Sleep and neuromuscular disease: bilevel positive airway pressure by nasal mask as a treatment for sleep disordered breathing in patients with neuromuscular disease

Christian Guilleminault, Pierre Philip, Anstella Robinson

Abstract

***Objective*—Investigation of the therapeutic effects of bilevel positive airway pressure delivered by nasal mask in patients with neuromuscular disease.**

***Methods*—20 patients with neuromuscular disease were evaluated for symptoms of nocturnal sleep disruption. These symptoms included daytime tiredness, fatigue, sleepiness, and complaints of insomnia. The patients were studied with nocturnal polysomnograms and daytime multiple sleep latency tests (MSLT). Their immediate and long term responses to bilevel positive airway pressure were also investigated. The study took place at the Stanford University Sleep Disorders Clinic. Some of the polygraphic evaluations were performed with portable equipment in the patients' homes. The reported population comprised 20 patients, all of whom had progressive neuromuscular disease. Five of the patients were women. Four patients had muscular dystrophy, six had myotonic dystrophy, and two patients each had mitochondrial myopathy and glycogen storage disease. Two patients had post-traumatic lesions, one bulbar and the other phrenic. The remaining patients had vascular myopathy, unclassified myopathy, syringomyelia, and slow evolving spinocerebellar degeneration.**

***Results*—19 of the 20 patients accepted some form of non-invasive ventilation. All but one of these were initially maintained on bilevel positive airway pressure spontaneous (S) mode, although one patient required a switch to the timed (T) mode within a year. The mean expiratory positive airway pressure (EPAP) used was 4.5 with a range of 4 to 5 cm H_2O. The mean inspiratory positive airway pressure (IPAP) was 11.5, range 9 to 14 cm H_2O. Before treatment the MSLTs were $\leqslant$ 8 minutes in 11 of the patients. The overall mean score was 8.2 (SD) 1.3 minutes. After long term treatment the mean MSLT was 12.5 (SD 2) minutes and the mean ESS score was 7 (SD 3). During the mean 3.5 years of follow up, three patients needed supplemental oxygen at a flow of 0.5 to 1.0 l/min bled into their masks. Three patients with myotonic dystrophy presented continued daytime somnolence despite apparent adequate treatment of their sleep disordered breathing. This required the addition of stimulant medication to their regimen. During this time three additional subjects had to be switched to nasal mask intermittent positive pressure ventilation delivered by traditional volume cycled home ventilator (volume controlled NIPPV).**

***Conclusions*—Bilevel positive airway pressure delivered by nasal mask may be used successfully to treat sleep disordered breathing associated with neuromuscular disease. This device can be employed to assist nocturnal ventilation by either the spontaneous or timed mode. In the United States it is less expensive and easier to institute than volume controlled NIPPV and may be as efficacious as this mode if close surveillance and regular re-evaluation of the patient's status is maintained.**

(*J Neurol Neurosurg Psychiatry* 1998;**65**:225–232)

Keywords: neuromuscular disease; daytime sleepiness; multiple sleep latency test; bilevel positive airway pressure treatment

Stanford Sleep Disorders Clinic and Research Center, Stanford University School of Medicine, Stanford, CA, 94305, USA
C Guilleminault
A Robinson

Sleep Clinic, Bordeaux University School of Medicine, Bordeaux, France
P Philip

Correspondence to:
Dr Christian Guilleminault, Sleep Disorders Center, 701 Welch Road, Suite 2226, Palo Alto, CA 94304, USA. Telephone 001 650 723 6965; fax 001 650 725 7341.

Received 24 March 1997 and in final revised form 23 December 1997
Accepted 13 January 1998

Patients with neuromuscular diseases have been successfully improved with ventilation through tracheostomy and more recently with intermittent positive ventilation applied by nasal mask (NIPPV).[1–7] Several types of equipment have been used, but most commonly prescribed are the PLV 100 (Lifecare, Aspen Colorado, USA) and the Monnal-D (Vitalair L' Air Liquide, Paris France).[7] Despite these reports, it has been our experience that clinicians fail to recognise sleep disordered breathing in neuromuscular patients until after patients have wake manifestations of their disease.[8] This occurs even though respiratory embarrassment during sleep is an earlier, albeit more subtle, clue to their illness. NIPPV is most commonly prescribed by pulmonary specialists. It is started when patients present obvious daytime (wake) breathing impairments, Or when the illness is brought to medical attention secondary to an acute respiratory episode with abrupt degradation of health.

Our sleep disorders clinic is located in the San Francisco Bay area, a region with many neurologists and three university hospitals within a 200 mile radius. All patients seen in the clinic and reported here had primary care

Table 1 Demographic variables

Patient	Diagnosis	Sex	Age	EDS	NSD	BMI
1	MD 1	M	37	Y	Y	24.0
2	MD 2	M	33	Y	Y	22.0
3	MD 3	M	29	Y	Y	21.0
4	MD 4	M	41	Y	Y	21.5
5	MD 5	M	43	Y	Y	22.0
6	MD 6	M	36	Y	Y	23.0
7	Vasc myop	F	32	Y	N	22.0
8	Mito myop	F	44	Y	Y	26.0
9	Mito myop	F	37	Y	Y	23.0
10	Gly sto dz	M	32	Y	N	24.5
11	Gly sto dz	M	28	Y	Y	22.0
12	Limb gir MD	F	17	Y	Y	23.5
13	Duchenne MD	M	12	Y	N	18.0
14	Duchenne MD	M	14	Y	N	20.0
15	Duchenne MD	M	14	Y	Y	19.0
16	Myo unclass	F	43	Y	Y	27.0
17	Post tr phrenic	M	51	Y	Y	26.0
18	Post tr bulbar	M	24	Y	Y	23.0
19	Syringomyelia	M	39	Y	Y	21.0
20	Slow SCD	M	49	Y	Y	23.0
Mean	—	—	32.75	—	—	22.58
SD	—	—	11.66	—	—	2.27

