	Intervention *N* = 41	Total *N* = 84	*P*-value
Age†	Years	57.5 (15.1)	62.1 (10.7)	59.8 (13.3)	0.11
Gender‡	Male	29 (67)	23 (56)	52 (62)	0.37
BMI§	kg/m^2	31 (28–37)	36 (31–41)	34 (30–39)	0.04
AHI§		29 (20–53)	39 (23–55)	35 (21–53)	0.23
AHI‡	Severe (≥30)	21 (49)	27 (66)	48 (57)	0.13
ESS†		11.2 (4.9)	10.7 (5.8)	10.9 (5.3)	0.65
NQ†		19.6 (11.1)	18.5 (10.8)	19.1 (10.9)	0.66
CPAP†	cmH_2O	9.4 (2.5)	9.7 (2.9)	9.6 (2.7)	0.56
Results at follow up					
ESS†		11 (5.3)	7.7 (5.5)	9.4 (5.6)	0.006
NQ†		19.6 (10.9)	18.2 (15.5)	18.9 (13.3)	0.64
Duration of follow-up‡	Weeks	15 (7–22)	8 (8–12)	12 (8–16)	0.017
Average duration of use§	(h/day)	N/A	6.6 (1.2)		
Pressure§	(cmH_2O)		10.2 (3.3)		
Mask	Face		25 (61)		
N (%)	Nasal		16 (39)		

Summary measures are †mean (standard deviation) with *P*-values from Student's *t*-test, ‡frequency (%) with *P*-values from Pearson's Chi-squared test or §median (interquartile range) with *P*-values from Wilcoxon's rank-sum test. AHI, apnoea hypopnea index; BMI, body mass index; CPAP, continuous positive airway pressure; ESS, Epworth sleepiness score; NQ, Nijmegen questionnaire.

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Table 2 Subset analysis: restricted to those with NQ > 19 at baseline

Variable	Category/units	Control $N = 21$	Intervention $N = 19$	Total $N = 40$	*P*-value
Age†	Years	55.6 (14.1)	63.8 (8.9)	59.5 (12.5)	0.035
Gender‡	Male	15 (71%)	8 (42%)	23 (57%)	0.11
BMI§	kg/m^2	30 (28–37)	37 (33–41)	35 (30–39)	0.018
AHI§		39.4 (24.3)	48.2 (36.2)	43.6 (30.4)	0.37
AHI‡	Severe (≥30)	11 (52%)	13 (68%)	24 (60%)	0.35
Results at follow up					
ESS†		13.0 (4.8)	11.5 (5.6)	12.3 (5.2)	0.36
NQ†	Baseline	28.4 (7.5)	28.1 (6.4)	28.3 (6.9)	0.87
NQ†	Follow up	24.6 (11.4)	22.1 (16.9)	23.4 (14.2)	0.52
CPAP†	cmH_2O		9.8 (3.5)	9.9 (3.2)	0.94
Duration of follow up§	Weeks	20 (7–26)	10 (8–12)	12 (8–21)	0.033

Summary measures are †mean (standard deviation) with *P*-values from Student's *t*-test, ‡frequency (%) with *P*-values from Pearson's Chi-squared test or §median (interquartile range) with *P*-values from Wilcoxon's rank-sum test. AHI, apnoea hypopnea index; BMI, body mass index; CPAP, continuous positive airway pressure; ESS, Epworth sleepiness score, NQ, Nijmegen questionnaire.

Of 93 patients enrolled in the study, 2 declined after enrolment and 7 were lost to follow up. Of the 84 patients included in analyses, 40 (47.6%) had DB with an elevated NQ, 52 (62.5%) were male and the mean age was 60 (±13) years. Median BMI was significantly higher in the treatment group ($P = 0.04$) (Table 1).

