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Long term noninvasive ventilation and continuous positive airway pressure in children with neuromuscular diseases in France

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A B S T R A C T

The aim of the study was to describe the characteristics of children with neuromuscular diseases treated with long term noninvasive ventilation or continuous positive airway pressure in France. On June 1st 2019, 387 patients (63% boys, mean age 11.2 ± 5.5 years) were treated with long term noninvasive ventilation/continuous positive airway pressure. Thirty three percent of patients had spinal muscular atrophy, 30% congenital myopathy/dystrophy, 20% Duchenne muscular dystrophy, 7% Steinert myotonic dystrophy, and 9% other neuromuscular diseases. Ninety-four percent of patients were treated with long term noninvasive ventilation and 6% with continuous positive airway pressure. Treatment was initiated electively for 85% of patients, mainly on an abnormal overnight gas exchange recording (38% of patients). Noninvasive ventilation/continuous positive airway pressure was initiated during a respiratory exacerbation in 15% of patients. Mean duration of noninvasive ventilation/continuous positive airway pressure was 3.3 ± 3.1 years. Mean objective long term noninvasive ventilation/continuous positive airway pressure use was 8.0 ± 3.1 h/24. Spinal muscular atrophy, congenital myopathy/dystrophy, and Duchenne muscular dystrophy represented 83% of children with neuromuscular diseases treated with long term noninvasive ventilation in France. Screening for nocturnal hypoventilation was satisfactory as noninvasive ventilation /continuous positive airway pressure was predominantly initiated electively.

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Keywords:
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Introduction

Respiratory muscles are rarely spared in children with neuromuscular disease (NMD), putting them at risk for alveolar hypoventilation. Noninvasive ventilation (NIV) is a method of noninvasive ventilatory support that includes continuous positive airway pressure (CPAP) and noninvasive ventilation (NIV) *sensu stricto*. The role of NIV is to assist or "replace" the weakened respiratory muscles to correct alveolar hypoventilation by maintaining an adequate tidal volume and minute ventilation [1]. Because breathing is physiologically less efficient during sleep, NIV will initially be used at night, but as respiratory muscle weakness progresses, NIV may be extended into daytime. Although children with NMD represent a large population requiring long-term NIV, there are no validated criteria for initiating NIV [1,2]. There is a consensus to initiate long-term NIV in case of isolated nocturnal hypoventilation, before the onset of daytime hypercapnia, and/or in case of acute respiratory failure requiring any type of ventilatory support [2,3]. NIV is associated with a correction of nocturnal and diurnal gas exchange, an increase in sleep efficiency and survival [2].

In France, all children treated with long term NIV/CPAP at home are followed within the French national paediatric NIV network. A survey performed by this network and published in 2021, revealed that 1447 patients aged less than 20 years were treated with NIV/CPAP for at least 3 months on June the 1st 2019 [4]. The mean age of the patients was 9.8 ± 5.8 years and the most frequent underlying disorders were: (1) upper airway obstruction (46%), (2) NMD (28%), (3) central nervous system disorder (13%), (4) cardiorespiratory disorder (7%), and (5) congenital bone disease (4%).

The aim of the present study was to analyse in detail the characteristics of the subgroup of patients with NMD of the 2019 national survey [4].

Material and methods

The study was a national cross-sectional survey performed among all the centres of the French national paediatric NIV/CPAP network which gathers 27 paediatric university centres distributed among 24 cities [4]. The study was a follow up survey conducted 19 years later after the original survey study which was published in Pediatric Pulmonology in 2003 [5].

For the present survey, the detailed methodology has been published in the original survey [4] but in summary, all the centres filled in an anonymous questionnaire for every child with any NMD aged ≤ 18 years treated since at least 3 months with NIV or CPAP on June the 1st, 2019. Some young adults aged 18–22 years who were still followed in these centres since childhood, and who could not be followed by adult centres because of their rare/genetic diseases, were also included. The questionnaire comprised the following information: date of birth, gender, primary and secondary diagnosis, the investigations performed before the NIV/CPAP initiation, the parameters that led to the decision of NIV/CPAP treatment, NIV/CPAP duration, the mean objective adherence to treatment during the last month obtained from the device built-in software, the type of interface and NIV/CPAP device (life support ventilator: for use ≥ 16 h/24, full range of alarms, internal + external batteries ≥ 8 h and allows patient's mobility; intermediate: use between 8 and 16 h/24, basic alarms, internal battery ≥ 2 h; standard: use at night, no alarms, no battery), and the use of additional technologies such as supplemental oxygen therapy, mouthpiece ventilation, or airway clearance devices. The patients with NMD were classified into five diagnostic groups: spinal muscular atrophy (SMA), congenital myopathy-dystrophy, Duchenne muscular dystrophy

