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Nocturnal nasal positive pressure ventilation for chronic obstructive pulmonary disease

Key Messages

1. Non-invasive ventilation is well-tolerated by hypercapnic chronic obstructive pulmonary disease (COPD) patients during exacerbations and quickly results in improvements of acidosis.
2. However in the severe stable phase, the tolerance for bilevel positive airway pressure is very poor and patients do not perceive the benefit as in acute exacerbations.
3. Concomitant obstructive sleep-disordered breathing (overlap syndrome) occurred in 13% of our patients, whose prevalence was no higher than in other populations. Most COPD patients with sleep-disordered breathing are not sleepy and hence routine sleep study is not recommended for patients with COPD.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a common cause of respiratory failure and the fourth leading cause of death in Hong Kong. Many patients present with recurrent exacerbations requiring hospital admission. Long-term oxygen therapy (LTOT) with usage of at least 15 hours daily may improve 5-year survival in patients with respiratory failure due to COPD. Nocturnal non-invasive positive pressure ventilation (NPPV) may confer further advantages by improving carbon dioxide responsiveness of the respiratory centre and facilitating respiratory muscle rest. During acute exacerbations of COPD, there is level-one evidence supporting the efficacy of NPPV. For example using a bilevel positive airway pressure (BiPAP) device reduces the need for intubation, hospital length of stay, and complications In severe stable COPD, the use of NPPV is highly controversial with conflicting data.[1]

Obstructive sleep apnoea syndrome (OSA) is a common form of sleep-disordered breathing (SDB) characterised by repetitive episodes of partial or complete upper airway obstruction causing sleep fragmentation and symptoms. Sleep may have adverse effects on respiration in patients with COPD as a consequence of hypoventilation and impaired ventilation/perfusion matching with recumbency and sleep onset.[2,3] The combination of SDB and COPD, the so-called overlap syndrome, may lead to more profound hypoxaemia and worsening pulmonary hypertension.[4]

The objectives of this study were to (1) assess whether severe stable COPD patients, with hypercapnic respiratory failure already on LTOT, would benefit from the addition of domiciliary NPPV; (2) evaluate the prevalence and symptoms of SDB, and the acceptance of nasal continuous positive airway pressure (CPAP) treatment among our patients with stable COPD; and (3) review the tolerance and outcome of patients with severe COPD in acute exacerbations and type-2 respiratory failure in general medical wards, who were nevertheless not deemed to require intubation but given NPPV treatment.

Methods

This study was conducted from September 1999 to February 2003, and was staged:

(1) Project 1: 46 patients with severe stable hypercapnic COPD on LTOT were recruited for assessment with arterial blood gases (ABG), polysomnography (PSG) to rule out significant SDB (defined as an apnoea-hypopnoea index [AHI] of ≥20/hour), Epworth sleepiness scale (ESS), and St George Respiratory Questionnaire (SGRQ). Patients were started on a trial of NPPV with BiPAP device; end-points included progress of ABG, quality of life, lung function, exercise capacity, and hospital admission rates.

(2) Project 2: 100 consecutive COPD patients in stable phase were recruited from the respiratory clinic for PSG, ESS, SGRQ assessment. Patients with an AHI of ≥10/hour were given a trial of nasal CPAP treatment.

(3) Project 3: a retrospective review of 72 patients admitted over a period of 18 months, not deemed for intubation but given BiPAP treatment for severe hypercapnic respiratory failure, with reference to factors predicting outcome.

Table 1. Distribution of symptoms related to sleep-disordered breathing in the Sleep and Health Questionnaire

Symptom	% of total patients, n=91			
	Not affected	Mild	Moderate	Severe
Impaired performance ability*	50	18	13	8
Daytime sleepiness†	25	36	13	13
Snoring frequency†	51	19	4	9
Witnessed apnoea†	82	3	0	0
Nocturnal awakenings†	46	29	6	8

* Using 6-point Likert scale: 1-2 (not affected), 3-4 (mild), 5 (moderate), and 6 (severe)
† Using 5-point frequency scale: not affected, rarely or <once/week (mild), sometimes or 1-2/week (mild), frequently or 3-4/week (moderate), and almost always or 5-7/week (severe)

Statistical analysis

All data were presented as mean±standard deviation, unless otherwise stated. Nominal data were analysed with the Chi squared test. Unpaired *t* test was used for continuous data. For comparisons between patients with AHI of ≥20/hour vs <20/hour, unpaired *t* test was used for normally distributed variables and Mann-Whitney *U* test for non-normally distributed variables. For comparisons between patients who died versus survivors, unpaired *t* test was used for normally distributed variables and Mann-Whitney *U* test for non-normally distributed variables. The Wilcoxon signed ranks test was used for comparing changes in ABG parameters at different time points within each group. Statistical significance was set at P<0.05. Data analysis was performed with the Statistical Package for the Social Sciences 10.0 for Windows (SPSS Inc, Chicago [IL], US).

