

Outcome of patients with severe asthma in the intensive care unit

Abdulaziz Alzeer, Ahmed BaHammam, Mohammed Masood, Sayed Jani Basha, Esam Alhamad, Sayed Sohail

BACKGROUND: Because little has been reported about the outcome of severe asthma outside the US and western Europe, we performed a retrospective case analysis of patients treated in the medical intensive care unit (MICU) of a university hospital in Riyadh, Saudi Arabia, to determine the management, complications and outcome of severe asthma requiring ICU admission.

METHODS: The records of patients with severe asthma admitted to the MICU between the periods of January 1996 to December 2003 were reviewed. Sixty-one episodes from 54 patients were studied, of which 27 (44%) were male.

RESULTS: All patients were hypercapnic; 23 (38%) were ventilated. The Acute Physiological and Health Evaluation (APACHE) score II was significantly higher in the ventilated group ($P < 0.0001$). The pH was significantly lower and PaCO_2 was significantly higher in the ventilated group ($P < 0.0001$). All patients survived. Only 42% of patients our series received inhaled corticosteroids before admission.

CONCLUSION: Our results suggest that severe asthma requiring ICU admission is now safely managed in ICUs. Our results are comparable to recently published data on the treatment of severe asthma in the ICU.

*From the Department of Medicine,
King Khalid University Hospital,
Riyadh, Saudi Arabia*

*Correspondence and reprint requests:
Abdulaziz Alzeer, MD
King Khalid University Hospital
Department of Medicine
P.O. Box 18321
Riyadh 11415
Saudi Arabia
T: +966-1-467 1521
F: +966-1-467 9495
alzeerahm@yahoo.com*

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The rate of hospital admissions for asthma has increased in recent years with potentially serious consequences,¹⁻⁴ especially for those cases that require intensive care.^{5,6} Despite reports of increased overall asthmatic fatalities, ICU mortality has shown a favorable outcome in the last decade.⁶⁻⁸ This has been attributed in part to a reduction in the incidence of barotrauma from mechanical ventilation, achieved through permissive hypercapnia, and to closer monitoring.⁶⁻⁸ Although only a small minority of severe asthma attacks required mechanical ventilation,⁶ the procedure is still associated with serious complications such as barotrauma, atelectasis, mucous plugging, hypotension, endotracheal tube malposition, pneumonia or neuropathy of critical illness.⁹⁻¹¹ As most of the previous reports of severe asthma in the ICU have come from Western Europe or the United States of America, little has been reported about severe asthma from other places, which could have different presentations. Therefore, we decided to describe our experience with severe asthma in the ICU, including management, complications and outcome.

Methods

This was a retrospective case analysis conducted in the medical intensive care unit (MICU) of King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia. All charts of patients admitted with severe asthma between

January 1996 and December 2003 were reviewed. Severe asthma was defined according to the National Heart, Lung and Blood Institute Expert Panel, as a patient who presented with severe respiratory symptoms not responding to initial inhalation therapy or intravenous (IV) steroid.¹² Severe asthma was the primary reason for admission. Patients admitted with other obstructive conditions, such as bronchiectasis or chronic obstructive pulmonary disease (COPD) evident by radiographic findings and pulmonary function tests were excluded. All clinical data including age, sex, the initial symptoms, and previous hospital or ICU admissions were reviewed. The duration of each asthma attack was recorded. A history of atopy or aspirin sensitivity was recorded. The management of the patient was also reviewed. The Acute Physiological And Chronic Health Evaluation (APACHE II) score was calculated using the worst score in the first 24 hours.¹³ According to hospital protocol, immediately after a clinical evaluation of the patient with near fatal asthma in the emergency room, treatment was started with frequent salbutamol and ipratropium-bromide nebulisations, IV methylprednisolone (1 mg/kg body weight every 6 hours), and IV broad spectrum antibiotics if signs of respiratory tract infection were observed. Serial arterial blood gases and peak expiratory flow rate (PEFR) were done before and after starting treatment. If there was no improvement in symptoms, PEFR or blood gases, patients were transferred to MICU for further management. If the patient deteriorated further as evidenced by a decreased level of consciousness or by developing cardiorespiratory arrest despite the above therapy, endotracheal intubation was considered either in the emergency room or in MICU. Ventilated patients were put mainly on volume-cycled mode. Four patients were ventilated using pressure-regulated volume control mode. The duration of mechanical ventilation was recorded. Also, the duration of muscle relaxant use was calculated in patients who were intubated and received neuromuscular blockade. Once the clinical status of these patients improved based on PO_2 , PCO_2 , pH and hemodynamics, extubation was considered.