BMI=body mass index (kg/m^2); EDS=excessive daytime sleepiness; NSD=nocturnal sleep disruption (Y=yes, N=no); MD=myotonic dystrophy; Vasc myop=vascular myopathy; Mitoch myop=mitochondrial myopathy; Glyc sto dz=glycogen storage disease; Limb gir MD=limb girdle dystrophy; Post tr phrenic=post-traumatic phrenic nerve paralysis; Post tr bulbar=post-traumatic bulbar lesion; Slow SCD=slow evolving spinocerebellar degeneration.

neurologists and 80% had at least one consultation at one of the three university hospitals in the area for their clinical symptoms, all had appropriate diagnosis of their neurological or muscle disorders. None had been treated for their sleep disordered breathing, despite the presence of sleep related symptoms for at least 12 months before initial presentation. Patients were seen in our own specialised clinic for their sleep related complaints.

Bilevel positive pressure treatment delivered by nasal mask (NPSV) has been widely used in patients with obstructive sleep apnoea syndrome with or without hypoventilation; and in chronic obstructive pulmonary disease. We think that it is underutilised as a first step in the treatment of patients with neuromuscular disease. Such patients most commonly not only have impairment of chest bellows that eliminates nasal continuous positive airway pressure (CPAP) as a treatment alternative, but may also have impairment of muscles located in the upper airway, particularly the airway dilators, which may be too weak to generate the necessary negative pressure to trigger a positive pressure ventilator. This is particularly true when patients present with sleep related problems, as repetitive arousals and sleep fragmentation ensue. The equipment can be easily titrated during one night of polygraphic recording. It has the advantages of simplicity and is a less costly machine than classic volume cycled home positive pressure ventilators. The specialist, however, must know the limits of this pressure based equipment and the type of follow up that is necessary to obtain the best result. This report focuses on the results obtained with nasal bilevel positive airway pressure (BiPAP™) treatment.

Table 2 Results of clinical trials at time T=0

Patient	RDI	Central %	ESS	SaO_2%	$ETCO_2$	TCO_2	MSLT
1	22	59	17	83	42	—	8
2	28	68	16	83	—	40	7
3	18	86	16	85	43	—	6.5
4	33	91	18	80	43	—	7.25
5	29	81	15	82	—	42	6
6	35	83	12	81	—	44	8
7	20	77	16	86	—	43	9
8	45	72	14	78	—	51	8.25
9	40	79	13	82	—	47	8.5
10	26	85	15	83	—	44	9
11	29	84	12	84	45	—	8.75
12	27	92	—	80	41	—	9.5
13	17	96	—	87	—	41	7
14	19	91	—	86	—	41	8
15	29	88	15	87	—	42	9.25
16	47	83	12	79	—	48	6.5
17	21	97	—	80	46	—	10
18	37	82	12	80	51	—	9
19	19	77	10	87	—	40	7
20	22	74	—	88	—	43	11
Mean	28.20	78.25	14.20	83.10	44.43	43.54	8.18
SD	8.96	8.00	2.27	3.07	3.36	3.31	1.30

RDI=respiratory disturbance index; Central %=percentage of RDI that is central apnoeas; ESS=Epworth sleepiness scale; SaO_2%=lowest saturation recorded overnight; $ETCO_2$=end tidal CO_2; TCO_2=transcutaneous CO_2; MSLT=multiple sleep latency test.

Patients and methods

POPULATION

The reported population comprised 20 patients (five women) who were seen for complaints of daytime sleepiness, tiredness and fatigue, nocturnal sleep disruption, and impairment of work and sociofamilial activities due to daytime somnolence. Table 1 presents demographics and diagnoses made by neurological clinics after clinical evaluations, EMG, nerve conduction velocity studies, and muscle biopsies. This population involved a wide array of neuromuscular diseases and thus formed a heterogeneous group, with some patients affected with rapidly evolving disorders whereas others had only a slowly progressive or nearly static disorder. Referrals to the sleep clinic came from neurologists in 50% of the cases (10 patients), pulmonary specialists in five cases, and from general practitioners in five cases. Referrals were made for suspicion of sleep disordered breathing in five cases, complaints of insomnia and nocturnal disrupted sleep in four cases, and unexplained daytime "fatigue-sleepiness" in 11 cases. All patients were seen during a 24 month period.

METHODS

All patients' clinical charts were reviewed; they then underwent a clinic interview and evaluation. They all had pulmonary function tests performed by their respective primary care centre within 8 weeks of having been seen by the sleep centre, sometimes after the sleep evaluation (4) but most often before the evaluation. They were asked to respond to a validated questionnaire with 800 questions on sleep and wakefulness (sleep questionnaire and assessment of wakefulness SQAW).[9] Sixteen were also asked to fill in a validated sleepiness scale, the Epworth sleepiness scale (ESS).[10 11] All patients then received polygraphic recordings during nocturnal sleep followed by a multiple sleep latency test (MSLT).[12] This is a daytime test wherein the patients are requested to take a nap at about two hour intervals, in standardised conditions, and where latency to sleep onset and latency to possible appearance of REM sleep is measured (table 2).

