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Long-term noninvasive ventilation in children and adolescents with neuromuscular disorders

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Long-term noninvasive ventilation in children and adolescents with neuromuscular disorders. U. Mellies, R. Ragette, C. Dohna Schwake, H. Boehm, T. Voit, H. Teschler. ©ERS Journals Ltd 2003.

ABSTRACT: The aim of the current study was to investigate the long-term impact of nocturnal noninvasive (positive-pressure) ventilation (NIV) on sleep, sleep-disordered breathing (SDB) and respiratory function in children and adolescents with progressive neuromuscular disorders (NMD).

Thirty patients (12.3±4.1 yrs) with various inherited NMD were treated with NIV for ventilatory insufficiency (n=14) or symptomatic SDB (n=16). Patients were prospectively followed with sleep studies, spirometry and peak inspiratory muscle pressure. Ten patients were studied before and after 3 nights withdrawal from NIV.

NIV normalised nocturnal gas exchange in all patients and diurnal gas exchange in patients with ventilatory insufficiency. The effects persisted over 25.3±12.7 months. Nocturnal transcutaneous partial pressure of carbon dioxide improved from (baseline *versus* latest control) 7.1±1.3 to 5.5±0.6 kPa (53.7±9.9 to 41.6±4.8 mmHg), diurnal carbon dioxide arterial tension from 6.3±1.6 to 5.4±0.5 kPa (47.5±11.9 to 40.6±3.6 mmHg).

NIV improved respiratory disturbance index, arousals from sleep, nocturnal heart rate and sleep architecture. Vital capacity decreased in five adolescents with Duchenne muscular dystrophy -183±111 mL·yr^{-1} but remained stable in 25 children with other conditions (8±78 mL·yr^{-1}). Three nights withdrawal of NIV in 10 previously stable patients resulted in prompt deterioration of SDB and gas exchange back to baseline but could be instantly normalised by resumption of NIV.

Noninvasive (positive-pressure) ventilation has favourable long-term impact on nocturnal and diurnal gas exchange and sleep and in patients with non-Duchenne neuromuscular disorders on vital capacity as well. It is indicated in children and adolescents with symptomatic sleep-disordered breathing or ventilatory insufficiency due to neuromuscular disorders.

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Respiratory muscle weakness is the inevitable consequence of many childhood neuromuscular disorders (NMD). It causes severe ventilatory restriction, results in progressive respiratory failure, and is the major cause of early death. Respiratory failure relates directly to the loss of respiratory muscle force and vital capacity and shows characteristic evolution from normal ventilation during daytime and sleep-induced hypopnoeas at mild degrees of ventilatory restriction, to rapid eye movement (REM) and non-REM sleep hypoventilation in severe ventilatory restriction [1, 2]. Continuous hypoventilation, common at inspiratory vital capacity (IVC) <40% predicted, precedes daytime hypercapnia. Daytime respiratory failure is highly prevalent at IVC <20% pred [2], and represents an accepted indication for supportive noninvasive (positive-pressure) ventilation (NIV). NIV, applied intermittently and preferably during sleep, relieves respiratory muscles from the work of breathing and augments alveolar ventilation [3–5].

In adolescents with Duchenne muscular dystrophy (DMD) and adults with various slowly progressive NMD or restrictive thoracic disease it has been shown that NIV applied during sleep, consistently improves diurnal and nocturnal gas exchange [5–8], symptoms and quality of life [9–12] and survival [6, 13]. NIV, therefore, is considered as a highly effective treatment of chronic respiratory failure due to NMD and a consensus conference has recently published guidelines on the initiation of NIV including NMD [14]. Evidence of benefit, however, is only based on nonrandomised studies and remains scant in the paediatric setting, particularly in NMD other than DMD [15, 16]. One earlier study of 10 children with nocturnal hypoventilation reported effective treatment but poor tolerance in patients <10 yrs [17]. Another recent study including mixed NMD reported immediate improvements of nocturnal gas exchange in 21 subjects and good mask tolerance over time, but presented no long-term data on gas exchange or lung function [18]. The gap between expanding use of NIV in the paediatric setting and understanding of its long-term effects in children therefore remains wide [19].

