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Non-invasive ventilatory approach to treatment of acute respiratory failure in neuromuscular disorders. A comparison with endotracheal intubation

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Abstract *Objective*: Prospectively to investigate the efficacy of non-invasive positive pressure ventilation (NPPV) combined with cricothyroid "mini-tracheostomy" (CM) as a first-line intervention in patients with acute respiratory failure (ARF) of neuromuscular origin, in comparison with positive pressure ventilation (PPV) via endotracheal intubation (ETI).
Design: Prospective analysis of the short-term outcomes of 14 non-consecutive patients suffering from ARF of neuromuscular origin who were administered NPPV and comparison with the outcomes of 14 matched historical control patients receiving conventional mechanical ventilation (MV) via ETI.
Setting: Adult five-bedded respiratory intensive care unit in a university hospital.
Patients and interventions: Fourteen neuromyopathic patients who developed hypercapnic ARF and were submitted to NPPV (group A) and fourteen matched historical control patients, who were administered PPV via ETI (group B). Seven subjects receiving NPPV also underwent CM.
Outcome measures: Mortality during ICU stay and treatment failure were evaluated; treatment failure was defined as death or the need for ETI for the NPPV group and as death or the inability to wean from MV for the control group. Length of stay in the ICU and time to improvement, defined as the time required for a significant relief of dyspnea and neurologic impairment and for correction of arterial blood gases, were also compared.
Results: Intra-hospital mortality and treatment failure were lower in the NPPV group than in the conventional PPV via ETI group (2 vs 8 cases and 4 vs 11 cases, respectively). In addition, the duration of ICU stay for subjects who underwent NPPV was shorter than for patients who were intubated (13.6 ± 9.7 vs 47.1 ± 51.9 days). "Mini-tracheostomy" was well tolerated and no significant side effects were encountered. Two patient were excluded from the study because they showed a severe inability to swallow and needed to be intubated to protect the upper airway from the risk of aspiration.
Conclusions: Non-invasive positive pressure ventilation in combination with CM may be considered as a safer and more effective alternative to ETI in the treatment of patients with neuromuscular disorders (NMD) who develop ARF and require MV; nevertheless, patient selection remains important, since a significant proportion of neuromyopathic patients might have to be excluded from NPPV because of severe risk of aspiration.

Key words Neuromuscular disorder · Acute respiratory failure · Non-invasive positive pressure ventilation

Introduction

The onset of acute respiratory failure (ARF) (in most cases due to infection of the respiratory tract, heart failure, administration of sedative drugs and/or metabolic irregularities) is a common event in subjects affected with neuromuscular disorders (NMD) and has a grim prognosis [1, 2, 3, 4].

In current practice, positive pressure ventilation (PPV) with a translaryngeal endotracheal tube constitutes the conventional approach for treating patients with ARF who require ventilatory support. However, placing this artificial airway presents several disadvantages, including tracheal injury, the need for sedation, inability of patients to swallow or talk and increased risk of infections such as pneumonia and sinusitis [5, 6, 7].

Disadvantages linked to mechanical ventilation (MV) via endotracheal intubation (ETI) are even more pronounced in neuromyopathic patients, due to the more prolonged duration of ventilatory treatment and the increased length of stay in the intensive care setting. In particular, pneumonia occurs with a higher frequency and a more elevated rate of mortality [8]. In addition, these patients frequently develop a myosin-depleting myopathy, associated with the use of neuromuscular blocking agents and steroids, which may exaggerate weakness of the respiratory muscles, thus delaying weaning from MV [9].

The interest in non-invasive positive pressure ventilation (NPPV), administered through a nasal, face or mouth mask, for neuromuscular chronic respiratory failure has led to a reassessment of the use of NPPV in ARF. NPPV, in fact, offers several potential advantages over PPV via ETI for the treatment of ARF, including improved patient comfort, avoidance of tracheal injury, preservation of airway defense mechanisms and, with nasal ventilation, continued ability to speak and swallow.