The following variables were systematically recorded during nocturnal sleep: EEG (C_3/A_2-

Table 3 Results of clinical trials at time T+4 weeks

Patient	*RDI*	*Central %*	*ESSS*	*SaO_2%*	*TCO_2*	*MSLT*
1	1.8	100	6	92	41	12
2	1.5	100	7	92	40	12
3	2.1	100	6	92.5	40	11
4	3	100	14	91	42	9.25
5	1.8	100	5	93	41	10
6	4	100	15	90	42	13
7	1	100	4	93	41	15
8	1	100	5	94	42	14
9	1.2	100	3	94.5	41	14.25
10	0.7	100	4	93	41	14.5
11	1.7	100	5	94	41	13
12	1.5	100	5	92	40	13.5
13	1.3	100	7	91	41	12
14	—	—	—	—	—	—
15	2	100	9	96	40	8.5
16	2.7	100	5	92	40	10.5
17	1	100	5	92	41	14
18	1	100	3	92	40	14.25
19	1.2	100	6	91	41	11.25
20	1	100	5	90	40	15
Mean	1.66	100	5.59	92.4	40.8	12.47
SD	1.00	0	2.00	1.4	1.1	1.97

C_4/A_1-O_1-O_2), chin and leg EMG, electro-oculogram, ECG (modified V_1), oronasal airflow, thoracic and abdominal efforts through bands, oesophageal pressure, pulse oximetry (Nellcor™) (Sao_2), transcutaneous CO_2 ($TcPo_2$) (Sensormedics™) or end tidal CO_2 ($ETco_2$) position, and intercostal diaphragmatic activity through two EMG electrodes placed in the 6th, 7th, or 8th right intercostal space depending on the best EMG response while awake supine. Oesophageal pressure monitoring, $TcPco_2$, Sao_2, leg and intercostal EMGs, oronasal airflow, and thoracoabdominal efforts were not monitored during the following daytime MSLT.

Respiratory events during sleep were characterised as central, mixed, or obstructive apneoas and hypopnoeas. Obstructive and mixed apnoeas and hypopnoeas were defined based on the presence of decreased or absent airflow and increased thoracoabdominal effort indicated by analyses of oesophageal pressure, cutaneous impedance bands, and intercostal EMG. Central apnoea was defined as the absence of airflow and thoracoabdominal inflection or oesophageal pressure changes. Central hypopnoeas were defined as a decrease in inspiratory effort based on analysis of oesophageal pressure (P_{ES}) with peak end inspiratory pressure of −3 cm H_2O, decrease in thoracoabdominal movements, and airflow not lasting longer than 120 seconds. Associated decreases in Sao_2 were confirmatory of abnormal breathing events. Hypoventilation was defined as presence of CO_2 retention for a minimum of 5 minutes, without the presence of apnoea or hypopnoea as here defined.

Once the diagnostic tests had been performed and demonstration of abnormal breathing during sleep and its type had been appropriately documented, patients came back to the laboratory within 1 to 15 days for titration of nasal BiPAP (the figure shows follow up plans). The same variables monitored during night 1 were again recorded. Titration was performed with the goal of eliminating any type of apnoea, hypopnoea, or hypoventilation during the first part of the night along with the associated EEG arousals. If, despite appropriate elimination of these breathing events, oxygen saturation was noted below 92%, low flow (0.25 to 1.0 l/m) 100% oxygen was then bled into the nasal mask through one of the lateral ports. Patients were sent home with this equipment for four weeks with the bilevel positive airway pressure device in the S mode—that is, NPSV. All patients were then brought back to the sleep laboratory and restudied during nocturnal sleep with re-evaluation of equipment settings and the need for low flow oxygen. This recording was performed with the patient's own mask and heated humidifier placed into the circuit. A repeat MSLT was performed and subjective response to treatment was assessed by a standard questionnaire (table 3). If the patient presented good control of his or her sleep disordered breathing and daytime sleepiness, they were again sent home with equipment as titrated and requested to contact the clinic if problems occurred. Home care companies regularly visited patients placed on low flow oxygen. Six months after the initial treatment, if no problems had occurred earlier, all patients had a clinic visit and an unattended ambulatory recording using a validated portable unit (Edentrace™). One year after the initiation of treatment, systematic overall re-evaluation was performed using the same standardised questionnaires, polygraphic recording, and MSLT (table 4). This yearly follow up re-evaluation was applied regularly to patients with long term follow up. Abnormalities in the ambulatory recording led to a new complete polygraphic evaluation. If intercurrent problems occurred, an ambulatory polygraphic recording was obtained as the first diagnostic intervention. If spontaneous breathing was not sufficient to maintain a respiratory rate at or above 12 bpm in the absence of apnoeas, hypopnoeas and falls in Sao_2, the T ventilation mode was used (pressure cycled nasal positive pressure ventilation ; NPPV). The imposed respiratory rate delivered continuously by the equipment was set during a new, formal, polygraphic recording. Patients started on this treatment mode had a routine follow up recording with the

