EMA Emergency Medicine Australasia

Emergency Medicine Australasia (2019) **31**, 756–762 doi: 10.1111/1742-6723.13242

ORIGINAL RESEARCH

Treatment and outcome of adult patients with acute asthma in emergency departments in Australasia, South East Asia and Europe: Are guidelines followed? AANZDEM/EuroDEM study

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For the members of the AANZDEM and EuroDEM study groups see Acknowledgements.

Accepted 9 January 2019

Key findings

- Treatment of asthma in Europe and South East Asia/Australia is similar.
- Compliance with guideline-recommended treatment is sub-optimal, in particular the under-use of systemic corticosteroids.
- Further efforts to improve compliance with guideline-recommended treatment are needed.

Abstract

Objective: Asthma exacerbations are common presentations to ED. Key guideline recommendations for management include administration of inhaled bronchodilators, systemic corticosteroids and titrated oxygen therapy. Our aim was to compare management and outcomes between patients treated for asthma in Europe (EUR) and South East Asia/Australasia (SEA) and compliance with international guidelines.

Methods: In each region, prospective, interrupted time series studies were performed including adult (age >18 years) patients presenting to ED with the main complaint of dyspnoea during three 72 h periods. This was a planned substudy that included those with an ED primary diagnosis of asthma. Data was collected on demographics, clinical features, treatment in ED, diagnosis, disposition and in-hospital outcome. The results of interest were differences in treatment and outcome between EUR and SEA cohorts.

Results: Five hundred and eighty-four patients were identified from 112 EDs (66 EUR and 46 SEA). The cohorts had similar demographics and co-morbidity patterns, with 89% of the cohort having a previous diagnosis of asthma. There were no significant differences in treatment between EUR and SEA patients – inhaled beta-agonists were administered in 86% of cases, systemic corticosteroids in 66%, oxygen therapy in 44% and antibiotics in 20%. Two thirds of patients were discharged home from the ED.

Conclusion: The data suggests that compliance with guideline-recommended therapy in both regions, particularly corticosteroid administration, is sub-optimal. It also suggests over-use of antibiotics.

Key words: *asthma, dyspnoea, emergency department, management, outcome.*

Introduction

Shortness of breath is a common reason for patients to attend an ED.[1] Patients with dyspnoea make up approximately 5% of all adult ED attendances, but importantly result in over 11% of ward admissions and nearly 20% of intensive care unit (ICU) admissions.[2] Research suggests that an acute exacerbation of asthma is responsible for approximately 13% of adult patients presenting to the ED with dyspnoea.[2]

The initial management of an exacerbation of asthma is well-established and described in several guidelines including those of the National Asthma Council (Australia), Global Initiative for Asthma, the British Thoracic Society and the Scottish Intercollegiate Guidelines Network.[3–6] These guidelines agree that initial management should include assessment of severity, administration of short-acting beta-agonists (SABAs), titrated oxygen therapy and administration of systemic corticosteroids. Antibiotics are not recommended unless there is clinical or radiological evidence of infection.

For patients with severe exacerbations, or who do not respond to initial treatment, the recommendations for additional therapy are less uniform between guidelines and may include inhaled anticholinergic medication,[7] intravenous administration of magnesium,[8] aminophylline,[9] parenteral beta-agonists,[10] or ketamine[11] and/or non-invasive or invasive ventilation.[12]

While there is local data for some regions, there is little comparative data regarding ED management and compliance with key guideline recommendations across regions around the world. The aim of this study is to describe and compare management and outcomes between patients treated for acute exacerbations of asthma in Europe (EUR) and South East Asia/Australasia (SEA), with an emphasis on compliance with international guideline recommendations, both overall and by region.