The present authors conducted this study to prospectively investigate the effects of nocturnal NIV on: 1) daytime and nocturnal gas exchange, 2) sleep and sleep-disordered

breathing (SDB), and 3) lung and respiratory muscle function in children with DMD and a wide variety of NMD other than DMD over a period of 3 yrs.

Methods

Subjects

Since 1997 nocturnal NIV had been started in 38 children with progressive NMD. Eight children had been excluded from the study; six <5 yrs because no lung function could be obtained and two because no regular follow-up had been possible. The remaining 30 children and adolescents, 16 female and 14 male (aged 12.3±4.1 yrs, range 6–19 yrs) were studied.

Indications for NIV were daytime ventilatory insufficiency (n=14) or symptomatic SDB (n=16). Nine subjects had congenital muscular dystrophy (12.2±3.4 yrs), five had DMD (16.6±1.5 yrs), six had intermediate spinal muscular atrophy type I–II (SMA, 7.7±1.0 yrs), five had SMA type II (10.0± 3.3 yrs), two had the juvenile type of acid maltase deficiency (17 and 19 yrs) and one each had hereditary motor and sensor neuropathy type I (12 yrs), centronuclear myopathy (8 yrs), or nemaline myopathy (14 yrs). A paediatric neurologist had assessed all patients and the diagnosis had been confirmed at the histopathological and at the molecular level where applicable. Eighteen patients (10 subjects with SMA, seven with CMD and one with DMD) experienced $\geqslant$3 chest infections per year necessitating antibiotic treatment. Twenty-three subjects had moderate-to-severe scoliosis of whom 14 underwent spinal stabilisation prior to initiation of NIV, 24 subjects were wheelchair users.

Lung and respiratory muscle function

IVC, forced expiratory volumes (forced vital capacity (FVC), forced expiratory volume in one second (FEV1)) and peak inspiratory muscle pressure (PIP) were measured with a hand-held spirometer/manometer (ZAN Meßgeräte, Obertulba, Germany). The best of three consistent efforts (<5% variability) was used. Predicted values of IVC were derived from published data [20, 21], predicted values of PIP (kPa) were calculated with the equation 2.43+(age×0.34) [21]. Arterial blood gas tensions were determined on room air from arterialised ear lobe blood in an automated blood gas analyser (AVL 500, AVL LIST; GmbH Medizintechnik, Graz, Austria). Ventilatory insufficiency was defined as daytime carbon dioxide arterial tension (Pa,CO_2) >6 kPa (>45 mmHg).

Sleep studies

Initial sleep studies were performed as full polysomnography (PSG, n=22) or cardiorespiratory polygraphy (n=8) including transcutaneous partial pressure of carbon dioxide (Ptc,CO_2 Radiometer, Copenhagen, Denmark) measurements. They were recorded onto a computerised work station (Embla 2.0, Flaga Medical Devices, Reykjavik, Iceland) scored manually and interpreted according to current guidelines [22, 23]. The Ptc,CO_2-device was calibrated before every measurement and adjusted to the patient's Pa,CO_2. No oxygen was supplemented. Studies were terminated prematurely in two subjects, one with diurnal respiratory failure and the other with severe nocturnal hypoxaemia, for immediate institution of NIV. SDB was considered present if the respiratory disturbance index was >10 events per hour, and nocturnal hypoventilation was defined as Ptc,CO_2 >6.7 kPa (>50 mmHg) for >50% of total sleep time [24].

