

PEDIATRIC ASTHMA

Demographics, Clinical Course, and Outcomes of Children with Status Asthmaticus Treated in a Pediatric Intensive Care Unit: 8-Year Review

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Objective. This study was done to understand the demographics, clinical course, and outcomes of children with status asthmaticus treated in a tertiary care pediatric intensive care unit (PICU). **Methods.** The medical charts of all patients above 5 years of age admitted to the PICU at Nationwide Children's Hospital, Columbus, OH, USA, with status asthmaticus from 2000 to 2007 were reviewed retrospectively. Data from 222 encounters by 183 children were analyzed. **Results.** The mean age at admission in years was 11 ± 3.8 . The median PICU stay was 1 day (range, 1–12 days) and median hospital stay was 3 days. The ventilated group ($n = 17$) stayed a median of 2 days longer in the PICU and hospital. Nearly half of the children ($n = 91$; 50%) did not receive daily controller asthma medications. Adherence to asthma medications was reported in 125 patient charts of whom 43 (34%) were compliant. Exposure to smoking was reported in 167 of whom 70 (42%) were exposed. Among patients receiving metered dose inhaler (MDI), only 39 (18%) were using it with a spacer. Among 105 patient charts asthma severity data were available, of them 21 (20%) were labeled as mild intermittent, 29 (28%) were mild persistent, 26 (25%) were moderate persistent, and 29 (28%) were severe persistent. Compared to children with only one PICU admission during the study period ($n = 161$), children who had multiple PICU admissions ($n = 22$) experienced more prior emergency department visits and hospitalizations for asthma symptoms. There were no fatalities. **Conclusion.** Asthmatics with any disease severity are at risk for life-threatening asthma exacerbations requiring PICU stay, especially those who are not adherent with their daily medications.

Keywords asthma, children, mechanical ventilation, PICU, status asthmaticus

INTRODUCTION

Childhood asthma is a significant public health problem in the United States (1–4) and more than six million US children (9.1% of children) are diagnosed with asthma (3). Childhood asthma is associated with significant morbidity leading to >500,000 emergency department (ED) visits, and >150,000 hospitalizations annually (3). Status asthmaticus is a severe asthma exacerbation associated with increased morbidity and mortality (5). Though the rate of hospital admissions for children with status asthmaticus is decreasing, significant proportion of patients still require intensive care for status asthmaticus (6,7).

The goal of this study was to improve our understanding of the epidemiology, clinical course, and outcomes of children with asthma who present with status asthmaticus in order to prevent pediatric intensive care unit (PICU) admissions and improve asthma care. This study reports the demographic and clinical characteristics of children with status asthmaticus who were treated in a tertiary care PICU over an 8-year period.

METHODS

We retrospectively reviewed the medical records of all patients 5–20 years of age admitted between 2000 and 2007 to the PICU at Nationwide Children's Hospital, Columbus, OH, with status asthmaticus (493.91) as their primary diagnosis. This study was approved by the local Institutional Review Board (IRB08-00212). Two hundred and forty-seven children were admitted on 281 occasions; 22 patients had >1 admission. Twenty-one encounters were excluded because of incomplete information. Twenty-five patients were excluded because of significant co-morbidities (congenital anomalies $n = 3$, severe developmental delay $n = 13$, neuromuscular disease $n = 3$, severe bronchopulmonary dysplasia, primary immunodeficiency, obstructive sleep apnea, ingestion, and empyema). The final sample included 222 PICU admissions of 183 children. Group comparisons of primary interest in this study were single versus multiple PICU admissions for asthma during the study period, mechanical ventilation (MV) therapy versus no MV, and MgSO₄ therapy versus no MgSO₄.

Medical records were reviewed for information such as age, gender, asthma severity, asthma medications, and compliance with home medications, exposure to smoking, and family history of asthma. We also evaluated the hospital course, therapies used in PICU, complications, and clinical outcomes.

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ANALYSIS

Descriptive statistics were calculated for each variable. Differences in demographic and clinical variables between groups were calculated with independent *t*-tests for normally distributed variables (age at admission, duration of symptoms), independent samples Mann–Whitney *U* tests for non-normally distributed variables (pH, pCO₂, duration of hospital, and PICU stay), and *z*-tests for the proportion of dichotomous variables. Related samples Friedman's two-way analysis of variance by ranks was used to evaluate change over time in capillary blood gas (CBG) values. An alpha level of ≤ 0.05 was considered significant. Odds ratios and 95% confidence intervals were calculated from 2 × 2 contingency tables, simple regression, or logistic regression as appropriate.