Table 4 Results of clinical trials at time T+12–14 months

Patient	*BMI**	*RDI*	*Central %*	*ESSS*	*SaO_2%*	*TCO_2*	*MSLT*
1	23	3	100	9	93	41	12.5
2	22.5	1	100	10	92	40	11
3	21	2	100	8	92	42	12
4	21	3.8	100	14	90	43	8
5	22.2	1	100	11	92	43	10.5
6	23.1	8	98	9	89	44	10
7	21.7	0.8	100	6	94	40	14
8	26.3	0.9	100	7	95	42	14.25
9	22	1	100	8	95	41	14
10	25	0.5	100	3	94	41	15
11	22.2	2	100	5	93	42	14
12	23	2	100	8	92	40	11
13	19	1.5	100	9	91	43	10
14	—	—	—	—	—	—	—
15	17.8	3.2	100	12	95	44	9
16	26	3	100	11	91	41	11
17	25.8	1	100	4	92	41	15
18	23.8	0.8	100	7	92.5	42	13.5
19	20.5	1.5	100	9	90	42	12
20	23.2	0.6	100	6	91	40	13.5
Mean	22.61	1.88	99.9	7.80	92.63	41.60	12.12
SD	1.61	1.10	1.1	2.05	1.40	1.03	2.02

*BMI was remeasured at the 1 year check up.

Table 5 Pulmonary function

	Initial evaluation Median % of predicted (SD)	*Measurement 12 to 14 months Median % of predicted (SD)*
FVC (Sitting)	73 (20.6)	68.3 (23.3)
FEV_1 (Sitting)	69 (20.2)	67.9 (27.9)
MIF (cm H_2O)	43 (11.0)	36.8 (13.7)
MEF (cm H_2O)	43 (16.0)	40.0 (20.2)

ambulatory monitoring equipment at home about 4 weeks after this titration. If any further adjustment was needed, a second ambulatory study was performed within 7 days. Surveillance ambulatory monitoring was obtained every 3 months thereafter during the first 6 months in patients without complaints. At the yearly follow up all patients also had pulmonary function tests and evaluation of locomotor and neurological handicap performed by the appropriate laboratories and clinics (table 5; see flow chart).

Results

PATIENT SELECTION

The 20 patients reported here were part of a total group of 28 patients with neuromuscular disorders who were seen during the same time period. The eight patients not included in this report were within the same age range and the sex ratio was closely related. These eight patients were seen in relation to complaints of a sleep disorder, but were treated differently. One patient already had a tracheostomy and was ventilated through it at night. Four patients received 4 l/m 100% oxygen through nasal prongs during the daytime and were treated at night with NIPPV. One patient had mixed and obstructive sleep apnoea and was treated with nasal CPAP. The last two patients had no need for nocturnal ventilation, one with myasthenia gravis improved with the use of a long acting anticholinesterase medication at bedtime; the other had depression and insomnia.

PATIENTS CONSIDERED FOR NASAL BILEVAL POSITIVE PRESSURE VENTILATION

Diagnostic evaluation

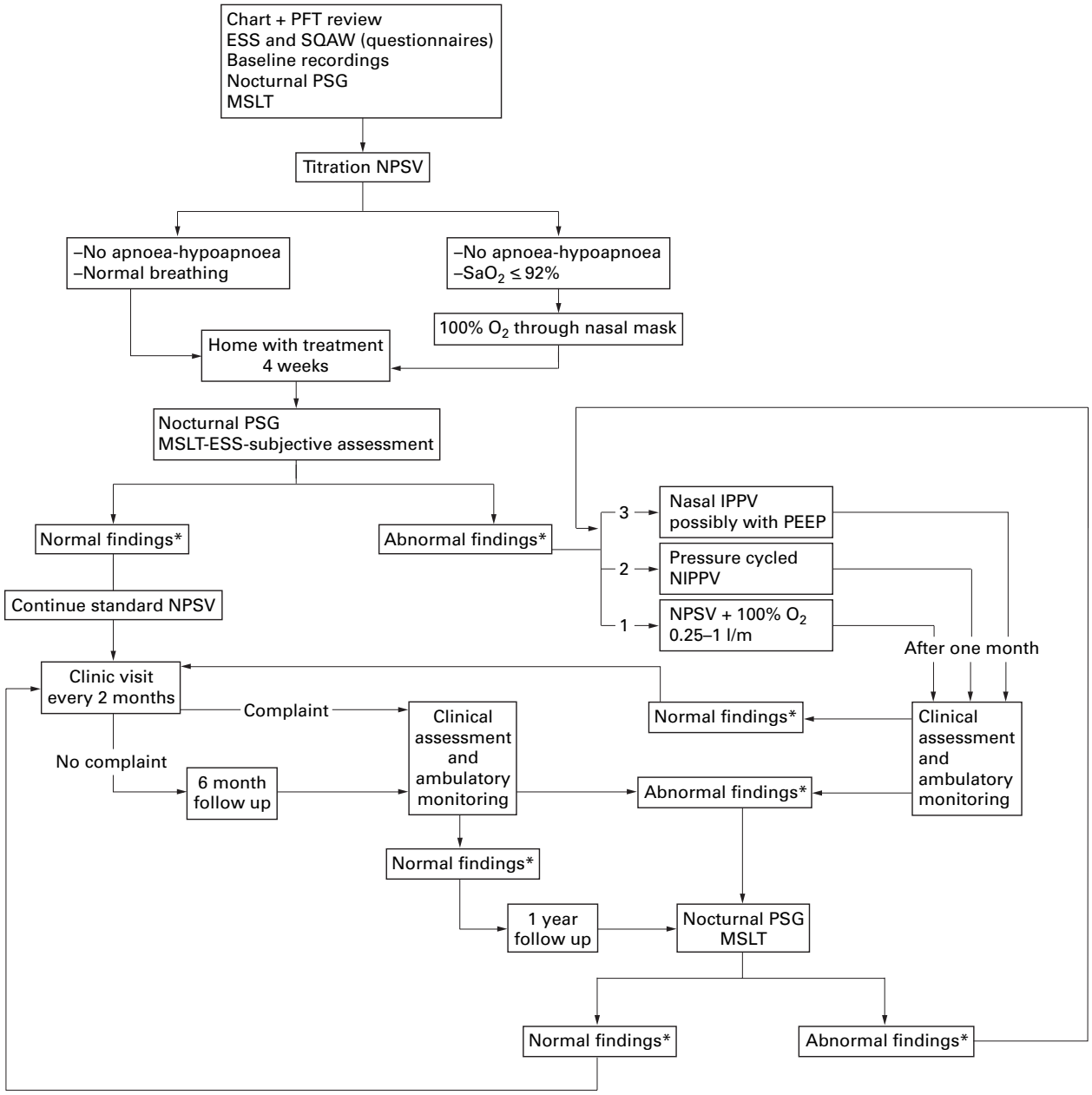
Our patients were all ambulatory and with a moderate neurological handicap when first seen—that is, 15 could climb stairs without support and five required assistance with stairs. Table 1 presents the ESS scores, nocturnal polygraphy, and MSLT results obtained at initial evaluation. Some ESS results are missing as the test was not available at the time of this evaluation for four patients. There was a discrepancy between the ESS scores and the results of the MSLT. All patients presented an ESS score>9 (reported as pathological in the validation studies of the scale[9 10]), although eight of the 16 patients with available ESS had an initial MSLT >8 minutes. MSLTs were≤ 8 minutes in only 11 of the studied patients; however, the overall mean score of 8.18 (SD 1.30) minutes was low.[13]