To date, two uncontrolled trials exploring the use of NPPV in acute respiratory insufficiency have included patients affected with NMD and severe restrictive pulmonary impairment; the results demonstrated that the application of this technique may result in a reversal of blood gas abnormalities, with regression of clinical symptoms [10, 11]. Nevertheless, to our knowledge no ventilatory trials evaluating the success rate and outcome of NPPV have been targeted specifically to neuromyopathic patients with ARF.

The encouraging results of our initial experience in the treatment of neuromuscular ARF with NPPV [12] prompted us prospectively to investigate the efficacy of NPPV as a first-line intervention in patients with ARF of neuromuscular origin, in comparison with PPV via ETI. To this end, we analyzed the clinical course of 14 subjects with advanced NMD who developed hypercapnic ARF and were submitted to nasal ventilation, and compared the results with the outcomes of 14 matched historical control patients receiving conventional ETI. In particular, we evaluated whether NPPV would outperform PPV via ETI in terms of mortality, treatment failure and length of ICU stay. In our study, some patients receiving NPPV were also administered cricothyroid "mini-tracheostomy" (CM), in order to facilitate the elimination of airway secretions and to avoid mucus plugging and atelectasis.

Material and methods

We compared the short-term outcomes in 14 patients suffering from ARF of neuromuscular origin who were administered NPPV (group A) with the outcomes of 14 matched historical control patients (group B) receiving conventional MV via ETI. The criteria adopted for administering MV were the same in groups A and B, and the two groups received similar pharmacologic therapy (antibiotics, steroids and diuretics, when needed).

Patients

Fourteen non-consecutive patients affected with advanced NMD and admitted, because of acute hypercapnic respiratory failure (ARF), to the ICU of the Respiratory Pathophysiology Department of the City Hospital of Padova between 1995 and 1997 were recruited for administration of NPPV. The diagnosis of NMD was based on standard clinical, enzymatic, electromyographic and biopsy criteria. Upon admission all of the patients met clinical and physiologic parameters suggesting the urgent need for MV, as indicated by the following criteria: (1) difficulty in breathing as expressed by the patient, (2) lethargy, (3) hypercapnia and (4) acute respiratory acidosis [13].

Before starting MV, the neurologic status of each patient was assessed by the Glasgow Coma Score [14] and the Kelly and Matthay Neurologic Status Score [15]. The only criterion for excluding patients from the study was severe inability to swallow, as assessed by the Gilardeau score [16], with need for ETI to protect the airways. Informed consent (as approved by the institutional review board) was obtained from the patients or from the parents of patients whose clinical condition rendered them unable to express their wish.

The control group was selected from a group of 30 patients admitted to the ICU of our Department between 1992 and 1994. For each patient treated with NPPV, a matching control patient was selected according to the following criteria: same sex and similar age (within 5 years) to that of the treated patient; same type of neuromuscular disease; similar degree of swallowing impairment, as assessed by the Gilardeau score [16]; severity of neurologic dysfunction on admission within two points of that of the treated patient, as assessed by the Kelly and Matthay Neurologic Status Score; arterial pH on admission within 0.03 units of the value for the treated patient; arterial partial pressure of carbon dioxide ($PaCO_2$) on admission within 0.7 kPa of the value for the treated patient when the value was below 9.3 kPa and within 1.4 kPa when it was 9.3 kPa or higher. These criteria were similar to those employed by other authors [17, 18]. Severe cardiomyopathy was excluded, both in the patients recruited for the study and in the matched historical controls, by clinical, ECG and radiographic findings.

Ventilatory treatment

Non-invasive pressure ventilation was delivered by a Puritan-Bennett 7200 ventilator (Puritan-Bennett) using the assist/control mode. At the start of MV the ventilator was adjusted to obtain a tidal volume (Vt) of 10 ml/kg and a respiratory rate of less than 25 breaths/min; the ventilator setting was then readjusted based on measurements of arterial blood gases, with the goal of maintaining arterial oxygen saturation (SaO_2) over 90 % and $PaCO_2$ below 6.7 kPa. Supplemental oxygen was delivered when necessary to raise SaO_2 above 90 %; external positive end-expiratory pressure (PEEP) was never added. Patients were connected to the ventilator by means of a light-weight, elastic, custom-made nasal interface that was well-fitted to the patient's face (Coltene, Altstatten, Switzerland). Special care was taken to avoid air leaks through the mouth by the application of chin straps.