Results

Project 1

Of 22 patients who met the inclusion criteria, 17 (77%) had no significant obstructive SDB and were offered a trial of nocturnal NPPV (BiPAP Harmony, ST mode, Respironics, Pennsylvania, US). Their mean age was 70±6 years and body mass index (BMI) was 19.4±3.2 kg/m^2. Pre-intervention testing revealed the following mean values: ESS 5.8±5.8; forced expiratory volume in one second (FEV_1) 25±9% of predicted; forced vital capacity (FVC) 41±18% of predicted, FEV_1/FVC ratio 48±20%; 6-minute walk distance 90±14 m; arterial blood pH 7.37±0.04; PO_2 9.6±2.0 kPa, PCO_2 8.2±1.5 kPa; SGRQ score 59±16. All except one patient could not tolerate two nights of BiPAP titration. The only patient who agreed to try BiPAP, dropped out after a 3-month trial, as there was no perceived benefit.

Project 2

Ninety-one patients met the inclusion criteria and consented to enter the study. There were eight females and 83 males with a mean age of 71±8 years, Pre-intervention mean values were as follows: BMI 21.8±4.3 kg/m^2; neck circumference 37±6 cm; FEV_1 0.9±0.5 L (47±24% of predicted); FVC 1.7±0.7 L (67±28% of predicted) post-bronchodilator; arterial blood pH 7.4, PCO_2 6.3 kPa, PO_2 10.9 kPa; ESS score 5.2±4.7. The distribution of symptoms is shown in Table 1. The PSG revealed a total mean sleep time of 5.0±2.2 hours, and arousal index 26±15/hour. The numbers of patients with AHI values of ≥10, ≥15, and ≥20 were 28 (31%), 17 (19%), and 12 (13%), respectively. Only three (3%) of the patients had OSA with an AHI of ≥20 and an ESS of ≥10.

Factors that might predict significant SDB among the patients with COPD were assessed by comparing data from those with AHI values of ≥20/hour (n=12) and <20/hour (n=78). No statistically significant difference was found with reference to mean values for pulmonary artery systolic pressure (43.3±12.3 vs 39.1±17.3), PCO_2 (6.7±1.4 vs 6.2±1.6), PO_2 (11.3±3.3 vs 10.8±2.5), arterial oxygen percent saturation (SaO_2; 92.3±5.3% vs 93.4±4.0%), arousal index (29.1±9.3 vs 25.8±15.7), and FEV_1 (0.6±0.3 vs 0.8±0.5). Those with more significant SDB tended to have lower mean minimum SaO_2 values during sleep (76.6±20.0 vs 84.1±10.6, p=0.05).

All 28 patients with an AHI of ≥10/hour were offered a 30-minute trial of nasal CPAP with the AutoSet titrating device at 4-cm H_2O for acclimatisation in the afternoon. However, 21 patients refused to take part in the overnight CPAP titration study after the daytime trial, while overnight CPAP titration was successfully performed in seven (25%) patients with a mean level of 12.1±4.0 cm H_2O.

The characteristics and baseline sleep study of these seven patients were compared with those who refused CPAP titration study (n=21). Those who accepted and completed CPAP titration study were similar in age, BMI, and ESS, but had a larger neck circumference (40.1±1.4 vs 37.5±2.9 cm, P=0.03), more severe OSA (as reflected by an AHI of 33.1±12.2 vs 19.7±14.3, P<0.01), and higher PCO_2 (7.1±1.4 vs 5.7±1.5, P=0.02). Only three patients agreed to proceed to home treatment; one on CPAP and two on BiPAP (after failing CPAP for a short period). Objective CPAP compliance over 1 and 3 months, as measured by the De Vilbiss CPAP timeclock, was 6.2 and 3.1 hours/night respectively. There was no timeclock available to check compliance with the BiPAP device. The ESS was 8.0±2.8 at the end of 3 months.

