Ventilatory Management in Patients with Status Asthmaticus

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Abstract

Objectives: To investigate the outcome of patients with status asthmaticus (SA) treated in a respiratory intensive care unit (RICU).
Design: A retrospective study conducted in the RICU of a training hospital on 12 consecutive patients with SA admitted to RICU between March 2001-December 2003.
Results: All cases were previously diagnosed and being followed up for 2-30 years. Female/male ratio was 11/1, mean age was 57±12 yrs. Initial APACHE II score: 19±4 (11-27); pH: 7.21±0.95; $PaCO_2$: 92±18 mmHg; PaO_2: 51±17 mmHg. Out of 12 patients, 6 received NIMV (IPAP: 10±1, EPAP 5±1 cmH_2O) for 1-3 days (9±5hrs/day) with a success rate of 50%. A total of 9 cases underwent intubation. IMV was administered initially with volume-controlled mode in all patients and subsequently it was switched to a pressure-controlled mode in three cases because of the high airway and plateau pressures. The mean duration of the weaning period was 45±37 hrs and total duration of IMV was 123±82 hrs. Out of 9 patients, 7 were sent to the hospital ward with improvement. Two cases, one for a technical problem on the 2nd day and the other due to development of a cerebrovascular accident on the 14th day, were sent to another hospital. We were informed that both were discharged from that hospital in good condition.
Conclusion: It is vital to have facilities for NIMV and IMV in every chest disease hospital for the management of life threatening events in asthmatics with severe attacks.

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Introduction

The prevalence of asthma in adults varies between 2% and 12% (1). Asthmatic attacks also vary greatly in severity from mild to life-threatening. The asthmatic attack that is unresponsive to intensive medical therapy and progresses to acute respiratory failure (ARF) is referred to as status asthmaticus (SA) (2). Mortality of patients with ARF caused by SA is generally lower than deaths from ARF due to other causes. Mortality rate due to ARF in SA was reported to be as high as 42% in 1977 (3), but has been reduced to lower than 10% in the last decade (4-11). Braman, who reported 0% mortality in 80 episodes of SA, stated that previous high complication rates and mortality in SA could be avoided (4). Still, SA carries a significant risk of morbidity and mortality in intensive care units (ICU). Severe asthmatic attacks can best be prevented by early intervention in the outpatient setting (12). In this report, we aim to analyze the clinical course, in-hospital complications and mortality in patients with SA treated in our

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respiratory intensive care unit (RICU) over a 2-year study period; and to discuss optimal ventilatory management in such patients.

Materials and Methods

The hospital records of 12 consecutive patients with SA admitted to our respiratory intensive care unit (RICU) between March 2001 and December 2003 were retrospectively evaluated. All patients were previously diagnosed as asthma according to GINA (Global Initiative for Asthma) criteria (13) and were being followed for 2-30 years. The presence of respiratory acidosis ($PaCO_2$>45mmHg, pH<7.35) in the analysis of arterial blood gases (ABG) was accepted to reflect status asthmaticus. The age and sex of the patients duration of asthma, smoking status, duration of symptoms prior to this attack, previously obtained pulmonary function tests (in 6 patients), acute physiology and chronic health evaluation (APACHE) II scores (14) calculated in the first 24 hours and arterial blood gases (ABG) obtained on admission while receiving fractionated inhaled oxygen ≥0.28 were all recorded.

Ventilatory management

The decision to use mechanical ventilation invasively or noninvasively was based on the judgment of the RICU attending pulmonary physicians (TY, ZK). Initially, noninvasive mechanical ventilation (NIMV), with the full-face mask was used if the patient had no contraindication for NIMV. In the presence of hemodynamic instability, altered mental status, severe respiratory distress and unsuccessful noninvasive trial (progressive deterioration with increasing distress or physical exhaustion and/or worsening ABG values), the patients underwent endotracheal intubation (ETI) and received invasive mechanical ventilation (IMV). These patients were initially ventilated with volume-controlled ventilation (VCV) using low respiratory rate (10-12 breaths/min), low tidal volume (6-8mL/kg) and high flow rate (40-100L/min). As the patient's airway and plateau pressures increased above acceptable levels (peak inspiratory pressure >40cm H_2O; plateau pressure >35 cm H_2O), the ventilatory mode was immediately switched to pressure-controlled ventilation (PCV). Auto-PEEP was measured by using the expiratory pause button of the ventilator. Static and dynamic compliance at the initiation of mechanical ventilation were calculated from the recorded peak airway pressure, positive end-expiratory pressure (PEEP), plateau pressure, and tidal volume. Respironics Bi-PAP-S, -ST or Puritan-Bennett 760 model ICU ventilators were used for NIMV interventions, and Puritan-Bennett 760 model ventilators were used for all IMV interventions.

