

Clinical course and outcome of children with status asthmaticus treated in a pediatric intensive care unit: a 15-year review

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Background and purpose: The purpose of this study was to analyze the clinical course and outcomes of children with status asthmaticus treated in a pediatric intensive care unit (PICU) in Taiwan.

Methods: The medical charts of all patients aged from 2 to 18 years with status asthmaticus who were admitted to the PICU National Taiwan University Hospital, Taipei, Taiwan, from 1990 to 2006 were reviewed retrospectively.

Results: Twenty eight children were admitted on 33 occasions; 4 patients had more than 1 admission. The mean age was 6.23 years (range, 2-17 years). No control medication was regularly used prior to admission for 81.8% of the episodes. The mean PICU stay was 2.55 days (range, 1-13 days) and, for 78.8% of episodes, the patients were discharged from the ICU within 2 days. For 11 episodes (33.3%), the patients required mechanical ventilation for a mean duration of 3.6 days. The mortality rate was 3.3% ($n = 1$). Complications included bronchopneumonia (57.6%), hemodynamic compromise (9.1%), neurologic symptoms (6.1%), and air leak (3.3%). Patients requiring mechanical ventilation had significantly lower initial pulse oximeter oxygen saturation ($<90\%$), lower blood gas pH (<7.25), higher partial pressure of carbon dioxide, and longer duration of PICU and hospital stay ($p < 0.05$) when compared with patients not requiring mechanical ventilation. For patients with a history of repeated PICU admissions for asthma, the intubation rate was 77.7%.

Conclusions: The prognosis for childhood status asthmaticus is favorable. The most common trigger factors were respiratory tract infection and poor asthma control.

Key words: Intensive care units, pediatric; Status asthmaticus

Introduction

The prevalence of childhood asthma has increased markedly in many countries, including Taiwan [1,2]. Status asthmaticus is a potentially life-threatening medical emergency, which is defined as progressive respiratory failure due to asthma for which conventional forms of therapy have failed [3]. Admission to an intensive care unit (ICU) for asthma is a marker of its severity and may be a precursor of asthma mortality [4]. However, the features of children admitted to the ICU for status asthmaticus in Taiwan have not

been fully studied previously. The purpose of this study was to analyze the clinical course and outcomes of children with status asthmaticus treated in a pediatric ICU (PICU).

Methods

In this retrospective study, the medical charts of all patients aged from 2 to 18 years with status asthmaticus who were admitted to the PICU of the National Taiwan University Hospital, Taipei, Taiwan, from November 1990 to August 2006 were reviewed. The patients were either admitted directly via the Emergency Department or transferred from a general ward. Admission to the PICU and the need for mechanical ventilation were based on the judgment of the primary

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care physicians. Non-invasive ventilation was tried first. Data recorded from the medical records included age, sex, age at diagnosis of asthma, asthma control use, duration of symptoms prior to admission, management in the PICU, laboratory data, complications, and clinical outcomes.

Statistical analysis

Asthma episodes requiring or not requiring mechanical ventilation and episodes with or without repeated PICU admission were compared. For categorical data, the Pearson chi-squared test was used. For continuous data, the Mann-Whitney *U* test was used. Logistic regression analysis was used to identify risk factors for mechanical ventilation for status asthmaticus. Variables analyzed included age, sex, regular asthma control use, repeated PICU admission for asthma, initial pulse oximeter oxygen saturation (SpO_2 ; $<90\%$, $\geq 90\%$), blood gas partial pressure of carbon dioxide (PCO_2 ; ≤ 55 mm Hg, >55 mm Hg), and pH (<7.25 , ≥ 7.25). The final model was obtained after examining model fitting by removing the variables sequentially. If the reduced model showed a poorer fit to the data than the full model, the variable was retained in the final model. Statistical significance was defined as $p < 0.05$ and all computations were made using the Statistical package for the Social Sciences (Version 13.0; SPSS, Inc., Chicago, IL, USA).

Results

Twenty eight children were admitted to the pediatric ICU for status asthmaticus on 33 occasions. Four patients (14.3%) had more than 2 admissions; 2 patients had 2 admissions, but 1 admission was before 1990 and was not included in the study, and 2 patients had 3 admissions. Eleven admissions occurred between 1990 and 2000 and 22 admissions occurred from 2001 to 2006. There was no obvious seasonal predilection of PICU admissions for status asthmaticus (Fig. 1).

