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Nocturnal hypoxemia and hypercapnia in children with neuromuscular disorders

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Abstract

The aim of the study was to identify daytime predictors of nocturnal gas exchange anomalies in children with neuromuscular disease (NMD) and normal daytime gas exchange.

Lung function tests, respiratory muscle evaluation and nocturnal gas exchange were obtained as part of routine evaluation.

We included 52 consecutive children with Duchenne muscular dystrophy (n=20), spinal muscular atrophy (n=10), and other NMD (n=22). Twenty patients had nocturnal hypoxemia defined by minimal pulse oximetry (SpO_2) <90% for at least 2% of night time and 22 had nocturnal hypercapnia defined by maximal transcutaneous carbon dioxide ($PtcCO_2$) value >50 mmHg for at least 2% of night time. Forced vital capacity and helium functional residual capacity correlated with minimal nocturnal SpO_2 (p=0.009 and p=0.01, respectively). Daytime pH correlated negatively with maximal nocturnal $PtcCO_2$ (p=0.005) and daytime $PaCO_2$ correlated with the percentage of time with a $PtcCO_2$>50 mmHg (p=0.02). Sniff nasal inspiratory pressure correlated with minimal nocturnal SpO_2 (p=0.02). Daytime $PaCO_2$ was a weak predictor of nocturnal hypercapnia (sensitivity 80%, specificity 57%).

Daytime lung function and respiratory muscle parameters correlate poorly with nocturnal hypoxemia and hypercapnia in children with NMD and normal daytime gas exchange which pleads for more systematic sleep studies in these children.

Key words: child, hypercapnia, hypoxemia, neuromuscular disease, polysomnography, sleep.

Introduction

Children with neuromuscular disorders (NMD) are at risk for sleep disordered breathing and nocturnal hypoxemia and hypercapnia as respiratory muscle weakness progresses. The physiological drop of alveolar ventilation is exacerbated in NMD, especially during rapid eye movement sleep, a period of maximal muscle hypotonia [1]. The type of NMD may influence the onset of abnormal nocturnal gas exchange as the involvement of respiratory muscles, and in particular the diaphragm, differs among diseases [2]. Patients with NMD characterized by a predominant involvement of the diaphragm are at greater risk of nocturnal hypoventilation than patients with preserved diaphragm [3, 4].

Nocturnal hypoxemia and hypercapnia should be diagnosed at an early stage to prevent the deleterious neurocognitive and cardiac consequences as well as the risk of acute respiratory failure. Indeed, non-invasive positive pressure ventilation (NPPV) has proven its efficacy in correcting abnormal nocturnal gas exchange over prolonged time periods and preventing acute respiratory exacerbations [5-9].

Unfortunately, nocturnal hypoxemia and hypercapnia are rarely symptomatic because of their progressive onset [10, 11]. Symptoms may be subtle and non-specific, and frequently, children become aware of their poor sleep quality after having started NPPV. In young children, symptoms are reported by the parents, who may underestimate their presence or severity.

It is unclear when first to search for nocturnal hypoventilation [12, 13]. If the magnitude of sleep-related hypoventilation is related to the progression of the disease, then it might be expected to relate to daytime measures reflecting severity of respiratory muscle weakness. Identification of daytime predictors of severity of nocturnal hypoventilation could permit selection of those patients in whom the possibility of hypoventilation is sufficiently high to justify a sleep study.

Vital capacity (VC) [14], forced expiratory volume in one second (FEV1) [15], and a rapid and shallow breathing [14] have been shown to correlate with nocturnal hypercapnia in adult patients with Duchenne muscular dystrophy (DMD), whereas peak inspiratory pressure and

inspiratory VC correlated with sleep disordered breathing and the severity of nocturnal hypercapnia in children with NMD [10]. However, studies on the predictive factors of nocturnal hypoventilation in patients with NMD are scarce, and most of them have small sample sizes, or are confined to adults with one type of NMD, such as DMD [14, 15]. Importantly, respiratory muscle tests adapted to young children, such as the sniff nasal inspiratory pressure (SNIP) or gastric pressure during cough (Pgas cough) have not been evaluated in these studies [2, 16].

