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M. M. Fernández
A. Villagrá
L. Blanch
R. Fernández

Non-invasive mechanical ventilation in status asthmaticus

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M. M. Fernández (✉) · A. Villagrá · L. Blanch · R. Fernández
Intensive Care Department,
Corporació Sanitària Parc Taulí s/n,
08208 Sabadell, Spain
E-mail: MFernandez@CSPT.es
Phone: +34-93-7458323Ext2 11 53
Fax: +34-93-7 23 38 63

Abstract *Objective*: To evaluate our clinical experience with the use of non-invasive mechanical ventilation (NIMV) in patients with an acute asthmatic attack.
Design: Seven-year period retrospective observational study.
Setting: General intensive care department (ICU) of a county hospital.
Patients: From 1992 to 1998, we documented clinical data, gas exchange and outcome of every asthmatic patient admitted to our ICU because of status asthmaticus (SA) refractory to initial medical therapy.
Interventions: Clinical charts were reviewed and patients were allocated to two groups according to their suitability as participants in an NIMV trial. Patients who arrived in respiratory arrest and those who ultimately improved with medical management alone were not considered candidates for NIMV. For the present analysis, the rest of the patients were considered candidates for NIMV, while the decision to start a NIMV trial or to perform endotracheal intubation (ETI) remained at the discretion of the attending physician. When patients failed to improve with NIMV, standard mechanical ventilation (MV) with ETI was initiated.
Measurements and results: Fifty-eight patients were included in the study. Twenty-five patients (43 %) were not eligible for NIMV: 11 patients (19 %) because of respiratory arrest on their arrival at the Emergency Room and 14 patients (24 %) because of improvement with medical management (bronchodilators, corticoids and oxygen). The remaining 33 patients were eligible for NIMV (57 %): 11 patients (33 %) received invasive MV and 22 patients (67 %) were treated with NIMV. Three NIMV patients (14 %) needed ETI. We compared data at baseline, 30 min, 2–6 h and 6–12 h after the onset of ventilatory support. Significant differences were observed in arterial blood gases on admission to the Emergency Room between MV and NIMV: $PaCO_2$ (89 ± 29 mmHg vs 53 ± 13 mmHg, $p < 0.05$), pH (7.05 ± 0.21 vs 7.28 ± 0.008, $p < 0.05$) and HCO_3^- level (22 ± 5 mmol/l vs 26 ± 6 mmol/l, $p < 0.05$). No differences were found in the median length of ICU stay (4.5 vs 3 days), median hospital stay (15 vs 12 days) and mortality (0 vs 4 %).
Conclusion: Face mask NIMV appears to be a suitable method for improving alveolar ventilation and can reduce the need for intubation in a selected group of patients with SA.

Key words Asthma · Mechanical ventilation · Hypercapnia · Non-invasive ventilation

Introduction

The prevalence, severity and morbidity of asthma have risen in recent years [1, 2], leading to an increase in the number of asthmatic patients requiring admission to the intensive care unit (ICU).

Patients with status asthmaticus (SA) present significant increases in both inspiratory and expiratory indexes of airway obstruction and high levels of dynamic hyperinflation. The inspiratory muscles maintain their contraction throughout the entire respiratory cycle, but chest overdistension shortens these muscles and reduces their efficiency. Finally, respiratory muscle fatigue and increased physiological dead space lead to respiratory acidosis and ventilatory failure [3, 4, 5]. Endotracheal intubation (ETI) and mechanical ventilation (MV) are required in patients with asthma and hypercapnia who develop exhaustion of the ventilatory muscles or life-threatening complications such as hypotension, arrhythmias and decreased level of consciousness. Nevertheless, ETI and invasive MV are associated with substantial morbidity and mortality rates [6, 7, 8]. As a result, less harmful methods of providing ventilatory support need to be found.