(DMD), Steinert's myotonic dystrophy, and other NMD. Of note, of the 398 patients with NMD or skeletal disease included in the nation-wide study [4], 11 patients were excluded for the present study because they did not have a NMD: 7 patients with scoliosis (without NMD), 2 patients with ischio-vertebral dysplasia, one patient with a thoracic neuroblastoma, and one patient with glycogenosis type 4. All questionnaires were centralised and analysed by the NIV centre of Necker hospital in Paris. The study was approved by the local institutional board (Comité d'Ethique de Necker Enfants malades, CENEM, n°CENEM19-5-BF) on March the 7th 2019, and all the patients aged >6 years and all parents gave their informed consent.

Descriptive statistics summarized patient's characteristics and NIV/CPAP technology. Group comparisons were done using the One Way Analysis of Variance test or the Kruskal-Wallis One Way Analysis of Variance on Ranks test in case of non-parametric data. Comparisons between 2 groups were done using the t-test, or the Mann-Whitney Rank Sum test in case of non-parametric data. Comparisons of quantitative data were done using the chi-square test. A p value <0.05 was considered for significance.

Results

Three hundred and eighty-seven patients were included in the study with 242 (60%) boys (Table 1). The number of patients per centre ranged from 0 to 41 patients. Twenty-three (6%) patients were older than 18 years. The most frequent NMD were: SMA (33%), congenital myopathy-dystrophy (30%), DMD (20%), and Steinert myotonic dystrophy (8%) (Fig. 1). The other NMD (9%) included arthrogryposis multiplex congenita ($n = 13$), congenital myasthenic syndromes ($n = 7$), diaphragmatic disorders ($n = 6$), Pompe disease ($n = 7$), and mitochondrial cytopathy ($n = 2$) (Table 1). The patients with DMD or Steinert myotonic dystrophy were older at NIV initiation as compared to the patients of the other diagnostic groups ($p < 0.001$). Patients with SMA or congenital myopathy-dystrophy were ventilated for a longer time than patients with DMD ($p = 0.002$). Ninety-four percent of the patients were treated with NIV and 6% with CPAP ($p < 0.001$). The use of CPAP was more common in patients with "other" NMD (23%) as compared to the other diagnostic groups ($p < 0.001$). Treatment was initiated electively for 85% of children while 15% of the patients were started on long term NIV/CPAP after a respiratory exacerbation. This percentage was higher in patients with SMA (23%) as compared to the other diagnostic groups ($p < 0.001$) (Table 1).

Prior to NIV/CPAP initiation, the majority of patients (39%) had exclusively a nocturnal pulse oximetry (SpO_2) with a transcutaneous carbon dioxide monitoring (PtcCO_2) recording. A polysomnography (PSG) or respiratory polygraphy (PG) was performed in 33% of patients (Table 2). Of note, 63% of the patients with Steinert myotonic dystrophy had a P(S)G with a PtcCO_2 recording ($p < 0.05$ as compared to the other diagnostic groups).

The criteria that led to NIV/CPAP initiation are shown in Table 3. In 20% of the patients, NIV/CPAP was initiated on "other criteria" comprising: abnormal blood gases (2%), clinical criteria (3%), the relay of invasive ventilation and/or the impossibility to wean the patient from NIV/CPAP initiated during a respiratory exacerbation (9%), prior to elective surgery (1.5%), restrictive lung disease on lung function tests (1%), or thoracic deformity (0.3%).

Mean objective NIV/CPAP use was 8.0 ± 3.1 h/24 (Table 4). Only 2% of the patients used their NIV/CPAP ≥ 16 h/24. The use of a nasobuccal interface was significantly more common in patients with Steinert myotonic dystrophy (41%) as compared to the other diagnostic groups ($p < 0.001$). A target volume mode was used by 15% of the patients, which tended to be more frequent (23%) in the patients with congenital myopathy/dystrophy. Only 5 patients,

Table 1
NIV/CPAP characteristics according to the diagnostic groups.

