ORIGINAL RESEARCH

Increasing Severity of Status Asthmaticus in an Urban Medical Intensive Care Unit

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BACKGROUND: Life-threatening status asthmaticus (SA) requiring intensive care is a major concern given the rising prevalence of asthma. We examined episodes of SA requiring admission to the medical intensive care unit (MICU) of an urban hospital center.

METHODOLOGY: The charts of patients admitted to the MICU of an urban hospital center with a diagnosis of SA during the 5-year period 2002–2006 were reviewed retrospectively. These results were compared with those of a previously published experience at our institution from 1995 to 1999.

RESULTS: The medical records of 84 MICU admissions for SA were reviewed. There were 61 women (5 pregnant). The mean age was 44 years. Use of cigarettes or illicit drugs was found in 51% and 30%, respectively. Mechanical ventilation (MV) was required in 76% of admissions. Noninvasive ventilation was used in 10 patients. Neuromuscular blockade (NMB) was needed in 9% of admissions. The highest average $PaCO_2$ during the first 24 hours was 67 mm Hg. Median duration of MV was 4.4 days. Six patients died, 3 of whom sustained prehospital cardiac arrest. Compared with the patients in the preceding 5-year period, the more recent patients had greater use of illicit drug and cigarettes. Patients presented with more severe asthma, as reflected by a higher $PaCO_2$ and an increased duration of MV.

CONCLUSIONS: During the recent 5-year period, we found a trend toward increasing severity of SA, as indicated by the degree of respiratory acidosis, need for NMB, and longer duration of MV. Access to medical care and cigarette and illicit drug use remain potential targets of primary intervention. ***Journal of Hospital Medicine*** **2008;3:206–211.**

KEYWORDS: status asthmaticus, intubation, noninvasive ventilation, permissive hypercapnia, asthma and pregnancy, neuromuscular blockade.

Status asthmaticus, although a relatively infrequent cause of admission to the intensive care unit, carries a significant risk of mortality and complications of critical care.[1] Asthma prevalence has risen,[2] and recent data have suggested an improvement in overall mortality.[3] Yet there may remain a subgroup of patients with the most severe asthma in whom this outcome benefit may not be seen. Asthma severity and mortality may be concentrated in certain urban areas, and there may even be disparities within cities. One recent study found a trend toward fewer and less severe presentations of ICU patients with status asthmaticus.[4] Our clinical experience in an urban hospital suggested otherwise, and we undertook an examination of status asthmaticus and compared these data with those of our previously published experience at this center.[5]

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TABLE 1
Characteristics of Patients

	n (%)
Age (± SD)*	44 ± 15
Sex	
Men	23 (27%)
Women (5 pregnant)	61 (73%)
Race/ethnicity	
African American	46 (55%)
Hispanic	35 (42%)
Substance use	
Cigarettes	40 (51%)
Illicit drugs	22 (30%)

* Standard deviation.

TABLE 2
Emergency Department Presentation

	n (%)
Medications	
Albuterol	72 (91%)
Inhaled steroids	22 (27%)
Leukotriene antagonist	29 (36%)
Inhaled combination*	41 (51%)
Prednisone	29 (36%)
Noncompliance	20 (45%)
Arterial blood gas	
$PaCO_2$ (mm Hg)	12 ± 5
APACHE II score†	12 ± 5
Chest radiograph (NAPD)‡	70 (83%)
NIV§	10 (12%)

* Includes inhaled steroids and long-acting beta agonist.
† Acute physiology and chronic health evaluation.
‡ No acute pulmonary disease.
§ Noninvasive ventilation.

MATERIALS AND METHODS

A retrospective review was performed of all patients with status asthmaticus admitted to the medical intensive care unit (MICU) of St. Luke's Hospital during the 5-year period January 2002 through December 2006. St. Luke's Hospital is a university-affiliated hospital in New York City. Patients were identified by discharge diagnosis of status asthmaticus through a computerized medical record database. Demographic data, initial presentation data, MICU course, and outcome were collected. Results were compared to our previous study during the 5-year period 1995–1999 at this institution.[5] Data are presented as means ± standard deviations.