Median follow-up time was significantly longer in controls (15 weeks) compared to the treatment group (8 weeks). Average duration of CPAP use per night in the treatment group was 6.6 h (±1.2). Mean NQ values at follow up did not differ significantly between groups; results were consistent after adjusting for baseline values, gender and BMI in regression models. Data on participant comorbidities, medications, smoking status and residual AHI on CPAP were not collected and therefore not used in regression modelling. Mean ESS was significantly lower at follow up in the treatment group compared to the control group. On linear regression modelling, mean ESS scores were 2.8 units (95% CI: 0.8–4.8) lower at follow up in patients treated with CPAP compared to controls after adjusting for BMI and baseline ESS values. The effect was more marked for patients who used the device for an average of more than 7 h per night (coefficient: 4.3 units (95% CI: 1.9–6.6)).

Descriptive statistics for the subset of patients with confirmed DB (baseline NQ values >19) are shown in Table 2. There was no statistically significant improvement in NQ in the treatment group compared to controls in patients with confirmed DB.

We defined a clinically significant change in NQ as 6 units (0.5 * standard deviation of the observed distribution of the change). Among patients who had DB at baseline and were treated with CPAP, 5/19 (26%) experienced a clinically significant reduction in NQ compared to 1/21 in the control group. In the CPAP group, 10/19 (53%) had an increase in NQ values compared to 8/21 (38%) in the control group. There was no difference in baseline characteristics when comparing those who responded to those who did not, however statistical strength was limited by small numbers.

Discussion

Our study found that DB is common in patients with OSA, and that CPAP therapy does not seem to be effective in improving DB symptoms. Even when the analysis was restricted to the 47.6% of patients who had an elevated NQ score (>19), and thus a diagnosis of DB, no improvement was observed. Patients treated with CPAP had an improvement in their daytime sleepiness symptoms indicating effective CPAP therapy was administered.

The nature of the abnormality reflected in an elevated NQ score is related to stress, respiration and anxiety.[3] The authors of the NQ describe the tool as a measure of 'functional respiratory complaints' where the term respiratory refers to ventilation, dyspnoea and breathing movement and the term functional refers to the relationship with stress and anxiety. An elevated Nijmegen score is abnormal and in recent studies has been used to identify patients whose complaints may not be related to a medical condition but rather a psychological one. The implication being that conventional therapy may not provide symptomatic improvement to a patient's symptoms.[3]

The reason the NQ score did not improve with CPAP may be because the pathophysiology that drives dyspnoea in patients with OSA includes impaired respiratory mechanics[5] and increased central respiratory drive[14] which may not be addressed by CPAP during wakefulness. Despite these observations, investigating whether

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CPAP improves complaints of daytime dyspnoea was warranted because of the complex and subjective nature of this complaint and because of the high prevalence of DB in this patient group.

Limitations of our study warrant further consideration. The study methodology raises the possibility of uncontrolled bias. Inclusion bias was managed by enrolling consecutive patients attending sleep studies, however patients and researchers were unblinded. Patients self-selected themselves to be in the treatment group if they followed physician recommendations or conversely self-selected themselves to be in the control group if they did not. There are many reasons why patients who are advised to use CPAP do not, including cost, intolerance or perceived intolerance and social reasons. Ideally a randomised control trial (RCT) would be done to better control for bias, however it may be considered unethical to randomise patients with confirmed OSA into an observation group when a proven and effective treatment for OSA (i.e. CPAP) exists.

The average follow-up time in the treatment group was 8 weeks. It is likely that most of the patients in this group have been suffering OSA for years with prolonged disruption to the chemical control of their respiratory centre.[14] For this reason, the follow-up time in the treatment group may have been too short to demonstrate an improvement in DB through rectification of chemical control of respiration.

DB is very common in patients with newly diagnosed OSA, occurring in almost half of all patients. CPAP therapy is an effective treatment for OSA associated daytime sleepiness. However, based on the results of our study it is not possible to advise patients with DB and OSA that CPAP will improve their dysfunctional breathing symptoms. Future research may need to explore non-CPAP therapies that may assist in the management of the dysfunctional breathing symptoms since such therapies, if combined with CPAP may ultimately improve the quality of life of a considerable proportion of patients with OSA.

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