	Total population(n = 387)	SMA(n = 129)	Congenital myopathy/dystrophy (n = 117)	DMD(n = 77)	Steinert myotonic dystrophy(n = 29)	Other(n = 35)
Age (years)	11.2 ± 5.5 (0.3–21.9)	8.9 ± 5.5 (0.3–20.3)	10.8 ± 4.9 (0.3–20.4)	15.8 ± 2.7* (7.7–21.9)	14.1 ± 4.2* (3.3–20.2)	8.6 ± 5.6 (0.7–16.6)
Age at initiation (years)	7.9 ± 5.5 (0–21.2)	5.1 ± 4.5 (0–16.8)	7.0 ± 4.9 (0–18.5)	13.6 ± 3.1 (3.3–21.2)	11.3 ± 4.6 (1.3–16.9)	6.1 ± 5.5 (0–16.0)
Duration of CPAP/NIV (years)	3.3 ± 3.1 (0–15.4)	3.7 ± 3.3 (0–15.4)	3.8 ± 3.4 (0–15.4)	2.3 ± 2.4 (0–11.2)	2.7 ± 2.5 (0–11.0)	2.5 ± 2.3 (0–7.8)
<i>Ventilatory mode</i>						
NIV (n, %)	361 (94%)	127 (99%)*	109 (93%)	73 (95%)	26 (90%)	26 (74%)
CPAP (n, %)	24 (6%)	1 (1%)	8 (7%)	4 (5%)	3 (10%)	8 (23%)*
<i>NIV/CPAP initiation</i>						
Electively	302 (85%)	82 (75%)	93 (88%)	70 (95%)	26 (90%)	31 (94%)
Respiratory exacerbation	53 (15%)	31 (25%)	13 (12%)	4 (5%)	3 (10%)	2 (6%)
	<i>n = 32</i>	<i>n = 16</i>	<i>n = 11</i>	<i>n = 3</i>		<i>n = 2</i>

Abbreviations: SMA: spinal muscular atrophy, DMD: Duchenne muscular dystrophy, Other: other neuromuscular disorder (arthrogryposis multiplex congenita (n = 13), congenital myasthenic syndrome (n = 7), diaphragm disorder (n = 6), Pompe disease (n = 7), mitochondrial cytopathy (n = 2)), NIV: noninvasive ventilation, CPAP: continuous positive airway pressure.

Data are given as mean ± standard deviation (range).

In italic: number of missing data.

* $p < 0.001$ as compared to patients with SMA, congenital myopathy-dystrophy and other neuromuscular disorders

$p < 0.001$ as compared to the other diagnostic groups.

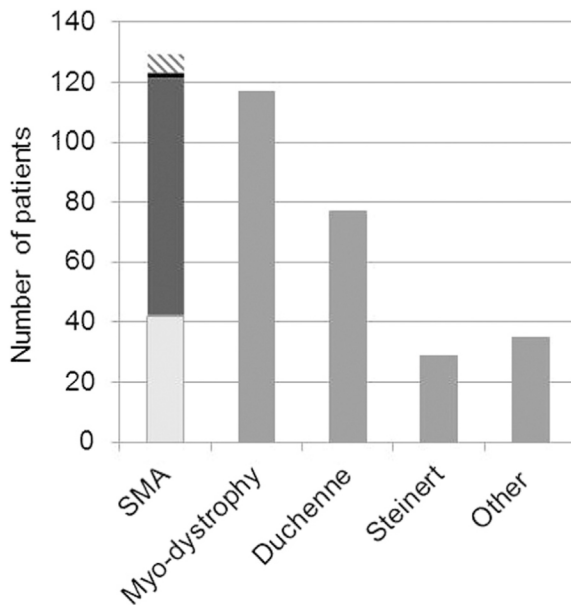


Fig. 1. Number of patients in the different diagnostic groups.