We performed thus a study including children with NMD without overt daytime hypercapnia and no need for NPPV during their routine annual evaluation. The aim of the study was to identify daytime parameters that could predict nocturnal gas exchange anomalies and/or respiratory events in children with NMD having daytime gas exchange within the normal range.

Material and methods (see Online content for detailed information)

Patients

All consecutive stable patients with NMD with a daytime partial arterial carbon dioxide pressure ($PaCO_2$) < 50 mmHg were included. The institutional review board of Armand Trousseau hospital approved the conduct of the study and all the parents, and patients if possible, provided written informed consent.

Lung function and respiratory muscle tests

Breathing pattern was determined from flow tracing, allowing the calculation of tidal volume (V_T), minute ventilation (V_E), and the rapid and shallow breathing index which is the ratio of breathing rate to V_T (f_R/V_T) [17].

After a period of rest, capillary arterial blood gases with determination of HCO_3^- were obtained [18], followed by the functional residual capacity by helium dilution (FRCHe), forced vital capacity (FVC) [19, 20], maximal static inspiratory (Pimax) and expiratory (Pemax) pressures [21], and maximum sniff nasal inspiratory pressure (SNIP) [16].

Afterwards, an oesogastric catheter was inserted pernasally (Gaeltec, Dunvegan, Isle of Skye, UK) with assessment of the appropriate placement of the oesophageal pressure (Pes) transducer [22]. Pdi was obtained by subtracting on line the Pes signal from the gastric pressure (Pgas) signal. Paradoxical breathing was assessed by calculating the ratio of the Pgas swing to the Pdi swing (ΔPgas/ΔPdi) [23]. The patient's inspiratory effort was assessed by measuring Pes and Pdi swings, and the oesophageal (PTPes) and diaphragmatic (PTPdi) pressure-time products [24]. Dynamic lung compliance ($C_L$dyn) and inspiratory airway-lung resistance ($R_L$insp) were measured [25] as well as maximal Sniff Pes and Sniff Pdi and gastric pressure during a maximal cough. (Pgas cough) [26]. The diaphragmatic (TTdi) and oesophageal (TTes) tension time indexes, which estimate the endurance of the diaphragm and the global inspiratory muscles, were calculated [27].

Overnight pulse oximetry and transcutaneous carbon dioxide recording

An overnight pulse oximetry (SpO_2) and transcutaneous carbon dioxide ($PtcCO_2$) recording was performed in room air by a combined SpO_2/$PtcCO_2$ monitor (SenTec AG, Therwil, Switzerland) [28], allowing the calculation of mean and minimal SpO_2, number of desaturations ≥ 4%/hour of recording, percentage of total night time spent with a SpO_2 < 90%, mean and maximum $PtcCO_2$, and percentage of total night time spent with $PtcCO_2$ > 50 mmHg. In this diagnostic study, as the patients were not expected to have abnormal nocturnal gas exchange, nocturnal hypoxemia was defined by a minimal SpO_2 <90% for at least 2% of night time [15] and nocturnal hypercapnia by a maximal $PtcCO_2$ >50 mmHg for at least 2% of night time [29].

Polysomnography

Polysomnography (PSG) was performed in room air [30]. Obstructive apnoea was defined as a drop in thermal sensor amplitude by ≥ 90% of baseline for at least 2 respiratory cycles, with continued or increased inspiratory effort during reduced airflow. Central apnoea was defined as a drop in thermal sensor amplitude by ≥ 90% of baseline in absence of inspiratory effort, either with a

duration ≥ 20 sec or at least 2 missed breaths and associated with arousal, awakening or ≥ 3% desaturation. Mixed apnoea was defined as a drop in thermal sensor amplitude by ≥ 90% of baseline for at least 2 respiratory cycles with the absent inspiratory effort initially, then resumption of effort during latter part of event. Hypopnoea was defined as a drop in nasal air pressure transducer amplitude by ≥ 50% for a duration ≥ 2 missed breaths, associated with arousal, awakening or ≥ 3% desaturation [31]. Apnoea-hypopnoea index (AHI) was calculated as the sum of apnoea and hypopnoea events per hour of total sleep. Sleep disordered breathing was defined as a AHI over 5 events/h.