Pulmonary function tests, performed during the daytime, indicated that the median forced expiratory vital capacity (FVC) for the total population was 73 (SD 20.6)% of predicted when sitting. The median supine FVC (n=5) was 69.8 (SD 24.2)% of predicted, median forced expired volume in the first second (FEV_1) sitting was 69 (SD 20.2)% of predicted, median maximal static inspiratory force (MIF) was 43 (SD 11)% of predicted, and median maximal static expiratory force (MEF) was 43 (SD 16)% of predicted. There was a poor (although significant) correlation (Spearman *r*) between FVC and respiratory disturbance index at night (−0.26, $p<0.05$). There was no significant change in the pulmonary function tests one year after initial evaluation and treatment. The median sitting FVC was 68.3 (SD 23.3)% of predicted. The sitting FEV_1 was 67.9 (SD 27.9)% of predicted, the MIF was 36.8 (SD 13.7) cm H_2O and the MEF was 40.0 (SD 20.0) cm H_2O (table 5).

Transcutaneous CO_2 ($TcPCO_2$) was replaced by measurements of end tidal CO_2 ($ETCO_2$) in several patients, during nocturnal PSG. Tables 2, 3, and 4 show the respiratory disturbance index and lowest Sao_2. All patients presented a pathological number of apnoeas and hypopnoeas during sleep. These abnormal breathing events during sleep were scores of "central" type defined based on monitoring not only of airflow and thoracoabdominal bands, but also determination of effort as indicated by oesophageal pressure monitoring in more than 92% of the cases of the surveyed population. Nocturnal disrupted sleep was associated with these events and the mean percentage of stage 1 NREM sleep was 36 (SD 7)%. (Normal value for the laboratory in age matched controls=10 (SD 3)%.)

Initial results with BiPAP

Initially, 18 patients had satisfactory control of their sleep disordered breathing patterns with NPSV as shown by the follow up recording. Again, this was 4 weeks after the full nocturnal polygraphic recording during which the original calibration of the equipment was performed. The mean expiratory positive airway pressure (EPAP) was 4.5 with a range from 4 to 5 cm H_2O. The mean inspiratory positive airway pressure (IPAP) was 11.5, range 9 to 14 cm H_2O. Three subjects had low flow 0.5 l 100% oxygen bled into the mask. Patient 14 (20th subject) could not tolerate the equipment, and was unable to be treated with this approach. After treatment the mean MSLT was 12.47 (SD 1.97) minutes and the mean ESS score was 5.95 (SD) 2.00. The results of the post-treatment MSLT (MSLT2) presented in tables 1 and 5 are those obtained after the first demonstration of control of the sleep disordered breathing syndrome, 4 weeks after initial evaluation. Two patients (4 and 6) with myotonic dystrophy still complained of daytime somnolence and had ESS scores of 14 and 15 respectively at follow up, yet they had no objective findings of persistent sleep disordered breathing. MSLTs were mildly improved in these two patients with scores of 9 minutes 15 seconds and 8 minutes 30 seconds respectively. None of the patients presented increases in $TcPCO_2$ when monitored while using the ventilator. There was no statistical difference in the $TcPCO_2$ throughout the period of follow up



How patients were followed up showing the steps taken once a patient was recognised as needing bilevel positive airway pressure by nasal mask. It indicates, depending on the examination findings, the clinical conclusions drawn and the follow up treatment approach taken.

although there was a trend toward improvement (43.54 (SD 3.31) at evaluation 1 *v* 40.80 (SD 1.10) at evaluation 2 and 41.60 (SD 1.03) at evaluation 3 (tables 2, 3, and 4)).