Project 3

The study included 72 patients (57 males) with a mean age of 70±7 years. Initial ABG testing revealed pH of 7.2±0.1,

Table 2. Comparison of chronic obstructive pulmonary disease patients who died in hospital and those who were discharged home or to rehabilitation unit

	Died (n=16)	Discharged to rehabilitation/home (n=56)	P value
Age (years)	73±7	70±8	0.053
Arterial blood gases			
Before bilevel positive airway pressure (BiPAP)			
pH	7.20±0.10	7.20±0.07	0.905
PCO_2 (kPa)	13.0±3.0	13.0±3.1	0.928
PO_2 (kPa)	9.8±4.6	11.3±6.4	0.397
SaO_2	86.8±8.6	86.3±10.1	0.772
O_2 requirement	7.7±6.2	4.6±4.2	0.064
2 hours after BiPAP			
pH	7.21±0.12	7.25±0.07	0.200
PCO_2 (kPa)	12.4±2.9	11.1±2.5	0.137
PO_2 (kPa)	10.9±4.9	10.7±4.4	0.878
O_2 requirement	6.1±3.6	5.5±3.6	0.483
4 hours after BiPAP			
pH	7.27±0.13	7.30±0.09	0.626
PCO_2 (kPa)	10.9±4.0	9.9±2.5	0.409
PO_2 (kPa)	11.6±4.4	10.5±3.9	0.740
O_2 requirement	6.8±3.2	4.8±2.6	0.101
4-24 hours after BiPAP			
pH	7.27±0.11	7.30±0.42	0.016
PCO_2 (kPa)	11.1±2.6	8.7±2.0	0.001
PO_2 (kPa)	13.3±9.5	11.0±4.1	0.824
O_2 requirement	6.5±3.6	4.1±2.1	0.026
1-2 days after BiPAP			
pH	7.30±0.14	7.38±0.05	0.082
PCO_2 (kPa)	10.0±2.4	8.3±1.9	0.036
PO_2 (kPa)	12.5±4.2	11.2±3.0	0.328
O_2 requirement	5.3±3.2	3.5±1.8	0.083

PCO_2 of 13.1±3.0 kPa, PO_2 of 11.1±6.2 kPa, and HCO_3 of 37.3±7.3 mmol/L. The mean inspiratory and expiratory positive airway pressures were 16±3 and 5±1 cm H_2O while the mean time for normalising pH and PCO_2 was 1.5±1.2 days and 2.3±1.8 days respectively. The time on BiPAP was 5.2±3.4 days. Sixteen (22%, 14 males and 2 females) patients died on our medical wards, whereas the remainder were discharged home or to our rehabilitation unit.

The initial ABG values were not associated with in-hospital mortality. Among those who survived, the improvements in pH and PCO_2 were sustained and significant at 2 hours, 4 hours, between 4 and 24 hours, and within 2 days of commencing BiPAP (P<0.001 for all). Those who died only had transient, though significant improvements in pH at 4 hours (P=0.017) [Table 2 and Fig].