Sedation protocol

Continuous midazolam infusion (0.15-0.3 mg/kg/h) was given for sedation. The lower and upper dose limits for midazolam were calculated on an individual basis and the infusion was initially given at a rate of 0.15 mg/kg/h. Infusion rate was titrated to obtain deep sedation adequate to suppress spontaneous breathing at least 24 hours. Fentanyl citrate (bolus or infusion) was given to patients in whom respiration was not suppressed despite the highest dose of midazolam. Neuromuscular blocking agent (NMBA), vecuronium bromide in bolus (0.05 to 0.1 mg/kg) or infusion doses (0.05 mg/kg/h), was administered to patients with patient-ventilator asynchrony or uncontrolled airway pressure. As bronchoconstriction subsided, ABG values improved and airway and plateau pressures decreased, paralytic agents and fentanyl citrate were stopped in respective order and midazolam dose was reduced by 2 mg steps per hour to achieve the lowest midazolam dose providing comfort to the patient, facilitating cooperation and nursing care and patient interaction with the ventilator. If the patient became ready for a weaning trial, midazolam dose was gradually decreased and the drug was finally discontinued.

Medical management

Inhaled β2-agonists such as salbutamol were administered with a mouth-piece in a dose of 2.5 mg every 20 min for the first hour, then every 1-4 hours as indicated by the patient's clinical course (15). In patients who had undergone IMV, salbutamol was used with a metered-dose inhaler (MDI) with a chamber device placed into the ventilator circuit. The dose and intervals of salbutamol administration in patients with IMV was adjusted according to the patient's airway pressures and auscultation findings. The first dose of salbutamol was at least 4-8 puffs (400-800μg), followed with 4 puffs (400μg) at 1-4 hours intervals (16,17). Intravenous methylprednisolone, 80-250 mg/day, was administered to all patients in the first 3 days, then tapered gradually. Theophylline was administered intravenously 5-6 mg/kg over 20-30 min, followed by a continuous infusion of 0.6 mg/kg/h. Antimicrobial therapy was used in patients with high fever, leucocytosis and pneumonia.

Statistical analysis

Statistical analysis was performed using SPSS 11.0 version. Results are given as means ± SDs. Comparisons between groups were made using the Mann-Whitney U test. All p values of <0.05 were considered statistically significant.

Results

During the study period, a total of 566 patients were admitted to RICU. Seventeen of these patients (3%) were asthmatics with severe attacks and 12 episodes were identified as SA in these 17 patients. The demographic and clinical characteristics of the cases are shown in Table 1. Nearly all of the patients (11/12) were female. Out of 12, 9 patients had a history of irregular treatment. Four cases had co-morbid dise-

ases, two with panic attack and the other two cases with diabetes mellitus. Leucocytosis (>12x10^9/L) was found in 9 cases and signs of pneumonia in the chest X-ray in 4 cases. S. pneumoniae was identified in the culture of endotracheal aspiration material in one of the patients with pneumonia.

Noninvasive mechanical ventilation (NIMV) was used in 6 (50%) cases who showed no contraindication for NIMV; while the other 6 patients were immediately intubated because of severe respiratory distress, severely altered mental status or unconsiciousnes. Demographic and initial clinical characteristics and the ABG values of the IMV and NIMV groups were found to be similar, although APACHE II score was higher in the IMV group (Table 2).

NIMV was administered with a full-face mask for 1-3 days. Mean period of daily administration was 9±5 hours. Mean inspiratory pressure (IPAP) was 10±1 cmH_2O and mean expiratory pressure (EPAP) was 5±1 cmH_2O in these patients. Out of 6, three cases improved rapidly and sent to the hospital ward within 3 days. The other 3 cases receiving NIMV underwent intubation due to worsening of ABG values and clinical status after 4-20 hours of NIMV intervention.

Mean initial inspiratory airway pressure, plateau pressure, auto-PEEP, static and dynamic compliance values in the 9 patients who received IMV, are summarized in Table 3. VCV was used as the initial mode for all cases and subsequently it was switched to PCV in 3 cases because of high airway and plateau pressure. All cases managed with IMV received midazolam in a dose of 0.2±0.05 mg/kg/h as the primary sedative agent. In 5 cases, it was deemed necessary to use fentanil citrate for deep sedation and vecuronium was administered in 4 cases for 19-35 hours because of ventilator-patient disharmony. Ventilator associated pneumonia (VAP) caused by methicillin resistant Staphylococcus aureus (MRSA) developed in one case on the 4th day and was treated succesfully with teicoplanin. Out of the 9, two cases, one for a technical problem on the 2nd ventilator day and the other due to development of a cerebrovascular accident on the 14th day, were transferred to another hospital. We were informed that both had been subsequently discharged from that hospital on the 5th and 25th hospital days. The remaining 7 cases received IMV with a total duration of 123±82 hrs (range 58-292 hrs) and a weaning duration of 45±37 hrs (17-126 hrs). The me-