Technique of noninvasive ventilation

NIV was applied by pressure-preset ventilators cycling in pressure-assist mode (BIPAP harmony; Respironics, Murrisville, PA, USA; Helia; Saime, Savigny Le Temple, France; VPAP II ST; Resmed Ltd., Sydney, Australia). Ventilator settings were chosen at the bedside with help of individual pressure-volume titration curves, and with the aim to increase tidal ventilation, suppress patient respiratory trigger effort, and optimise patient-ventilator synchrony. Adjustments were made during the following overnight sleep study with the aim of normalisation gas exchange (mean oxyhaemoglobin saturation (Sa,O_2) $\geqslant$95% and mean Ptc,CO_2 $\leqslant$6.7 kPa ($\leqslant$50 mmHg)) and completely suppressing SDB. Ventilator setting averaged as follows: inspiratory positive airway pressure 13.9±3.1 cmH_2O (range 8–19 cmH_2O), expiratory positive airway pressure 4.4±1 cmH_2O (range 3–8 cmH_2O), backup respiratory rate 19.6±2.5 beats per minute (bpm) (range 14–24 bpm).

Masks were selected to ensure comfortable but air-tight seal. The mirage full face mask (Resmed, Sydney, Australia, n=10) was used most frequently, besides custom-made masks [25] covering nose and mouth (n=7) and nose only (n=8), and other commercial nose masks (n=5). Ventilators for patients using a face mask were equipped with battery and low pressure and power failure alarms. Patients and caregivers were trained in equipment use. Eighteen subjects with frequent chest infections or a peak cough flow <150 $L \cdot min^{-1}$ were also instructed in assisted coughing using an intermittent positive-pressure breathing device for hyperinsufflation.

Follow-up

Follow-up after initial investigation and institution of NIV was at 3–6 (n=30), 12–18 (n=30), 24–30 (n=20), and $\geqslant$36 months (n=9). It included lung and respiratory muscle function tests, arterial blood gas (ABG) on room air after at least 8 h of spontaneous breathing, and PSG/polygraphy with capnometry during nocturnal NIV. Changes of ventilator settings or masks were made where necessary. Self-reported NIV use was controlled by reviewing the gauge of the ventilator. Thirteen patients were included in a study examining the impact of NIV on quality of life [9, 12].

Withdrawal from noninvasive ventilation

After at least 6 months of successful NIV all patients were asked to take a 3 night break from NIV prior to the following control visit. It was emphasised that patients should resume NIV in case of recurring symptoms. Ten of the 30 patients who completed the trial were re-evaluated after 3 nights without NIV and after 2 nights resumption of NIV.

Statistical analysis

Influence of NIV on gas exchange, lung function and sleep was analysed using the paired Wilcoxon test and the Spearman's rank correlation test. Group comparison between the distinct NMD and the impact of NIV withdrawal was tested using analysis of variance (ANOVA). All results are presented as mean±SD. The p-value $p<0.05$ was considered as significant.

Table 1. – Influence of noninvasive ventilation (NIV) on nocturnal and daytime gas exchange

NMD	Patients n	Duration month	Sa,O_2 %		Ptc,CO_2 mmHg		Pa,O_2 mmHg		Pa,CO_2 mmHg	
			Before NIV	During NIV	Before NIV	During NIV	Before NIV	After NIV	Before NIV	After NIV
MD	5	29.4±9.8	94.4±1.9	95.6±1.2	52.0±4.5	42.8±7.1*	82.8±16.2	88.8±11.6	45.9±7.4	41.9±2.4
Congenital MD	9	20.7±10.9	89.7±8.9	96.2±1.4*	56.6±8.1	42.2±3.9**	74.5±20.5	85.6±7.5	49.7±12.1	41.1±2.7
Neuropathy	12	25.3±11.7	92.5±5.9	96.7±2.0*	48.7±8.9	40.0±4.8	80.7±18.1	89.8±12.7*	41.9±10.1	38.6±3.7
Other myopathies	4	30.0±21.8	81.2±10.0	96.2±0.5**	64.5±12.8	43.8±2.8**	65.3±18.8	93.3±8.8	60.9±12.8	44.1±3.3**
Mean±SD	30	25.3±12.6	90.5±7.9	96.3±1.5***	53.7±9.9	41.6±4.8***	77.2±18.6	88.8±10.4***	47.5±11.9	40.6±3.6***