Patients' characteristics

Fifteen patients (53.6%) were boys and 13 (46.4%) were girls. The mean age was 6.23 years (range, 2-17 years). The age distribution of the episodes was as follows: 2 to 5 years, 63.6%; 6 to 12 years, 15.2%, and 13 years or older, 21.2%. The median duration between first asthma diagnosis and PICU admission was 8 months (range, 1-133 months). Therapy prior to PICU admission was as follows:

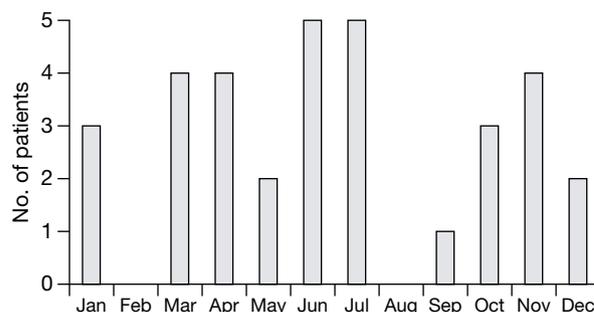


Fig. 1. Cumulative monthly distribution of pediatric intensive care unit admissions for status asthmaticus from 1990 to 2006.

inhaled corticosteroid only, 3.3%; inhaled corticosteroid combined with long-acting β_2 -agonist, 18.2%; aminophylline, 12.1%; and montelukast, 3.3%. However, no control drugs were used prior to admission in 81.8% of the episodes, including 9.1% of patients who used a short-acting β_2 -agonist for wheezing.

Intensive care unit course and outcomes

The indications for admission to the PICU were deterioration of blood gas status and overt or impending respiratory failure. The mean duration from presentation to the emergency department to PICU admission was 4.4 h (range, 1-29 h). In 9.1% of the episodes, the patients had repeated emergency department visits before PICU admission.

Based on initial blood gas data, in 57.6% of the episodes, the patients had hypercapnia (PCO_2 , >45 mm Hg) and in 48.5%, the patients already had acidemia (pH, <7.3). Although all of the patients received oxygen, significant hypoxia (oxygen pressure, <60 mm Hg) was still found in 42.4% of episodes (Table 1).

The mean PICU stay was 2.55 days (range, 1-13 days). The distribution of PICU stay was as follows: 1-2 days, 78.8%; 3-7 days, 15.2%; and ≥ 8 days, 6.1%. For 11 of the 33 admissions (33.3%), the patients required invasive mechanical ventilation, and the mean duration was 3.6 days (range, 1-10 days). The distribution of mechanical ventilation duration was as follows: 1-2 days, 45.5%; 3-7 days, 45.5%; and ≥ 8 days, 9.1%. Six intubations were performed electively in the PICU, while emergency intubation was performed in the emergency department and general wards on 4 and 1 occasions, respectively.

In addition to oxygen and adequate hydration, medications used in the PICU for asthma treatment are summarized in Table 2. Nebulized β_2 -agonist

Table 1. Initial blood gas results for patients with status asthmaticus admitted to the pediatric intensive care unit by episode (n = 33).

Parameter	No. of episodes (%)
pH	
<7.0	2 (6.1)
7.0-7.3	14 (42.4)
>7.3	17 (51.5)
Partial pressure of carbon dioxide (mm Hg)	
>45	19 (57.6)
35-45	7 (21.2)
<35	7 (21.2)
Oxygen pressure (mmHg) ^a	
<60	14 (42.4)
60-100	10 (30.3)
>100	9 (27.3)

^aPatients received variable oxygen concentrations.

Table 2. Medication history and complications of patients with status asthmaticus admitted to the pediatric intensive care unit by episode (n = 33).

Parameter	No. of episodes (%)
Medications	
β ₂ -Agonist (nebulized)	33 (100)
Steroid (intravenous or oral)	29 (87.9)
Steroid (inhaled)	1 (3.0)
Aminophylline (intravenous)	18 (54.5)
Ipratropium bromide (nebulized)	16 (48.5)
Isoproterenol	2 (6.1)
Azithromycin	18 (54.5)
Other antibiotics	15 (45.4)
Complications	
Death	1 (3.3)
Bronchopneumonia	19 (57.6)
Hemodynamic compromise	3 (9.1)
Neurologic symptoms	2 (6.1)
Air leak	1 (3.3)

was used as a first-line therapy for all admissions, and systemic corticosteroids were given for 87.9% of admissions. If these initial medications were not effective, second-line treatment include intravenous aminophylline and nebulized ipratropium bromide. Patients in 72.7% of the admissions had respiratory tract infection. For patients for whom mycoplasma serology test results were available, the positivity rate was 7 of 24 admissions (29.2%). Azithromycin was used in 54.5% admissions and other antibiotics were used in 45.4% to treat concomitant respiratory tract infections.

Multiple allergen simultaneous test results were available for 17 patients (Table 3). House dust mite was the most predominant inhalational allergen (n = 12), followed by cockroach (n = 4), house dust

Table 3. Trigger factors for patients with status asthmaticus admitted to the pediatric intensive care unit by episode (n = 33).