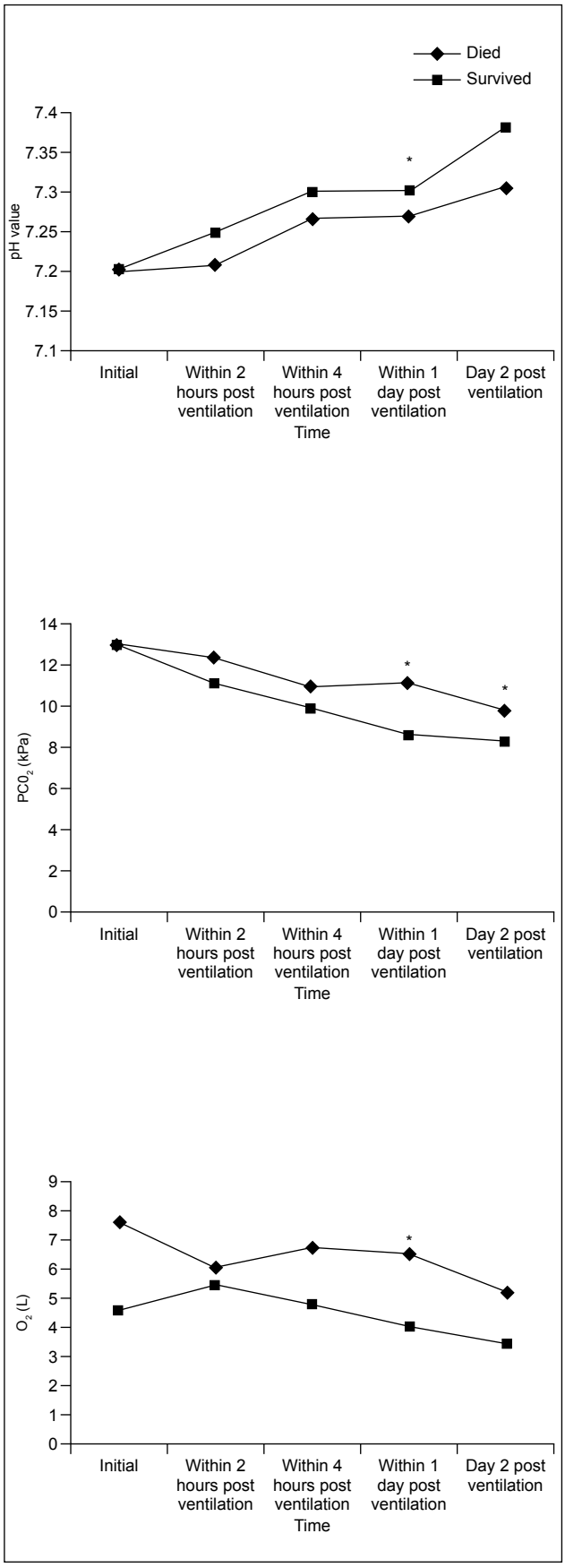
Discussion

Chronic obstructive pulmonary disease is a common disease, with a substantial morbidity and mortality worldwide. During acute exacerbations, many patients with advanced COPD develop worsening respiratory failure with hypercapnia. In acute exacerbations of COPD, pH is the best marker of severity and reflects acute as opposed to stable (chronic) alveolar hypoventilation. A pH of <7.26 is associated with a poor prognosis; death occurred in 10/39 (26%) of episodes with such a pH.[5,6] The mortality rates in a 1-year prevalence study of COPD patients admitted to hospital were 7% for patients with a normal pH, increasing to 14% for those who were acidotic (pH of <7.35) after initial medical treatment.[7] It is thus important to prevent tissue hypoxia and control acidosis and hypercapnia with ventilatory support, while medical treatment can help to maximise lung function and reverse the precipitating cause of the exacerbation. The main strategies include oxygen therapy, non-invasive ventilation, and invasive mechanical ventilation.

In our retrospective study of 72 COPD patients with severe hypercapnic respiratory failure (pH of 7.2±0.1) not deemed suitable for intubation, the mortality (n=16, 22%) was substantial but the majority (n=56, 78%) improved and could be weaned off NPPV after a mean of 5±3 days and discharged from our general medical wards after a stay of 12±8 days.[8] Thus, the use of NPPV may be justifiable for patients not deemed for intubation, who have acutely reversible COPD exacerbations.

Among the 17 patients with stable hypercapnic COPD, only one agreed to a 3-month trial of nocturnal NPPV after two initial nights of pressure titration. There was no significant improvement in the parameters examined for that patient and he declined further NPPV at the end of the trial period.

Our study has shown that the frequencies of patients with an AHI of ≥10, ≥15, and ≥20 were 28 (31%), 17 (19%), and 12 (13%) respectively.[9,10] The majority of our COPD patients were not sleepy (ESS score of 5.2±4.7). Three (3%) of the patients in our study had OSA, defined as those with an AHI of ≥20 and ESS of ≥10.[9-11] Those who



* Significantly different

Fig. Serial changes in arterial blood gas parameters after commencement of non-invasive ventilation with bilevel positive airway pressure

had significant SDB tended to have a lower minimum SaO_2 during sleep but their pulmonary artery systolic pressure was not significantly higher. Tolerance of CPAP was poor and only one patient was prescribed home CPAP, whereas another two were started on BiPAP treatment. Our previous study with ischaemic stroke patients (mean age of 64 years) showed a high prevalence of obstructive SDB (AHI of ≥20/hour) in 49% compared with 24% of normal controls.[12] Patients with ischaemic stroke were also non-sleepy (ESS of 6.8±3.6) and few could tolerate CPAP.[12] Poor CPAP tolerance among our COPD patients is not surprising, as in general, OSA patients who are symptomatic show better compliance with CPAP treatment.[13]

Conclusion

Severe COPD patients with hypercapnic respiratory failure have very poor tolerance or acceptance of nocturnal BiPAP in the stable phase. During acute exacerbations, our COPD patients, even though they had severe disease and were not deemed for intubation, tolerated BiPAP well in the general medical wards, although the mortality was substantial (22%). The prevalence of 'overlap syndrome' with concomitant SDB (defined as an AHI of ≥20/hour) was 13%, which is not higher than in the general population. Most COPD patients with concomitant SDB are not sleepy and hence cannot accept CPAP treatment.

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