FOLLOW UP

At the six month follow up one patient (15) presented repetitive falls in Sao_2 on his ambulatory study with a lowest Sao_2 of 79%. This patient was restudied with a nocturnal polygraphic recording. He presented again with a predominance of central apnoeas during sleep and was switched to low flow oxygen bled in the mask and to bilevel positive airway pressure treatment with equipment in the T mode. In his case response to the treatment was poor at first year follow up, with continued disordered breathing during sleep. Similarly, within the first 24 months, patients 12, 13, and 18 failed on treatment with bilevel positive airway pressure. All were switched to volume cycled NIPPV with a low positive end expiratory pressure (PEEP). This improved nocturnal ventilation for some time in each case. Patient 15 also had to be placed on volume cycled NIPPV after 18 months of follow up. In general, the Sao_2 improved with treatment, as would be expected (tables 2, 3, and 4). Overall, the RDI was reduced very significantly from initial evaluation to 12 to 14 months follow up; 28.65 (SD 7.05) at initial evaluation compared with 1.66 (SD 1.00) at 1 month and 1.88 (SD 1.10) at 1 year. Concomitantly, the relative percentage of central apnoeas rose to 100 (from 78.25 (SD 8.00)% at evaluation 1). Although at initial evaluation there was a discrepancy between the ESS score and MSLT in some patients there was a significant

decrease in the mean ESS score after one year—that is, the mean score decreased from 14.20 (SD 2.27) to 7.80 (SD 2.05) over a 1 year period. One month after the initial overnight polysomnogram the body mass index was not re-evaluated; however, it was not significantly changed one year later.

Statistical analyses of the results of the ESS, Sa_{O_2}, T_{CO_2}, and MSLT over the time of the three studies (about 1 year) were significantly different. Multivariate repeated measures analysis using the Wilks' lambda test yielded a p value<0.01 in each case. Also, repeated measures of analysis of variance (ANOVA) over the three studies showed significant *F* values for ESS, Sa_{O_2}, TcP_{CO_2}, and MSLT.

Currently, the mean follow up is 3.5 years with a range from 30 months to 5 years. Some IPAP adjustments had to be performed in 10 patients and low flow 100% oxygen (0.5 l/min) had to be added in two patients.

In conclusion, one patient could not tolerate the nasal mask from the start, four patients had to be switched to volume cycled NIPPV during the first 2 years, and 10 patients needed adjustment of the initially determined EPAP and IPAP. Six patients needed low flow oxygen bled into their masks, three of whom subsequently switched to volume cycled NIPPV. Despite appropriate control of sleep disordered breathing, daytime sleepiness was still significant in three patients (3, 4, 5) with myotonic dystrophy (two of them nearly from the start); and stimulant medications had to be add to their daily medical regimen.

We had no skin lesions involving nose or cheek and no chronic eye irritation noted in our population (although this does not eliminate the possibility of these chronic problems of nocturnal nasal ventilation occurring). We systematically used heated humidifiers that improve comfort and probably avoided some chronic reactive rhinitis. Oral leaks were minimal.

Comments

NASAL BILEVEL POSITIVE AIRWAY PRESSURE VERSUS OTHER VENTILATORY TECHNIQUES

Previously, volume cycled NIPPV has been used successfully in neuromuscular syndromes associated with sleep disordered breathing.[1–7] Bilevel positive airway pressure administered by nasal mask (NPSV mode or pressure cycled NIPPV mode) is less costly here in the United States. This method of ventilatory support is less complicated to initiate than volume cycled NIPPV; yet may improve quality of life of many patients whose sleep related symptoms are currently underdiagnosed. Undoubtedly, bilevel positive airway pressure given by nasal mask is not always as efficacious as traditional volume cycled ventilation. Recently, particularly in Europe, new equipment has been made available that can improve the performance of bilevel positive airway pressure devices. However, for mild to moderate sleep disordered breathing this approach may be successful for several years and the simpler and more economical spontaneous mode equipment may maintain appropriate ventilation during sleep. Improvements in ventilation are limited with bilevel positive airway pressure machines, as these devices generate a maximum inspiratory pressure of only 30 cm H_2O compared with volume cycled home ventilators. The new generation of variable flow pressure cycled devices are equipped with a "rise time" as well as the expanded range of pressures; this functions as a rudimentary flow adjustment.

Statistical evaluation of different indices of quality of sleep (including subjective and objective measures) in our patients showed a significant improvement of each over time. There was a significant reduction in daytime sleepiness after treatment as measured by the Epworth sleepiness scale and multiple sleep latency test. Sa_{O_2} and TcP_{CO_2} were also greatly improved after the institution of bilevel positive airway pressure therapy. This improvement was still present at the 18 month follow up.

A study of nasal intermittent positive pressure ventilation over 18 months in eight patients disclosed an improvement of lung function and blood gas indices during the day.[14] Unlike most of the literature available this was a cohort of patients with pure neuromuscular disease (no chronic obstructive lung disease). The RDI was essentially eliminated and sleep architecture and efficiency improved. The patients in this study were treated with a volume cycled portable ventilator.