A standard monitoring ICU system was applied to all the patients; an indwelling arterial catheter was inserted into the radial artery for continuous recording of arterial blood pressure and frequent blood gas analysis, SaO_2 was continuously monitored via a pulse oximeter, and ECG and respiratory rate were continuously recorded by classic means. The proper use of the ventilator and tolerance were monitored by the attending physician and specialized nurses experienced with NPPV; patients were also regularly examined at 2-h intervals to verify their subjective response to ventilatory treatment (i. e., degree of dyspnea and mental alertness) and their ability to clear secretions and to protect the airways. Arterial blood gases were measured within 2-h, 2- to 6-h and 6- to 12-h intervals following initiation of NPPV.

Non-invasive positive pressure ventilation was initially delivered continuously, except for brief periods of "rest" (10–20 min), to allow the patients to receive dietary liquid supplements, drink water and speak. Continuous MV was administered until satisfactory clinical conditions and blood gas exchange were restored; the criteria for discontinuation of NPPV were the following: $PaCO_2$ below 6.7 kPa and pH above 7.35 for at least 24 consecutive hours; respiratory rate less than 25 breaths/min; improvement of clinical signs and chest radiograph image. Afterwards, daily ventilator use was intermittent (approximately 3–4 h, 2 times per day), until $PaCO_2$ was stabilized at about 5.5–6 kPa and pH at 7.38–7.40; when necessary, supplemental oxygen was delivered during spontaneous breathing by nasal cannula or a Venturi mask, to maintain SaO_2 above 90 %. In all cases, nocturnal ventilation via nasal mask was continued after the resolution of ARF, until discharge from the ICU. When NPPV was unable to reduce dyspnea and lethargy and/or to improve blood gas exchange within the first 6–12 h of application, this ventilatory technique was judged to be inadequate: under these circumstances, ETI was administered.

The ventilator setting and weaning protocol were similar for the control subjects who were administered ETI in our ICU between 1992 and 1994. Patients were weaned from MV following improvement in respiratory failure by adjusting periods off MV to patient tolerance and objective findings; after extubation, all the patients were administered nocturnal NPPV until discharge from the ICU. Subjects who had required tracheostomy were administered nocturnal PPV via tracheostomy tube.

Cricothyroid "mini-tracheostomy"

Cricothyroid "mini-tracheostomy" is a procedure of percutaneous tracheal cannulation with a small-bore tube that provides constant tracheal access for sputum suction, which has been successfully utilized for patients undergoing thoracic surgery; CM usually does not alter the ability to speak and swallow and thus does not compromise the patient's quality of life [19].

Seven subjects receiving NPPV showed severe inability to clear bronchial secretions, with frequent need for broncho-aspiration, in spite of assisted cough and bronchial drainage; they all underwent CM in order to facilitate the elimination of airway secretions and avoid mucus plugging. The "mini-tracheostomy" was performed with a Mini-Trach II kit (Portex, UK).

Study end points and statistical analysis

To assess the efficacy of NPPV in comparison with PPV via ETI, primary study end points were defined as mortality during ICU stay and treatment failure. Treatment failure was defined as death or the need for ETI in the NPPV group, and as death or the inability to wean from MV for the control group. Secondary study end points were time to improvement, defined as the time required for a significant relief of neurologic impairment and for correction of arterial blood gases, and length of stay in the ICU. The Fisher exact test was used to compare categorical variables (mortality and treatment failure), and the Student's *t*-test was used to compare continuous variables (anthropometric data, pulmonary function and blood gas data at study entry). The Mann-Whitney nonparametric test was used to compare time to improvement and the duration of ICU stay. A p value less than 0.05 was considered as statistically significant.