Methods

This is a planned sub-study of two international, multi-centre, prospective, observational, interrupted time series cohort studies. They were designed to evaluate the epidemiology and outcomes of adult patients (age >18 years) presenting to the ED with shortness of breath as the main complaint. This sub-study focused on those patients who received an ED diagnosis of acute exacerbation of asthma. The European Dyspnoea in Emergency Medicine (EuroDEM) study (NCT02060799) was conducted in 66 European EDs in Belgium (n = 3), Finland (n = 5), France (n = 5), Germany (n = 5), Italy (n = 1), the Netherlands (n = 16), Romania (n = 7), Spain (n = 1), Turkey (n = 7) and UK (n = 16). The AANZDEM study was conducted in 46 Asia-Pacific centres in Australia (n = 33), New Zealand (n = 4), Singapore (n = 3), Hong Kong (n = 4) and Malaysia (n = 2). The Asia, Australia and New Zealand Dyspnoea in Emergency Medicine (AANZDEM) study methodology have been previously published.[13] The study sample was generated with consecutive patients attending EDs during three study periods of 72 h in different seasons throughout 1 year.

A specifically designed data collection tool was developed by each regional steering committee. Data collected included patient demographics, co-morbidities, mode of arrival, usual medications, initial assessment (clinical assessment and vital signs), investigations performed and results, treatment in the ED, ED diagnosis (diagnosis at ED discharge), outcome after the ED including disposition and in-hospital mortality. Local investigators at each hospital were provided with detailed information and instructions (including a data dictionary) to increase the reliability of data collection.

The outcomes of interest for this study were differences in management and clinical outcomes between EUR and SEA patient cohorts and compliance with guideline-recommended treatment, overall, by region and by disposition group (as a surrogate for severity). Results are presented as frequencies or as medians with interquartile range (IQR). The χ^2 test or Fisher's exact test (as appropriate) were used to compare categories. Continuous variables were compared using the t-test (parametric) and the Wilcoxon test (non-parametric). A Bonferroni

correction was applied to account for the multiple comparisons undertaken, with a *P*-value of 0.00116 comparable to a *P*-value of 0.05 from a single comparison. Statistical analysis was performed using SAS version 9.1 software (SAS Institute, Cary, NC, USA).

The study was performed in accordance with the Declaration of Helsinki. Ethics committee approvals were obtained for all sites according to local requirements. If requested by the local ethics committee, patient consent for data collection was obtained.

Results

Five hundred and eighty-four patients were studied; 387 from SEA and 197 from EUR. The median age was 45 years and 38% of patients were male. Median duration of symptoms prior to ED presentation was 2 days (IQR 1–4 days). The demographics of the cohorts were similar, including co-morbidity pattern. Eighty-nine percent of cases had a past history of asthma (95% CI 86–91%) and 18% were documented to be currently smoking (95% CI 15–22%). Seventy percent of cases reported use of inhaled beta-2 agonists (95% CI 66–74%); however, the proportion was significantly higher in the SEA cohort (75% *vs* 61%; $P < 0.01$). Inhaled corticosteroid use was low (44%, 95% CI 40–49%) but not significantly different between cohorts. Oral steroid use was also similar between cohorts (14%, 95% CI 11–17%) (Table 1). About a third of patients arrived at ED by ambulance (32%, 95% CI 28–36%); similar between the cohorts. Clinical severity (Appendix S1) was also similar in the two cohorts.

There were no statistically significant differences in management between the EUR and SEA cohorts. Inhaled SABA were administered in 86% (95% CI 83–89%) and systemic corticosteroids in 66% (95% CI 61–69%). Ventilatory support occurred in 14 patients (2.4%, 95% CI 1.4–4%): non-invasive support in 13 and mechanical ventilation in one

