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ORIGINAL ARTICLE

Gender and Status Asthmaticus

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ABSTRACT

Background. Adult women may be more susceptible to asthma than men. **Hypothesis.** Women are more likely to develop status asthmaticus (SA) requiring critical care. **Methods.** The medical records of patients admitted to our medical intensive care unit (ICU) for SA between 1994 and 2000 were examined. A number of demographic and physiologic variables were extracted from the medical records. **Results.** Of 103 total admissions, 53 (of 37 patients) were age < 50 years and had clinical evidence suggesting SA. Among these 37 patients, the average ($\pm$ SE) age was 30.8 ± 1.0 y with average acute physiology and chronic health evaluation (APACHE) II of 9.5 ± 0.8 . Seventeen patients were Hispanic, 13 were black, and 7 were white. Twenty-four patients (accounting for 37 admissions) were female and 13 patients (16 admissions) were male. Although women accounted for a greater absolute number of endotracheal intubations (ETI; 17 vs. 12) and were more likely to be admitted to ICU more than once (7 vs. 3), men had a higher incidence of ETI (RR = 1.6; 95%CI = 1.04–2.6). The need for using therapeutic permissive hypercapnia and lengths of stay (ventilator, ICU, and hospital) were similar between men and women. Two patients, both women, died of causes not related to treatment of SA. **Conclusions.** These data suggest that although women accounted for more ICU admissions for SA, men were more likely to require ETI.

Key Words: Asthma; Status asthmaticus; Critical care; Mechanical ventilation; Permissive hypercapnia.

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Some data suggest that the prevalence of asthma is greater in women than in men (1). One published report demonstrated that women composed a greater absolute number of admissions to an intensive care unit (2). It has also been our clinical impression that women are more likely to be admitted to our intensive care unit with status asthmaticus and require mechanical ventilation and permissive hypercapnia more frequently than men. In this retrospective cohort study, we examined the hypothesis that women are more likely to require critical care for status asthmaticus and are at greater risk of having particularly severe cases requiring extreme therapies.

METHODS

Our medical intensive care unit (MICU) keeps a logbook of all admissions. Names and unit numbers of patients admitted to our MICU with the diagnoses of asthma or status asthmaticus between 1994 and 2000 were abstracted from the logbook and submitted to medical records. Medical records of these patients were examined to determine if they met consensus clinical criteria for status asthmaticus (3). Those older than age 50 y were excluded to reduce the likelihood of including patients with chronic obstructive pulmonary disease. The following were abstracted from the medical records: (1) age, (2) gender, (3) ethnicity, (4) admission acute physiology and chronic health evaluation (APACHE) II scores, (5) administered medications, (6) arterial blood gases, (7) ventilator parameters, (8) complications, (9) lengths of stay, and (10) outcomes.

The mean values of continuous variables were compared for men and women by nonpaired Student *t*-tests assuming unequal variances. Risk and odds ratios were computed for nonparametric variables where appropriate. Multiple logistic regression analyses (Statistica) were performed for selected clinical variables to identify independent risk factors for requiring mechanical ventilation and to adjust for potential confounding. In addition, gender ratios for emergency department (ED) visits of patients with acute exacerbations of asthma for 1996 and 1997 were ascertained from the hospital's data processing department. Observed gender ratios of critically ill asthmatics were adjusted for the gender ratio of patients presenting to the ED. All values are listed as mean $\pm$ standard error. A *P* value of $<.05$ signified statistical significance.

RESULTS

A total of 37 patients with 53 admissions into the MICU met the study's entry criteria. An additional 16 patients, with 50 admissions, were not included because they were aged 50 years or more or failed to fulfill strict criteria for status asthmaticus. Among the 37 patients, the average age was 30.8 ± 1.0 y with average APACHE II of 9.5 ± 0.8 . Seventeen patients were Hispanic, 13 were black, and 7 were white.

Twenty-four patients, accounting for 37 admissions, were female and 13 patients, accounting for 16 admissions, were male. Ten patients had multiple (2–5) admissions. These included seven women with 20 total admissions and three men with 6 total admissions. Between 1996 and 1998 there was a total of 2943 ED visits, of which men accounted for 1310 (44.5%). On the contrary, men accounted for only 30.2% of ICU admissions. Table 1 lists comparisons of demographic and physiologic variables of men versus women.

Thirty-nine (73.5%) patients required endotracheal intubation. Overall, arterial blood gas pH was lower (7.19 vs. 7.37) and PCO_2 was higher (64 vs. 36 mm Hg) in those who were intubated. Women accounted for a greater absolute number of endotracheal intubations (17 vs. 12) and were more likely to be admitted to ICU more than once (7 vs. 3). However, men treated in our ICU had a greater risk of endotracheal intubation ($\text{RR} = 1.6$; $95\% \text{CI} = 1.04\text{--}2.6$) and were 2.8 times ($95\% \text{CI} = 0.5\text{--}14.5$) as likely as women to have >1 intubation over the period. Ventilator mechanics, the need for permissive hypercapnia and lengths of (ventilator, ICU, and hospital) stay were similar for men and women. Two patients, both women, died. One arrived to the ED with severe brain injury and the other had coincident fibroblastic sarcoidosis that contributed to her death.