Results

Two patients showed a severe inability to swallow with high risk of aspiration (stage 4 of Gilardeau classification). They required intubation to protect the upper airway and were excluded from the study; subsequently, they underwent tracheostomy and were submitted to long-term home mechanical ventilation, since they failed to wean from MV.

Tables 1 and 2 report diagnoses related to neuromuscular disease and to ARF, anthropometric data, Glasgow Coma Score and the degree of encephalopathy as assessed by the Kelly and Matthay Score, results of the last pulmonary function test obtained prior to admission (recording time: 1–3 months before the acute illness) and blood gas data at detection of ARF. Forced vital capacity (FVC) is expressed as an absolute value and as a percent of the predicted value; reference values are those of the European Community [20] or of Polgar and Promadhar [21] for subjects older or younger than 18 years, respectively. Arm span was used for determining percent predicted values in patients with severe scoliosis. Subjects in groups A and B who received NPPV and PPV via ETI, respectively, were very closely matched.

Severe respiratory infection (bronchitis or pneumonia), in most cases due to aerobic gram-negative agents, was the cause of acute decompensation in all patients in both groups; in subjects 3A and 12B respiratory infection was combined with abuse of sedative drugs. At ad-

Table 1 Anthropometric, clinical, pulmonary function and blood gas data at study entry, course of PPV and clinical outcome of patients submitted to NPPV (group A) and to PPV via ETI (group B). (DMD = Duchenne's Muscular Dystrophy; ALS = Amyotrophic Lateral Sclerosis; CMD = Congenital Muscular Dystrophy; CM = Congenital Myopathy; MSN = Motor-Sensory Neuropathy; GCS = Glasgow Coma Score; KMS = Kelly and Matthay Score; TI = Time to Improvement)

Patient, no	Type of NMD	Diagnosis related to ARF	Age, yr	BMI	GCS	KMS	FVC, L	FVC, %	PaO_2, kPA	$PaCO_2$, kPa	pH	Complications and Clinical outcome	TI, hrs	ICU stay, days
1A	DMD	Bronchitis	24	11.3	12	2	0.18	6	9.2	8.9	7,31	Discharged from ICU	10	4
2A	DMD	Pneumonia	24	21.5	14	2	0.54	13	9.3*	6.9	7,31	"Minitracheostomy"; discharged from ICU	4	9
3A	DMD	Pneumonia, sedative drugs	22	22	7	3	NA	NA	7.1	10.2	7,31	"Minitracheostomy"; ineffective NPPV; died	–	5
4A	DMD	Bronchitis	24	18.4	10	3	1.40	26	4.4	12.3	7,26	Discharged from ICU	8	15
5A	DMD	Pneumonia	19	9.2	12	2	0.32	7	10.6*	6.1	7,30	"Minitracheostomy"; discharged from ICU	9	20
6A	DMD	Bronchitis	14	25	10	4	0.35	8	10.3*	10.3	7,26	"Minitracheostomy"; ventricular arrhythmia; died	–	5
7A	DMD	Pneumonia	24	22.6	12	2	0.47	9	8.6*	7.8	7,35	Discharged from ICU	12	15
8A	ALS	Pneumonia	63	24	12	2	2.59	53	8.4	9.3	7,34	"Minitracheostomy"; discharged from ICU	4	40
9A	ALS	Bronchitis	69	22.5	6	5	NA	NA	16*	12	7,18	Ineffective NPPV; intubated, tracheostomy	–	14
10A	CMD	Bronchitis	51	15	11	3	0.80	18	7.7	9.3	7,27	Discharged from ICU	9	9
11A	MSN	Bronchitis	68	25.9	12	2	1.92	40	7.2	9.5	7,26	Discharged from ICU	12	10
12A	ALS	Bronchitis	69	23	12	2	3.20	75	9.5*	9.3	7,35	Ineffective NPPV; intubated; tracheostomy	–	25
13A	ALS	Bronchitis	62	22.2	12	2	1.20	41	8.7	9.3	7,32	"Minitracheostomy"; discharged from ICU	8	7
14A	CM	Bronchitis	10	20.1	8	4	0.36	19	8	10.6	7,28	Discharged from ICU	8	11
1B	DMD	Bronchitis	27	20.2	9	3	0.23	6	5.1	9.3	7,31	Cardiac failure; died	2	9
2B	DMD	Pneumonia	19	13	12	2	0.30	12	10.6*	6.8	7,34	Superimosed pneumonia; died	4	90
3B	DMD	Bronchitis	24	26	7	4	0.47	9	5.3	11.3	7,30	Superimosed pneumonia; died	2	75
4B	DMD	Pneumonia	25	11.3	10	3	0.23	5	13.5*	12	7,24	Tracheostomy; discharged from ICU	2	15
5B	DMD	Bronchitis	17	NA	10	4	NA	NA	9.1*	6.7	7,27	Cardiac failure; died	6	3
6B	DMD	Bronchitis	15	20	8	4	0.19	3	5.3	10.7	7,29	Discharged from ICU	2	20
7B	DMD	Bronchitis	19	19.9	10	4	0.30	8	6.3	8.5	7,34	Superimosed pneumonia; died	5	35
8B	ALS	Pneumonia	64	26	12	2	2.10	45	9.5*	10	7,33	Superimosed pneumonia; died	3	41
9B	ALS	Bronchitis	64	26	6	5	NA	NA	12.9*	11.2	7,15	Tracheal stenosis; pneumonia; died	3	180
10B	CMD	Bronchitis	54	17.6	10	3	0.89	23	4.3	10.1	7,29	Discharged from ICU	4	7
11B	MSN	Pneumonia	67	28	9	4	NA	NA	4.9	10.6	7,23	Tracheostomy; discharged from ICU; long-term MV	2	20
12B	ALS	Bronchitis, sedative drugs	70	24.1	8	4	NA	NA	14.4*	9.7	7,32	Tracheostomy; discharged from ICU; long-term MV	1	40
13B	ALS	Bronchitis	67	20.1	12	2	NA	NA	4.8	10.6	7,29	Superimosed pneumonia; died	1	120
14B	CM	Bronchitis	5	12	8	4	NA	NA	15.1*	9.3	7,31	Tracheostomy; discharged from ICU; long-term MV	2	9

