Long-Term Non-Invasive Positive Pressure Ventilation among Cystic Fibrosis Patients Awaiting Lung Transplantation

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Abstract

Background: Pulmonary disease is the most frequent cause of morbidity and mortality in cystc fibrosis patients. New techniques such as non-invasive positive pressure ventilation have resulted in prolongation of life expectancy in CF patients with end-stage lung disease.

Objectives: To determine the role of NIPPV in CF patients awaiting lung transplantation.

Methods: Between 1996 and 2001 nine CF patients (5 females) with end-stage lung disease were treated with bi-level positive airway pressure ventilation in the "spontaneous" mode.

Results: The patients' mean age at initiation of BiPAP was 15 years (range 13–40 years) and the mean duration of BiPAP usage was 8 months (range 3–16 months). Four patients underwent successful lung transplantation, three patients died while awaiting transplantation, and the remaining two are still on NIPPV while waiting for transplantation. Patients' body mass index increased significantly ($P < 0.05$) during BiPAP therapy (from 16.1 to 17.2 kg/m^2). Blood pH, p_aCO_2, and bicarbonate improved significantly (from 7.31 to 7.38, 90.8 to 67.2 mmHg, and 48.9 to 40.3 mEq/L, respectively). Pulmonary function tests were not affected by BiPAP usage. The patients experienced a significant alleviation in morning headaches and improvement in quality of sleep ($P < 0.003$). There were no major complications during BiPAP usage.

Conclusions: We demonstrated that long-term NIPPV can stabilize and improve physiologic parameters such as ventilation, arterial blood gases and body mass index, as well as subjective symptoms such as sleep pattern, daily activity level, and morning headaches in CF patients with end-stage lung disease. Further prospectively controlled studies are needed to evaluate the potential of BiPAP therapy and its influence on morbidity and mortality in the post-lung transplantation period.

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Pulmonary disease remains the most frequent cause of morbidity and mortality among patients with cystic fibrosis. When forced expiratory volume in 1 second approaches 30% of predicted, 2 year mortality is greater than 50% [1]. In the last decade improvement in the overall management of CF patients together with the development of new techniques, such as non-invasive positive pressure ventilation, resulted in the prolongation of life expectancy among CF patients with end-stage respiratory disease [2].

Bi-level positive airway pressure is a non-invasive mode of ventilation administered through a tight-fitting mask. The device cycles spontaneously between the preset levels of inspiratory and expiratory positive airway pressures [3]. For some patients BiPAP may be a beneficial alternative to endotracheal intubation [2]. BiPAP has been used successfully in CF, neuromuscular disease, obstructive sleep apnea, and congenital central hypoventilation syndrome [4–6]. However, difficulty in handling upper airway secretion, heavy sedation, impending intubation, and coma are some of the contraindications for its use.

Studies using a BiPAP device demonstrated improvement in PaO_2, decreased $PaCO_2$ and reduction in surface diaphragmatic electromyography activity in patients with chronic obstructive pulmonary disease [7]. Moreover, other studies showed a successful outcome in patients with acute lung injury, acute respiratory distress syndrome, and status asthmaticus [8,9]. Furthermore, Sood at al. [2] demonstrated a beneficial effect of BiPAP in CF patients with acute respiratory failure hospitalized in an intensive care unit. Recently, BiPAP was used in CF patients with end-stage lung disease as a bridge to transplantation [3,10,11].

The aim of the present study was to determine the effect of NIPPV on subjective and objective parameters in CF patients awaiting lung transplantation.

Patients and Methods

From 1996 to 2001, nine CF patients were treated with NIPPV in our center. These patients, who had end-stage pulmonary disease and were accepted to the lung transplantation program, were given NIPPV treatment while awaiting lung transplantation.

All patients used the same BiPAP device (model S/T Respironics, Monroeville, PA, USA) applied through a full face mask (Respironics). The initial setting of the inspiratory cycle peak pressure was 6 cm H_2O while the expiratory positive airway pressure was set at 2–3 cm H_2O on the "spontaneous" mode of ventilation. Pressures were increased in increments of 2 cm H_2O and were adjusted to optimize patients' comfort, breathing pattern, chest excursion, breath sounds, hemoglobin saturation and blood gases. The maximal BiPAP settings reached an inspiratory positive pressure of 14–18 cm H_2O and an expiratory positive pressure of 4–6 cm H_2O. The BiPAP

CF = cystic fibrosis
NIPPV = non-invasive positive pressure ventilation
BiPAP = bi-level positive airway pressure ventilation

Table 1. Subjective assessment of patients' quality of life and work of breathing

	1	2	3	4
Activity tolerance	Bedridden	Active with O_2 supplement	Active without O_2 supplement	Normal activity
Sleep pattern	Restless with frequent arousal	Frequent arousal	Daytime somnolence	Good sleep
Morning headache	None	Mild	Moderate	Severe

The work of breathing was evaluated by heart rate, respiratory rate and accessory muscle.
The need for supplemental O_2 was quantified in liters.