Statistical analysis

Data are presented as median and interquartiles. Interrelationships between lung function, respiratory muscle function, polysomnographic parameters, and gas exchange were analyzed using the Spearman's rank test. Group comparisons were performed using the Mann-Whitney U test and Kruskal-Wallis rank sum test. Stepwise multiple regression analysis on rank was performed to determine the major determinant of the nocturnal dependent variable, when necessary. Predictive values of nocturnal hypoxemia, hypercapnia and sleep disordered breathing were computed using the receiver operator curves (ROC). Cut-off points were calculated by bi-dimensional analysis at equal sensitivity to specificity ratio. The dependent variable with the maximal area under the curve (AUC) was considered to be the strongest predictor. A p value of less than 0.05 was considered statistically significant.

Results

Patients

Fifty-two patients were included in the study (Table 1). Twenty patients had DMD (*DMD group,* age range 7-19 years), 10 patients had spinal muscular atrophy (*SMA group,* age range 7-19 years), and 22 patients suffered from other NMD (*Other group,* age range 5-17 years): Steinert

myopathy (n=2), central core myopathy (n=3), Ulrich myopathy (n=1), Friedrich myopathy (n=1), merosine deficiency (n=2), facioscapulohumeral myopathy (n=1), laminopathy (n=1), unknown myopathy (n=11). Twenty patients had nocturnal hypoxemia and 22 had nocturnal hypercapnia. Paradoxical breathing was present in one patient with *DMD* patient and 3 patients within the *Other group*.

Correlation of daytime parameters with nocturnal hypoxemia and hypercapnia

Lung function

FVC and FRCHe correlated positively with minimal nocturnal SpO_2 (r=+0.384, p=0.009, and r=+0.368, p=0.01, respectively) in the total population (Figure 1). However, when the three NMD subgroups were considered separately, only FVC correlated with minimal nocturnal SpO_2 in the *Other group* (r=+0.695, p<0.001), but also with mean nocturnal SpO_2 and the percentage of time with SpO_2<90% (r=+0.652, p=0.002, and r=-0.677, p<0.001, respectively). None of the lung function parameters correlated with nocturnal $PtcCO_2$.

Diurnal gas exchange

Daytime pH correlated negatively with maximal nocturnal $PtcCO_2$ and mean nocturnal $PtcCO_2$ in the total population (r=-0.400, p=0.005, r=-0.544, p=0.002, respectively) and with maximal nocturnal $PtcCO_2$, mean nocturnal $PtcCO_2$ and the percentage of time with $PtcCO_2$>50mmHg in the *Other group* (r=-0.477, p=0.03; r=-0.586, p=0.02 and r=-0.483, p=0.03, respectively). Daytime $PaCO_2$ correlated with the percentage of time with $PtcCO_2$>50 mmHg in the total population (r=+0.345, p=0.02) and in the *Other group* (r=+0.445, p=0.04) (Figure 2), and with mean nocturnal $PtcCO_2$ in the total population (r=+0.444, p=0.01). When the patients were separated in those who were hypercapnic during the night or not, the only parameter that differed significantly between the two groups was daytime $PaCO_2$, which was significantly higher in the

hypercapnic patients (p=0.009) (Figure 3). However, no daytime parameter differed between the patients with and without nocturnal hypoxemia.

Respiratory mechanics

No correlation was found in the total population and the subgroups with any of the respiratory mechanic parameters.

Respiratory muscles

SNIP correlated negatively with minimal nocturnal SpO_2 in the total population (r=-0.358, p=0.02) and with minimal and mean nocturnal SpO_2 in the *Other group* (r=-0.554, p=0.01, and r=-0.632, p=0.004). Moreover, Pgas cough correlated positively with minimal and mean nocturnal SpO_2 in the total population (r=+0.316, p=0.04, and r=+0.372, p=0.03, respectively) and with mean nocturnal SpO_2 in the *Other group* (r=+0.639, p=0.003). SNIP was the only parameter that correlated with mean nocturnal $PtcCO_2$ in the *DMD group* (r=+0.626, p=0.04).