RESULTS

Demographics

In the total sample of 222 children admitted to the PICU for asthma, the mean age at admission was 11 ± 3.7 years and the male:female ratio was 128:94 (Table 1). Twenty-two of the children were previously not known to have asthma. The median PICU stay was 1 day (range = 1–12) and median hospital stay was 3 days (range 1–15). Other demographic and clinical characteristics of the sample are listed in Table 1. During the first 4 years of the study (2000–2003), the total number of patients admitted to PICU was 108, with an average stay of 3.7 days, compared to the last 4 years (2004–2007) when 97 children were admitted, with an average stay of 3.6 days. Adherence to asthma medications was documented in 125 patient charts; among them only 43 (34%) patients were adherent (Table 1). Asthma severity documentation was available in 105 patient charts; among whom 21 (20%) mild intermittent, 29 (28%) mild persistent, 26 (25%) moderate persistent, and 29 (28%) severe persistent (Table 1).

Clinical Course

During their PICU admission, daily inhaled corticosteroids (ICS) were started for 66 (30%) children, and leukotriene receptor antagonist (LTRA) was added for 22 (10%) patients. Combination therapy (ICS + long-acting beta-agonist (LABA)) was started for 36 (16%) patients, and an additional 11 (5%) patients, daily dose of combination therapy (ICS + LABA) was increased. Eight patients (3.6%) received non-invasive ventilation (continuous positive airway pressure/bilevel positive airway pressure for a mean duration of 1 day (range 0.5–2). Two patients received less than 1 day of a helium–oxygen mixture. Seventeen patients (8%) underwent MV for a mean of 2 days (range 1–6). Sixty-two patients (28%) were still receiving supplemental oxygen when they were transferred from PICU to regular units. All patients survived.

At admission to PICU, 88 patients had capillary blood gases drawn and among them 60 had follow up capillary blood gases done during their PICU stay. Details of CBG data are in Table 1. Complications included

TABLE 1.—Demographic and clinical characteristics of the total sample of children hospitalized in the PICU for asthma.

Characteristics	Total sample	
	Mean	SD
Age at admission (yrs)	11	3.7
Duration of symptoms (yrs)	9.2	4.5
	Frequency	%
Sex		
Male	128	58
Female	94	42
Known asthmatic	200	90
Family h/o asthma	84	38
Asthma severity		
Mild intermittent	21	20
Mild persistent	29	28
Moderate persistent	26	25
Severe persistent	29	28
Previous hospital admissions	140	67
Previous ED visits	162	79
Exposure to smoking	70	42
Daily home medications		
ICS	46	21
LTRA	92	41
ICS/LABA	63	28
Medication adherence	43	34
Delivery system		
MDI	74	33
MDI with spacer	39	18
Nebulizer	39	18
Hospital therapies		
Continuous albuterol	201	91
Terbutaline	152	69
Steroids	214	96
MgSO ₄	57	26
MV	17	8
Chest X-ray: airspace disease	57	51
	Median	IQR
Median pH on first CBG	7.36	7.29–7.40
Median pH on PICU CBG	7.36	7.3–7.4
Median pCO ₂ on first CBG	38	34–49
Median pCO ₂ on PICU CBG	34	31–40
PICU stay (days)	1	1–2
Hospital stay (days)	3	2–4

bronchopneumonia and/or atelectasis in 57 patients and air leak in four patients. None of the patients with air leak received invasive or non-invasive ventilation. Two patients developed chest pains with ST depression and both were receiving continuous albuterol and **terbutaline** and improved with discontinuation of therapy.

Single Versus Multiple PICU Admissions

This was the first asthma-related PICU admission for 161 children, while 22 of the children had multiple PICU admissions during the study period. We compared the demographic characteristics and clinical course between these two groups (Table 2). Children who experienced multiple PICU admissions were nearly 3 years older ($p = .001$; OR = 1.20) than the single PICU admission group, and experienced asthma symptoms for an

TABLE 2.—Demographic and clinical characteristics of patients with a single versus multiple PICU admissions.