The means of the groups were compared using the Student *t* test.

RESULTS

There were 89 MICU admissions for status asthmaticus; the records of 84 patients were available for review. The hospital admission rate for asthma remained stable at 1.6% of admissions during the period 2002–2006, compared with 1.4% of hospital admissions during the previous study period of 1995–1999. In the current study, 3% of asthma admissions required MICU care compared with 5% in the prior era.

Between the 2 study periods, there were no changes in MICU admission criteria or new protocols for management of status asthmaticus in the emergency department. The only difference in ICU management of intubated patients is that in the most recent study period there was an emphasis on earlier identification of patients for extubation. A new sedative, propofol, was available for ICU sedation during the current study period.

Two patients were admitted to the MICU 4 times, and 9 patients were admitted twice. Each presentation was counted as a separate admission and was analyzed individually. Seven patients (8%) had sustained a cardiopulmonary arrest prior to MICU admission. All were intubated in the field by emergency medical services. Characteristics of the patients are shown in Table 1. African American and Hispanic patients constituted 96% of the group. Half the patients were current cigarette smokers, and 30% admitted to current use of illicit drug. Fifty-five percent of patients reported allergies (dust, pollen, pets), and 59% had previously been intubated for asthma.

Status asthmaticus was associated with an upper respiratory tract infection in 54%, illicit drug use in 15%, allergies in 12%, and a recent corticosteroid taper in 8% of exacerbations. Almost all patients had used a short-acting beta-2 agonist, and 78% had been prescribed inhaled corticosteroids either alone or in combination. Thirty-six percent had used oral prednisone. Nonadherence was self-reported by 45% of patients (Table 2).

Emergency department management for all patients included inhaled beta-2 agonist therapy administered continuously, intravenous corticosteroid therapy (methylprednisolone 125 mg once), and magnesium sulfate (2 g intravenously).

TABLE 3
Patients Treated with NIV (n = 10)

	NIV successful	NIV required intubation
Number of patients	6	4
Age	52 ± 20	52 ± 5.6
Admission $PaCO_2$ (mean)	50 ± 13	76 ± 17 $P = 0.044$
Admission pH (mean)	7.33 ± 0.09	7.18 ± 0.04 $P = 0.007$

Noninvasive ventilation was initiated in 10 patients (Table 2).

MICU Management

All patients in the MICU initially received aerosolized bronchodilator therapy every 1 to 2 hours and high-dose intravenous corticosteroid therapy (40–125 mg methylprednisolone every 6 hours). The standard ventilator modality was assist control and permissive hypercapnia. The tidal volume averaged 8 ± 1.5 mL/kg, and mean respiratory rate was 12 ± 1.7 breaths/minute. Plateau pressure and intrinsic PEEP were inconsistently recorded.

The highest $PaCO_2$ during the first 24 hours of ventilation averaged 67 ± 27 mm Hg and exceeded 100 mm Hg in 8 episodes; neuromuscular blockade was used in 5 of these episodes. The highest $PaCO_2$ recorded during controlled mechanical ventilation in a patient who survived was 159 mm Hg.

Of the 10 patients who were given a trial of noninvasive ventilation (NIV), 4 subsequently required intubation. The average time on NIV before intubation was 2 hours. Patients who were intubated after a trial of NIV had a significantly higher initial $PaCO_2$ than those who were successfully managed with NIV (Table 3). There were no deaths among patients treated with NIV. Table 4 demonstrates the main differences between patients requiring invasive ventilation and those successfully managed with noninvasive ventilation.

Sedation and Neuromuscular Blockade

Propofol was used for sedation in almost all patients (97%). The addition of lorazepam was required in 27 patients (42%). Neuromuscular blockade with cisatracurium was initiated in 6 episodes after high levels of 3 sedatives (propofol, opiates, and benzodiazepines) were used for continued respiratory efforts and evidence of severe dynamic hyperinflation. These patients were younger and manifested a significantly greater degree of respiratory acidosis while receiving mechanical ventilation (Table 5). Duration of neuromuscular blockade averaged 2 days, and their use was associated with significantly longer durations of mechanical ventilation and MICU stay and a greater risk of complications. However, none of these patients died (Table 5).