Pa,O_2: arterial oxyhaemoglobin tension; Pa,CO_2: arterial carboxyhaemoglobin tension; Sa,O_2: mean nocturnal oxyhaemoglobin saturation; Ptc,CO_2: mean nocturnal transcutaneous carboxyhaemoglobin tension; NMD: neuromuscular disorders; Muscular dystrophy (MD) comprised four subjects with Duchenne muscular dystrophy and one subject with Becker muscular dystrophy, neuropathy comprised 11 subjects with spinal muscular atrophy and one subject with hereditary motor and sensor neuropathy type I, other myopathies comprised two subjects with juvenile type of acid maltase deficiency, one with nemaline myopathy and one with centronuclear myopathy. Conversion factor for mmHg to kPa (×0.133). *: p<0.05; **: p<0.01; ***: p<0.001.

Results

The observation period (time from institution of NIV to the latest follow-up) averaged 25.3±12.7 months (range 8–60 months, table 1). During the observation period patients' height and weight increased from 141±21 cm to 145±20 cm and 32.8±20.4 kg to 35.8±20.7 kg, respectively (p<0.005).

In 26 patients/parents self-reported use of nocturnal NIV was 8–12 h during at least 6 nights a week. Four patients/parents reported an intermitted use of 3–4 h of sleep during most days of the week. Eight patients used NIV intermittently during naps and episodes of upper airway infections. Patients/parents reports were concordant to the ventilator gauge in all cases.

Noninvasive ventilation effect on gas exchange

Long-term NIV improved or normalised mean Sa,O_2 and Ptc,CO_2 (90.5±7.9% to 96.3±1.5% and 7.1±1.3 kPa to 5.5±0.6 kPa (53.7±9.9 mmHg to 41.6±4.8 mmHg), p<0.001), nadir Sa,O_2, maximum Ptc,CO_2 and per cent of sleep time spent in hypoxaemia and hypercapnia (fig. 1). Nocturnal heart rate dropped from 104.7±14.3 bpm pre-ventilation to 86.4±12.6 bpm during NIV (p<0.01).

NIV also caused sustained improvement in daytime gas exchange, apparent from ABG drawn ⩾8 h of spontaneous breathing (table 1). In the patients with diurnal ventilatory insufficiency (n=14) arterial oxygen tension (Pa,O_2) increased from 8.7±1.8 to 11.3±1.1 kPa (65.3±13.2 to 85.1±8.5 mmHg), pH from 7.33±0.05 to 7.38±0.03, and Pa,CO_2 fell from 7.5±1.3 to 5.7±0.3 kPa (56.4±9.5 to 42.8±2.6 mmHg) (p<0.01 for all). Individual data are shown in figure 2.

Noninvasive ventilation effect on sleep and sleep-disordered breathing

Paired full PSG before initiation of NIV and during NIV could be performed in 17 patients. NIV effectively suppressed SDB and improved sleep (table 2). During NIV respiratory disturbances and associated electroencephalogram (EEG)-arousals normalised. The proportion of light sleep (stage 1 and 2) decreased and slow wave sleep (stage 3 and 4) increased.

Withdrawal from noninvasive ventilation

Eight patients refused NIV-withdrawal, 12 made an attempt but resumed back to NIV mainly during the first night because significant symptoms occurred. Finally ten patients, seven with diurnal respiratory failure and three with SDB, completed 3 nights without NIV. In these patients withdrawal resulted in prompt deterioration of nocturnal and diurnal hypoventilation nearly back to baseline. Resumption of NIV during the following nights immediately normalised nocturnal respiration and diurnal blood gases within 2 nights/days (fig. 3). There was no significant difference in lung and respiratory muscle function between the measures made after withdrawal and after resumption of NIV.