Characteristics	Single PICU admission, <i>N</i> = 161		Multiple PICU admissions, <i>N</i> = 22		<i>p</i> ^a	Odds ratio	95% Confidence interval
	Mean	SD	Mean	SD			
Age at admission (yrs)	10.6	± 3.7	13.4	± 3.6	.001*	1.20	1.07–1.35
Duration of symptoms (yrs)	8.0	± 4.7	13.3	± 2.6	.006*	1.30	1.05–1.61
	Frequency	%	Frequency	%	<i>p</i> ^b		
Sex							
Male	98	61	11	50	.330	1.56	0.64–3.80
Female	63	39	11	50			
Known asthmatic	139	86	22	100	.065	1.16	1.09–1.23
Family h/o asthma	51	32	9	41	.387	1.49	0.60–3.72
Asthma severity							
Mild intermittent	21	35	0	0	.007*	0.72	0.61–0.85
Mild persistent	20	33	4	27	.621	0.73	0.21–2.57
Moderate persistent	14	23	3	20	.783	0.82	0.20–3.33
Severe persistent	5	8	8	53	.001*	12.57	3.21–49.30
Previous hospital admissions	88	58	19	91	.004*	7.02	1.58–31.19
Previous ED visits	109	73	18	95	.039*	6.61	0.85–51.11
Exposure-smoking	43	34	7	54	.158	2.25	0.712–7.12
Daily home medications							
ICS	38	24	3	14	.293	0.51	0.14–1.82
LTRA	52	32	11	50	.101	2.10	0.85–1.25
ICS/LABA	27	17	9	41	.008*	3.4	1.34–8.84
Medication adherence	37	36	3	30	.693	0.75	0.18–3.09
Delivery system							
MDI	49	30	9	41	.322	1.58	0.64–3.95
MDI with spacer	28	17	4	18	.927	1.06	0.33–3.36
Nebulizer	23	14	5	23	.302	1.77	0.59–5.25
Hospital therapies							
Continuous albuterol	144	90	57	93	.832	1.18	0.25–5.50
Terbutaline	106	66	18	82	.133	2.34	0.75–7.24
Steroids	155	96	21	96	.581	0.81	0.09–7.09
MgSO ₄	40	25	5	23	.829	0.89	0.31–2.57
MV	13	8	1	5	.559	0.54	0.07–4.36
Chest X-ray: airspace disease	48	60	4	57	.882	0.89	0.19–4.2
	Median	IQR ^c	Median	IQR	<i>p</i> ^d		
Median pH on first CBG	7.36	7.3–7.4	7.31	7.2–7.4	.063	0.65	1.0–4.12
Median pH on PICU CBG	7.38	7.3–7.4	7.30	7.2–7.4	.017*	2.71	0.44–16.53
Median pCO ₂ on first CBG	37	33–44	44	35–67	.017*	4.12	0.44–38.83
Median pCO ₂ on PICU CBG	34	30–38	35	31–45	.321	0.61	0.10–3.73
PICU stay (median days)	1	1–2	1	1–3	.422	1.04	0.86–1.27
Hospital stay (median days)	3	2–4.5	3	2–4	.733	0.97	0.78–1.22

Note: ^aIndependent *t*-test.^bz-Test for differences between proportions.^cIQR, interquartile range.^dIndependent samples Mann-Whitney *U* test.

SD, standard deviation.

**p* ≤ .05.

average of 5 years longer ($p = .006$; OR = 1.30) (Table 2). Only one-third of the children in both groups were adherent to their daily medication regimen. In children with multiple PICU admissions compared to those with a single PICU admission, initial CBG revealed similar median pH levels, but significantly higher median pCO₂ levels ($p = .017$).

Compared to children with a single PICU admission, the odds were 12.5 times greater that children who would experience multiple PICU admissions in the future were previously diagnosed with severe persistent asthma, seven times greater that they had more previous hospital admissions for asthma, 6.6 times greater that they had more previous ED visits for asthma, and 3.4

times greater that they were prescribed daily ICS/LABA medication (Table 2). Other variables that were statistically significant between the two groups but had odds ratios <3.0 and/or a 95% confidence interval <1.0 may require further examination to evaluate their clinical significance (Table 2).