Factor	No. of episodes (%)
Inhalational allergen allergy	
House dust mite	12/17 (70.6)
Cockroach	4/17 (23.5)
House dust	2/17 (11.8)
Dog dander	2/17 (11.8)
Cat dander	1/17 (5.9)
Respiratory tract infection	
Upper respiratory tract infection	5/33 (15.2)
Bronchopneumonia	19/33 (57.6)
Mycoplasma	7/24 (29.2)
Lack of control medication use	27/33 (81.8)
Undetermined	4/33 (12.1)

(n = 2), dog dander (n = 2), and cat dander (n = 1). No significant differences for house dust mite sensitization were noted between patients requiring (3/5) and not requiring (9/12) mechanical ventilation.

Complications included bronchopneumonia (57.6%), hemodynamic compromise (9.1%), neurologic symptoms (6.1%), and air leak (3.3%) (Table 2). One patient died. The patient was a 15-year-old girl who had an 11-year history of asthma and 1 previous PICU admission for status asthmaticus. She had received a full course of subcutaneous desensitization for house dust mite with minimal effect and used a β₂-agonist and aminophylline for control. Severe respiratory distress occurred suddenly at home, which was unresolved by bronchodilator inhalation. Apnea suddenly ensued. When the girl presented to the emergency room, she was comatose. Initial blood gas revealed severe hypercapnia with both respiratory and metabolic acidosis, indicating hypoxia with shock. Despite aggressive management, she died 1 day after PICU admission.

Compared with patients not requiring mechanical ventilation, patients requiring mechanical ventilation had significantly lower initial SpO₂, lower pH, and higher PCO₂ in the initial blood gas tests, and longer duration of both PICU and hospital stay (*p* < 0.05) [Table 4]. Compared with patients without a history of repeated ICU admission for asthma, patients with repeated PICU admissions had significantly lower pH and higher PCO₂ in initial blood gas tests (*p* < 0.05). There was also a trend for longer PICU stay among these patients (*p* = 0.06) [Table 5].

Despite high asthma control use prior to admission (88.9%), the intubation rate of episodes for those

Table 4. Comparison of mechanical ventilation use for patients with status asthmaticus admitted to the pediatric intensive care unit by episode (n = 33).

	Mechanical ventilation	No mechanical ventilation	<i>p</i>
Age (years; mean ± SD)	7.28 ± 4.8	5.7 ± 4.2	NS
Sex (male/female)	6/5	14/8	NS
Hospital stay (days; mean ± SD)	8.18 ± 4.33	4.72 ± 1.77	<0.05
PICU stay (days; mean ± SD)	4.81 ± 3.57	1.41 ± 0.50	<0.05
Onset to PICU (days; mean ± SD)	1.18 ± 0.40	1.22 ± 0.53	NS
Initial pulse oximeter oxygen saturation (%; mean ± SD)	80.1 ± 16.1	90.1 ± 6.94	<0.05
pH (mean ± SD)	7.18 ± 0.17	7.34 ± 0.07	<0.05
Partial pressure of carbon dioxide (mm Hg; mean ± SD)	67.03 ± 29.37	43.81 ± 11.12	<0.05
White blood cell count (μL; mean ± SD)	16544 ± 6713	14681 ± 5457	NS
C-reactive protein (mg/dL; mean ± SD)	3.79 ± 7.85	1.44 ± 2.37	NS

Abbreviations: SD = standard deviation; PICU = pediatric intensive care unit; NS = not significant.

Table 5. Comparison history of repeat pediatric intensive care unit admissions for patients with status asthmaticus (n = 33).

	Repeat PICU admission	No repeat PICU admission	<i>p</i>
Age (years; mean ± SD)	7.41 ± 4.46	5.81 ± 4.40	NS
Sex (male/female)	8/1	12/12	NS
Intubation no. (%)	7/9 (77.7)	4/24 (16.6)	<0.05
Hospital stay (days; mean ± SD)	7.55 ± 4.9	5.25 ± 2.23	NS
PICU stay (days; mean ± SD)	4.77 ± 4.08	1.71 ± 0.99	0.06
Onset to PICU (days; mean ± SD)	1.22 ± 0.44	1.21 ± 0.51	NS
Initial pulse oximeter oxygen saturation (%; mean ± SD)	81.25 ± 19.85	88.70 ± 6.23	NS
pH (mean ± SD)	7.18 ± 0.18	7.33 ± 0.08	<0.05
Partial pressure of carbon dioxide (mm Hg; mean ± SD)	68.04 ± 30.70	45.37 ± 13.63	<0.05
White blood cell count (μL; mean ± SD)	17315 ± 5201	14547 ± 6025	NS
C-reactive protein (mg/dL; mean ± SD)	1.91 ± 4.19	2.32 ± 5.19	NS

Abbreviations: PICU = pediatric intensive care unit; SD = standard deviation; NS = not significant.

with a history of repeated ICU admissions for status asthmaticus was 77.7%, much higher than for those without this history (16.6%) [*p* < 0.05]. Logistic regression analysis showed that the significant risk factors were initial blood gas pH <7.25, initial SpO₂ <90%, and prior PICU admission history for asthma.

