

Short papers

Domiciliary nocturnal intermittent positive pressure ventilation in patients with respiratory failure due to severe COPD: long term follow up and effect on survival

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Abstract

Background—There is increasing interest in the use of non-invasive nocturnal intermittent positive pressure ventilation (NIPPV) in the management of patients with chronic hypercapnoeic (type II) respiratory failure. Although this treatment enables patients requiring mechanical ventilatory support to be treated more readily at home, few studies have been done to demonstrate its long term benefits in chronic obstructive pulmonary disease (COPD) and the application of NIPPV in these circumstances remains controversial.

Methods—Eleven patients in severe stable chronic type II respiratory failure due to COPD who were unresponsive to conventional treatments experienced symptomatic hypercapnia when receiving sufficient supplementary oxygen to result in an arterial oxygen saturation (Sa_o) of >90%. They were assessed for treatment with NIPPV, and its effects were observed for over two years using arterial blood gas tensions, spirometric parameters and body mass index (BMI), survival, hospital admissions, use of general practitioner resources, and patient satisfaction.

Results—Hospital admissions and GP consultations were halved after one year compared with the year before NIPPV and there was a sustained improvement in arterial blood gas tensions at 12 and 24 months when breathing air, despite progressive deterioration in ventilatory function. BMI did not change during the period of observation. The median survival was 920 days, with no patient dying within the first 500 days.

Conclusions—Domiciliary NIPPV results in improvements in arterial blood gas tensions which are sustained after two years of treatment and reduces both hospital admissions and general practitioner visits by patients with severe COPD in hypercapnoeic respiratory failure. It is well tolerated and, although there was no control group, survival appears to be prolonged

when these results are compared with those of the NOTT and MRC (LTOT) trials.

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Keywords: home ventilation; chronic obstructive pulmonary disease; outcome measures

Non-invasive positive pressure ventilation (NIPPV) is a well established form of treatment for chronic hypercapnoeic (type II) respiratory failure in patients with neuromuscular disease or skeletal deformity. Although there has been increasing interest in its use for patients in chronic type II respiratory failure due to chronic obstructive pulmonary disease (COPD), its use remains controversial in this group of patients with conflicting reports of its efficacy and acceptability.^{1,2}

Methods

Eleven patients, all ex-smokers in severe type II respiratory failure, were electively admitted between 1991 and 1995. All were diagnosed as having COPD and were receiving maximal drug therapy. Long term oxygen therapy (LTOT) sufficient to correct hypoxaemia (Sa_o >90%) resulted in symptomatic hypercapnia, especially morning headaches and excessive diurnal somnolence. Sleep apnoea syndrome was excluded (apnoea/hypnoea index <10) but patients 1, 3, 7, 8, 9, and 10 (table 1) experienced severe sleep hypoventilation.

Four patients (nos 2, 5, 6, and 8) had been intubated and ventilated on a total of seven occasions prior to NIPPV. All patients received supplementary oxygen. Seven were already on LTOT prior to NIPPV (mean 37 months) and continued with it, in addition to ventilation. Three further patients (nos 4, 6, and 7) were commenced on oxygen during the induction process. In one case (no. 4) NIPPV was accompanied by nocturnal oxygen therapy.

The pressure set, time cycled "Nippy" ventilator (Friday Medical, London) was used with nasal or full face masks (Respironics, Pennsylvania, USA and Friday Medical, London, UK). Settings were made initially according to patient comfort, then adjusted according to

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Table 1 Patient characteristics and pretreatment lung function