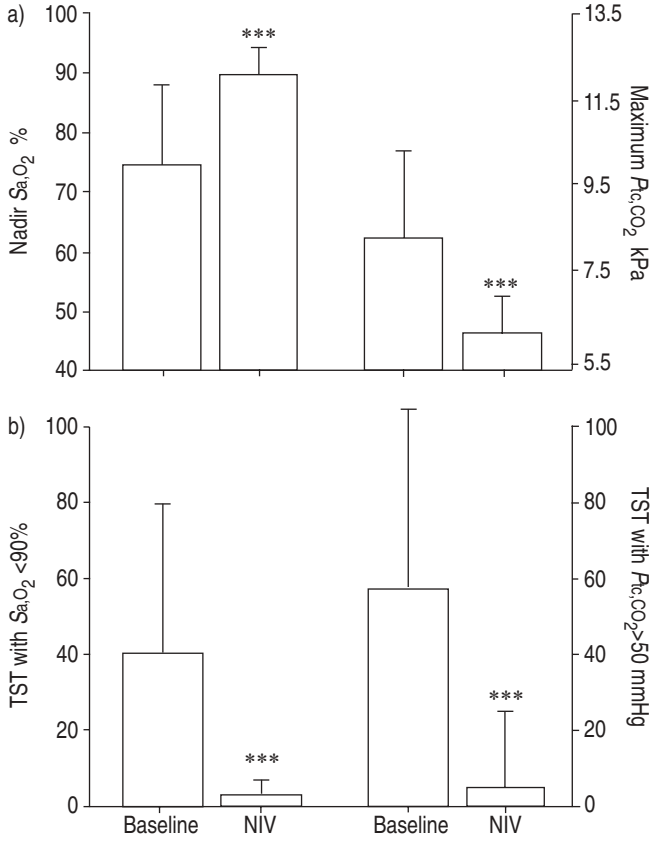

Fig. 1. – a) Impact of noninvasive ventilation (NIV) on nadir oxyhaemoglobin saturation (Sa,O_2) and maximum transcutaneous carbon dioxide tension (Ptc,CO_2), and b) on sleep time spent with hypoxaemia and hypercapnia. Baseline study before institution of NIV and during NIV at the latest control visit 25.3±12.7 months later. % TST: per cent of total sleep time; n=30; ***: p<0.001.