Abbreviations: SMA: spinal muscular atrophy, light grey: SMA type I, dark grey: SMA type II, black: SMA type III, hatched: type not available, myo-dystrophy: congenital myopathy-dystrophy, Duchenne: Duchenne muscular dystrophy, Steinert: Steinert myotonic dystrophy, other: other neuromuscular disorders.

aged 12 to 20 years, used daytime ventilation by means of a mouthpiece. Nine (2%) patients had additional oxygen therapy with NIV. For CPAP, mean level was 8 ± 2 cmH₂O with 62% of the patients using a standard device.

Airway clearance devices were used by 254 (66%) of patients but more frequently by patients with SMA and congenital myopathy/dystrophy as compared to the other diagnostic groups ($p < 0.001$) (Table 5). The majority of the patients (71%) had one device while the other patients (29%) had two or more devices.

Patients with SMA represented the largest group of patients on chronic NIV/CPAP with 42 (34%) patients having a type I or I bis, 79 (64%) a type II and 2 (2%) patients a type III (for 6 patients, the type of SMA was not reported) (Table 6). All the patients, but one patient with SMA type III, were treated with NIV. The age at NIV

initiation was lower in patients with SMA type I as compared to patients with SMA type II ($p < 0.001$). A life support device was used more often by patients with SMA type I (83%) as compared to patients with SMA type II (45%, $p < 0.001$). NIV was initiated electively for 42% of patients with SMA type I and 75% of those with SMA type II ($p < 0.05$). The decision to initiate NIV was mainly based on “other criteria” and an abnormal nocturnal SpO₂ and PtcCO₂ recording. Airway clearance devices were used by 79% of patients with SMA type I and 87% of patients with SMA type II. The type of device was mainly an IPPB device for both groups, followed by a MI-E device.

Discussion

This survey is the first to give a recent, national, and complete overview of all children with NMD treated with long term NIV/CPAP in France. The main observations are that 93% of the patients were treated with NIV, SMA represented the most important diagnostic group, NIV/CPAP was started electively in 85% of cases, and mean adherence to NIV/CPAP was around 8 h/24.

This survey confirms the large increase of the number of children with NMD treated with long term CPAP/NIV in France during the last two decades. Indeed, this number increased from 35 in 2000 [5] to 387 in 2019 [4]. However, although the number of NMD patients has risen sharply, the percentage of patients with NMD treated with long term NIV/CPAP has remained relatively stable, from 34% in 2000 to 27% in 2019, due to the large increase in children treated with CPAP for severe upper airway obstruction [4,6,7]. This increase in the number of children treated with long term NIV or CPAP and the change in the relative percentage of the different diagnostic groups have been observed worldwide. An extensive review on pediatric NIV and CPAP published in 2018 observed that obstructive sleep apnea was the most common condition (29%), with SMA and other NMD representing 8% and 5% of the total population, respectively [6]. Another study published the same year by the same authors revealed that NIV incidence and prevalence increased five and three-fold over a ten year period (2005–2014) in their centre, with upper airway anomalies representing 60% of the 622 patients, and musculoskeletal and NMD 15% [7].

This increase in the number of children with NMD treated with long term NIV may be in part explained by a better diagnosis and

Table 2

Investigations performed prior to NIV/CPAP initiation.

Investigations, n (%)	Total population(n = 387)	SMA(n = 129)	Congenital myopathy / dystrophy(n = 117)	DMD(n = 77)	Steinert myotonic dystrophy(n = 29)	Other(n = 35)
Nocturnal SpO ₂ + PtcCO ₂ recording	149 (39%)	49 (38%)	45 (38%)	31 (40%)	6 (21%)	18 (51%)
PG/PSG + nocturnal PtcCO ₂ recording	86 (22%)	13 (10%)	29 (25%)	18 (23%)	17 (59%)*	9 (26%)
PG/PSG	41 (11%)	6 (5%)	14 (12%)	11 (14%)	4 (14%)	6 (17%)
Nocturnal SpO ₂ recording (alone)	3 (1%)	1 (1%)	2 (2%)	0	0	0
Blood gases	2 (0.5%)	2 (1.5%)	0	0	0	0
	n = 32	n = 16	n = 11	n = 3		n = 2

Abbreviations: SMA: spinal muscular atrophy, DMD: Duchenne muscular dystrophy, Other: other neuromuscular disorder, PG: respiratory polygraphy, PSG: polysomnography, SpO₂: pulse oximetry, PtcCO₂: transcutaneous carbon dioxide pressure, ICU: intensive care unit.