TABLE 4
Invasive Versus Noninvasive Ventilation for Status Asthmaticus

	Intubated patients	Patients managed only with NIV
Number of patients	64	6
Age	45 ± 16	52 ± 20
Admission $PaCO_2$ (mean)	64 ± 22	50 ± 13 $P = 0.057$
Admission pH (mean)	7.2 ± 0.15	7.33 ± 0.09 $P = 0.021$
Length of MICU stay (days)	5.8 ± 4.4	3 ± 4.2 $P = 0.012$
Hospital mortality	6	0

TABLE 5
Characteristics of Patients Receiving Neuromuscular Blockade (NMB)

	(−) NMB	(+) NMB	*P* value
Number of patients	58	6	
Age	47 ± 15	24 ± 2	
Highest $PaCO_2$ (mean)	68 ± 21	119 ± 35	0.015
Lowest pH (mean)	7.18 ± 0.14	6.96 ± 0.13	0.007
Barotrauma	1 (2%)	2 (33%)	
Myopathy	10 (17%)	2 (33%)	
Duration of MV (days)	4 ± 3.7	7.5 ± 1.2	0.0001
Length of MICU stay (days)	5.3 ± 4.3	10 ± 3	0.007
Length of hospital stay (days)	8 ± 6	14 ± 3.4	0.006
Mortality	6 (10%)	0 (0%)	

The complications of status asthmaticus are shown in Table 6. Three patients suffered barotrauma (2 patients with pneumomediastinum and 1 with pneumothorax requiring chest tube placement). MICU complications, including suspected ventilator-associated pneumonia and catheter-related infection, were predominantly seen in patients who required mechanical ventilation for more than 5 days. Excessive sedation was noted in 7 patients, prompting additional investigations (brain imaging and electroencephalograms).

Outcomes

Table 6 shows the outcomes for the patients. Duration of mechanical ventilation averaged 4.4 ± 3.7 days. Eighty-four percent of patients were extubated successfully. Three patients required a tracheostomy for prolonged ventilatory support. Duration of MICU stay averaged 4.8 ± 4.2 days.

TABLE 6
Complications and Outcome

	n (%)
Complication	
Ventilator-associated pneumonia	14 (21%)
Catheter-related infection	7 (11%)
Barotrauma	3 (3.5%)
Myopathy	12 (19%)
Outcome	
Duration of MV (days)	4.4 ± 3.7
Length of hospital stay (days)	7.78 ± 5.7
Discharge home	69 (82%)
Mortality	6 (7%)

Following the MICU course, only 21% of patients were seen by pulmonary specialists in the hospital, and on hospital discharge, only 45% were referred to the outpatient pulmonary specialty clinic (Table 7). Most patients (82%) were discharged home.

There were 6 deaths (7%). Three patients sustained a prolonged cardiopulmonary arrest prior to MICU admission and were determined to be brain dead. One young patient who was intubated for status asthmaticus and lobar pneumonia rapidly developed hyperthermia, rhabdomyolysis, and multiorgan failure; in addition to antibiotics to treat sepsis, empiric treatment of malignant hyperthermia was initiated. Unfortunately, autopsy was declined. Two patients died after a prolonged hospital stay complicated by nosocomial infection and multiorgan failure.

Comparison to Prior 5-Year Period

Table 7 compares the current study to the prior 5-year period. Demographic features and ventilator management remained stable, but we noted more use of NIV, increased use of propofol and cisatracurium, increased severity of respiratory acidosis, increased duration of ventilation, and a higher mortality rate.