Hypercapnia was defined as a $PaCO_2 \geq 45$ mm Hg on initial blood gases.¹⁴ Sepsis was defined according to the guidelines of American College of Chest Physicians/Society of Critical Care Medicine.¹⁵ Complications were recorded. A favorable outcome was defined as discharge from the hospital. Statistical analysis was performed using Student's t test for continuous variables and chi-square tests for categorical variables. A *P* value equal or less than 0.05 was considered statistically significant.

Results

Fifty-four patients with 62 episodes of acute severe asthma were admitted to the MICU. The mean age of the patients was 39 ± 19 years (range, 15-56 years). These admissions represented 0.4% of total admissions throughout the period, January 1996 to December 2003. One patient file was missing and was therefore excluded. There were 27 (44%) males and all patients survived ICU and were discharged home. Demographic and clinical variables for the 61 asthmatic patients are shown in Table 1. There were no statistically significant differences in these variables between ventilated and non-ventilated patients. Table 2 shows additional clinical variables of non-ventilated and ventilated patients. There was no statistically significant difference between the groups in term of asthma duration, duration of attack, respiratory rate or blood pressure on admission. The groups were also not different in peak expiratory flow rate (PEFR). However, the APACHE II score was significantly lower in the non-ventilated group (*P* value < 0.0001). The pH was significantly lower in the ventilated group and PCO_2 was significantly higher ($P < 0.0001$) for both. Ventilated patients were tachycardic compared to those who were not ventilated ($P < 0.006$). All patients received β_2 -agonist and IV corticosteroids on their initial presentation to the emergency room. The mean duration of ventilation was 3.2 ± 3.4 days. Muscle relaxant was used in 18 ventilated patients and the mean duration was 12.56 hours (range, 4-30 hours). The range of ICU stay was 1 day to 21 days with mean of 5.6 ± 3.5 days.

Eight patients from the ventilated group and ten patients from the nonventilated group (statistically non-significant difference) received subcutaneous epinephrine 1:1000 when they did not respond to the initial inhalation therapy. Three patients received IV salbutamol and 2 patients received continuous IV ketamine for 24 hours. Twenty-five patients, all in the intubated group, had complications. Four (6%) patients had barotrauma, 8 (13%) hypokalemia, 2 (3%) supra-ventricular tachycardia, 8 (13%) lactic acidosis, 2 (3%) sepsis and 1 (1.6%) had myopathy.

Discussion

We described the clinical presentation, ICU management and outcome of patients with severe asthma. All of our patients made a complete recovery and were discharged home. Our results suggest that patients with severe asthma can be managed safely in the ICU and have a favorable outcome. Earlier studies had shown mortality figures as high as 38%.⁵ In a retrospective study by

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Table 1. Demographic and clinical variables of 61 ventilated and non-ventilated severe asthmatic patients treated in the medical intensive care unit.

Study Variables	Ventilation		Test statistic	P value
	No N = 38 (%)	Yes N = 23 (%)		
Sex				
- Male	14 (36.8)	13 (56.5)	1.53*	0.217
- Female	24 (63.2)	10 (43.5)	-	
Age	34.3±18.8	43.7±19.8	- 1.86 †	0.068
Smoking	4 (10.5)	-	-	0.192
History of allergies	15 (39.5)	5 (21.7)	1.32	0.251
History of aspirin use	6 (15.8)	5 (21.7)	-	0.398**
History of NSAID use	2 (5.3)	3 (13.0)	-	0.271**
On inhaled steroid	14 (36.8)	12 (52.2)	0.82	0.365
Compliance with treatment	23 (60.5)	9 (39)	1.84	0.175
Used more than 3 medications	11 (28.9)	5 (21.7)	0.10	0.749
On oral steroids	7 (18.4)	4 (17.4)	-	0.610
Regular follow-up	11 (28.9)	8 (34.8)	0.037	0.84

Values are mean±standard deviation.

*Chi-square; **Fisher's Exact test P value; † t value; NSAID: Non-steroidal anti-inflammatory drug

Table 2. Additional clinical variables of 61 ventilated and non-ventilated severe asthmatic patients treated in the medical intensive care unit.