Mechanical Ventilation

In the total sample of 222 PICU admissions, there were 205 (92%) children who did not require MV ($n = 205$), while 17 (8%) of the children were mechanically ventilated (Table 3). Among the 17 mechanically ventilated children, 12 (71%) were admitted during the first 4 years of the study with a mean annual rate of 10.7% compared

TABLE 3.—Demographic and clinical characteristics of patients who did not receive MV versus patients who were mechanically ventilated.

Characteristics	Not mechanically ventilated, <i>N</i> = 205		Mechanically ventilated, <i>N</i> = 17		<i>P</i> ^a	Odds ratio	95% Confidence interval
	Mean	SD	Mean	SD			
Age at admission (yrs)	11	3.7	12	3.6	.263	1.08	0.95–1.23
Duration of symptoms (yrs)	9.5	4.4	4.8	3.6	.023*	0.76	0.59–0.98
	Frequency	%	Frequency	%	<i>p</i> ^b		
Sex							
Male	118	58	10	59	.919	0.95	0.35–2.59
Female	87	42	7	41			
Known asthmatic	184	90	16	94	.563	1.83	0.23–14.47
Family h/o asthma	76	37	8	47	.415	1.51	0.56–4.08
Asthma severity				33			
Mild intermittent	19	19	2	33	.400	2.11	0.36–12.35
Mild persistent	28	28	1	17	.537	0.51	0.51–4.54
Moderate persistent	26	26	0	0	.145	0.92	0.87–0.98
Severe persistent	26	26	3	50	.227	2.69	0.51–14.19
Previous hospital admissions	129	67	11	69	.854	0.11	0.37–3.39
Multiple PICU admissions	57	28	4	24	.704	0.80	0.25–2.55
Previous ED visits	148	79	14	88	.405	1.89	0.41–8.67
Exposure smoking	68	33	2	17	.066	0.26	0.54–1.21
Daily home medications							
ICS	45	22	1	6	.116	0.22	0.03–1.72
LTRA	85	42	7	41	.982	0.99	0.36–2.70
ICS/LABA	57	28	6	35	.510	1.42	0.50–4.01
Medication adherence	39	34	4	36	.886	1.10	0.30–1.10
Delivery system							
MDI	68	33	6	35	.858	1.10	0.39–3.10
MDI with spacer	33	16	6	35	.046*	2.84	0.98–8.22
Nebulizer	37	18	2	12	.513	0.61	0.13–2.76
Hospital therapies							
Continuous albuterol	190	93	11	65	.001*	0.15	0.05–0.45
Terbutaline	139	68	13	77	.460	1.54	0.49–4.91
Steroids	198	97	16	94	.600	0.57	0.07–4.89
MgSO ₄	51	25	6	35	.345	1.65	0.58–4.68
Chest X-ray: airspace disease	47	50	10	59	.478	1.46	0.51–4.15
	Median	IQR ^c	Median	IQR	<i>p</i> ^d		
Median pH on first CBG	7.37	7.3–7.4	7.27	7.1–7.3	.001*	0.11	0.10–0.81
Median pH on PICU CBG	7.36	7.3–7.4	7.26	7.2–7.4	.046*	0.92	0.28–2.95
Median pCO ₂ on first CBG	37	33–44	49	40–82	.003*	1.06	0.34–3.31
Median pCO ₂ on PICU CBG	33	31–37	43	33–62	.016*	1.00	0.31–3.23
PICU stay (median days)	1	1–2	3	1–6	.002*	1.21	1.01–1.45
Hospital stay (median days)	3	2–4	5	2.5–8	.039*	1.29	1.06–.57

Note: ^aIndependent *t*-test.^bz-Test for differences between proportions.^cIQR, interquartile range.^dIndependent samples Mann–Whitney *U* test.

SD, standard deviation.

**p* ≤ .05.

to five patients (29%) during the last 4 years with the mean annual rate of 5.3%. Thus, there was a trend toward fewer patients requiring MV over time. The MV group had a shorter history of asthma symptoms (4.8 years versus 9.5 years; *p* = .023) and significantly higher percent of patients in MV group were using MDI with spacers (35 % versus 16%; *p* = .046). Most other demographic and pre-hospitalization clinical characteristics were similar between groups. However, the clinical course of ventilated patients was significantly different from non-ventilated patients. Mechanically ventilated children were less likely to receive continuous albuterol during hospitalization (65% versus 93%; *p* = .001). The first CBG taken in the emergency department as well as

CBG in the PICU indicated significantly lower median pH levels and higher median pCO₂ levels in the ventilated group. This group stayed a median of 2 days longer in the PICU (*p* = .002; OR = 1.21) and in the hospital (*p* = .039; OR = 1.29) (Table 3).