In italic: number of missing data.

Sixty two patients had no investigation and NIV/CPAP was initiated on other criteria.

* $p < 0.05$ as compared to the other diagnostic groups.

Table 3

NIV/CPAP initiation criteria.

Initiation criteria, n (%)	Total population(n = 387)	SMA(n = 129)	Congenital myopathy/ dystrophy (n = 117)	DMD(n = 77)	Steinert myotonic dystrophy(n = 29)	Other(n = 35)
Nocturnal SpO ₂ + PtcCO ₂	149 (39%)	43 (33%)	48 (41%)	31 (40%)	9 (31%)	18 (51%)
AHI	50 (13%)	7 (5%)	15 (13%)	13 (17%)	8 (28%)	7 (20%)
AHI + SpO ₂ + PtcCO ₂	54 (14%)	9 (7%)	2 (2%)	12 (16%)	9 (31%)	6 (17%)
SpO ₂	5 (1%)	3 (2%)	2 (2%)	0	0	0
PtcCO ₂	8 (2%)	3 (2%)	18 (15%)	2 (3%)	0	1 (3%)
AHI + SpO ₂	5 (1%)	0	2 (2%)	2 (3%)	0	1 (3%)
AHI + PtcCO ₂	3 (1%)	0	2 (2%)	0	1 (3%)	0
Other criteria	77 (20%)	44 (34%)	17 (14%)	14 (18%)	2 (7%)	0
	n = 36	n = 20	n = 11	n = 3	0	n = 2

Abbreviations: SMA: spinal muscular atrophy, DMD: Duchenne muscular dystrophy, Other: other neuromuscular disorder, PG: respiratory polygraphy, PSG: polysomnography, SpO₂: pulse oximetry, PtcCO₂: transcutaneous carbon dioxide pressure, AHI: apnea-hypopnea index.

In italic: number of missing data.

Table 4

NIV/CPAP adherence and equipment.

	Total population(n = 387)	SMA(n = 129)	Congenital myopathy/ dystrophy(n = 117)	DMD(n = 77)	Steinert myotonic dystrophy(n = 29)	Other(n = 35)
<i>Adherence (hours/night)</i>	8.0 ± 3.1 (0–24)	8.6 ± 2.3 (0–16)	8.0 ± 3.6 (0–24)	7.0 ± 2.6 (0–11)	7.0 ± 2.9 (0–12)	9.0 ± 4.2 (3–24)
<4 h/24 (n, %)	27 (7%)	3 (2%)	11 (9%)	9 (12%)	3 (10%)	1 (3%)
≥ 16 h/24 (n, %)	6 (2%)	1 (1%)	3 (3%)	0	0	2 (6%)
	n = 30	n = 11	n = 6	n = 9		n = 4
<i>Interface</i>						
Nasal (n, %)	304 (79%)	119 (92%)	88 (75%)	53 (69%)	15 (52%)	29 (83%)
Nasobuccal (n, %)	49 (13%)	2 (2%)	18 (15%)	13 (17%)	12 (41%)*	4 (11%)
Nasal prongs (n, %)	21 (5%)	5 (4%)	5 (4%)	9 (12%)	0	2 (6%)
Total face (n, %)	2 (1%)	0	0	1 (1%)	1 (3%)	0
	n = 11	n = 3	n = 6	n = 1	n = 1	
<i>Ventilatory mode</i>						
NIV n, %	361 (94%)	127 (98%)	109 (93%)	73 (95%)	26 (90%)	26 (74%)
CPAP n, %	24 (6%)	1 (1%)	8 (7%)	4 (5%)	3 (10%)	8 (23%)
	n = 1	n = 1				
<i>Type of NIV device</i>						
Standard (n, %)	46 (12%)	7 (5%)	11 (9%)	11 (14%)	10 (34%)	7 (20%)
Intermediate (n, %)	109 (28%)	37 (29%)	34 (29%)	23 (29%)	9 (31%)	6 (17%)
Life support (n, %)	194 (50%)	77 (60%)	62 (53%)	37 (48%)	7 (24%)	11 (31%)
	n = 12	n = 6	n = 2	n = 2		n = 2
<i>NIV settings</i>						
Mean IPAP (cmH ₂ O, range)	14.3 ± 3.9 (7–30)	14.4 ± 4.1 (7–30)	15.3 ± 4.1 (8–28)	13.5 ± 3.3 (8–26)	13.5 ± 3.2 (8–21)	12.7 ± 3.6 (8–21)
Mean EPAP (cmH ₂ O, range)	4.6 ± 1.2 (0–10)	4.6 ± 1.1 (2–9)	4.5 ± 1.4 (0–10)	4.7 ± 1.2 (0–7)	4.9 ± 1.1 (3–8)	4.8 ± 0.7 (4–6)
BUR (breaths/min)	18.7 ± 5.4 (10–50)	20.1 ± 5.6 (10–50)	19.4 ± 5.2 (10–40)	15.9 ± 3.6 (10–30)	15.9 ± 3.4 (10–25)	20.7 ± 6.8 (10–36)
<i>CPAP setting</i>						
Mean CPAP (cmH ₂ O, range)	8.0 ± 2.1 (5–12)	9	7.1 ± 1.5 (6–10)	9.5 ± 2.4 (7–12)	10	7.4 ± 2.3 (5–12)