TABLE 1. *Patient characteristics*†

	Total *N* (%)	AANZDEM *N* (%)	Missing data	EuroDEM *N* (%)	Missing data	*P*-value
N (%)	584 (100)	387 (66)	–	197 (34)		
Demographics						
Age, median [Q1–Q3] (years)	45 (30–60)	45 [31–60]	1	43 [27–61]	2	0.43
18–40 years	236 (40)	149 (41)	–	87 (44)	–	0.53
41–60 years	193 (33)	136 (35)	–	57 (29)	–	
61–75 years	87 (5)	55 (14)	–	32 (16)	–	
>75 years	53 (9)	36 (9)	–	17 (9)	–	
Male, *N* (%)	223 (38)	154 (40)	1	69 (35)	0	0.30
Duration of symptoms, median [Q1–Q3] (days)	2 [1–4]	2 [1–4]	8	2 [1–7]	24	0.16
Co-morbidities, *N* (%)						
Prior history of asthma	519 (89)	351 (91)	1	168 (85)	1	0.07
Smoker	106 (18)	62 (16)	3	44 (23)	2	0.07
COPD	32 (5)	23 (6)	3	9 (5)	6	0.56
Chronic medication use, *N* (%)						
Inhaled beta-2 agonists	410 (70)	289 (75)	1	121 (61)	0	<0.001
Inhaled corticosteroids	260 (45)	177 (46)	0	83 (42)	0	0.43
Oral corticosteroids	80 (14)	52 (13)	3	28 (14)	0	0.90
Xanthines	‡	11 (3)	3	No data available		
Home oxygen	5 (1), missing data *n* = 3	4 (1)	3	1 (0.5)	0	0.67
Mode of arrival, *N* (%)						
By ambulance	185 (32), missing data *n* = 9	115 (30)	5	70 (36)	4	0.12

†Data are presented as number (percentage) or median (interquartile range). ‡Fisher's exact test. COPD, chronic obstructive pulmonary disease.

TABLE 2. *Management at the ED and outcomes*†

	Total	AANZDEM	Missing data	EuroDEM	Missing data	*P*-value
Treatment in the ED, *N* (%)						
Oxygen therapy	252 (44)	155 (40)	0	97 (49)	9	0.009
Inhaled beta-2 agonists	504 (86)	339 (88)	1	165 (85)	2	0.37
Corticosteroids (IV or oral)	380 (66)	268 (69)	1	112 (58)	3	0.006
NIV combined	13 (2.3)	8 (2.1)	0	5 (2.7)	9	0.76‡
Mechanical ventilation	1 (0.2)	0 (0)	3	1 (0.5)	9	0.33‡
Antibiotics	117 (20)	89 (23)	3	28 (15)	7	0.02
Discharge from the ED, *N* (%)						
Home	385 (66)	253 (65)	0	131 (68)	5	0.64 omnibus χ^2
Ward	180 (31)	123 (32)	0	57 (29)	5	
Intensive care unit	15 (2.3)	11 (2.8)	0	4 (2.1)	5	
Death in ED	0 (0)	0 (0)	0	0 (0)	5	
In-hospital outcome, *N* (%)						
Mortality	1 (0.2)	0 (0)	0	1 (0.5)	8	0.34‡

†Data are presented as number (percentage). ‡Fisher's exact test.

patient. Antibiotics were administered in 20% of patients overall (95% CI 17–23%) (Table 2).

Two thirds of patients were discharged home from the ED (66%, 95% CI 62–70%), 15 (2.3%, 95% CI 1.4–4%) were admitted to ICU, and the remainder was transferred to an inpatient ward (31%, 95% CI 27–35%). In total, there was one death (0.2%, 95% CI 0.03–1%), occurring in the European cohort.

Discussion

This study explores the treatment and outcomes of adult patients presenting to ED with acute dyspnea because of asthma exacerbations across two major global regions. Our findings suggest that compliance with guideline-recommended treatment is similar between the regions but that it is sub-optimal, particularly under-use of systemic corticosteroids and potential over-use of antibiotics.