Magnesium Sulfate Therapy

Among 222 encounters, 57 patients (26%) received MgSO₄ (Table 1). All received MgSO₄ in PICU and not in ED. Compared to children who did not receive MgSO₄ in the PICU, children who received MgSO₄ stayed in the PICU and hospital 1 day longer (*p* = .033; *p* = .003), even though their acute illness was not significantly worse as observed by their initial

CBG, need for MV, or presence of air space disease on chest radiographs. Compared to children who did not receive MgSO_4 in the PICU, children who received MgSO_4 , revealed significantly higher median pH levels on last CBG (7.44 versus 7.39; $p = .009$). There were no differences between the groups in demographic or pre-hospitalization measures

DISCUSSION

Asthma is a very common chronic childhood disease and can have significant morbidity and may result in life-threatening exacerbations requiring intensive care.

Currently, despite new guidelines and therapeutic options, asthma morbidity and mortality rates in US are increasing (8,9). Examination of the characteristics of children who present with life-threatening asthma exacerbations (status asthmaticus) may lead to better patient care and improve morbidity and even mortality from asthma.

Factors associated with severe life-threatening asthma exacerbations include failure to diagnose asthma, inadequate therapy of prior asthma, poor compliance with therapy, delay in seeking help, and history of previous asthma admissions (10,11). Hon et al. (11) reported that only one-third of their children received maintenance inhaled corticosteroids, while Chiang et al. (12) noted that about 80% of children admitted to intensive care unit (ICU) for status asthmaticus received no daily asthma medications.

Status asthmaticus is a life-threatening asthma exacerbation that does not respond to acute asthma care (13). Many children may require ICU care which includes aggressive and early treatment with bronchodilators, corticosteroids, and oxygen (13–16), and mechanically assisted ventilation in more severe cases (13–17).

The percentage of patients with status asthmaticus requiring MV varies from study to study. In single center studies with small numbers of patients, rates varied from 15% to 30% (11,12,18–20), whereas in large multi-center studies, rates varied from 9% to 14% (6,7).

Bratton (7) reviewed data from 41 pediatric hospitals during 2000–2003 and noted about 14% of patients admitted to PICU required MV. Interestingly, there were differences between ICUs from 6% to 27% reflecting center to center variation in management and possibly in outcomes. In single center studies, percent of patients requiring MV is high, but most of these studies are older; most of them have small numbers of patients. In our study, 8% required MV and among patients admitted to PICU for status asthmaticus, patients requiring MV during first 4 years (2000–2003) was 10.7% per year compared to 5.3% per year in the later 4 years (2004–2007). Thus, there was a trend toward both lower numbers and percent of children in PICU for status asthmaticus requiring MV over time, though difference was not significant probably secondary to limited number of patients. This change was noted though there was no significant difference in admission rate to PICU during those periods (108 versus 97, respectively). Though we noted a trend in our study toward less need for MV over time, our study is a single center study with limited

number of patients. It is possible that decrease in % of PICU patients requiring MV is due to more aggressive management of status asthma in PICU over time.

Studies also revealed that MV increased length of stay in PICU. In Hartman et al. (6) study, both hospital and ICU length of stay were longer in hospitals with PICU compared to adult hospitals, and length of stay of ventilated children was almost twice that of hospitals with PICU (8.2 versus 4.2 days; $p = .002$). From our cohort in a large pediatric hospital, non-mechanically ventilated patients had a median hospital stay and PICU stay of 3 and 1 days, respectively, compared to 5 and 3 days in patients requiring intubation and MV ($p = .002$ and $p = .039$, respectively). Hartman et al. (6) noted that almost half (46%) of ventilated children in hospitals with PICU were ventilated for 4 or more days. Our data revealed that only 5 out of 17 (29%) children requiring MV stayed in PICU 4 days or more. We also noted that significantly higher percent of patients in MV group were using MDI with spacers (35 % versus 16%; $p = .046$) compared to non-MV group, which may indicate that asthma was less controlled in MV group and many of them might have felt a need to add spacers to MDI to improve drug delivery to lungs for better symptom control.