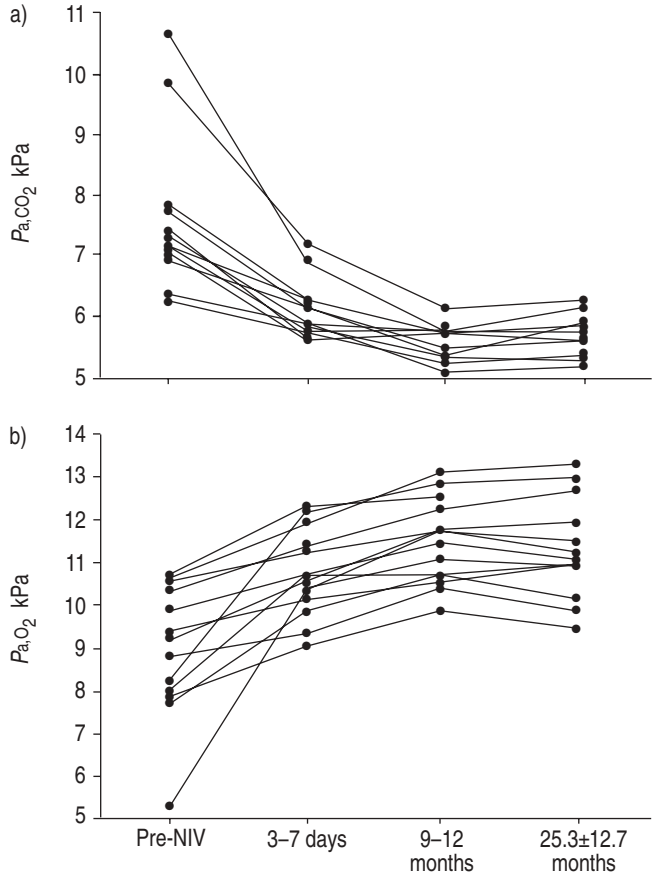

Fig. 2. – Impact of noninvasive ventilation (NIV) on a) diurnal arterial carbon dioxide tension (P_{a,CO_2}), and b) diurnal arterial oxygen tension (P_{a,O_2}) before institution (pre-NIV), 3–7 days after institution of NIV, at a control visit 9–12 months after institution of NIV and at the latest control visit at 25.3±12.7 months. Blood gas samples were obtained after at least 8 h spontaneous breathing. n=14; p<0.001 for the difference between blood gas tensions before (pre-NIV) and at any of the controls after initiation of NIV.

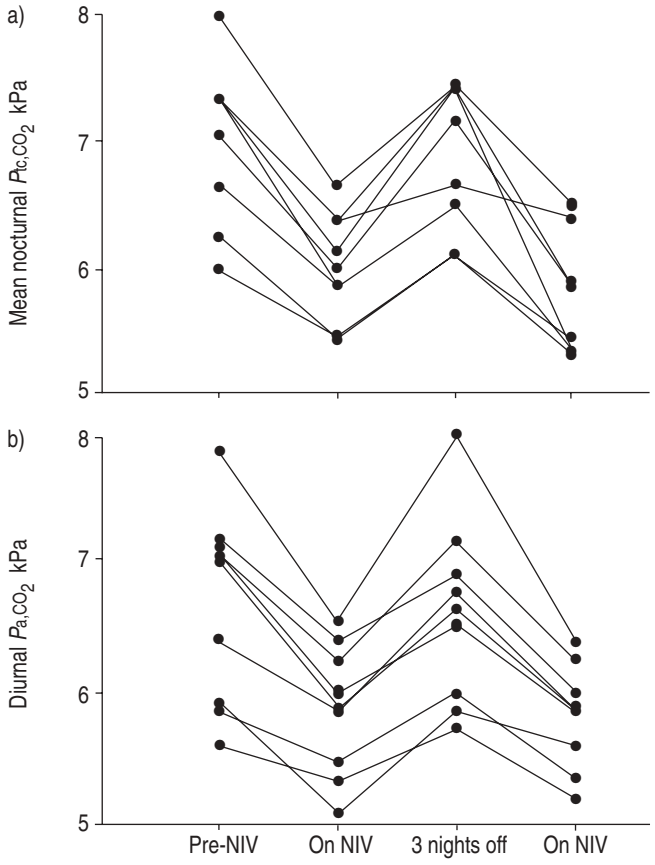

Fig. 3. – Impact of noninvasive ventilation (NIV) withdrawal on a) nocturnal transcutaneous carbon dioxide tension (P_{tc,CO_2}) and b) diurnal arterial carbon dioxide tension (P_{a,CO_2}). Measurements were obtained before institution of treatment (pre-NIV), at a subsequent control visit (on NIV), after 3 nights NIV-withdrawal (3 nights off) and after 2 days re-institution of NIV. Blood gas samples were obtained after at least 8 h spontaneous breathing. n=10; p<0.001 (ANOVA) for the differences between all measurements at the different dates (between pre-NIV and on NIV, on NIV and 3 nights off, and 3 nights off and the following control on NIV).

Noninvasive ventilation effect on lung and respiratory muscle function

Restrictive ventilatory defect (IVC 27.2±15.3%) was present in all patients at study entry. During the observation period IVC decreased by 82±246 mL, or 2% predicted per year. Change in IVC varied among the different diagnostic entities of NMD (table 3). It declined 183±111 mL·yr^{-1} in adolescents with DMD, who did not grow and had no progression of scoliosis, but on average did not change significantly in patients with other conditions. In the younger children with SMA and congenital muscular dystrophies, the majority of the study patients, IVC course was highly heterogeneous, showing improvement in seven, stability in five, and slow or rapid decline in nine patients, associated with the progression of scoliosis.