Several studies suggest that non-invasive mechanical ventilation (NIMV) added to the standard pharmacological therapy may be involved in various forms of hypercapnic acute respiratory failure. NIMV mainly works by improving alveolar ventilation and ameliorating muscle fatigue, relieving dyspnoea and avoiding the unnecessary risks and discomfort associated with the endotracheal tube [9, 10, 11, 12, 13]. The term NIMV encompasses a range of techniques for augmenting alveolar ventilation without an artificial airway. Continuous positive airway pressure (CPAP) and non-invasive intermittent positive pressure ventilation (NPPV) via a face mask are the most common methods. In asthmatic patients, Martin et al. [14] studied the effects of CPAP during histamine-induced bronchospasm. They found that CPAP reduced airway resistance and the workload of the inspiratory muscles, improving their efficiency and decreasing the cost of breathing. To our knowledge, the only report of experience with NPPV as a first line treatment in SA is by Meduri et al. [2]. With their highly skilled team, they showed that face mask NPPV was highly effective in correcting gas exchange abnormalities, with low rates of intubation.

As there are currently few data on the clinical use of NIMV in SA, we performed this study with the following objectives in mind: (1) to review the data of severely asthmatic patients admitted to our ICU after the introduction of this ventilatory support as a clinical routine, and (2) to compare the clinical profile, arterial blood gases (ABG) and outcome between patients treated with invasive MV and those treated with NIMV.

Materials and methods

We reviewed the clinical charts of asthmatic patients admitted to our ICU from 1992 to 1998 with the diagnosis of refractory SA. The diagnosis of asthma was based on clinical history and normal pulmonary function tests after the crisis.

Status asthmaticus was defined as a severe asthmatic attack with patients showing one or more of the following symptoms: dyspnoea precluding speech, accessory muscle use, respiratory rate more than 35/min, pulsus paradoxus above 18 mmHg, tachycardia higher than 140 beats/min, peak expiratory flow rate less than 100 l/min and hypercapnia. Refractoriness was defined as deterioration of these symptoms despite maximal therapy [3]. In this period, NIMV was available for clinical use at the discretion of the attending physician, as a first-line therapy in patients who failed to respond to conventional medical management. Our drug protocol during this period was based on inhaled beta-adrenergic agonists, inhaled cholinergic antagonists (ipratropium), inhaled budesonide, intravenous methylprednisolone or hydrocortisone and intravenous adrenaline in the most severe cases.

For the present analysis, patients were categorised in two groups: candidates and not candidates for NIMV. We considered candidates for NIMV those patients with clinical indication of MV that met at least two of the following criteria: (1) severe dyspnoea at rest, (2) a respiratory rate (RR) above 30 breaths/min, (3) PaO_2 below 60 mmHg while breathing room air or below 80 mmHg with additional oxygen, (4) $PaCO_2$ of 50 mmHg or more, (5) arterial pH of 7.30 or less and (6) active contraction of the accessory muscles of respiration or paradoxical abdominal motion. Exclusion criteria were: immediate ETI for cardiopulmonary resuscitation, ETI because of impaired consciousness (coma or seizure disorders), severe haemodynamic instability, life-threatening arrhythmia and facial deformities.

Non-invasive mechanical ventilation was discontinued and ETI was performed when patients presented any of the following criteria: (1) worsening of ABG, (2) haemodynamic instability or life-threatening arrhythmia, (3) face mask intolerance, (4) development of any clinical condition requiring ETI or (5) patient request.

Face mask NIMV was available in two different modes: CPAP or pressure support ventilation (PSV), which were applied at the discretion of the attending physician. The head of the bed was raised to an angle of 45° or greater and kept elevated during NIMV to minimise the risk of aspiration. PSV was supplied by commercial ventilators (Servo Ventilator 900 C, Siemens Elema, Solna, Sweden, and Evita 2 and 4, Draeger, Lubeck, Germany) with a standard circuitry connected to a pneumatic sealed face mask (Downs CPAP Mask, Vital Signs, Totowa, N.J.) fixed with rubber head straps. The trigger sensitivity was adjusted to 0.5 cmH_2O. PSV was titrated to achieve a minimum of 400ml of expired V_T, and was increased in steps of 3 cmH_2O in accordance with the patient's requirement and lack of improvement of breathing pattern or ABG. Positive end-expiratory pressure (PEEP) was applied until a substantial improvement in the effort required to trigger the ventilator was noted.