Early administration of systemic corticosteroids has been shown to reduce the need for hospital admission in ED patients with asthma,[13] and is an established component of acute asthma management. It is unclear why one third of patients presenting with an acute exacerbation of asthma including 25% of those who were admitted to hospital were not administered systemic steroids, and this may be a focus for further research. Possible reasons include very mild disease only requiring reliever medication and/or prehospital administration of corticosteroids by ambulance paramedics or general practitioners. The data available did not allow us to test these hypotheses.

It is notable, also, that approximately 20% of patients in the cohorts were given antibiotics, increasing to approximately 40% in admitted patients. The reasons for this are unclear. In most cases, asthma exacerbations are because of viral rather than bacterial pathogens.[14] Unnecessary or excessive use of antibiotics for asthma has been documented in various settings, including the USA[15] and Kuwait.[16] A recent large study of adult patients with exacerbations of asthma found that the addition of azithromycin to usual treatment did not result in any clinical benefit.[17] Interestingly, a significant proportion of patients screened for eligibility in that study were excluded because of prior initiation of antibiotics,[18] suggesting that antibiotic overuse is a widespread problem in this setting.

Poor compliance with evidence-based asthma guidelines has been noted in both adult and paediatric populations – across many settings.[15,16,19,20] Attempts to improve the quality of asthma care include clinical pathways, treatment protocols and computerised asthma management systems.[21–23] To date, these interventions have, for the most part, been implemented in paediatric ED, with varying results.

That almost 20% of patients overall are smokers is of concern as it reduces the effectiveness of inhaled steroids and increases the risk of hospital admission.[24] Also concerning is the low use of regular inhaled corticosteroids. This study was not designed to assess reasons for this, but they may include limited access to primary healthcare or poor compliance. We did not have access to data on what proportion of patients had asthma action plans. That a low proportion of patients reported taking oral steroids at presentation is suggestive that the proportion with action plans was low and/or that patients did not known when or how to implement them.

Our study has some limitations that should be considered while interpreting our results. We have combined two datasets, one from Europe and one from the Asia/Pacific region, which differed slightly in design. This has led to some minor differences in data collection; however, we do not consider that this significantly influenced our findings. The size of the cohort and the diversity of ED is a strength of the study as it supports the generalisability of our findings. Data on some specific aspects related to asthma management were not collected because of the nature of the parent study including the use of inhaled anticholinergic medications, the choice of inhalation therapy between hand-held inhaler and nebuliser therapy and the use of intravenous bronchodilator medication such as aminophylline and magnesium. We consider this a minor weakness as our intention was to focus on widely accepted, core management. We were also unable to analyse treatment stratified by severity, as this data was not collected in the parent study. There is also a small amount of missing data from some patients; however, this is unlikely to have influenced our results. The sample was defined by the final ED diagnosis, which may have been subject to miscoding or error. This pragmatic approach reflects real-world practice.

Conclusion

The data suggests that compliance with guideline-recommended therapy in both regions, particularly corticosteroid administration, is sub-optimal. It also suggests over-use of antibiotics. Further efforts to improve and sustain compliance with existing treatment guidelines are required.

Acknowledgements

EuroDEM study was performed under the supervision of the EUSEM Research Committee. Data management in Europe was facilitated by the Jeroen Bosch Hospital.

AANZDEM study was supported by a grant from the Queensland Emergency Medicine Research Foundation, grant number EMPJ-108R21-2014.

The work of JM was supported by the Research Council of Lithuania (grant no. MIP-049/2015).

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We thank Toine van den Ende and Ans Kluivers for their assistance in collecting data in Europe.

Author contributions

AMK and SL had the concept for the studies; the steering committees contributed to refinement of the protocol, ethics applications, data collection, interpretation of the results and refinement of the manuscript. AMK, SC and WSK performed the analysis and drafted the manuscript.

Competing interests

AMK is a member of the Editorial Board of *Emergency Medicine Australasia*. No other competing interests are declared.

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Supporting information

Additional supporting information may be found in the online version of this article at the publisher's web site:

Appendix S1. Clinical signs at admission.