Abbreviations: NIV: noninvasive ventilation, CPAP: continuous positive airway pressure, SMA: spinal muscular atrophy, DMD: Duchenne muscular dystrophy, Other: other neuromuscular disorder, IPAP: inspiratory airway pressure, EPAP: expiratory airway pressure, BUR: back up rate.

Data are given as mean standard deviation or (ranges).

In italic: number of missing data.

* $p < 0.01$ as compared to the other diagnostic groups

Table 5
Use of airway clearance devices at home.

	Total population(n = 387)	SMA(n = 129)	Congenital myopathy / dystrophy(n = 117)	DMD(n = 77)	Steinert myotonic dystrophy(n = 29)	Other(n = 35)
IPPB alone (n,%)	112 (29%)	42 (32%)	38 (32%)	24 (31%)	5 (17%)	3 (8%)
MI-E alone (n,%)	62 (16%)	25 (19%)	17 (15%)	15 (19%)	5 (17%)	0
IPV alone (n,%)	6 (1%)	2 (2%)	3 (3%)	1 (1%)	0	0
IPPB + MI-E (n,%)	54 (14%)	25 (19%)	13 (11%)	14 (18%)	2 (7%)	0
IPPB + IPV (n,%)	8 (2%)	6 (5%)	2 (2%)	0	0	0
MI-E + IPV (n,%)	10 (3%)	5 (4%)	3 (3%)	0	0	2 (6%)
IPPB + MI-E + IPV (n,%)	1 (1%)	1 (1%)	0	0	0	0
None (n,%)	133 (34%) <i>n = 1</i>	23 (18%)	40 (34%) <i>n = 1</i>	23 (30%)	17 (59%)	30 (86%)

Abbreviations: SMA: spinal muscular atrophy, DMD: Duchenne muscular dystrophy, Other: other neuromuscular disorder, IPPB: intermittent positive pressure breathing device, MI-E: mechanical in-exsufflator device, IPV: intrapulmonary percussive ventilation.
In italic: data not available.

Table 6
Characteristics of patients with spinal muscular atrophy.

	SMA type I (n = 42)	SMA type II (n = 79)
Age (years)	6.2 ± 5.4 (0.7–18.6)	10.6 ± 4.9 (0.5–20.3)
Age at initiation (years)	3.7 ± 2.0 (0.1–6.9)*	6.4 ± 4.4 (0–16.8)
Duration of NIV (years)	3.1 ± 3.1 (0.1–15.4)	4.3 ± 3.4 (0–13.5)
<i>Type of NIV device</i>		
Standard (n, %)	1 (2%)	5 (6%)
Intermediate (n, %)	4 (10%)	33 (42%)
Life support (n, %)	36 (86%)* <i>n = 1</i>	36 (46%) <i>n = 5</i>
<i>NIV initiation</i>		
Electively	18 (43%) [#]	60 (76%)
Acute respiratory failure	14 (33%) <i>n = 10</i>	14 (18%) <i>n = 5</i>
<i>Initiation criteria</i>		
AHI	3 (7%)	3 (4%)
Nocturnal SpO ₂ + PtcCO ₂	7 (17%)	32 (40%)
AHI + SpO ₂ + PtcCO ₂	2 (5%)	7 (9%)
SpO ₂	1 (2%)	2 (3%)
PtcCO ₂	0	3 (4%)
AHI + SpO ₂	0	0
AHI + PtcCO ₂	0	0
Other criteria	16 (38%) <i>n = 13</i>	26 (33%) <i>n = 6</i>