Table 2. Patient characteristics

Patient	Gender	Age (yrs)	Genetics	BiPAP (months)	Trans-plant	Echo	Before BiPAP				During BIPAP			
							FEV_1	FVC	RR	HR	FEV_1	FVC	RR	HR
1	M	40	W1282X/W1282X	12	DL	Normal	13	19	35	105	15	15	30	95
2	M	34	ΔF508/W1282X	3	LR, BLT	Mild TR	14	30	36	90	14	15	36	90
3	F	25	W1282X/unknown	10	DL	Mild TR	16	30	40	90	16	30	35	95
4	F	22	ΔF508/ΔF508	3	DL	Rt CHF	17	26	35	100	17	26	35	100
5*	M	22	W1282X/G542X	12		Normal	15	25	40	100	15	26	30	85
6	M	27	ΔF508/?unknown	18		Normal	14	29	39	95	18	37	27	75
7	F	31	W1282X/W1282X	14		Mild TR	19	30	35	100	22	35	30	100
8*	F	13	ΔF508/ΔF508	1		Right CHF	17	26	40	120	17	26	40	95
9*	F	17	ΔF508/ΔF508	12		Mild TR	13	20	41		13	22		

* Died
DL = double lung transplantation BLT = blood clot lysis time RR = respiratory rate
TR = tricuspid valve regurgitation CHF = congestive heart failure HR = heart rate

was used during the night sleep as well as during day naps. All patients received oxygen supplementation ranging from 3 to 5 L/min during BiPAP therapy.

Prior to initiating BiPAP therapy, a pediatric pulmonologist explained the procedure, options and goals of therapy to the patients and their parents. The efficacy of BiPAP was determined by objective and subjective measures one year before and during utilization. Objective parameters included hemoglobin saturation, blood gases, body mass index as calculated by weight/height squared, and work of breathing (respiratory rate, heart rate, and accessory muscle use). Subjective parameters included sleep pattern, morning headaches, and physical activity. The assessments were performed monthly by the attending pulmonologist and were scaled ranging from 1 to 4, as suggested by Padman et al. [12] [Table 1].

Statistical analysis was performed using the BMDP statistical software (University of California Press, Los Angeles, CA). The data were analyzed using analysis of variance (ANOVA) with repeated measures. *P* values <0.05 were considered significant.

Results

From 1996 to 2001 nine patients with end-stage lung disease were evaluated (4 males, 5 females). The mean age at initiation of BiPAP was 25 years (range 13–40 years). The mean duration of BiPAP usage was 8 months (range 3–16 months). Patients' characteristics are given in Table 2.

Four patients underwent successful lung transplantation with 100% survival after 5 years of follow-up. Three patients died while awaiting lung transplantation. Two patients are still using BiPAP while waiting for transplantation. Most of the parameters assessed demonstrated an improvement after BiPAP usage.

Objective parameters [Table 3]
BMI increased significantly during NIPPV usage, from 16.1 to 17.2 kg/m^2 ($P < 0.05$). Blood gases also improved significantly. pH increased from 7.31 to 7.38 ($P = 0.01$), mean $PaCO_2$ decreased from 90.8 to 67.2 mmHg ($P = 0.003$), and bicarbonate levels decreased from 49.1 to 40.3 mEq/L ($P = 0.003$). However, PaO_2 did not change significantly. The work of breathing showed a tendency for improvement: the mean pulse of 100 beats per minute and the mean respiratory rate of 40 before NIPPV decreased to 88 and 37 respectively. Pulmonary function tests (FEV_1 and FVC) were not affected.

Subjective parameters
The subjective parameters all improved during the use of NIPPV. Morning headaches were significantly alleviated and sleep pattern

BMI = body mass index
FEV_1 = forced expiratory volume in 1 second
FVC = forced vital capacity

Table 3. Objective parameters

Patient	pH		PaO_2		$PaCO_2$		HCO_3-		BE		Hospitalizations*		BMI	
	Before BiPAP	After BiPAP	Before BiPAP	After BiPAP	Before BiPAP	After BiPAP	Before BiPAP	After BiPAP	Before BiPAP	After BiPAP	Before BiPAP	After BiPAP	Before BIPAB	After BIPAB
1	7.3	7.33	47	47	100	55	47	35	14	7	4	2	17	18
2	7.3	7.4	43	52	85	50	50	33	14	9	2	3	17	18
3	7.3	7.4	40	45	122	85	59	40	25	14	4	4	17	18
4	7.3	7.4	70	46	90	65	52	40	14	9	4	2	19	22
5**	7.3	7.4	35	40	90	55	54	40	14	10	4	4	18	19
6	7.4	7.4	60	60	60	50	37	33	9	8	3	2	17	19
7	7.3	7.4	55	50	85	60	43	37	14	11	2	2	15	16
8**	7.3	7.3	42	50	96	95	50	50	17	17	3	4	12	12
9**	7.3	7.35	50	45	90	90	48	55	16	17			13	13

* Number of hospitalizations during the year preceding BiPAP and during the first year of BiPAP use.
** Died

improved ($P < 0.003$ and 0.002 respectively) while activity tolerance demonstrated a tendency towards improvement.