A recent study[15] compared volume cycled flow generators, bilevel positive airway pressure, and continuous positive airway pressure for effects on ventilation and inspiratory muscle support. The authors studied 12 patients, five of whom had chronic airflow obstruction and seven of whom had chest wall/neuromuscular disease. Unlike our patients they were all using nocturnal ventilatory support before enrollment in the study. Their pulmonary function tests were, on average, worse than those in our patients especially because of those persons with chronic airflow obstruction. The differences notwithstanding, the study disclosed volume cycled flow generators and bilevel positive airway pressure to be of equal efficacy in delivering non-invasive ventilatory support overnight in these patients. The authors suggest that bilevel positive pressure treatment delivered by nasal mask may be more accessible in those with chronic lung disease because of the lower cost. This was with the understanding that patients must be able to adequately trigger the ventilator.[15 16]

Another recent study investigated 11 wake patients with chronic ventilatory deficiency in a study wherein spontaneous ventilation, bilevel positive airway pressure, inspiratory positive airway pressure, volume cycled flow generators, and continuous positive airway pressure were compared.[17] As with the previously described study these patients were receiving non-invasive ventilation with volume cycled flow generators before the evaluation. As in the previous study six of the 11 patients had chronic airway obstruction. Five of the patients had kyphoscoliosis and one of those cases was complicated by asthma. Although their lung function was comparable except for worse CO_2

concentrations (while awake), this was primarily a physiological study of several variables, over short intervals (five minutes), in each modality. Nevertheless the authors concluded that there was no difference in efficacy between volume cycled flow generators and bilevel positive airway pressure techniques compared with spontaneous ventilation. Bilevel positive airway pressure caused the largest increase in tidal volume and reduction in respiratory rate. They both increased oxygen saturation and inspiratory muscle unloading to an equal degree. By contrast, continuous positive airway pressure worsened oxygen saturation.[17]

In 1995 Ferguson and Gilmartin[18] indicated that bilevel positive airway pressure ventilatory assistance may not necessarily reduce hypercapnia ($Paco_2$). As mentioned, our group of patients had no evidence of hypoventilation (CO_2 retention) as defined, with the monitoring equipment used. Undoubtedly some more severely affected patients with neuromuscular disease may present sleep related hypoventilation (particularly during REM sleep) even if hypoventilation is not seen during wakefulness. This may be related to the further decrease in inspiratory efforts due to the loss of non-specific respiratory stimuli with sleep onset, REM sleep related atonia, and sleeping position. There is a leak port in the mask but these authors[18] found that CO_2 may not always be cleared adequately when using the standard exhalation device. Despite an increase in minute ventilation, a relative hypercapnia was noted due to exhalation past the exhalation device and subsequent rebreathing of exhaled gases and increased dead space. The replacement of the usual valve by a non-rebreather valve eliminated CO_2 rebreathing and had no effect on the overall beneficial effect of the equipment. This finding emphasises again the need for regular follow up of these patients with appropriate sleep recordings. We have not seen this problem and, to date, have not needed to change any of the equipment valves for our patients.

An additional point must be made about using the classic intermittent positive pressure ventilation delivered by nasal mask and not BiPAP by nasal mask. Too often, follow up sleep studies are not done, and pressures are set to deliver a volume at a specific rate during sleep based on wake studies and the cycling ventilator is fitted at a negative pressure "x" and a positive pressure of 2 cm H_2O, sometimes 3 cm H_2O. In patients with neuromuscular disorders, particularly those with generalised disease, there may be an impairment of upper airway dilators, particularly during REM sleep. When the physiological REM sleep related atonia begins, a volume ventilator may induce mixed or obstructive events as the negative intrathoracic pressure necessary to trigger the device may be too large for the weakened upper airway dilators. The type of volume ventilator prescribed is important as a positive end expiratory pressure may have to be dialed to appropriately oppose this machine induced side effect. Also, investigation of patients with neuromuscular diseases with a simple pulse oximeter during sleep may not be sufficient as an arousal response can be triggered much before a drop in Sao_2 of 3% or more is seen. This arousal response will induce sleep fragmentation. Ambulatory monitoring equipment may miss this problem also as few of these monitor EEG. Those without EEG recording may, however, be helpful if attention is given to simultaneous abrupt and transient changes in amplitude in breathing associated with increase in heart rate, or if the equipment gives some indication of abrupt change in blood pressure, such as those measuring pulse transit time.

It is often questioned why CPAP is not used as a first line treatment in neuromuscular patients. Certain patients with "central" apnoea and hypopnoea may have "central" events during sleep, only because of hyperventilation after a short arousal and very rapid return to sleep, or secondary to an incompletely elucidated mechanism which involves upper airway reflexes with abrupt upper airway occlusion and secondary inhibition of diaphragmatic activity. The distinction between the different causes of central apnoeas during sleep should have been made at the diagnostic phase, before treatment is considered. If an upper airway occlusion during sleep is suspected in a neuromuscular patient (for example, in some patients with Shy-Drager syndrome or certain patients with postpoliomyelitis syndrome with predominant impairment of 12th cranial nerves), nasal CPAP may be helpful. But most commonly in neuromuscular patients, thoracoabdominal impairment during sleep is the primary defect and nasal CPAP is ineffective. This outlines the importance of a proper diagnostic monitoring during sleep before treatment selection.

From our experience, it seems that patients who require timed mode bilevel positive airway pressure or associated low flow oxygen have been the ones who went on to require volume controlled NIPPV.[19] This finding indicates the contribution of the central control of breathing, and the relative severity of the patient's disease. Whether this treatment approach should have started from the beginning is open to question. The point can be made, however, that instituting bilevel positive airway pressure is much more convenient; and that with close follow up, patient care is not compromised. Also, most probably, our patients were treated at an earlier stage of breathing impairment than previously reported. The complaint treated here was a sleep disorder that impinged on the daytime quality of life of the patient. It was not based on a significant pulmonary abnormal result at systematic follow up during the daytime in a pulmonary clinic.