Abbreviations: SMA: spinal muscular atrophy, NIV: noninvasive ventilation, AHI: apnea-hypopnea index, SpO₂: pulse oximetry, PtcCO₂: transcutaneous carbon dioxide pressure.

Data are given as mean standard deviation or (ranges).

In italic: number of missing data.

* *p* < 0.01 as compared to patients with SMA type II.

[#] *p* < 0.05 as compared to patients with SMA type II.

follow up of patients with NMD. Indeed, in France, all patients with rare diseases, including NMD, are managed by national reference centres for rare diseases who have elaborated national guidelines for optimal management (https://www.has-sante.fr/jcms/c_1340879/fr), with the recommendation for systematic sleep studies for numerous rare disorders, including NMD. The increase in the number of children with NMD is also explained by a global increase in the expertise in paediatric NIV/CPAP. Indeed, the paediatric NIV centres increased from approximately 4 in 2000 to 28 university paediatric NIV/CPAP centres in 2019 [4,5]. And finally, the management of infants with SMA type I has become more pro-active since the availability of innovative therapies [8,9]

Nearly all the patients (94%) were treated with NIV with only 6% of the patients being treated with CPAP. Children with NMD are usually treated with NIV and not CPAP [1,2,10,11]. NIV is indicated for disorders that cause disequilibrium in the respiratory balance, with the aim to assist or ‘replace’ the weakened respiratory muscles in order to correct alveolar hypoventilation [1]. CPAP is indicated in case of upper airway obstruction and

was more commonly used by patients with ‘other’ NMD (23%) such as arthrogyriposis multiplex congenita, congenital myasthenic syndromes, and mitochondrial cytopathy or in children who have a NMD with a predominance of obstructive events [12].

NIV/CPAP was started electively in 85% of the patients. This is explained by the fact that screening for sleep-disordered breathing in high risk populations has improved in France. The percentage of patients in whom NIV/CPAP was initiated during an acute illness (15%) is indeed within the low range as compared to those reported by other groups in Austria (29%) [13], Vancouver, Canada (47%) [14], Japan (66%) [15], or in some emerging countries such as Argentina (53%) [16], but similar to those reported in London (15%) [17] or Alberta, Canada (17%) [7]. However, these studies included also patients without NMD.

A PSG or a PG was performed before NIV/CPAP initiation in 33% of the total population, associated with a simultaneous PtcCO₂ recording in 22% of the patients. The majority of patients (39%) had only a nocturnal SpO₂ and PtcCO₂ recording. This may be explained in part by the limited access to sleep studies for children in some paediatric centres. Also, PtcCO₂ monitoring is recommended but also not available on a routine basis in all centres [2].

There are no validated criteria to start long term NIV in children [2,6,18]. In clinical practice, NIV may be initiated in (1) an acute setting, after invasive ventilation or NIV weaning failure in the paediatric intensive care unit, or (2) in a subacute or chronic setting, on abnormal nocturnal gas exchange alone or on the association of abnormal gas exchange and respiratory events on a PSG [2,18]. In the present study, in the majority of cases (42%), elective NIV/CPAP was initiated on an abnormal nocturnal SpO₂ and/or PtcCO₂ recording, as noticed by the European Respiratory Society Task Force on long term paediatric NIV [2]. In 13% of cases, NIV/CPAP was initiated on an abnormal AHI and in 16% of cases, on an abnormal AHI and SpO₂ and/or PtcCO₂ recording. Most sleep studies performed in children with NMD show no or few apnoeic events so that the AHI is often within the normal range or moderately increased [19–21]. As the major criterion to initiate NIV is alveolar hypoventilation, it is obvious that an abnormal overnight gas exchange represents the most common criteria to start NIV [2,18]. NIV/CPAP was initiated on ‘other criteria’ in 20% of the patients, comprising: abnormal blood gases, clinical criteria, the relay of invasive ventilation and/or the impossibility to wean the patient from NIV/CPAP initiated during a respiratory exacerbation, prior to elective surgery [22], restrictive lung disease on lung function tests, or thoracic deformity.