Representative data of 2 patients with preserved respiratory muscle strength and nocturnal hypercapnia, and 2 other patients having severe respiratory muscle weakness and normal nocturnal gas exchange are shown in Table 2.

Correlation of daytime parameters with PSG

A PSG was performed in 27 patients (Table 3). Median AI was 1.8 (interquartiles 0.3–4.8) events/hour with a maximal value of 63 and median AHI was 8.6 (3.3–19.5) events/hour. We found that 74% of apnoeas were obstructive, 21% were central and 5% were mixed. Nineteen patients had an AHI above 5 events/h. Daytime $PaCO_2$ and HCO_3^- correlated positively with the AHI in the total population (r=+0.491, p=0.009 and r=+0.467, p=0.01, respectively) and in the *DMD group* (r=+0.668, p=0.02, and r=+0.618, p=0.04, respectively). Lung function parameters, respiratory mechanics and respiratory muscle parameters were not correlated to the AI or AHI. When the

patients were separated in those with an AHI ≤ 5 or > 5, no daytime parameter differed significantly between the two groups.

Stepwise regression analysis and ROC

Using forward stepwise regression analysis on rank, we found that FVC explained 24% of the variability of minimal nocturnal SpO_2, daytime pH explained 30% of the variability of mean nocturnal $PtcCO_2$ and daytime $PaCO_2$ explained 26% of the variability of AHI.

Scatter plot and ROC curve obtained for daytime $PaCO_2$ showed that a $PaCO_2$ value > 38 mmHg had a 80% sensitivity but only 57% specificity for predicting nocturnal hypercapnia (Figure 3).

Discussion

This study is the first to analyze lung function, daytime blood gases, respiratory mechanics, respiratory muscle strength and endurance in a large group of children with NMD in order to identify daytime parameters that could predict the need for a sleep study. Although approximately 39% and 44% of the children had nocturnal hypoxemia and hypercapnia respectively, and 70% had sleep disordered breathing, no simple unique lung function or respiratory muscle parameter was able to accurately identify patients with altered nocturnal gas exchanges or sleep disordered breathing.

Two previous studies from our group compared DMD and patients with other NMD treated or not with NPPV and found that several tidal breathing and respiratory muscle parameters, such as f_R/V_T, SNIP, Pgas cough, and TTes and TTdi were more severely impaired in the patients treated with NPPV, as compared to those who did not need NPPV [2, 32]. However, patients treated with NPPV had a more advanced disease than the patients in the present study. This was also the case for the DMD patients in the study reported by Toussaint et al. who were mainly adolescents and young adults having a more advanced disease [14].

VC or inspiratory VC is the parameter that has been shown to correlate with nocturnal gas exchange in most studies [1, 10, 14]. This was confirmed in our study, as we found a relationship between FVC and nocturnal SpO_2. Moreover, FRCHe also correlated with nocturnal SpO_2. The role of FRC is based on the fact that it is the main "oxygen reservoir". Indeed, FRC has been shown to determine the apnoea-related desaturations regardless of the changes of apnoeas duration in adult patients with obstructive sleep apnea [33]. In preterm infants, a negative relationship has also been observed between FRC and the proportion of apnoeas with desaturation [34]. Moreover, it had been observed that a low FRC during awake state is associated with a greater loss of air in the dorsal lung region during sleep [35], exposing patients to greater desaturations and apnoea during sleep [36].

Respiratory muscle parameters correlated only with nocturnal oxygenation but not with nocturnal capnia. This may be explained by the fact that in patients with neuromuscular weakness, the severity of nocturnal hypoxemia is related to the postural fall in VC, suggesting that the degree of impairment of diaphragmatic function is an important determinant of nocturnal oxygenation, irrespective of involvement of other respiratory muscles [4]

As physiologically expected, a correlation was observed between daytime $PaCO_2$ and nocturnal $PtcCO_2$ in the present study and another paediatric study [10]. This study identified a $PaCO_2 > 38$ mmHg as the only daytime parameter that predicts nocturnal hypercapnia. However its predictive power was moderate and insufficiently relevant for clinical practice. Nevertheless, our results are in agreement with Mellies et al. who found that $PaCO_2$ was a strong predictor of nocturnal hypercapnic hypoventilation and that a value > 40 mmHg in NMD children should raise the suspicion of respiratory muscle fatigue and should prompt polysomnographic investigation [10].