NA = not available * supplemental oxygen

Table 2 Anthropometric, clinical, pulmonary function and blood gas data at study entry and outcomes of patients submitted to NPPV (group A) and to PPV via ETI (group B). Values are expressed as mean ± standard deviation

	Group A	Group B	P Value
Age, yrs	38.8 ± 23.1	38.4 ± 24.1	NS
BMI	20.5 ± 5.5	20.3 ± 5.6	NS
Glasgow Coma Score	10.7 ± 2.3	9.4 ± 1.9	NS
Kelly and Matthay Status Score	2.7 ± 1	3.4 ± 1	NS
FVC, L	1.1 ± 1	0.6 ± 0.6	NS
FVC, %	26.2 ± 21.7	13.9 ± 14	NS
PaO_2, kPa	8.9 ± 2.6	8.6 ± 4	NS
$PaCO_2$, kPA	9.5 ± 1.7	9.8 ± 1.6	NS
pH	7,29 ± 0,04	7,29 ± 0,05	NS
Death, No	2	8	0.046
Treatment failure, No	4	11	0.021
Time to improvement, hrs	8.4 ± 2.8	2.8 ± 1.5	0.0002
ICU stay, days	13.6 ± 9.7	47.1 ± 51.9	0.049

mission, all the patients in group A showed severe carbon dioxide retention, except for subjects 2A and 5A, in whom hypercapnia was moderate.

The response to NPPV and PPV via ETI is described in Table 1and 2. There was a clear trend indicating a lower mortality and a lower treatment failure among patients receiving NPPV compared with those who were intubated (mortality: 2 vs 8; treatment failure: 4 vs 11; Fisher exact p value = 0.046 and 0.021, respectively). Among patients of group A, nasal ventilation failed in three cases (3A, 9A and 12A) due to the inability to achieve an adequate alveolar ventilation, with progression of hypercapnia. Patient 3A was not administered ETI, as the parents expressed their wish to have ventilatory life support limited to a non-invasive approach; as a consequence, the patient died 5 days after the initiation of NPPV. Patients 9A and 12A were intubated and subsequently tracheostomized. Patient 6A developed severe ventricular arrhythmia after 72 h of successful NPPV and was intubated; a second episode occurred 24 h after intubation and led to cardiac arrest and death.