DISCUSSION

This study confirms that women composed a greater number of admissions for acute asthma to our ED and critical care unit. The unexpected finding of this study was that, although women accounted for a greater number of endotracheal intubations, men treated for status asthmaticus in our ICU were 60% more likely than were women to be endotracheally intubated.

Table 1. Demographic and physiologic characteristics of critically ill men vs. women presenting with status asthmaticus.

Parameter	Men (13)	Women (24)	P value
Number (admissions)	16	37	
Age	29.8 ± 1.7 29; 20–46	31.2 ± 1.2 30; 20–49	.51
APACHE II	10.6 ± 1.5 8.5; 3–24	9.1 ± 0.9 7; 3–30	.40
Race			
Black	3	10	.28
Hispanic	7	10	.49
Caucasian	3	4	.60
Albuterol (# 2.5 mg nebs in first hour)	2.4 ± 0.4	2.8 ± 0.1	.17
SQ epinephrine	5	7	.34
Magnesium	3	7	.99
Heliox trial	2	11	.18
Arterial blood gas			
PH	7.26	7.28	.63
PCO ₂	56	49	.31
Intubated	12	17	.05
R _{aw} /C _{rs}	23.9/25.2	31.7/28.5	.22/.41
Permissive ↑CO ₂	5	7	.33
Ventilator LOS (H)	33 ± 7.1 25.5; 8–81	71.4 ± 32.0 26; 6–552	.26
ICU LOS (d)	2.5 ± 0.5 2; 1–7	2.0 ± 0.3 1.5; 1–9	.37
Hospital LOS (d)	4.8 ± 0.5 4.5; 2–10	6.7 ± 2.0 4.0; 1–76	.34
Mortality	0	2	.29

APACHE = acute physiology and chronic health evaluation; SQ = subcutaneous; LOS = length of stay.

The reasons for these observed gender disparities are not altogether clear. Previous studies have demonstrated that childhood asthma is more prevalent in boys (4). During adolescence the ratio is nearly 1:1 (4). During adulthood, asthma is more prevalent in women (1). Data from Europe suggest a 6% excess prevalence of asthma in women compared with men (1). If a similar pattern exists in the United States, which has been suggested in some epidemiologic studies (5), the 11% excess ED visits by women for acute asthma cannot be explained solely by the higher disease prevalence in women. This confirms previous findings (2,5–8).

One possible explanation of these observations is that women with similar degrees of bronchoconstriction present for treatment more often than men. This could occur because of different health behaviors as has been demonstrated with other chief complaints (9). Another possibility is diagnosis/treatment bias—that our clinicians were more likely to diagnose

acute asthma in women. Alternative explanations are that either women experience more frequent exacerbations than men, or for the same degree of bronchoconstriction, women experience a greater degree of dyspnea. Earlier studies have suggested that women may perceive a greater degree of dyspnea than men at any given level of bronchoconstriction (10,11) and are more likely to demonstrate airway hyperresponsiveness after bronchoprovocation (12). It is possible that the smaller baseline airway aperture in women is more likely to reach a critical (perception threshold) diameter during bronchoconstriction. However, this remains conjecture.

The reason that women composed a 39.6% excess of admissions to our ICU is partly explained by the 11% excess ED visits compared with men. One possible explanation is that women are less likely to respond to initial therapies. Insofar as women are more likely than men to have slow-onset asthma (13), which may result from a greater degree

of airway inflammation (14), it is plausible that bronchodilator therapy in the ED is insufficient to reverse slow-onset asthma cases (i.e., it takes 12–24 hours for corticosteroids to begin affecting outcomes). Another possibility is that dyspnea is more pronounced in women than men with the same degree of bronchoconstriction—and respiratory distress is often a variable that precipitates ICU admission. It is unlikely that the excess of female admissions to the ICU can be based on gender-based treatment bias. Gender-based treatments, in general, tend to favor men; for example, women with myocardial infarction are *less* likely than men to receive “aggressive” treatment and invasive diagnostic procedures (15,16). When patients are intubated and mechanically ventilated (as in 55% of our sample), there would be no argument about whether admission to the ICU is appropriate, but indeed a greater proportion of men were intubated compared with women. Although our ICU uses physiologic admission/discharge criteria (i.e., respiratory rate > 30/minute, hypercapnic respiratory failure, heliox breathing), we cannot assure that these were strictly observed in all cases. Our sample was remarkably similar in the severity of physiologic abnormalities to a nearby sample of patients (2) and we observed no differences in severity between men and women. Nonetheless, we cannot entirely discount the possibility that our observations are explained by similar gender-based treatment bias amongst our hospital’s practicing intensivists.