Continuous positive airway pressure was supplied by a commercial system (Draeger CF 800, Lubeck, Germany) connected to the face mask. Valves of fixed values of 5 and 7.5 cmH_2O were used. Oxygen concentration was adjusted to the previously supplied level and was progressively reduced, provided that haemoglobin oxygen saturation remained above 90%, as continuously measured by pulse oximetry (HPM 1020 A, Palo Alto, Calif.).

Non-invasive mechanical ventilation was continuously applied, except for short periods of disconnection to allow the administration of bronchodilators, coughing, drinking and eating at the patient's request. Patients were weaned off NIMV when the acute

Table 1 Demographic and physiologic parameters on Emergency Room admission, expressed as means ± SD (*NIMV* non-invasive mechanical ventilation, *MV* mechanical ventilation, *NA* non-applicable)

	Candidates for NIMV		Not candidates	
	NIMV (n = 22)	MV (n = 11)	Respiratory arrest (n = 11)	Medical management (n = 14)
Female/male	16/6	8/3	8/3	8/6
Age (years)	48 ± 21	53 ± 19	58 ± 19	42 ± 14
APACHE II score	11 ± 5	16 ± 12	16 ± 12	11 ± 7
Type of asthma				
I	9	4	3	4
II	13	7	8	10
Dyspnoea score			NA	
Severe	9	10		7
Moderate	13[a]	1		5[a]
Mild	0	0		2
Accessory muscle use, n (%)	19 (86)	11 (100)	NA	11 (79)
Respiratory rate (breaths/min)	32 ± 6	30 ± 16	NA	33 ± 7
Heart rate (beats/min)	112 ± 26	111 ± 37	NA	118 ± 24
Mean arterial pressure (mmHg)	93 ± 20	109 ± 23	NA	85 ± 21[a]

[a] $p < 0.05$ compared to MV

phase had improved and after evaluation of their tolerance of breathing. If they were able to breathe without any assistance, NIMV was stopped, the mask removed and oxygen supplied at a low concentration by Venturi mask. If any sign of respiratory insufficiency appeared, NIMV was restarted and the tolerance test was repeated after a 12-h period of rest.

In patients considered unsuitable for NIMV by their attending physician or when NIMV was considered ineffective on the basis of the previous criteria, ETI and standard MV were performed. MV was supplied by the same volume-cycled ventilators with the following ventilatory parameters: volume-control mode, respiratory rate (8–10 cycles/min), inspiratory to expiratory ratios at 1:2 or 1:3 with a median PEEP of 8 cmH_2O. When they appeared, hypercapnia and respiratory acidosis were tolerated.

Patients were continuously monitored with our standard ICU equipment (Hewlett Packard M1166A, Palo Alto, Calif.): ECG, blood pressure (measured either non-invasively or by means of an indwelling arterial catheter), and haemoglobin oxygen saturation by pulse oximetry. Clinical data and ABG were collected on admission to the emergency room and at 30 min, 2–6 h and 6–12 h while on NIMV or on MV. The following data on admission were also recorded: age, sex, APACHE II score, RR measured by thoracic excursions, heart rate, use of accessory muscles of respiration and type of asthma. Type of asthma was classified as type I, when the clinical condition deteriorated in days or weeks, and type II, when deterioration developed acutely in minutes or hours [3]. The degree of dyspnoea was assessed by the modified Borg dyspnoea scale: 4–5 severe, 2–3 moderate, 1 mild and 0 none. Outcome was evaluated as length of ICU stay, hospital stay, complications and mortality.

For statistical analysis, discrete variables on admission were compared by using the chi-square test. Patients were evaluated at baseline, at ICU admission, 30 min, 2–6 h and 6–12 h after starting ventilatory support, either invasive or non-invasive. We compared average responses for each variable at the evaluation times by using ANOVA. A difference was considered statistically significant when the p value was lower than 0.05.