Several factors may explain the poor correlation between daytime parameters and nocturnal hypoventilation in our patients. First, the patients in the present study may have a too modest impairment of their respiratory muscle performance. Indeed, none of our patients fulfilled the unanimously accepted criteria for nocturnal NPPV, i.e. a daytime $PaCO_2 > 50$ mmHg and/or a history of a severe respiratory exacerbation [37, 38]. But the present study is in line with daily

practice that recommends regular screening for nocturnal hypoventilation in patients in a stable state [38]. The poor correlation between the daytime lung and respiratory muscle function parameters and sleep related parameters suggest that other factors may play a role in the preservation or deterioration of nocturnal gas exchange in children with NMD. Overweight and obesity, but also chest deformity with scoliosis, macroglossia and craniofacial deformity, cardiomyopathy and central nervous system involvement may all contribute to sleep-disordered breathing in patients with NMD. However, none of the patients included in the present study had severe scoliosis justifying arthrodesis or enlarged tonsils and only 2 patients had a BMI z-score > +2.

We acknowledge that our study has some limitations. There are no unanimously accepted criteria for the definition of nocturnal hypoxemia and hypercapnia. We have arbitrarily chosen two criteria which have been used previously [15, 29], but we agree that the frequency of nocturnal hypoxemia and hypercapnia would have been different with other criteria. Despite the fact that our study is one of the largest paediatric studies reported to date, the number of patients in each NMD subgroup was relatively small. Predictive factors that are specific for one group of NMD patients could thus have been missed. Invasive parameters were not available for all patients because some patients refused the oesogastric catheter and two patients had a severe nausea reflex that made the placement of the catheter too uncomfortable. The AI and AHI were only available for 27 patients. Because nocturnal hypoventilation is more common in patients with NMD than apnoeic events, we prioritised our search on predictors of nocturnal hypoventilation.

In conclusion, even if respiratory muscle tests correlate poorly with nocturnal gas exchange, regular monitoring of simple non-invasive tests are recommended in children with NMD. VC, even if not all children are able to perform a reliable and reproducible forced VC manoeuvre [2], is a simple and non-invasive test that is a global indicator of respiratory muscle strength and of diaphragm performance when comparing its value in the prone and supine position. The SNIP is an easy volitional test to assess inspiratory muscle strength which has proved its feasibility and

reproducibility in young children; a normal value excluding inspiratory muscle weakness, but a low value requiring the recording of oesophageal pressure [16]. Both tests are useful for the longitudinal monitoring of an individual patient, the indication of cough assisted techniques and peri-operative NPPV in case of scheduled surgery such as arthrodesis. However, as these tests correlate poorly with nocturnal gas exchange, more systematic sleep studies are recommended in children with NMD.

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Table 1: Patients' characteristics and lung and respiratory muscle function.