Hon et al. (11) noted that the only significant difference between ventilated and non-ventilated group was the presence of CO_2 retention and therefore theorized that CBG can be useful, especially if clinical improvement on standard therapy is slow. Our patients requiring MV had significantly worse median pH and pCO_2 at presentation. There was improvement in pH and pCO_2 over time in both MV and non-ventilated patients.

Status asthmaticus is one of the most common causes of admission to a PICU. Complications, including pneumonia (either aspiration or ventilator-associated) and air leak (pneumomediastinum or pneumothorax) occur at higher rates in children admitted to PICU (8–22%) (21) and are higher for mechanically ventilated children (21). Children who require intubation and MV can have a protracted ICU course, and thus a longer hospital stay with increased risk of developing further complications (21,22). Some may argue that bronchopneumonia and atelectasis may be part of the severity of disease process and may not be considered as complications. Hartman et al. (6) noted a concomitant diagnosis of pneumonia in 22% among those admitted to hospitals with PICU for status asthmaticus. In their report, 16% received ICU care and 9.6% of ICU patients required MV; pneumonia was noted in 33.5% of ventilated children compared to 20% of non-ventilated children. Chiang et al. (12) noted that bronchopneumonia was present in 57% of patients who required ICU care for status asthmaticus. Our series revealed that 112 children had a chest radiograph and among them 57 (51%) had evidence of air space disease (pneumonia or atelectasis). Seventeen (8%) children admitted to PICU with status asthmaticus required MV and air space disease (pneumonia versus atelectasis) was noted in 10 (59%) of children requiring MV compared to 47 (49%) of non-ventilated children.

Studies have revealed a positive role of single dose of intravenous MgSO_4 in status asthmaticus, especially in ED

in adults and older children with severe status asthmaticus not improving on standard initial therapies (23). In our cohort, 57 patients (26%) received MgSO_4 but they stayed in the PICU and hospital 1 day longer even though severity of their status asthmaticus was not significantly worse than those not receiving MgSO_4 . As use of MgSO_4 was a choice of managing team, it is possible that it was perception of the managing team that status asthmaticus in some children was more severe requiring MgSO_4 . Such perception might have lead to their longer stay in PICU as median pH on last CBG in PICU in the group which received MgSO_4 was significantly higher compared to the group not receiving MgSO_4 . Thus perception of severity of status asthmaticus by managing team is an important factor in determining length of PICU stay and/or hospital stay. As patients received MgSO_4 in PICU and not in ED, it is possible that potential delay in receiving MgSO_4 might have been a factor as studies have shown its positive role when given in ED (23).

Our data supported previous observation of Robertson et al. (24) that asthma severity does not accurately predict risk for hospital admission, PICU admission, or death, although it was a significant factor in predicting repeated PICU stays. While our report indicates survival of all patients, asthma management that requires PICU admission may still be associated with morbidity and even mortality. Our study has limitations as it is a retrospective descriptive study from a single center. Study lacks a comparison group, data are missing on some patients and adherence is reported by parents which cannot be confirmed. Study is also limited as no standardized clinical asthma scores were used to quantify illness severity. Even with these limitations, study has provided some significant trends in demographics and in management of sub-group of children with status asthmaticus which are admitted to PICU.

CONCLUSION

The prognosis for childhood status asthmaticus is favorable. Lack of adherence to controller therapy, previous hospital admissions and ED visits, presence of air space disease on chest radiograph, and exposure to smoking are noted in large proportion of patients admitted to PICU for status asthmaticus. A small number of these patients with increased acidosis or hypercarbia on capillary blood gases at the time of their initial presentation in the ED required MV. Risk of recurrent PICU admission is significantly higher in patients with longer duration of asthma and those with previous hospital admissions and/or ED visits. Attempts to decrease risk of PICU admission would include improved diagnosis, avoidance of smoking exposure, adequate therapies, and adherence to therapies.

DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

No potential conflict of interest exists with any companies or organizations whose products and services may be discussed in this article. There is no conflict of interest to report.

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