Results

Over the 7-year period of the study, 58 patients with hypercapnic exacerbation of asthma were admitted to the general ICU of the Hospital of Sabadell. Demographic and physiological parameters on admission are shown in Table 1. Drugs and doses used in the emergency room are shown in Table 2. Twenty-five patients (43 %) were not eligible for NIMV: 11 (44 %) because of respiratory arrest on arrival at the hospital and 14 (56 %) because of improvement with intensive medical management. Thirty-three patients (57 %) were classified as eligible for NIMV. Eleven of these 33 patients (33 %) were directly submitted to MV, while the remaining 22 (67 %) underwent an NIMV trial (7 CPAP and 15 NPPV). Three of these 22 patients were intubated because of impaired consciousness, impaired alveolar ventilation or intolerance to mask ventilation. For the purposes of the study, we compared the evolution of patients considered eligible for NIMV, regardless of whether or not they actually received this non-invasive treatment. The mean time in the emergency room before ICU admission was 50 ± 20 min.

When NIMV was applied the first disconnection was after a median time of 300 min (25^{th} and 75^{th} percentiles were 180 and 540 min, respectively). No cases of severe facial skin necrosis or clinically important gastric distension were observed. Pain in the nasal bridge area was frequent, but easily alleviated in most patients by applying a skin patch over this region. The technique was well tolerated and none of the 19 non-intubated patients required sedation. Anxiety was relieved by low doses of benzodiazepines in this group. Only one patient developed mask intolerance and needed ETI.

Table 2 Drugs and dosage used in the Emergency Room in each group of patients (*beta$_2$* beta$_2$-adrenergic-receptor agonists)

Route of administration	Drug	Candidates for NIMV		Medical management	*p* value
		NIMV	MV		
Inhaled	Beta$_2$	2.23 ± 1.72	0.86 ± 0.47	3.84 ± 2.01	0.06
Inhaled	Ipratropium	0.15 ± 0.11	0.62 ± 0.84	0.38 ± 0.27	0.26
Inhaled	Budesonide	0.734 ± 0.658	0.418 ± 0.025	0.092 ± 0.012	0.49
Nebuliser	Beta$_2$	10.35 ± 9	4.72 ± 2.4	5.95 ± 4	0.68
Intravenous	Beta$_2$	0.87 ± 0.74	0.69 ± 0.46	1.88 ± 2.33	0.56
Intravenous	Methylprednisolone	58 ± 40	62 ± 35	68 ± 53	0.69
Intravenous	Hydrocortisone	213 ± 150	174 ± 115	206 ± 201	0.09
Intravenous	Adrenaline	0	1.32 ± 0.004	0.96 ± 0.33	0.83

Doses are expressed as medians ± SD in milligrams/hour

Table 3 Evolution of arterial blood gases on hospital admission, on ICU admission, within 2 and 6 h, and within 6 and 12 h after ventilatory support (*MV* mechanical ventilation, *NIMV* non-invasive mechanical ventilation)