TABLE 7
Comparison of the Two 5-Year Periods

Years	1995–1999	2002–2006
Number of admissions	88	89
Sex (women)	63 (72%)	61 (73%)
Pregnancy	3	5
Age (mean)	45	44
Nonwhite	78 (90%)	81 (97%)
Smoker	27 (31%)	40 (51%)
Illicit drugs	16 (18%)	22 (30%)
Initial $PaCO_2$ (mm Hg)	54.9	61
Cardiopulmonary arrest prior to MICU	6 (7%)	7 (8%)
Mechanical ventilation	75 (87%)	64 (76%)
NIV	0	10 (12%)
Highest $PaCO_2$ (mm Hg)	60.2	67
Duration of MV (days)	3	4.4
Sedatives: propofol	0 (0%)	62 (97%)
NMB	1 (1%)	6 (9%)
Barotrauma	5 (6%)	3 (4%)
Mortality	2 (2.3%)	6 (7%)
Discharge home	83 (95.4%)	69 (82%)

DISCUSSION

We identified greater severity of status asthmaticus among patients requiring admission to our urban intensive care unit. Despite reports of improvement in outcome[3] and reduction in the severity and number of MICU admissions by other investigators[4] in New York City, patients with status asthmaticus admitted to the MICU suffered significant mortality and morbidity. During the recent 5-year period, compared with the period reported in our previous report,[5] these patients had greater respiratory acidosis, more frequent need for neuromuscular blockade, longer duration of mechanical ventilation, increased complications, and higher unadjusted mortality.

There remain few large series of status asthmaticus. Episodes of life-threatening asthma occur more frequently in specific high-risk areas. We had the benefit of a prior study in our institution in order to compare trends in status asthmaticus. With greater attention to asthma severity, treatment, access to information, and medical care, a change in demographic features may have been expected. Yet we found that noncompliance with medications and smoking and illicit drug usage increased in this recent 5-year period compared with the prior study period. Minority populations are also at particular risk for severe asthma.[6]

Noninvasive ventilation has been shown to be effective in acute hypercapnic respiratory failure in patients with chronic obstructive lung disease.[7,8] A small study of asthma found that NIV was associated with a reduction in $PaCO_2$ during the early hours of use and that mortality and complications were not increased in those who subsequently required intubation.[9] However, in another study of 27 patients managed with NIV, 2 of the 5 patients requiring intubation died.[10] In

the 1 randomized controlled study of NIV in severe asthma, Soroksky et al. found that NIV significantly improved lung function and decreased hospitalization rate compared with the use of conventional therapy alone. The average $PaCO_2$ and pH of these patients were 33.59 mm Hg and 7.41, respectively.[11] Meduri et al. reported a small series of 17 patients with severe asthma treated with NIV, 2 of whom were subsequently intubated. The initial pH and $PaCO_2$ of these patients averaged 7.25 and 65 mm Hg, respectively.[12] In our series, NIV was used in 10 patients, 4 of whom were subsequently intubated. The average time on NIV before intubation was 2 hours, and there were no deaths in this group. Patients who were intubated after NIV had a statistically significant lower pH (7.17) and higher $PaCO_2$ (76 mm Hg) on admission than those who were successfully managed with NIV, with the pH and $PaCO_2$ of the latter group 7.32 and 50 mm Hg, respectively.

Improvement in mortality of status asthmaticus over the past decades has been attributed to improved ventilatory strategy using permissive hypercapnia. This approach has been credited with a decrease in barotrauma, hemodynamic instability, and mortality.[5,13] The latter complications were mainly a result of the dynamic hyperinflation found in patients with severe asthma. Decreasing the respiratory rate and tidal volume as well as increasing the inspiratory flow rate will lead to an increase in expiratory time and will subsequently decrease the dynamic hyperinflation. With this approach, hypercapnia may occur. Hypercapnia ($PaCO_2$ level up to 90 mm Hg) is generally well tolerated when oxygenation is maintained.[14] Sedation is crucial to achieving optimal ventilation. Because of its short duration of action and bronchodilator effects,[15,16] propofol was the main sedative used in our MICU. Additional sedatives were required for half our patients. A prolonged sedative effect was noted in several cases, which prompted additional neurologic evaluation. It is conceivable that higher doses of sedatives are required for ventilatory control of young patients with a strong respiratory drive.