	All patients (n=52)	DMD group (n=20)	SMA group (n=10)	Other group (n=22)
Patient characteristics				
Age (yrs)	14.9 (10.1–16.1)	16.1 (14.9–17.9)*	11.3 (9.5–15.0)	12.5 (7.6–15.6)
Weight (kg)	37.0 (24.7–59.5)	46.5 (35.5–60.5)	29.2 (18.0–38.0)	33.0 (24.0–51.0)
Height (cm)	151 (125–164)	168 (159–174)	138 (126–164)	145 (124–168)
BMI z-score	-0.56 (-2.00–0.90)	-0.45 (-2.00–0.37)	-2.00 (-2.00–0.84)	-0.48 (-2.00–1.36)
Lung function parameters				
FVC (% predicted)	36.5 (29.0–48.0)	34.0 (28.0–42.3)	30.5 (24.5–61.5)	42.0 (32.5–61.5)
FRCHe (% predicted)	66.5 (52.0–83.0)	69.0 (61.0–85.0)	52.0 (44.0–77.0)	66.0 (52.8–84.0)
Daytime blood gases				
Daytime PaO_2 (mmHg)	92.0 (84.0–97.8)	89.5 (83.5–97.5)	92.5 (83.0–100.0)	92.0 (85.0–95.8)
Daytime $PaCO_2$ (mmHg)	39.0 (37.0–42.0)	38.5 (36.5–41.5)	37.5 (34.0–42.0)	39.0 (38.0–42.0)
pH	7.42 (7.40–7.43)	7.42 (7.40–7.44)	7.42 (7.41–7.43)	7.41 (7.40–7.43)
HCO_3^- (mmole/L)	24.18 (22.75–26.30)	24.23 (22.79–26.22)	22.70 (21.36–26.33)	24.31 (23.00–26.31)
Respiratory parameters				
VT (ml/kg)	7.0 (5.0–9.1)	6.5 (5.0–8.7)	9.7 (7.8–11.2)	6.9 (4.6–9.0)
fR (breaths/min)	22.8 (17.6–25.5)	20.0 (17.5–22.9)	23.0 (16.0–26.5)	24.0 (20.9–28.4)
VE (L/min)	5.9 (5.2–6.6)	6.0 (5.3–6.8)	5.7 (4.9–7.0)	5.9 (5.2–6.6)
fR /VT (breaths/min/ml)	0.08 (0.06–0.12)	0.07 (0.05–0.08)	0.06 (0.05–0.12)	0.11 (0.06–0.14)
ΔPgas/ΔPdi	0.32 (0.20–0.52)	0.29 (0.20–0.40)	0.55 (0.40–0.69) †	0.34 (0.18–0.42)
$C_L$dyn (ml/cmH_2O)	41 (24–58)	64 (44–80)*	29 (15–41)	32 (24–55)
$R_L$insp (cmH_2O/L.s^{-1})	6.6 (3.4–8.1)	5.2 (3.4–7.2)	5.9 (3.4–11.0)	6.7 (3.7–8.4)
Respiratory muscle performance				
SNIP (cmH_2O)	-27.5 (-39.0 – -19.5)	-22.0 (-33.5 – -12.5)	-27.0 (-38.5 – -18.0)	-35.0 (-40.0 – -23.5)
Sniff Pes (cmH_2O)	-30.5 (-45.0 – -25.0)	-25.0 (-35.5 – -22.3)	-32.0 (-60.0 – -23.3)	-32.0 (-47.0 – -26.0)
Sniff Pdi (cmH_2O)	37.4 (25.2–57.0)	27.0 (19.2–36.7)**	56.0 (33.0–77.8)	40.0 (28.0–58.0)
Pgas cough (cmH_2O)	38.1 (21.0–51.0)	23.0 (14.5–36.3)*	37.2 (27.5–47.3)	50.5 (37.3–68.3)
PeMax (cmH_2O)	33.0 (22.0–43.5)	28.5 (21.0–34.9)	20.5 (8.0–33.0)	42.0 (24.4–64.1)
PiMax (cmH_2O)	-30.5 (-40.2 – -20.2)	-37.4 (-41.3 – -21.0)	-30.0 (-30.8 – -24.0)	-28.0 (-41.8 – -16.1)
Respiratory muscle endurance				
TTes	0.05 (0.02–0.07)	0.06 (0.04–0.08)	0.03 (0.02–0.08)	0.05 (0.02–0.06)
TTdi	0.15 (0.08–0.26)	0.25 (0.12–0.40)	0.11 (0.07–0.19)	0.17 (0.09–0.21)