Table 1. Patient characteristics at admission to RICU

Number of patients	12
Sex, F/M	11 / 1
Mean age, years (range)	57±12 (29-76)
Mean asthma duration, years (range)	10±8 (2-30)
Smoking status, n	3 (>20pac/y)
Mean duration of symptoms prior to attack, days (range)	5±5 (1-15)
Pulmonary function tests* (means and SD)	
FVC, mL (% pred.)	2145±1393 (63±25)
FEV_1, mL (% pred.)	1080±650 (39±15)
FEV_1/FVC, %	68±1
APACHE II mean score at admission (range)	19±4 (11-27)
ABG values at admission, mean ± SD (range)	
pH	7.21±0.95 (7.02-7.34)
Pa_{CO2}, mmHg	92±18 (75-130)
Pa_{O2}, mmHg	51±17 (27-73)
Pulse oximetry, %	69±21

* PFTs were available in six patients' files (during the past one year period).

Abbreviation:

FVC: Forced vital capacity

FEV_1: Forced expiratory volume in 1 second

APACHE: Acute physiology and chronic health status

Table 2. Comparison of patients receiving NIMV and IMV by ABG values and APACHE II scores (mean and SD values at admission).		
	NIMV	IMV
Number of patients	6	6
pH	7.26±0.05	7.16±0.01
Pa_{CO2}, mmHg	93±15	92±25
APACHE II score	16±3	23±3*
* p<0.05		

Table 3. Auto-PEEP, static compliance, dynamic compliance, inspiratory airway pressure and plateau pressure values in patients receiving IMV (means and SD)	
Ppeak, cm H_2O	35±8 (25-50)
Pplateau, cm H_2O	27±6 (20-40)
Auto-PEEP, cm H_2O	5.3±1.4 (4-8)
Static compliance, mL/cm H_2O	20.4±4.5 (13-28)
Dynamic compliance, mL/cm H_2O	15±4 (10-21.4)

an length of RICU stay in these cases was 9±5 days (3-18 days) and the mean length of hospital stay was 13±6 days (7-25 days).

Discussion

In this study, over a 2-year period, only 3% of RICU admissions were asthmatics. Indeed, due to the recent advances in the treatment and management of asthma, this condition has become a less frequent cause for admission to the ICUs in the last decades. Frequency of asthma as a cause for admission to the ICU has been reported as 4% over a 10-year period (4). In another report, it was stated that only 7% of severe asthmatics presenting to 37 different emergency departments in France were transferred to an ICU (18).

Nearly all of the patients (92%) were female in our study. Similarly, previous investigators have reported a female predominance in asthma ICU admissions (7,9,19). Women also report more symptoms and worse quality of life than men with similar or even less severe asthmatic attacks (19-21).

Because older patients are less likely to have asthma and differential diagnosis with other diseases that occur commonly in the elderly might present difficulties, many studies on acute asthma have excluded patients aged over 55-years and some have excluded patients over 40-years (7,22,23). Contrary to widespread belief, asthma is not rare in this age group. In an article by Braman, epidemiologic, clinical and pharmacologic aspects of asthma in the geriatric population have been reviewed in detail (24). In a recent trial, Enright and co-workers noted that asthma was both underdiagnosed and undertreated in elderly persons and it was reported that 10% of asthma hospitalizations occurred in persons aged over 66 years (25, 26). Another study showed that patients aged over 55 accounted for a meaningful rate (21%) of adult emergency visits for asthma (18). Furthermore, it was reported that patients at highest risk of severe asthma were those between 15 and 24-years-old and those over 55-years old (27). For reasons stated above, we did not exclude patients older than 55-years in our study. Six of patients in our series were in this age group.

There are many different factors which trigger asthmatic attacks. Exposure to indoor or outdoor allergens, air pollutants, respiratory infections, exercise, nonsteroid anti-inflammatory drugs and emotional factors are the main triggers which can be identified clinically (28). Also, patients who do not comply to the treatment are more likely to have severe attacks than patients who receive regular treatment. In our series, there were 9 patients who were not receiving treatment regularly, which suggested that these patients were non-compliant to treatment. Nine of these patients had leucocytosis and pneumonia was diagnosed in 4 of these cases. These findings indicate that infections and irregular treatment were the most outstanding causes of severe attacks in this study. In 2 cases who were suffering from panic attacks, asthmatic symptoms were possibly exacerbated by extreme emotional stress.