The administration of therapeutic paralysis is generally avoided in patients with status asthmaticus treated concurrently with corticosteroids. Myopathy may develop in the setting of neuromuscular blockade and corticosteroid administration and prolong ventilatory failure.[17] In our earlier series, only 1 patient received a paralytic agent; in the current series, neuromuscular paralysis was needed in 6 episodes despite maximum sedative infusion. Patients requiring neuromuscular blockade were younger and had a significantly lower pH and higher $PaCO_2$ than did those not receiving neuromuscular blockade. These patients developed more complications, including prolonged weakness, supporting the general approach of avoiding paralytic use unless absolutely necessary. It is noteworthy that despite this greater degree of respiratory failure and subsequent ICU complications, no patients in this group died.

The median duration of mechanical ventilation was 4.4 days. Complications included ventilator-associated pneumonia, catheter-related infection, excessive sedation, and prolonged weakness. These events occurred primarily in patients who received paralytics and patients whose mechanical ventilation was prolonged. The average duration of mechanical ventilation for patients who had ventilator-associated pneumonia and catheter-related infection was 22 and 31 days, respectively.

Status asthmaticus in pregnancy deserves special attention, and its course has not been well described in the literature. We report finding that in the current study period there were 5 pregnant patients requiring ICU management for status asthmaticus, all with dramatic degrees of hypercapnia and acidosis during controlled mechanical ventilation; the highest $PaCO_2$ and lowest pH averaged 101 mm Hg and 7.06, respectively. Management of status asthmaticus in pregnancy is no different than in nonpregnant individuals, but there are concerns about the effects of hypercapnia and acidosis on the fetus.[18] In all 4 patients who delivered, the pregnancies resulted in healthy babies. In the 1 patient who suffered a pneumomediastinum during early labor, the decision was made for cesarean delivery because of concerns about potential worsening of the barotrauma and maternal cardiopulmonary condition. This patient did not require intubation prior to or during the cesarean delivery. Collaboration with the obstetrician is essential in the management of these cases.

Despite advances in ventilator management and critical care, there remains a mortality risk in patients with status asthmaticus.[17,19,20] In our study, 6 patients (7%) died; 3 patients died after suffering pre-MICU cardiac arrest, and 3 patients died of multiorgan failure. Regular asthma clinic follow-up, to include counseling about smoking

cessation and illicit drugs, is essential. Unfortunately, only 45% of our patients had specialty clinic referral on discharge. Lack of patient understanding of their illness may also complicate their care, as demonstrated by nonadherence to medication and medical appointments. Five of our patients left against medical advice, 4 of them within a day of extubation.

Our study had several limitations. Patients were identified based on admission diagnosis by the attending physician; the coexistence of chronic obstructive pulmonary disease could not always be definitely excluded. However, all patients had a prior diagnosis of asthma and had been treated for asthma. The young age of the patient group is consistent with that reported in the literature.

It is difficult to compare studies of status asthmaticus, given the dynamic nature of the airways disease and individual clinician judgments about intubation and extubation. We believe that longer duration of ventilation reflects more severe asthma, especially in this time when clinicians attempt noninvasive ventilation and daily trials of spontaneous breathing for earlier extubation.

In conclusion, this report describes an increase in the severity of status asthmaticus in patients admitted to an urban MICU. The reason for the increase in severity compared to our previous study is uncertain. Possible factors include: cigarette and substance use, refractoriness to therapy because of environment or smoking, inadequate medical care, poor understanding of illness, and adherence to therapy. As the ICU management is supportive, the best approach is prevention, targeting at-risk minority populations with education, counseling for smoking and drug cessation, and specialty care. Once status asthmaticus has developed, a careful, limited trial of NIV in selected patients may offer benefits in the management of ventilatory failure and avoidance of ICU complications.

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