Ten subjects receiving NPPV (1A, 2A, 4A, 5A, 7A, 8A, 10A, 11A, 13A and 14A) responded well, with an uncomplicated course; clinical and physiologic improvement was evident after a mean of 8.4 h (range 4–12) on continuous nasal ventilation. The mean ICU stay for subjects who underwent NPPV was significantly lower than for patients who were intubated (13.6 ± 9.7 vs 47.1 ± 51.9 days; p = 0.049). The nasal mask was well-tolerated by all the patients and did not produce significant side-effects. Cricothyroid "mini-tracheostomy" was well tolerated by all seven patients who received it (2A, 3A, 5A, 6A, 8A, 9A and 10A) and no significant side effects arose after placement of the cannula. An initial difficulty was encountered during tracheal cannulation of patient 5A, due to the presence of severe cervical scoliosis with tracheal deviation.

All the patients in group B initially responded well to MV via ETI and the time required for the correction of gas exchange abnormalities was shorter than for patients submitted to NPPV (time to improvement: 2.8 ± 1.5 vs 8.4 ± 2.8 h; p = 0.0002). Nevertheless, 11 patients developed severe complications. Five patients (2B, 3B, 7B, 8B and 13B) died as a consequence of unresolved pneumonia complicated by irreversible septic shock. Patient 9B developed tracheal stenosis and underwent tracheostomy; subsequently he died as a consequence of unresolved pneumonia. Patients 1B and 5B died due to cardiac failure after 9 and 3 days, respectively, of continuous MV. Patients 11B, 12B and 13B were tracheostomized due to the need for prolonged MV; subsequently, they could not be weaned from MV and were submitted to long-term home mechanical ventilation approximately 24 h per day.

The remaining three patients (4B, 6B and 10B) had successful clinical courses. Patients 6B and 10B were extubated after 4 and 8 days of MV, respectively; following extubation they were administered nocturnal NPPV until discharge from the ICU. Case 4B was tracheostomized because of the need for prolonged MV; at discharge from ICU the tracheostomy tube was removed and replaced by a Montgomery T-tube, due to the persisting need for bronchial suction.

Discussion

The onset of ARF with need for ventilatory support is a common event in patients affected with neuromyopathies and has a grim prognosis. With this condition, the administration of PPV by a non-invasive route might be preferred to ETI, on the basis of improved patient comfort, avoidance of tracheal injury, preservation of airway defense mechanisms and, with nasal ventilation, continued ability to speak and swallow.

To our knowledge, this is the first study evaluating NPPV as a first-line intervention in patients affected with NMD who develop ARF requiring MV. The results obtained by comparing two groups of neuromyopathic patients with similar clinical features and levels of respiratory function allowed us to determine whether this approach would reduce mortality and length of ICU stay compared to PPV via ETI.

Although our study presents well-known limits due to the fact that we used matched historical controls [22], it provides several elements of information. First of all, our results suggest that the application of NPPV tends to reduce mortality and treatment failure in comparison with PPV via ETI. In fact, mortality was lower in the NPPV group than in the conventional PPV via ETI group (2 and 8 patients, respectively). Moreover, the majority of patients in group A were successfully ventilated and discharged from the ICU; in contrast,

only 3 of the 14 subjects receiving MV via ETI had an uncomplicated clinical course. Our study also demonstrates that the duration of ICU stay for subjects who underwent NPPV was significantly shorter than for patients who were intubated, even though the time initially required for obtaining a significant clinical and physiologic improvement was longer for group A than for group B.