	MV (n = 11)	NIMV (n = 22)	Medical management (n = 14)	*p* value
Emergency Room				
PaO_2 (mmHg)	60 ± 21	68 ± 31	109 ± 76	0.04
$PaCO_2$ (mmHg)	89 ± 29	53 ± 13	63 ± 25	0.001
HCO_3^- (mmol/l)	22 ± 5	26 ± 6	23 ± 3	0.08
pH	7.05 ± 0.21	7.28 ± 0.008	7.17 ± 0.20	0.003
PaO_2/FIO_2	212 ± 106	261 ± 79	314 ± 113	0.09
ICU admission[a]				
PaO_2 (mmHg)	207 ± 173	153 ± 144	117 ± 64	0.31
$PaCO_2$ (mmHg)	61 ± 17	63 ± 24	48 ± 17	0.02[b]
HCO_3^- (mmol/l)	21 ± 8	26 ± 7	23 ± 3	0.09
pH	7.22 ± 0.18	7.24 ± 0.11	7.27 ± 0.16	0.20
PaO_2/FIO_2	323 ± 200	326 ± 244	351 ± 121	0.92
2–6 h				
PaO_2 (mmHg)	123 ± 70	121 ± 49	93 ± 12	0.60
$PaCO_2$ (mmHg)	41 ± 8	51 ± 24	43 ± 8	0.41
HCO_3^- (mmol/l)	25 ± 3	26 ± 8	23 ± 4	0.57
pH	7.39 ± 0.08	7.32 ± 0.15	7.33 ± 0.02	0.32
PaO_2/FIO_2	301 ± 106	314 ± 113	301 ± 68	0.94
6–12 h				
PaO_2 (mmHg)	127 ± 56	97 ± 21	92 ± 12	0.06
$PaCO_2$ (mmHg)	48 ± 12	48 ± 14	40 ± 3	0.25
HCO_3^- (mmol/l)	27 ± 2	27 ± 7	25 ± 2	0.75
pH	7.36 ± 0.11	7.36 ± 0.07	7.41 ± 0.02	0.28
PaO_2/FIO_2	285 ± 100	292 ± 83	324 ± 86	0.65

[a] Note that five patients in the MV group were already intubated when arterial blood gases were obtained

[b] NIMV versus medical management group

On admission to the Emergency Room there were no statistically significant differences between NIMV patients and MV patients in terms of clinical variables, but MV patients tended to be more acidotic and hypercapnic than NIMV patients. When patients were admitted to the ICU, statistically significant differences were found in the $PaCO_2$ level between NIMV patients and those treated with medical management alone (63 ± 24 vs 48 ± 17). Moreover, NIMV and medical management patients were clearly different, from a clinical point of view, in terms of the response to initial treatment in the Emergency Room. While the $PaCO_2$ of medically managed patients improved from 63 ± 25 to 48 ± 17 mmHg, hypercapnia worsened in NIMV patients from 53 ± 13 to 63 ± 24 mmHg. Both aspects were the main determinants for attending physicians to classify these patients as refractory to treatment and to start a trial of NIMV. With 2–6 h and 6–12 h of ventilatory support, there were no differences in blood gases (Table 3).

Improvement in RR in the NIMV group was slower and more progressive than in MV patients, but faster than in the medical management group (Fig. 1). The median PEEP level was 5 cmH_2O (25^{th} and 75^{th} percentiles: 3.0 and 7.62, respectively). The median PS level was 10 cmH_2O (25^{th} and 75^{th} percentiles: 10 and 15).

Three of the 22 NIMV patients (14 %) finally needed ETI because of deterioration of ABG and/or impaired consciousness. One of these three patients (4 % of