There were no major complications that necessitated discontinuation of BiPAP usage. Two patients had hemoptysis while using BiPAP, and BiPAP was stopped for a week and then restarted. Four patients exhibited pressure sores and discomfort over the nose bridge which resolved with reduction of strap tension and the addition of a nasal bridge interface.

Discussion

In the current study we showed that the use of long-term non-invasive positive pressure ventilation improved acid base balance, blood gases, body mass index, and work of breathing in CF patients with end-stage lung disease awaiting lung transplantation.

CF is characterized by the destruction of lung parenchyma and the presence of obstructive airway disease with mechanical disturbance of the respiratory muscles and diaphragm. Previous investigators demonstrated that NIPPV in CF patients acutely improved oxygenation, increased minute ventilation and effectiveness of alveolar ventilation, and improved inspiratory and expiratory muscle strength [13,14]. The reduction in work of breathing and in spontaneous inspiratory effort, and the increment of effective alveolar ventilation [13] might explain the improvement in our patients' arterial blood gases.

Like Hill et al. [15], we demonstrated an increase in the BMI of all patients when NIPPV was used for a sufficient period (3–16 months). The reduction of the spontaneous inspiratory effort [14,16] and the resulting decrease in work of breathing and muscle energy expenditure might explain the improvement in BMI. In turn, the increased BMI and intermittent rest of respiratory muscle might increase respiratory muscle strength [14,17–19] and contribute to the observed decrease in work of breathing. Moreover, the increase in BMI is of major importance because poor nutritional status, low BMI, and lean body mass depletion are important risk factors for morbidity and mortality, especially when accompanying end-stage lung disease, and during the waiting period for lung transplantation [20,21]. Furthermore, BMI below the 25th percentile or <17 kg/m^2 was found to be a risk factor for mortality during the first 90 days following lung transplantation [22,23].

In addition to the improvement in respiratory parameters, we observed a significant improvement in sleep quality and daily activity levels, and a reduction in morning headaches up to 16 months of follow-up. Better quality of life may be explained by the improvement in oxygen saturation and PaO_2 and the reduction in $PaCO_2$ during all sleep stages [11,24]. Better quality of life and improved daily activity are important therapeutic goals in CF patients with severe lung disease and may facilitate patient involvement in training programs prior to lung transplantation [14,15].

BiPAP therapy was well tolerated by our patients although we did observe minor complications, mainly pressure sores and discomfort over the nose bridge which resolved with reduced strap tension and the addition of a nasal bridge interface and did not necessitate discontinuation of BiPAP therapy. In two patients who showed mild hemoptysis with no hemodynamic changes during NIPPV, usage was stopped for a week and then restarted without recurrence of hemoptysis.

The use of NIPPV can decrease the need for artificial airway placement and maintains the ability to communicate verbally, to cough and to swallow. BiPAP has been proposed as a salvage therapy for patients awaiting lung transplantation [10]. Since the waiting period for lung transplantation is almost 2 years [25], a reduction in the number of pulmonary exacerbations and of hospitalizations, improvement in nutritional status and gas exchange, and avoidance of invasive mechanical ventilation may result in increased patient survival to transplantation and have a significant impact on the patient's pre-transplantation quality of life. Furthermore, this improvement in patients' pre-transplantation status may result in increased survival following transplantation [21].

Conclusion

We have shown that long-term NIPPV can stabilize and improve physiologic parameters such as ventilation, arterial blood gases and BMI, as well as subjective symptoms including sleep pattern, daily activity level and morning headaches in CF patients with end-stage lung disease. Further prospectively controlled studies are needed to evaluate the potential of BiPAP and its influence on morbidity and mortality in the post-transplantation period.

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Women like silent men. They think they're listening.

Anonymous

Capsule

Lenin's malady – syphilis or not?

Lerner et al. from the Ben-Gurion University in the Negev and Shaare Zedek Medical Center in Jerusalem tried to analyze the illness of Lenin as depicted in the literature and from his physician journals. The authors state that the health of heads of states is not always handled in the same way as an incapacitating disability in ordinary professionals. Instead of suspension of responsibilities, the health status of political leaders is concealed, especially when the illness is perceived as stigmatizing, such as organic mental impairment or sexual disorder. The authors analyze the malady of Lenin (1870-1924) in the light of relevant and new medical information. It is hoped that this will accentuate the need for transparency when the health of a statesman is concerned. The authors conclude that the symptoms described and the use of salvarsan in Lenin's treatment point to a diagnosis of syphilis.

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