Patient	Sex	Age	BMI	FEV ₁ % (l)	FVC% (l)	TLC% (l)	RV % (l)	TLCO % (ml/min/ mm Hg)	Kco (ml/min)	PaO ₂ (kPa)	Paco ₂ (kPa)	Paco ₂ with corrected Sao ₂ (kPa)	-HCO ₃ mmol/l	HCT	Smoking history (pack years)
1	F	63	56	53 (0.98)	69 (1.7)	81 (3.31)	103 (1.61)	72 (14.1)	5.6 (115%)	5.6	7.7	7.7	33	0.40	42
2	M	73	30	41 (1.02)	50 (1.8)	–	–	–	–	6.0	7.5	11.1	31	–	50
3	M	67	29	37 (1.05)	50 (2.01)	90 (5.82)	120 (2.71)	88 (22)	5.03 (124%)	6.0	9.7	10.3	37	0.50	90
4	M	65	42	36 (0.97)	43 (1.69)	86 (5.49)	104 (2.71)	94 (25.3)	–	5.3	8.8	10.1	31	0.50	60
5	M	62	26	23 (0.73)	45 (1.81)	84 (5.51)	130 (2.97)	70 (18.6)	5.69 (136%)	6.6	7.2	10.7	28	0.45	80
6	M	72	26	27 (0.62)	52 (1.73)	90 (5.11)	148 (3.22)	60 (12.7)	3.97 (105%)	6.5	10.8	11.7	34	0.48	18
7	F	48	42	43 (1.02)	66 (1.97)	97 (4.5)	158 (2.52)	71 (16.4)	5.70 (109%)	6.4	8.3	6.7	30	0.41	23
8	F	45	23	20 (0.44)	45 (1.19)	90 (3.6)	158 (2.07)	90 (19.8)	8.20 (155%)	5.3	8.0	8.0	33	0.46	45
9	M	66	33	47 (1.26)	61 (2.32)	100 (6.3)	143 (3.2)	80 (19.8)	4.30 (107%)	7.7	7.3	7.5	32	0.49	200
10	M	48	34	34 (1.19)	58 (2.68)	91 (6.3)	150 (3.3)	80 (24.5)	5.90 (124%)	7.7	7.3	8.0	33	0.55	55
11	M	51	26	19 (0.60)	44 (1.9)	100 (6.4)	195 (4.02)	32 (8.9)	2.10 (46%)	4.6	8.4	8.4	40	0.47	60
Mean values		60	33.3	34.5	53	82.6	128	67	4.2	6.02	8.08	9.12	32.9	0.42	65.7

FEV₁ = forced expiratory volume in one second; FVC = forced vital capacity; TLC = total lung capacity; RV = residual volume; TLCO = carbon monoxide transfer factor; Kco = carbon monoxide transfer coefficient; PaO₂, Paco₂ = arterial oxygen and carbon dioxide tensions.

diurnal Paco₂ values. During induction of treatment pulse oximetry and arterial blood gas tensions were regularly measured. Once respiratory variables had been stabilised and the patients were acclimatised, they were discharged and reviewed in the multidisciplinary sleep and breathing clinic.

Morbidity was assessed from a review of the general practitioner records. Consultations for respiratory reasons, general problems and home visits were recorded, together with hospital admissions in the year before and the year after starting NIPPV.

Patient compliance with NIPPV (number of nights/hours per night), experience of symptoms of hypercapnia since commencing NIPPV, side effects of mask ventilation, and overall satisfaction with the treatment were assessed by means of a locally developed postal questionnaire after two years of treatment. Patients were asked to respond on a scale of severity—for example, often/sometimes/never; every night/most nights/rarely.

To assess the effect of NIPPV on gas exchange the best blood gas measurements when spontaneously breathing air were taken in the month prior to starting NIPPV, and the worst (in the event of more than one measurement being available) at six, 12 and 24 month intervals after starting the treatment.

Spirometric testing, using a Vitalograph dry bellows spirometer, was repeated 12 and 24 months after commencing NIPPV. Body mass index (BMI) was calculated for the period before and six, 12, and 24 months after starting NIPPV. Lung volumes were measured using the multibreath helium dilution technique and carbon monoxide transfer factor using the single breath technique.³

STATISTICAL ANALYSIS

Comparisons were made of values before and after commencing NIPPV. Analysis of variance (Friedman non-parametric ANOVA) and paired *t* tests were used to examine differences

between these two periods in terms of blood gas tensions, lung function, admissions to hospital, use of general practitioner resources, and body mass index. The results of parametric measurements are presented as mean (SD), mean difference, 95% confidence interval, and statistical probability.

Results

ARTERIAL BLOOD GAS TENSIONS

Individual patient data are shown in table 1, all whilst breathing air spontaneously: PaO₂ improved from a mean (SD) of 6.0 kPa (0.97) prior to NIPPV to 7.5 (1.2), (mean difference 1.5, 95% CI 0.56 to 2.57, *p* = 0.006) at six months, 7.8 (1.2) kPa (mean difference 1.78, 95% CI 0.69 to 2.8, *p* = 0.004) at 12 months, and 7.2 (1.1) kPa at 24 months (mean difference 1.27, 95% CI 0.42 to 2.12, *p* = 0.003).