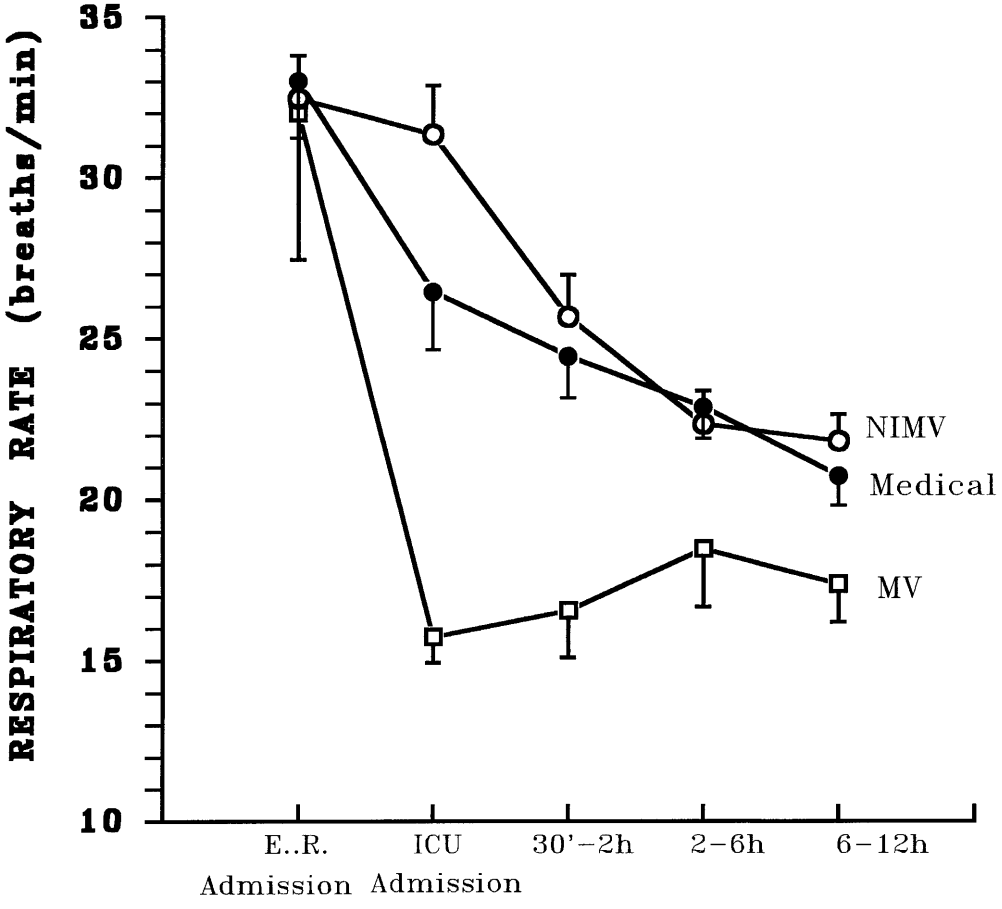

Fig. 1 Evolution of respiratory rate in the three groups of patients. Note that five patients in the mechanical ventilation group were already intubated when respiratory rate was registered

NIMV patients) died after 12 days in the ICU because of a ventilator-associated pneumonia. No additional complications were detected as a result of delaying intubation in the other two patients failing to respond to NIMV. The median length of ICU stay for NIMV patients was 3 days (25^{th} and 75^{th} percentiles: 2 and 5, respectively) and was 4.5 days (25^{th} and 75^{th} percentiles: 2 and 8, respectively) for MV patients (p NS). The median hospital stay for NIMV patients was 12 days (25^{th} and 75^{th} percentiles: 10 and 20, respectively), and was 15 days (25^{th} and 75^{th} percentiles: 11 and 21, respectively) for MV patients (p NS). The global mortality rate was 3% (1 patient out of 33 considered a candidate for NIMV).

Despite the fact that NIMV has been available since 1992, asthmatic patient did not receive this treatment in the first 2 years. From 1994 onwards, the proportion of asthmatic patients receiving NIMV has steadily increased, as Fig. 2 shows.

Discussion

The results of this study suggest that NIMV improves pulmonary function and is a safe treatment in patients with SA and hypercapnia, whose conditions fail to improve with initial medical management and who require MV.

The pathogenesis of airflow obstruction involves airway wall inflammation, smooth muscle mediated bronchoconstriction and intraluminal mucus plugging [1, 3, 4]. In spontaneously breathing asthmatics, progressive reductions in FEV_1 are followed by proportional increments in the inspiratory work of breathing. Substantial shortening of the inspiratory muscles, because of hyperinflation of the lung, reduces their mechanical efficiency and endurance, thereby increasing the risk of fatigue. As airway obstruction becomes more severe and the work of breathing becomes excessive, CO_2 production is greater than the CO_2 cleared by alveolar ventilation, and $PaCO_2$ increases [2, 3, 4, 5]. The rationale for NIMV in SA is its potential for improving alveolar ventilation, thereby decreasing the risk of respiratory muscle fatigue.