Inspiratory muscle pressure, too, was severely impaired prior to NIV. It improved slightly from 2.5±1.2 kPa (40±20 % pred) to 2.8±1.2 cm kPa (44±20% pred., p=0.11). This effect was observed in all patients, irrespective of NMD entity.

Table 2. – Influence of noninvasive ventilation (NIV) on sleep-disordered breathing and sleep

	Before NIV	During NIV	p-value
RDI·h^{-1}	10.5±13.1	3.1±3.5	<0.001
REM-RDI·h^{-1}	20.5±21.1	3.0±5.3	<0.001
Arousal index·h^{-1}	20.6±14.3	10.2±3.8	<0.001
Light-sleep %	55±12	44±13	<0.05
Slow-wave-sleep %	24±9	34±9	<0.05
REM-sleep %	18±6	20±6	0.18

RDI: respiratory disturbance index per hour sleep; REM-RDI: respiratory disturbance index per hour rapid eye movement (REM)-sleep; arousal index: electrocephalographic arousals per hour sleep.

Outcome

No patient died or experienced life threatening complications during the study period. Four patients required a total of six hospital admissions due to chest infections, amounting to 0.2 admissions per patient and year. All patients reported relevant improvement of symptoms. In 13 patients who had completed a validated questionnaire, a highly significant and relevant improvement in quality of life had been demonstrated [9, 12, 26].

Table 3. – Influence of noninvasive ventilation (NIV) on inspiratory vital capacity (IVC)

NMD	Patients n	IVC mL		IVC %		IVC-change mL·yr^{-1}
		Before NIV	With NIV	Before NIV	With NIV	
MD	5	1200±670	776±464*	26.2±11.4	16.2±7.3*	-183±111*
Congenital MD	9	514±305	493±212	21.3±6.9	19.4±7.0	2.4±91.7
Neuropathy	12	601±506	578±443	32.5±21.3	25.4±14.0	1.8±65.5
Other myopathies	4	717±207	747±327	25.8±8.7	22.3±9.0	38.3±92.5
Mean±SD	30	690±493	608±374	27.2±15.3	21.7±10.8**	-23.9±109.3*

NMD: neuromuscular disorders; Muscular dystrophy (MD) comprised four subjects with Duchenne muscular dystrophy and one subject with Becker muscular dystrophy, neuropathy comprised 11 subjects with spinal muscular atrophy and one subject with hereditary motor and sensor neuropathy type I, other myopathies comprised two subjects with juvenile type of acid maltase deficiency, one with nemaline myopathy and one with centronuclear myopathy. *: $p<0.05$; **: $p<0.01$.

Discussion

NIV over the past years has become standard therapy for acute and chronic respiratory failure of various causes, including adult neuromuscular diseases [27]. NIV improves gas exchange by increasing tidal ventilation, unloading respiratory muscles, and possibly by resetting respiratory centre chemosensitivity [4, 28, 29]. Favourable impact on morbidity, survival, and quality of life has been shown in adult neuromuscular disease and in adolescents with DMD, a disease of gradual and highly predictable progression [6, 13, 30, 31]. The evidence for benefit in other NMD is less clear, in part because concerns over undue prolongation of severely handicapped life, mask intolerance, and uncertainty about appropriate timing of initiation of NIV have hampered its widespread application. Concerns are likely to abate, however, over a recent report of NIV′s beneficial effect on gas exchange and good mask tolerance over time in even small children with NMD other than DMD [18].

The present study confirms the beneficial effect on gas exchange, but expands upon the existing data by demonstrating the consistency of the effect over an observation period of up to 5 yrs, coupled with marked improvement of sleep quality, stabilisation of lung and respiratory muscle function, and rapid deterioration of gas exchange during brief ventilation pause.