In our study, all patients received ventilatory support and half of them were initially administered NIMV with a success rate of 50%. Three cases treated with NIMV subsequently required intubation, and no deaths occurred. It requires considerable expertise to decide the timing of intervention of NIMV and the timing of intubation. We use NIMV as a first-line interventional therapy in eligible patients with ARF and our success rate with this intervention is over 80% in patients with hypercapnic ARF (29). Previous investigators demonstrated that NIMV can be used safely in carefully selected patients with SA, and NIMV is highly effective in correcting gas exchange abnormalities using a low inspiratory pressure (7,9,30-33).

Patients managed with NIMV in our study had shorter hospitalization than those who received IMV. This finding can be attributed to the fact that patients in the NIMV group were less ill than those patients in the IMV group (APACHE II score, 16 vs 23, respectively). Indeed, in Gehlbach's study also, duration of hospitalization was found to be significantly associated with increasing APACHE II score (7). In addition, most patients in the IMV group require deep sedation and/or neuromuscular blockage, interventions which may lead to a delay in extubation (34).

In our series, a total of 9 patients received IMV and all survived despite the fact that their mean APACHE II score was 23±3 (predicted death rate adjusted for asthma: 9.4%). Overall mean APACHE II score was 19 in our patients, ranging from 11 to 27, and it was statistically higher in the IMV group (p<0.05). An APACHE II score >25 has been reported to

be associated with higher mortality (9). Afessa and co-workers reported a mortality rate of 8.3% among intubated asthmatic patients (9). However, in the context of an editorial comment, Shapiro stated that this rate was strikingly high and gave the mortality rate in patients with SA in his hospital as 2.6% (35). In contrast to high mortality rates in such patients in early years, recent studies report much lower figures (Table 4) (34-9). Pneumothorax, nosocomial infections and co-morbidities were suggested as the most common causes of mortality in mechanically ventilated SA patients (7,9). Barotraumas can occur either during bag ventilation after endotracheal intubation or during invasive positive pressure ventilation (9).To prevent barotraumas and improve outcome, it is recommended that ventilatory strategy be chosen to minimize airway pressure, allowing sufficient time for completion of expiration by using low tidal volume (5-7mL/kg), low respiratory rate (8-10 breaths/min), high peak flow, minimal PEEP (<5cmH_2O) and limiting peak inspiratory pressure to <40 cmH_2O (36). We set the ventilator in accordance with the above recommendations and encountered no barotrauma complications. VAP developed in only one of our patients and a second patient suffered from a cerebrovascular accident.

Acute asthma attacks that require visits to an emergency department and admission to hospital are usually attributable to failure of long-term management and contribute to asthma severity (22). Many patients and physicians remain reluctant to intervene with a course of corticosteroids early in worsening asthma because of fear of side effects (12). The consequence of delay is often progression to severe disease requiring urgent care. Also, serious management errors are common in those admitted to hospital with acute severe asthma. In the French study, it is reported that systemic corticosteroids were not administered in 32% of patients with life-threatening attacks and in 49% of patients with severe attacks. In contrast, 49% of patients with mild or moderate attacks were receiving systemic corticosteroids (18). This situation suggests that physicians not only fear using corticosteroids because of side effects, and also that they cannot truly assess the severity of the attacks. Patients at high risk for a fatal attack of asthma are likely to have repeated hospitalizations, multiple emergency room visits and previous intubations and/or ventilatory assistance (37). They also have an increased prevalence of poorly controlled disease, take more ß-agonists, underuse corticosteroids and/or have more nocturnal symptoms than do case control subjects (38). A distinct pathological subtype of rapidly fatal disease known as "catastrophic", "brittle" or "sudden asphyxic" asthma, is a dramatic but rare happening. In this type of attack, intense bronchospasm occurs often over the course of 1-2 hours (36). Recovery appears to be rapid, which suggest that bronchoconstriction may be the predominant pathophysiological factor. In our series, no patient suffered from such a type of asthmatic attack.

Table 4. Mortality rates reported in some studies in mechanically ventilated patients with acute severe asthma

Authors/and reference no.	Year	Number of cases	Mortality %
Scoggin CH et al, 3	1977	19	42
Mansel et al, 11	1990	32	22
Braman SS et al, 4	1990	80	0
Williams TJ et al, 5	1992	51	0
Zimmerman JL et al, 8	1993	69	6
Afessa B et al, 9	2001	132	8.3
Gehlbach B et al, 7	2002	78	4
Current study	2004	12	0

In conclusion; mechanical ventilation, invasive or noninvasive, is a life-saving event for patients with ARF caused by status asthmaticus. In this study, 0% mortality in such patients is hopeful with respect to the high risk of death in severe asthmatic patients. We believe that improved survival in SA patients is strongly associated with the existence and availability of facilities for NIMV and IMV in every chest disease hospital for the management of life threatening events in asthmatics with severe attacks and also with the .experience of the team who are respomsible for the management of these patients.

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