Data are presented as median (interquartiles).
Abbreviations: DMD, Duchenne muscular dystrophy; SMA, spinal muscular atrophy; BMI, body mass index, FVC, forced vital capacity; FRCHe, functional residual capacity measured by the Helium dilution technique; PaO_2: partial arterial oxygen pressure, $PaCO_2$, partial arterial carbon dioxide pressure; VT, tidal volume; fR, respiratory rate; fR/VT, rapid and shallow breathing index; VE, minute ventilation; ΔPgas/ΔPdi, ratio of gastric pressure swing to transdiaphragmatic pressure swing during spontaneous breathing; $C_L$dyn, dynamic lung compliance; $R_L$insp: inspiratory lung resistance; SNIP, sniff nasal inspiratory pressure; Pes, esophageal pressure; Pdi, transdiaphragmatic pressure; Pgas cough, gastric pressure during a maximal cough maneuver; Pemax, maximal static expiratory pressure; Pimax, maximal static inspiratory pressure; TTes, tension time index of the inspiratory muscles; TTdi, tension time index of the diaphragm.

* Compared with SMA or Other groups; ** Compared with SMA group; † Compared with DMD or Other groups.

Table 2: Respiratory muscles and nocturnal gas exchanges measurements in 4 patients.

Patients	**#1**	**# 2**	**# 3**	**#4**
Respiratory muscles				
FVC (% predicted)	77	57	25	23
SNIP (cmH_2O)	-97	-38	-14	-12
Pgas cough (cmH_2O)	81	50	13	19
Nocturnal gas exchange				
SpO_2 min (%)	94	86	91	80
% nighttime with SpO_2 <90%	0	0	0	0
SpO_2 mean (%)	99	96	95	97
$PtcCO_2$ max (mmHg)	59	59	47	47
% nighttime with $PtCO_2$ >50 mmHg	66	56	0	0
$PtcCO_2$ mean (mmHg)	50	51	43	39

Patients #1 and 2 belong to the *Other group*, and are examples of preserved or moderate respiratory muscle weakness with altered nocturnal capnia; patients #3 (DMD) and #4 (SMA) show a severe respiratory muscle weakness with normal nocturnal gas exchanges.
Abbreviations: FVC, forced vital capacity; SNIP, sniff nasal inspiratory pressure; Pgas cough, gastric pressure during a maximal cough maneuver; SpO_2, pulse oximetry; $PtcCO_2$, transcutaneous carbon dioxide tension; min, minimal; max, maximal.

Table 3: Sleep parameters.

	All patients (n=27)	DMD group (n=11)	SMA group (n=6)	Other group (n=10)
AI (events/hour)	1.8 (0.3–4.8)	3.1 (0.5–8.0)	2.4 (0.0–4.8)	1.2 (0.0–2.2)
AHI (events/hours)	8.6 (3.3–19.5)	18.0 (9.4–26.7)	5.9 (3.0–10.8)	5.6 (2.0–9.4)
SpO_2 mean (%)	96 (94–97)	94 (93.5–97)	94 (91–97)	97 (94–98)
SpO_2 min (%)	84.0 (73.5–93.8)	82.5 (76.0–94.0)	66.0 (60.3–89.0)	88.0 (77.0–92.0)
% night time with SpO_2<90%	0.0 (0.0–8.0)	1.0 (0.0–9.5)	0.0 (0.0–17.5)	0.0 (0.0–2.0)
Desaturation Index	37.0 (8.0–64.8)	46.0 (8.3–76.0)	45.5 (6.0–58.0)	26.0 (3.0–47.0)
$PtcCO_2$ mean (mmHg)	44.2 (42.0–48.8)	44.1 (41.8–46.5)	40.7 (39.4–42.0)	48.0 (42.8–50.3)
$PtcCO_2$ max (mmHg)	50.0 (46.0–58.0)	48.5 (46.5–53.0)	48.5 (46.2–56.5)	52.0 (46.0–59.0)
% night time with $PtCO_2$>50mmHg	0.0 (0.0–9.8)	0.0 (0.0–4.5)	0.0 (0.0–0.0)	0.0 (0.0–55.0)

Data are presented as median (interquartiles).
Abbreviations: DMD, Duchenne muscular dystrophy; SMA, spinal muscular atrophy; AI, apnoea index; AHI, apnoea-hypopnoea index; SpO_2, pulse oximetry; $PtcCO_2$, transcutaneous carbon dioxide tension; min, minimal; max, maximal.