The reason for why men were more likely to be intubated is even more uncertain. Some data suggest that men with near-fatal asthma are more likely than women to experience “impaired dyspnea” (17). If this is the case, men may be more likely to present later in the course of an exacerbation, thereby increasing the risk of endotracheal intubation. Another possibility is that women are more likely to have slow onset of asthma symptoms, allowing more time to present for care. Men are more likely than women to have rapid-onset severe asthma (13). Rapid onset of symptoms could predispose to presentation with more severe bronchoconstriction requiring intubation/mechanical ventilation. Although we only had small numbers of patients, our data suggest that bronchoconstriction, measured by airway pressures and the need for permissive hypercapnia, was *not* greater in men. Note, however, that these variables index severity after intubation and it is possible that physiology changes as a result of intubation (either worsening secondary to airway

manipulation or improving secondary to augmented bronchodilator delivery).

In conclusion, this study reiterates that women compose a majority of patients treated in our intensive care unit for status asthmaticus but that men were more likely to be endotracheally intubated. Future studies may help to illuminate mechanisms to confirm and explain these findings.

REFERENCES

1. de Marco R, Locatelli F, Sunyer J, Burney P. Differences in incidence of reported asthma related to age in men and women. A retrospective analysis of the data of the European Respiratory Health Survey. *Am J Respir Crit Care Med* 2000; 162:68–74.
2. Trawick DR, Holm C, Wirth J. Influence of gender on rates of hospitalization, hospital course, and hypercapnea in high-risk patients admitted for asthma: a 10-year retrospective study at Yale-New Haven Hospital. *Chest* 2001; 119:115–119.
3. National Asthma Education Program; Expert Panel Report. Guidelines for the diagnosis and management of asthma. 1997.
4. Bjornson CL, Mitchell I. Gender differences in asthma in childhood and adolescence. *J Gend Specif Med* 2000; 3:57–61.
5. Yunginger JW, Reed CE, O’Connell EJ, Melton LJ 3rd, O’Fallon WM, Silverstein MD. A community-based study of the epidemiology of asthma. Incidence rates, 1964–1983. *Am Rev Respir Dis* 1992; 146:888–894.
6. Clark S, Camargo CA. Sex differences among inpatients with acute asthma: The UHC asthma clinical benchmarking project. *Am J Respir Crit Care Med* 2001; 163:A364.
7. McFadden ER, Elsanadi N, Dixon L, Takacs M, Deal EC, Boyd KK, Idemoto BK, Broseman LA, Panuska J, Hammons T, et al. Protocol therapy for acute asthma: Therapeutic benefits and cost savings. *Am J Med* 1995; 99:651–661.
8. Rodrigo G, Rodrigo C. First-line therapy of adult patients with acute asthma receiving a multiple-dose protocol of ipratropium bromide plus albuterol in the emergency department. *Am J Respir Crit Care Med* 2000; 161:1862–1868.
9. Verbrugge LM, Steiner RP. Physician treatment of men and women patients: sex bias or appropriate care? *Med Care* 1981; 19:609–32.



10. Devereux G, Hendrick DJ, Stenton SC. Perception of respiratory symptoms after methacholine-induced bronchoconstriction in a general population. *Eur Respir J* 1998 Nov; 12(5):1089–1093.
11. Killian KJ, Watson R, Otis J, St Amand TA, O'Byrne PM. Symptom perception during acute bronchoconstriction. *Am J Respir Crit Care Med* 2000; 162:490–496.
12. Kanner RE, Connett JE, Altose MD, Buist AS, Lee WW, Tashkin DP, Wise RA. Gender difference in airway hyperresponsiveness in smokers with mild COPD. The Lung Health Study. *Am J Respir Crit Care Med* 1994; 150:956–961.
13. Rodrigo GJ, Rodrigo C. Rapid-onset asthma attack: a prospective cohort study about characteristics and response to emergency department treatment. *Chest* 2000; 118: 1547–1552.
14. Strauss L, Hejal R, Galan G, Dixon L, McFadden ER Jr. Observations on the effects of aerosolized albuterol in acute asthma. *Am J Respir Crit Care Med* 1997; 155:454–458.
15. Mahon NG, McKenna CJ, Codd MB, O'Rourke C, McCann HA, Sugrue DD. Gender differences in the management and outcome of acute myocardial infarction in unselected patients in the thrombolytic era. *Am J Cardiol* 2000; 85:921–926.
16. Gan SC, Beaver SK, Houck PM, MacLehose RF, Lawson HW, Chan L. Treatment of acute myocardial infarction and 30-day mortality among women and men. *N Engl J Med* 2000; 343:8–15.
17. Turner MO, Noertjojo K, Vedal S. Risk factors for near-fatal asthma. *Am J Respir Crit Care Med* 1998; 157:1804–1809.



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