Non-invasive positive pressure ventilation generally does not lead to complications stemming from nosocomial infections, possibly due to the lack of invasion by ETI and improved preservation of the airway defense mechanisms [23]. This feature probably plays a determinant role in increasing the success rate of non-invasive ventilation in neuromuscular ARF: in fact, in our study, superimposed or unresolved pneumonia with septic shock was absent in individuals receiving nasal ventilation. In contrast, these complications represented the cause of failure in 6 of the 11 subjects unsuccessfully treated via translaryngeal tube, even though in all the cases an aggressive antibiotic regimen was administered, selected on the basis of microbiological investigations.

It should be emphasized that NPPV combined with cricothyroid "mini-tracheostomy" (CM) was successfully administered even to patients showing a severe inability to eliminate bronchial secretions. The need for constant access to the bronchial tree for sputum suction is generally considered as a factor contraindicating the administration of non-invasive ventilatory treatment and requiring ETI. Nevertheless, in our experience, by providing direct access to the upper airways, CM made the use of nasal ventilation possible even in patients with profuse bronchial secretions and ineffective cough, thus avoiding mucus plugging and atelectasis. This result supports our preliminary report [12] and confirms both the utility of CM in the management of severe sputum retention in neuromuscular disorders and its tolerance by the patients, who are still able to maintain their speech and swallowing abilities.

We believe that these results support extended use of NPPV combined with CM in neuromuscular ARF. There are, however, factors limiting the administration of NPPV in neuromyopathic patients which render ETI unavoidable sometimes. In our study, two patients had to be excluded from NPPV and intubated because they showed complete inability to swallow with severe risk of aspiration. Dysphagia is a common occurrence in neuromuscular disorders: it has been reported in at least 73 % of patients with amyotrophic lateral sclerosis [24], in more than one-third of individuals with spinal muscular atrophy and in 40 % of patients with myotonic dystrophy [25]. Thus, considering that the ability to protect the upper airway adequately is undoubtedly crucial to the success and safety of non-invasive ventilatory treatment, a significant proportion of neuromyopathic patients might have to be excluded from NPPV during ARF because of severe risk of aspiration. An unsuccessfully treated patient in group A (case 3A) who had developed ARF as a consequence of pneumonia and inappropriate administration of sedative drugs (i.e., benzodiazepines) died as a result of progression of hypercapnia, due to the inability of non-invasive ventilation to achieve adequate alveolar ventilation. This loss of effectiveness of NPPV could be explained by the fact that narcotics are reported to determine a failure of centrally mediated respiratory activity to compensate for sleep-related insufflational leakage in ventilator-users [26]; therefore, one could argue that the use of non-invasive ventilation may also be contraindicated when neuromuscular ARF is triggered by the administration of sedative drugs.

Finally, some ethical considerations must be weighed regarding the impact of NPPV and ETI on the ability of our neuromyopathic patients to decide about their lives. In our experience the application of NPPV allows patients to retain their cognitive abilities and to discuss their preferences about the levels of medical intervention. By contrast, ETI often requires sedation, thus denying patients a sufficient degree of mental capacity to decide whether or not to undergo tracheostomy; in the present study, three of the patients in group B were obliged to undergo this procedure. In this regard, it is important to consider that some mentally competent individuals with advanced NMD have expressed their wish to place limits on the use of life-support techniques [27] and that some neuromyopathic patients who have been tracheostomized without their prior consent said that they would not want to undergo tracheostomy if they could make the decision [28]. In addition, tracheostomized patients also seem to be likely to experience greater difficulty in establishing care at home [29]. Therefore, given that NPPV allows patients the possibility to participate in decisions about their management, avoiding the risk of undergoing tracheostomy without a fully informed discussion, we suggest that, from an ethical point of view, NPPV should be preferred to ETI as the initial ventilatory treatment for all cases of neuromuscular ARF.

In conclusion, the findings of our study provide support for considering NPPV, in combination with cricothyroid "mini-tracheostomy", as a safer and more effective alternative to ETI in the treatment of patients with NMD who develop ARF and require MV, with the caveat that patient selection remains important to the success of this ventilatory approach. Prospective, controlled studies are needed to assess fully the true benefit of NPPV as a first-line intervention in neuromuscular ARF.

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