NIV was instituted with the objective of achieving normocapnia during ventilation. The goal that was realised within 3–7 days of hospitalisation using flow-triggered, pressure-controlled modes of ventilation and, when necessary customised masks that covered the nose and mouth, minimised dead-space and air leaks and facilitated ventilator cycling. Much bedside effort went into finding optimal ventilator settings. When effectively unloaded, spontaneous respiratory rate quickly dropped to back-up rate, nocturnal heart rate dropped 15% from baseline and patients generally fell asleep shortly after initiation of ventilation.

Gas exchange normalised rapidly in the early treatment phase, and continued to improve over the first few months. Improvements of gas exchange persisted through the daytime interval of spontaneous breathing, an observation that has previously been reported and attributed to the resetting of the ventilatory control centre [4, 28].

The deleterious effects of respiratory muscle weakness, however, were demonstrated by rapid though fully reversible deterioration of nocturnal and diurnal gas exchange during only 3 days of ventilation pause in ten patients. In contrast to the study of HILL *et al.* [4] that included six adults with mainly restrictive chest wall disorders in whom 1 week withdrawal from NIV did not alter diurnal blood gases, in children with advanced respiratory muscle weakness the regular nightly use of NIV seems to be necessary to maintain the gains achieved.

By extending the indication for NIV to patients with symptomatic sleep hypopnoeas and nocturnal hypercapnia the question of appropriate timing of initiation of NIV is raised. Many neuromuscular diseases, particularly those included in the present study, are characterised by diffuse respiratory muscle involvement and progressive decline of lung and respiratory muscle function. SDB, nocturnal and diurnal hypercapnic hypoventilation are common complications that evolve as a function of ventilatory restriction [1, 2, 8]. Institution of NIV for symptomatic sleep hypopneas, although not recommended in a recent Cochrane Review [32] seems justified in the light of anticipated progression to nocturnal hypoventilation and chronic hypercapnia that is blunting central respiratory drive and probably triggering subsequent daytime respiratory failure. [4, 5]. Moreover, NIV improved sleep quality, evident by an increase in sleep efficiency and deep sleep, and a reduction of light sleep and arousals.

One limitation of the study is that symptoms and quality of life have not been followed systematically. However, 20 patients including 13 who had only SDB refused withdrawal from NIV because they had experienced significant symptoms when sleeping without NIV. All 10 patients who withdrew NIV experienced reappearance of sleep disturbance and daytime symptoms and had some difficulties tolerating the 3 nights without NIV. This simple trial and the children′s excellent compliance is providing convincing evidence that objective improvements in sleep during nocturnal ventilation go along with subjective improvements that are perceived as very beneficial. Furthermore 13 of the patients in the current study were included in another study and reported significant and relevant relief of symptoms and improvement in quality of live [9, 12].

The current authors strongly feel that it is no longer justified to withhold an effective therapy that is otherwise generally accepted in conditions such as nocturnal hypoventilation due to obesity or chronic obstructive pulmonary disease (COPD) from severely handicapped and symptomatic children.

NIV′s effects on lung function are less clear, in part because data on the natural course of lung function changes are scarce. In the non-DMD patients lung function stayed fairly stable or even improved slightly. In these patients a relevant decline in IVC was always accompanied by a progression of scoliosis. In contrast IVC decline was most pronounced in DMD patients. They lost 183 mL per year, an amount that is equal to the 200 mL·yr^{-1} previously reported [33].

Expectedly, inspiratory muscle pressure was markedly reduced in all patients. In contrast to previous observations in adults [34] it did not deteriorate but improved slightly during the ventilation period, in the DMD male children despite concurrent decline of vital capacity. This might suggest

that respiratory muscle rest and resetting of respiratory centre set point for CO_2 were the predominant mechanisms.

In summary, the present study shows that prolonged use of noninvasive ventilation is well tolerated and highly effective in reversing sleep-disordered breathing and chronic respiratory failure in children with neuromuscular diseases. Therefore, a regular and systematic evaluation including sleep studies is essential. Noninvasive ventilation should be recommended in children with sleep-disordered breathing when an initial trial is tolerated and symptoms improve, but it is mandatory long term once respiratory failure occurs.

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