Study Variables	Ventilation		t	P value
	No n=38	Yes n=23		
Duration of asthma (years)	8.6±7	9.8±6.7	-0.67	0.463
Duration of attacks (hours)	70.3±93	87.4±166	-0.52	0.762
Heart rate	122.9±21.3	99.7±42	2.85	0.006
Systolic blood pressure	127±21.5	134±50	-0.74	0.46
pH	7.3±0.096	7.0±0.095	10.13	<0.0001
PaCO2	50.7±11.8	86.5±22	-8.32	<0.0001
PaO2	76.7±40	84±74	-0.50	0.62
HCO3	23±5.8	23.8±5.5	-0.55	0.58
PEFR	115±110	95.6±99	0.69	0.49
APACHE II score	9.0±5.7	22±8	-7.0	<0.0001

Values are mean±standard deviation.

PEFR: peak expiratory flow rate; APACHE: Acute Physiological and Chronic Health Evaluation

Mountain et al in 1998, who reported on 229 patients admitted to the ICU, a third were hypercapnic; only 5 patients were ventilated and they reported no mortality.⁶ Almost all reports in the last decade have shown a favorable outcome.^{6-8,16,17} Braun et al reported no mortality following 80 episodes of severe asthma and they attributed their excellent outcome to close monitoring and repetitive of blood gas analysis.⁸ A recent study from the UK attributed the improved survival to repetitive bronchoscopic airway toilet and reduction of airway pressure. This improvement in survival happened despite an increased rate of mechanical ventilation.¹⁷ All our patients were hypercapnic and a third were mechanically ventilated using volume-cycled mode, allowing permissive hypercapnia to reduce peak airway pressure below 40 mm Hg as previously recommended.¹⁸ Four of our patients were successfully ventilated using pressure-regulated volume control mode, which assured adequate tidal volume with minimal peak airway pressure, although the mean airway pressure could have been high. This mode was recently used in pediatric asthmatic patients.¹⁹ We believe the reduction in airway pressure contributed to the improved survival in our patients. The other factor that contributed to the good outcome was the absence of anoxic brain damage. Earlier data had suggested that most asthma fatalities occur at home or on arrival to the emergency room. As some of these patients were subsequently admitted to the ICU with anoxic brain damage, this lead to the alteration of the overall asthma outcome in the ICU.^{8,18}

The APACHE II score was significantly higher in the ventilated group compared to the non-ventilated group ($P < 0.0001$). This reflects the rapid deterioration in the physiological status of the ventilated group, requiring intubation and mechanical ventilation, shortly after their admission. Wasserfallen et al described a group of asthmatics who deteriorated rather quickly and had sudden asphyxic asthma with hypercapnia requiring intubation.²⁰ This suggests that patients with severe asthma and a higher APACHE II score have a greater chance of intubation. Recent published studies have also shown that a high APACHE score in status

asthmaticus is associated with prolonged hospitalization and death.^{21,22}

Inadequate therapy and poor patient compliance are well known factors that precipitate severe asthma attacks.²³ Among our patients, only 31% were regularly attending a follow up clinic and only 42% were receiving inhaled corticosteroids. This highlights the inadequate therapy for asthma in this series of patients, despite the recent implementation of a National Asthma Program in Saudi Arabia.

The effectiveness of parenteral β -agonists has been debated, and there is a paucity of information concerning their use in severe asthma.^{24,25} Bloomfield et al compared intravenous β -agonist to inhaled salbutamol using a double blind, cross-over design and concluded that the two regimes were equally effective.²⁴ On the other hand, Williams et al have shown that a parenteral β -agonist resulted in more significant improvement in peak expiratory flow rate (PEFR) compared with nebulized β -agonist.²⁵ A significant number of our patients were given a subcutaneous β -agonist, which may have averted the need for mechanical ventilation. Apart from sinus tachycardia and hypokalemia, we encountered no other significant side effects. We therefore support the recommendation for using a parenteral β -agonist in severe asthma.²⁶ Myopathy was documented in one patient who had a history of left lower lobectomy requiring mechanical ventilation for 12 days. Previous studies have shown that up to 30% of asthmatics subjected to prolonged nondepolarizing neuromuscular blocking agents developed myopathy and muscle weakness.^{27,28} This complication occurred in 1.6% of our patients. This is attributed, we believe, to the short period of ventilation and limited use of neuromuscular blockade.

In summary, the findings of this study are in agreement with recent reports of low mortality in severe asthmatics managed in the ICU. Aggressive therapy with non-invasive modalities should not be delayed. However, should mechanical ventilation be needed, attention should be given to reducing the airway pressure, even at the price of permissive hypercapnia.

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