Paco₂ fell from a mean (SD) value of 8.1 (1.3) kPa to 6.4 (1.2) (mean difference -1.73, 95% CI -3.15 to -0.32, *p* = 0.021) at six months, 6.40 (1.1) kPa (mean difference -1.66, 95% CI -3.04 to -0.28, *p* = 0.023) at 12 months, and 6.7 (0.9) kPa at 24 months (mean difference -1.35, 95% CI -2.59 to -0.11, *p* = 0.03).

Plasma bicarbonate concentration fell from a mean (SD) of 33 (3.3) mmol/l before NIPPV to 29 (3.7) mmol/l at six months (mean difference -3.64, 95% CI -7.27 to -0.002), 29 (3.9) mmol/l at 12 months (mean difference -3.63, 95% CI -7.11 to -0.17), and 30 (3.8) mmol/l at two years (mean difference -2.7, 95% CI -6.46 to 1.06). These results were not statistically significant.

SURVIVAL

Two patients died, one (patient 4) after 820 days and the other (patient 5) after 1522 days of NIPPV treatment, both of acute respiratory failure. Median survival is 920 days (range 686–1240).

SPIROMETRIC DATA

During the year following NIPPV, FEV₁ decreased from a mean (SD) of 34 (11.2)% predicted to 27 (8.9)% (mean difference -7.09, 95% CI -12.06 to -2.12, *p* = 0.012), and in the second year further to 26 (9.9)% predicted (mean difference -9.09, 95% CI -15.79 to -2.39, *p* = NS), and FVC decreased from a mean of 53 (9.2)% predicted to 49 (13.0)% (mean difference -3.45, 95% CI -13.5 to 6.59, *p* = 0.01). During the first year the FEV₁/FVC ratio fell from 47% predicted to 41% predicted (*p* = 0.016), and to 39% at the end of the second year (*p* = NS).

HOSPITAL ADMISSIONS

The median number of admissions to hospital before NIPPV was two per year (range 0-5); the median difference in admissions to hospital before and after NIPPV was 1.00 (95% CI 0 to 2). The duration of stay in hospital decreased from a median of 16 days (range 0-47) to 7 days (range 0-15), *p* = 0.023, median difference 1.00 (95% CI for median difference 2 to 25).

GENERAL PRACTITIONER RESOURCES

"General" consultations at the GP surgery per year fell following NIPPV, although this was not statistically significant (median difference 4.0, 95% CI -1.0 to 10). "Respiratory" consultations were also reduced (median difference 3.0, 95% CI -1 to 8.0) after commencing NIPPV, as were house calls (median difference 1.0, 95% CI -1.0 to 7.0). Patients on NIPPV were supported by the clinical nurse specialist and a telephone contact number was made available. No patient requested a home visit; a mean of 1.4 visits were initiated by the specialist nurse in the first year.

PATIENT SATISFACTION AND COMPLIANCE

Of the patients who fulfilled the criteria for NIPPV none withdrew from treatment. After two years patients were using NIPPV for an average of 6.5 hours each night. All patients had experienced relief of morning headache and excessive diurnal somnolence, and claimed improved sleep quality. There was no improvement in breathlessness; 75% claimed to be "very satisfied" with the treatment, and dissatisfaction in the remainder was related to skin ulceration on the bridge of the nose caused by the mask, a problem which was resolved in most cases by careful adjustment of the head harness.

There was no significant change in BMI or haematocrit levels before and after commencing NIPPV.

Discussion

We describe a group of patients with COPD in whom the use of LTOT was associated with symptomatic hypercapnia. They tended towards obesity which resulted in lung compression, as evidenced by the raised Kco, and this probably contributed to the tendency to hypoventilate, especially during sleep. All had severe airways obstruction. Improvement in blood gas measurements during the period of

treatment cannot be attributed to weight reduction.

Treatment with NIPPV resulted in a marked improvement in blood gas tensions and in symptoms, and a striking reduction in the frequency and length of admissions, GP consultations, and house calls. The reduction in the use of resources was not simply due to transfer of care to the respiratory nurse specialist. Most admissions were for adjustment of ventilator pressures and were of short duration whereas previously they were for treatment of ventilatory failure. These outcomes were sustained for the two year period of observation, despite gradually worsening ventilatory function.