Figure legends

Figure 1

Relationship between minimal nocturnal SpO_2 and (A) FVC %predicted, and (B) FRCHe % predicted. SpO_2: pulse oxymetry; FVC: forced vital capacity; FRCHe: functional residual capacity by the Helium technique.

Symbols: black circles: Duchenne muscular dystrophy (DMD); grey triangles: spinal muscular atrophy (SMA); white squares: other neuromuscular disorders (Other).

Figure 1

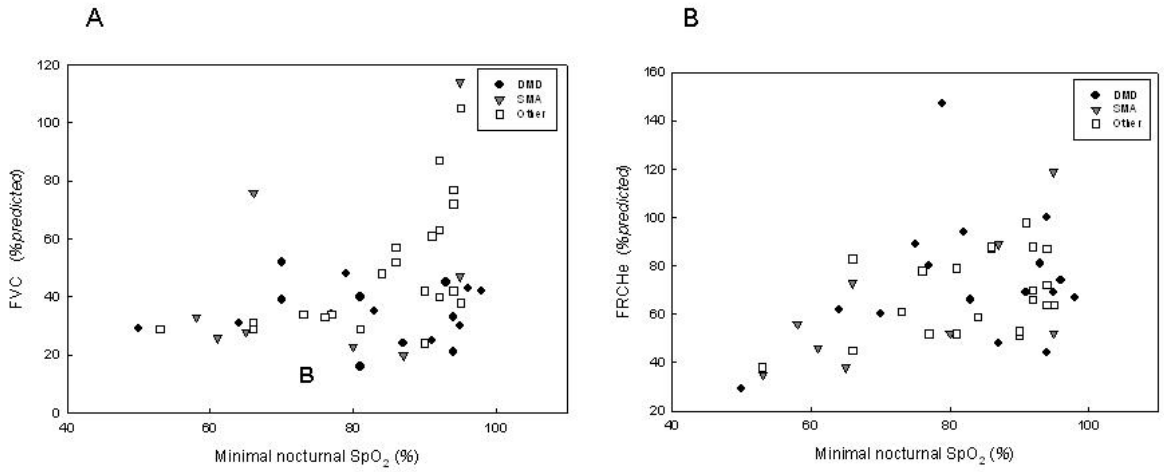

Figure 2

Relationship between daytime $PaCO_2$ and the percentage of night time spent with a $PtcCO_2$ >50 mmHg. $PaCO_2$: partial arterial carbon dioxide pressure; $PtcCO_2$: transcutaneous carbon dioxide tension.

Symbols: black circles: Duchenne muscular dystrophy (DMD); grey triangles: spinal muscular atrophy (SMA); white squares: other neuromuscular disorders (Other).

Figure 2

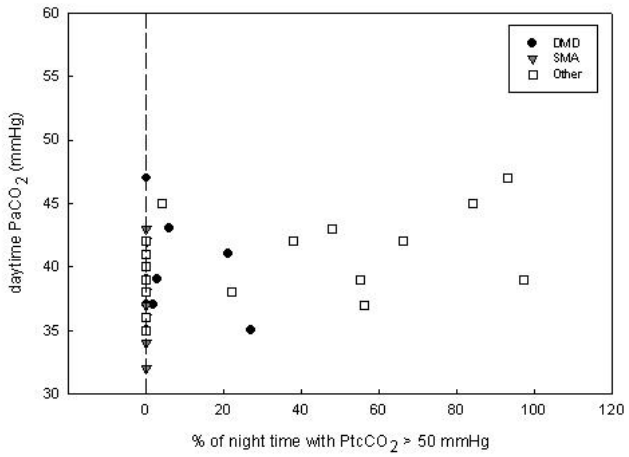

Figure 3

Predictive threshold of daytime $PaCO_2$ computed for nocturnal hypercapnia (NH). Left panel shows scatter plot, right panel the ROC plot with the area under the curve (AUC). The line indicates the optimal cut-off points for predictive value.

Symbols: black circles: Duchenne muscular dystrophy (DMD); grey triangles: spinal muscular atrophy (SMA); white squares: other neuromuscular disorders (Other).

Figure 3