DAYTIME PULMONARY STUDIES VERSUS NOCTURNAL RECORDING

It should also be re-emphasised that published studies comparing wakeful pulmonary function tests and sleep studies have failed to show a good correlation between wake and sleep findings. It is obvious, for example, that wakeful pulmonary function studies will not predict the frequency of sleep EEG arousals related to

the sleep related breathing changes seen in neuromuscular patients.

DAYTIME SOMNOLENCE, QUALITY OF LIFE, AND NEUROMUSCULAR DISORDERS

Daytime somnolence may not be completely controlled with appropriate treatment of sleep disordered breathing, particularly in patients with myotonic dystrophy. Independent of underlying dysfunction; daytime sleepiness may persist after treatment of the sleep related breathing disorder has been optimised, and stimulant medication may be an helpful adjunct.

QUALITY OF LIFE, ECONOMIC IMPACT, AND NASAL VENTILATION IN NEUROMUSCLAR DISORDERS

Our patient cohort is much too small for comparison with the large follow up investigation reported by Leger *et al* in 1994[7] on the use of nasal IPPV and its impact on the number of days spent in hospital before and after beginning treatment with nasal ventilation. This team did one of the rare outcome studies on the subject. Their patient population included 16 with Duchenne type muscular dystrophy and these authors emphasise that these 16 patients also spent fewer days in hospital during NIPPV ($p<0.003$) than before treatment. If this is confirmed, early recognition and appropriate treatment of sleep disordered breathing in neuromuscular patients should be important to obtain not only improved quality of life for patients but also for containment of healthcare costs.

This study was supported by General Clinical Research Center Grant 0070 from The National Institutes of Health. We are grateful to Molly Haselhorst for editing the manuscript and preparing the figure.

1 Leger P, Madelon J, Jennequin J, *et al.* Non-invasive home IPPV by nasal mask in ventilator dependent patients with musculoskeletal disorders: an efficient alternative to tracheostomy [abstract]. *Am Rev Respir Dis* 1987;**135**:A193.
2 Ellis ER, Bye PTB, Bruderer JW, *et al.* Treatment of respiratory failure during sleep in patients with neuromuscular disease. *Am Rev Respir Dis* 1987;**135**:148–52.
3 Kerby GR, Mayer LS, Pingleton SK. Nocturnal positive pressure ventilation by nasal mask. *Am Rev Respir Dis* 1987;**135**:738–40.
4 Carroll N, Branthwaite MA. Control of nocturnal hypoventilation by nasal intermittent positive pressure ventilation. *Thorax* 1988;**43**:349–53.
5 Leger P, Jennequin J, Gerard M, *et al.* Home positive pressure ventilation via nasal mask for patients with neuromuscular weakness or restrictive lung or chest wall disease. *Respir Care* 1989;**34**:73–9.
6 Branthwaite MA. Non-invasive and domiciliary ventilation: positive pressure techniques. *Thorax* 1991;**46**:208–12.
7 Leger P, Bedicam JM, Cornette A, *et al.* Nasal intermittent positive pressure ventilation: long term follow up in patients with severe chronic respiratory insufficiency. *Chest* 1994;**105**:100–5.
8 Labanowski M, Schmidt-Nowara W, Guilleminault C. Sleep and neuromuscular disease: frequency of sleep disordered breathing in a neuromuscular disease clinic population. *Neurology* 1996,**47**:1173–80.
9 Stanford Sleep Disorders Clinic and Research Center Sleep Questionnaire and assessment of wakefulness (SQAW). In: C Guilleminault, ed. *Sleep and waking disorders indications and techniques.* Menlo Park, CA: Addison-Wesley, 1982: 384–413.
10 Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991;**14**: 540–45.
11 Johns MW. Reliability and factor analysis of the Epworth sleepiness scale. *Sleep* 1992;**15**:376–81.
12 Carskadon MA, Dement WC, Mitler MM, *et al.* Guidelines for the multiple sleep latency test (MSLT); a standard measure of sleepiness. *Sleep* 1986;**9**:519–24.
13 Van der Hoed J, Kraemer H, Guilleminault C, *et al.* Disorders of excessive daytime somnolence; polygraphic and clinical data for 100 patients. *Sleep* 1981;**4**:23–37.
14 Barbe F, Quera-Salva MA, de Lattre J, *et al.* Long-term effects of nasal intermittent positive-pressure ventilation on pulmonary function and sleep architecture in patients with neuromuscular diseases. *Chest* 1996;**110**:1179–83.
15 Restrick LJ, Fox NC, Braid G, *et al.* Comparison of nasal pressure support ventilation with nasal intermittent positive pressure ventilation in patients with nocturnal hypoventilation. *Eur Respir J* 1993;**6**:364–70.
16 Meecham Jones DJ, Wedzicha JA. Comparison of pressure and volume preset nasal ventilator systems in stable chronic respiratory failure. *Eur Respir J* 1993;**6**:1060–4.
17 Elliott MW, Aquilina M, Green J, *et al.* A comparison of different modes of non-invasive ventilatory support: effects on ventilation and inspiratory muscle effort. *Anaesthesia* 1994; **49**:279–83.
18 Ferguson GT, Gilmartin M. CO_2 rebreathing during BiPAP ventilatory assistance. *Am J Respir Crit Care Med* 1995;**15**: 1126–35.
19 Strumpf DA, Carlisle CC, Millman RP, *et al.* An evaluation of the respironics bilevel CPAP patient device for delivery of assisted ventilation. *Respir Care* 1990;**35**:415–22.