The mean objective adherence was good as reported by other French studies [23–25]. This may be explained by the therapeutic education of the patients and caregivers and the expertise of the centres, associated with a well organised national home care

provider network. NIV adherence was slightly lower in patients with DMD or Steinert myotonic dystrophy and may be explained by the older age of the patients and consequently a physiologically lower sleep duration, or by the difficulty to accept NIV for teenagers with chronic conditions. The observed adherence is in agreement with paediatric guidelines that recommend that NIV/CPAP should be used during the patient's total sleep time [2].

Nasal masks were the most common interface (79%) as reported in many studies [26]. The use of a nasobuccal interface was significantly more common in patients with Steinert myotonic dystrophy due to a high prevalence of mouth breathing in these patients.

Most patients had a life support or intermediate device which may be explained by the fact that numerous of these patients were infants or young children whose weight is below the recommended minimal weight proposed by the manufacturer for a standard device. Indeed, the use of an inappropriate device precludes the detection of the patient's airflow and consequently the appropriate monitoring of the patient's respiratory data and adherence [27,28]. Second, because of a limited respiratory autonomy, 50% of the patients had a life support device. Interestingly, only a few patients (2%) required additional oxygen, which may signify that for the majority of diseases for which a ventilatory support is required, NIV is sufficient to normalize nocturnal gas exchange.

Concerning NIV settings, pressure support ventilation was largely used among the centres with settings that are in agreement with those reported in the literature [29]. Volume target ventilation was used by only 15% of the patients.

Airway clearance devices were used by 66% of patients with 20% of the patients using two devices. IPPB is commonly used in France, which explained why it was used by 46% of the patients while 31% of the patients used a MI-E. Finally, only 5 patients used mouthpiece ventilation, showing that this mode is exceptionally used in children, as compared to adult NMD patients in France (14%) [30]. Unfortunately, it was not possible to have the objective compliance with these airway clearance devices, the survey assessing only the devices that were prescribed at home.

Patients with SMA represented the largest group with 34% of patients having a type I, 64% a type II and 2% of patients a type III. As expected, the age at NIV initiation was lower for patients with SMA type I as compared to patients with SMA type II, with a more common use of a life support device (83%). NIV was initiated during a respiratory exacerbation in 33% of patients with SMA type I which was the highest rate observed in this survey [8]. The decision to initiate NIV was mainly based on "other criteria" including respiratory symptoms (recurrent respiratory infections, respiratory exacerbation) and chest deformity. Airway clearance devices were used by 82% of patients with SMA which was also the highest rate observed in the present survey.

We acknowledge that our survey has some limitations. Although data was complete for 26 centres, data was incomplete for one centre dealing mainly with patients with NMD, leading to a moderate underestimation of the number of patients. No information is available on the cut off values or the details of the abnormal parameters that prompted the NIV/CPAP initiation. Indeed, due to the lack of validated criteria or consensus, the threshold values and parameters were based on the routine clinical practice of each centre. The objective adherence with the airway clearance devices was not available. Unlike other countries, corticosteroids are not prescribed on a routine basis in France for DMD patients. Finally, this survey was performed before the availability of gene therapy for patients with SMA, their profile is thus expected to evolve in the coming years.

In conclusion, this survey showed the large increase in the number of children with NMD treated with long term

NIV/CPAP in France over the last two decades. SMA, congenital myopathy/muscular dystrophy and DMD represented the most important diagnostic groups. The expertise of the French paediatric NIV/CPAP network is reflected by the good mean objective adherence and the low percentage of NIV/CPAP initiation during a respiratory exacerbation. National surveys and registers are extremely informative for the natural history of children with NMD, in particular within the area of innovative therapies, such as gene therapy for children with SMA, which are expected to profoundly change the course of the NMD routine care. Finally, surveys and registers contribute also to provide optimal medical care and to help to define recommendations and guidelines for the NIV/CPAP initiation, follow up and weaning of this increasing challenging population.

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