In terms of severity of ventilatory function and respiratory failure, the patients were comparable to those in the MRC (LTOT)⁴ and NOTT⁵ series although insufficient data are available to make comparisons of BMI or lung mechanics. In those series the mean Pao₂ and Paco₂ were 6.7 kPa and 7.3 kPa, and 6.8 kPa and 5.8 kPa, respectively. A mean FEV₁ of 0.98 litres (37% predicted) in our patient group compares with 0.76 litres in the MRC trial and 29.5% predicted in the NOTT trial, and mean age and sex were similar. In the MRC (LTOT) trial about 45% of patients had died at three years, some 30% in the first 500 days whereafter the mortality fell to about 12% each year in the treated group. In the NOTT trial about 12% had died in the first 12 months, and 22% at two years. Those patients whose Sao₂ fell below 85% during sleep were at particular risk. Although arterial blood gas tensions of the patients in this series were more severely impaired, survival was considerably improved compared with those trials despite deteriorating pulmonary function. Although this is a group with a poor prognosis,⁶ no patient died during the first two years of treatment. The median survival was 920 days (the longest surviving for over four years), suggesting that intervention with NIPPV had a significant impact on survival.

Because there was no survival benefit until after 500 days (in men), the MRC trial suggested that patients with advanced disease might not be salvageable. The extended survival of our patients, however, lends support to the idea that NIPPV is an adjunct that should be considered in all cases of chronic type II respiratory failure unresponsive to LTOT, particularly where there is evidence of worsening hypoventilation during sleep. Addition of NIPPV to LTOT improves quality of life.⁷ LTOT alone does not,⁸ nor does it reduce the frequency of hospital admission.

Previous reports of the effects of NIPPV in type II respiratory failure due to chronic airways obstruction over shorter follow up periods have produced similar results, but not all patients in this category will respond so well.^{9, 10} Elliott *et al*¹¹ found that only seven out of 12 patients continued with treatment over 12 months. Those who did so had fewer symptoms (so may not have perceived the benefit), and others did so because of loss of confidence in equipment and possibly lack of training. We agree with Meecham Jones *et al*⁷ that these

patients take to their new treatment much more readily if they are stabilised during a period in hospital when the beneficial effects on excessive diurnal somnolence and intellectual function can be definitively demonstrated. Specialised nursing and medical support appears to be essential.

Domiciliary NIPPV produces significant and sustained improvements in arterial blood gas tensions in patients with severe COPD and hypercapnoic respiratory failure unresponsive to other treatments, reducing both hospital admissions and demand on general practitioner resources. Although the number of patients is small, the encouraging results of treatment suggest that prospective studies with clearly defined enrolment criteria in a larger group of patients are urgently required.

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Evidence for eosinophil activation in bronchiectasis unrelated to cystic fibrosis and bronchopulmonary aspergillosis: discrepancy between blood eosinophil counts and serum eosinophil cationic protein levels

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Abstract

Background—Increased serum levels of eosinophil cationic protein (ECP) have been detected in adolescent patients with cystic fibrosis. However, ECP concentrations in adult patients with bronchiectasis unrelated to cystic fibrosis have not been studied.

Methods—Eosinophil numbers and serum concentrations of ECP were determined in 14 patients with known or newly diagnosed bronchiectasis and compared with age and sex matched patients with allergic bronchial asthma, chronic obstructive pulmonary disease (COPD), and controls in whom bronchiectasis or obstructive pulmonary disease could be excluded.

Results—Serum ECP levels were significantly raised both in patients with bronchiectasis (median (range) 22.5 µg/l (7-85)) and allergic asthma (35.0 µg/l (7-128)) compared with the sex and age matched subjects suffering from COPD (6.7 µg/l (1.5-28); $p < 0.006$) and non-obstructive

normal controls (7.5 µg/l (3.5-19); $p < 0.003$). In contrast, significantly increased peripheral eosinophil numbers were observed in patients with bronchial asthma ($305 \times 10^6/l$; $p < 0.01$) but not in those with bronchiectasis ($10^2 \times 10^6/l$), COPD ($117 \times 10^6/l$), and healthy controls ($101 \times 10^6/l$).

Conclusions—The discrepancy between eosinophil counts and eosinophil numbers in patients with bronchiectasis suggests that serum ECP levels may be more relevant in assessing local eosinophil involvement than blood eosinophil numbers. (*Thorax* 1998;53:498-500)

Keywords: bronchiectasis; asthma; chronic obstructive pulmonary disease; eosinophil cationic protein

Bronchiectasis is associated with a vigorous bronchial inflammation due to frequent or persistent bacterial colonisation and increased numbers of neutrophils and neutrophil-derived products found in both bronchoalveolar lavage

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