Discussion

Asthma is a leading chronic illness in childhood, and status asthmaticus is a potentially fatal presentation. This study describes the clinical features of PICU admissions for status asthmaticus in a tertiary referral center in Taiwan in the past 15 years. The number of admissions that occurred from 2001 to 2006 were 2-fold those that occurred from 1990 to 2000. The explanation for this finding is unknown but might be related to the introduction of the National Health Insurance system and increased PICU availability in the hospital. This phenomenon also reflected the increasing incidence of asthma, increasing levels of air pollution, and increasing aeroallergen allergy in recent years. Since this study

describes the experience of only 1 medical center, a nationwide study would be valuable to clarify whether this is a general trend in Taiwan. Although some studies have indicated higher PICU admissions for asthma in the winter months [5], these data showed no obvious seasonal predilection, which might be related to climatic differences between countries.

Since the number of patients in this study was limited, further large-scale studies are needed to clarify the relationship between seasonal changes and the incidence of status asthmaticus in Taiwan. However, this study showed that there were many admissions for status asthmaticus outside the winter season and highlights the importance of asthma control in Taiwan even in the summer season.

In this study, concomitant respiratory tract infection and lack of regular maintenance therapy prior to admission seemed to be the most likely triggering factors for status asthmaticus. House dust mite sensitization may also have been a trigger (Table 3). Therefore, education on the importance of regular maintenance therapy and environmental control, and aggressive

monitoring for a possible asthma attack during respiratory tract infection are essential. Mycoplasma infection has long been associated with asthma [6]. In this study, the mycoplasma serology positive rate was about 30%. Thus concomitant mycoplasma infection must be considered during an asthma attack. Macrolides have been found to have both antimicrobial and anti-inflammatory effects [6]. When an asthma attack is combined with concomitant mycoplasma infection, early treatment with macrolides should be considered.

Clinically, status asthmaticus usually presents with cough and wheezing, followed by signs of dyspnea, increased difficulty in breathing, and anxiety. Overt respiratory failure or even cardiopulmonary arrest are also possible manifestations [3]. Hypoxia and hypocapnia are the earliest blood gas findings during a severe asthmatic attack. Hypercapnia indicates a failed compensation mechanism and impending respiratory failure [3]. In this study, initial blood gas tests showed hypercapnia in 57.6% of admissions. Moreover, patients in 9.1% of admissions had a history of repeated emergency department visits. These findings show that families of children with asthma and some medical staff may underestimate the initial presentation of severe asthma. Appropriate asthma care education and a high index of suspicion on behalf of the families and medical staff are required.

Management of status asthmaticus requires aggressive cardiopulmonary monitoring and a highly skilled critical care team. β_2 -Agonists and corticosteroids remain the first-line treatment. Adjunctive therapy includes anticholinergics, methylxanthines, and magnesium sulfate [7,8]. In intubated patients, inhalational anesthetics and ketamine have also been tried [9]. Non-invasive ventilatory support should be tried initially because the use of mechanical ventilation may result in dynamic hyperinflation and barotrauma [10,11].

When mechanical ventilation is needed, the volume-cycled ventilator is the most frequently recommended instrument. The aim is to correct hypoxia with permissive hypercapnia to minimize the risk of barotraumas and air leak [3,11]. The use of positive end-expiratory pressure is still controversial. In this study, the initial pH and PCO_2 in blood gas, SpO_2 , and a prior history of intubation for asthma were risk factors for the need for mechanical ventilation, which is consistent with previous studies [12-14]. The prognosis of childhood status asthmaticus in this study was favorable, with a low mortality rate and no obvious long-term complications for most patients.

A history of previous PICU admission for status asthmaticus was an important risk factor for respiratory failure requiring mechanical ventilation in this study, which is compatible with previous studies [15,16]. This finding may reflect the underlying asthma severity and status of asthma control. Recently, genetic polymorphism in the gene coding for the β_2 -adrenergic receptor has been found to affect airway hypersensitivity and response to bronchodilators, and has thus been associated with status asthmaticus [17,18]. Whether this genetic predisposition could explain the aforementioned phenomenon needs further prospective studies.

In conclusion, with appropriate management, the prognosis of childhood status asthmaticus is generally favorable. The most common trigger factors are respiratory tract infection and poor asthma control. Initial blood gas pH, initial SpO_2 , and prior history of PICU admission for asthma appear to be risk factors for the need for mechanical ventilation.

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