Several studies have demonstrated a beneficial effect of mask-CPAP by improving the pathophysiological

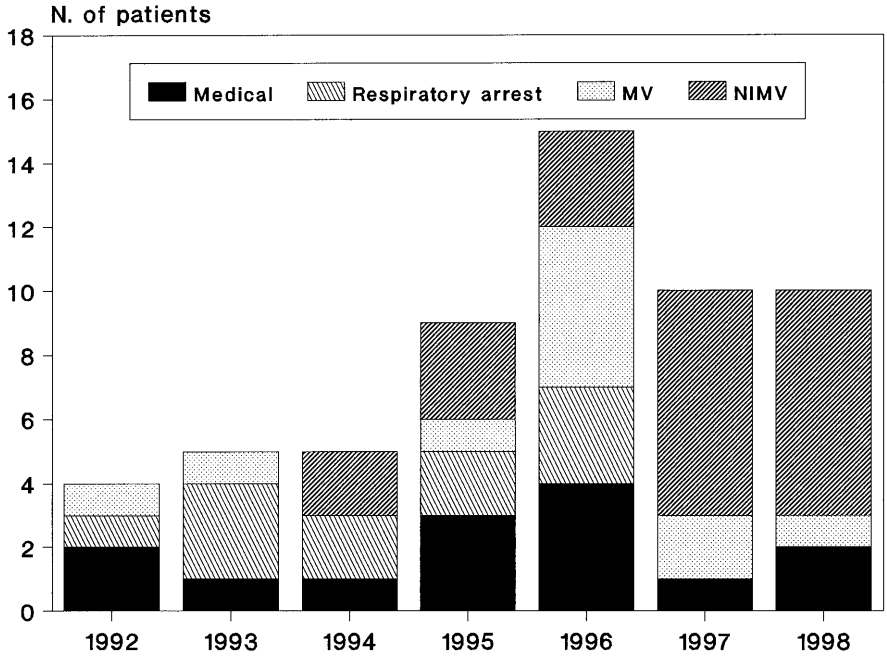

Fig. 2 Evolution of ICU admissions due to status asthmaticus classified according to the supplied ventilatory treatment

state of acute respiratory failure in acute asthma. Mask-CPAP produces bronchodilation and decreases airway resistance, expands atelectasis and promotes removal of secretions. Consequently, the work of the diaphragm and the inspiratory muscles is reduced and intrinsic PEEP may be offset. Additionally, CPAP decreases the adverse haemodynamic effects of large negative inspiratory swings in pleural pressure, which compromise right and left ventricular performance [3, 15, 16].

Non-invasive intermittent positive pressure ventilation with pressure support ventilation (PSV) offers the possibility to increase spontaneous tidal volume. Patients may maintain their own breathing pattern while the increased pressure available for flow delivers a higher tidal volume and allows for a reduction in inspiratory effort. Patients normally adapt their breathing pattern to this improved alveolar ventilation with a reduction in RR (as observed in this study), which increases expiratory time and reduces the burden on the respiratory muscles [2, 13].

Our results are in accordance with the pioneer study of the use of NIMV in SA [2]. No severe side effects, such as facial skin necrosis or gastric distension, were observed. The ETI rate, complications and mortality were low and comparable with the study performed by Meduri et al. [2]. However, we cannot rule out the possibility that the short delay of ICU admission may account for the low mortality rate observed.

This study has some limitations that should be emphasised. First, it is an observational report of our daily clinical experience. The decision to start a trial of NIMV was not controlled or randomised, but relied on the clinical judgement of the attending physicians. Second, our data strongly suggest that physicians decided on an NIMV trial in the patients whose ABG on admission indicated a less severe condition. Moreover, because of the retrospective design, we are unable to elucidate the possible effects of any other confounding factors, such as nutritional approach, changes in the hospital case-mix due to a better primary care of asthmatic patients and the possible learning curve for NIMV.

We conclude that NIMV via face mask appears to be a suitable method to improve alveolar ventilation which can reduce the intubation rate in a selected group of patients with SA. The observed low morbidity and mortality rate observed in patients with life-threatening asthma treated with NIMV and with invasive MV suggest that future trials should be focused on soft end-points, such as comfort and patient's choices.

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