Clinical Reviews

Acute Asthma in Adults: Controversies and Best Practice

M Schuhmann, FJH Brims, AJ Chauhan

Abstract

Asthma in the emergency care setting is common and may be life-threatening. Last year the British Thoracic Society updated their guidelines for the management of asthma, however some treatments remain controversial and there is variation in adherence to these and other national and international guidelines.

Keywords

Acute asthma, treatment, adults.

Introduction

Asthma is a chronic condition that affects all ages; when uncontrolled, asthma may result in hospital admission and can result in death. Globally there are an estimated 300 million individuals with asthma[1,2] and there is continued evidence that the prevalence is still rising in developed countries.[3-5] The United Kingdom has amongst the highest prevalence of asthma in the world with up to 15% of the population with a previous or current physician diagnosis of asthma.[6] In Europe the estimated cost of asthma is €17.7 (£13.3) billion a year; developed countries can expect 1–2% of their total healthcare budget to be spent on asthma.[1] Inpatient costs are a relatively small percentage of this, but still account for €0.5 (£0.38) billion across Europe per year.[7] In 2004-2005 there were 88,630 finished inpatient consultant episodes in the NHS as a result of asthma, and although mortality from asthma has fallen over the last decade, in 2004 there were 1381 deaths from asthma in the UK.[6] A variety of factors lead to deaths in acute asthma including psychosocial factors and inadequate control and medical management of acute disease. The burden of exacerbations lead to costs to both the patient and the health service: of the 5.2m people in the UK with asthma, 2.6 million experience severe symptoms and about 500,000 have very severe symptoms because currently available treatments are not effective. These 10% of asthmatics account for more than 30% of the costs of this disease to the NHS.[6]

In this review article we discuss aspects of management of adult acute asthma in the first 48 hours after presenting to hospital, examining areas of controversy, best practice and research. For a more comprehensive overview of all aspects of asthma management readers are encouraged to read the BTS/SIGN Guidelines.[8]

Recognising the Risk

Some individuals will have a higher risk of death from acute asthma, and it is important to recognise this early – this includes those with a history of severe asthma (previous ventilation, multiple admissions and ED attendances, requirement for oral steroids and multiple medications) as well as those with adverse behavioural or psychosocial features (such as non-compliance, poor outpatient clinic attendee, psychiatric illness, learning difficulties and obesity).

Managing Acute Asthma

Early recognition of the severity, differentiation from chronic obstructive pulmonary disease (COPD - Table 1) and prompt treatment are the cornerstones of the management of acute asthma.

	COPD	Asthma
Smoker or ex-smoker	Nearly all	Possibly
Symptoms under age 35	Rare	Often
Chronic productive cough	Common	Uncommon
Breathlessness	Persistent/progressive	Variable
Night time waking with breathlessness and or wheeze	Uncommon	Common
Diurnal or day to day variability of symptoms	Uncommon	Common

Table 1. Differentiating Asthma from COPD*
* Adapted from BTS/NICE COPD guidelines 2004.[9]

Dr Maren Schuhmann
MRCP
Specialist Registrar in Respiratory & GIM
Respiratory Department, Queen Alexandra Hospital, Portsmouth, UK

Dr Fraser Brims
MRCP MD
Specialist Registrar in Respiratory & GIM
Respiratory Department, Queen Alexandra Hospital, Portsmouth, UK

Professor Anoop Chauhan
FRCP PhD
Consultant in Respiratory Medicine
Respiratory Department, Queen Alexandra Hospital, Portsmouth, UK

Correspondence:
Prof Anoop J Chauhan
Respiratory Centre
Queen Alexandra Hospital
PO6 3LY
Portsmouth, UK
Email: anoop.chauhan@porthosp.nhs.uk

Moderate Asthma	– Worsening breathlessness or wheeze – Peak Expiratory Flow Rate (PEFR) 50–75% of best or predicted – No features of acute severe asthma
Acute Severe Asthma	**Any one of:** – Respiratory rate over 25/min – Heart rate over 110/min – PEFR 33–50% of best predicted – Unable to complete sentences
Life Threatening Asthma	**Any one of:** – PEFR less than 33% of predicted or best – O_2 saturation less than 92%; PaO_2 < 8kPa – $PaCO_2$ in normal range (4.6 – 6.0 kPa) – Silent chest – Cyanosis – Exhaustion, confusion, coma – Hypotension, bradycardia, dysrhythmia
Near Fatal Asthma	Raised $paCO_2$ and/or requiring mechanical ventilation

Table 2. Levels of ascending severity of acute asthma exacerbation.*
*Adapted from BTS/SIGN Guidelines 2009.[8]

The severity of asthma can be categorised using clinical features and peak expiratory flow (PEF) and are presented in Table 2; these should act as a guide to clinicians with respect to different management options. With correct recognition and treatment at least 80% of asthma patients presenting to the Emergency Department may be discharged after treatment with standard therapy.[10]

A brief summary of the areas covered in this dialogue is provided in Table 3 and discussed in detail below.

High Flow Oxygen

Patients are hypoxic during an asthma exacerbation.[11,12] Arterial Blood Gas (ABG) measurement should be performed in all patients with life-threatening features of asthma, or moderate to severe features with pulse oximetry <92%, or in those with significant clinical decline despite treatment. In acute asthma the risk of precipitating hypercapnic (Type II) respiratory failure with oxygen therapy is very low, and Table 1 can help if there is any diagnostic uncertainty about asthma and co-exiting COPD. The recent BTS guidelines on emergency oxygen recommend initial oxygen therapy via nasal cannulae at 2-6 L/min (preferably) or simple face mask at 5-10 L/min.[13] For patients not at risk of hypercapnic respiratory failure (i.e. no evidence of COPD) who have O_2 saturation <85%, treatment should be commenced with a reservoir mask at 10-15 L/mm. The recommended initial oxygen saturation target range is 94-98%. If oximetry is not available, oxygen is given until oximetry or blood gas results are available. A change to a reservoir mask is recommended if the desired saturation range cannot be maintained with nasal cannulae or simple face mask (at this stage the patient should be assessed by senior medical staff). In the not uncommon circumstance where a patient has features of both asthma and COPD (or other risk factors for hypercapnic respiratory failure), aim at a saturation of 88-92% pending blood gas results but adjust to 94-98% if the $PaCO_2$ is normal (unless there is a history of previous hypercapnic respiratory failure requiring NIV) and recheck ABGs within 30-60 minutes. Additional ABG measurements are not required if a patient responds to treatment. Nebulisers should be driven with oxygen with at least 6L/min of oxygen, or supplemental oxygen should be administered concurrently.

Nebulised Bronchodilators – Bolus, Continuous, and in combination

In acute asthma short acting β_2-agonists such as salbutamol can be inhaled via a large volume spacer every 10-20 min. In many cases however inhaler technique is poor and this has led to the widespread use of nebulised bronchodilators.

Bolus nebulisation of β_2-agonist every 15-30 minutes is adequate to manage most moderate to severe exacerbations. Continuous (or "back-to-back") nebulisers, delivering up to 10mgs of salbutamol per hour for example, are at least as effective as bolus nebulisation[14] and are likely to be more effective in severe cases. Thus continuous β_2-agonist nebulisation is recommended in cases that have not responded to initial bolus treatment.[8]

During the first days of an admission with acute severe asthma, many patients will require regular nebulisers; this remains especially important overnight and early morning (when poorly controlled asthmatics are characteristically at greater risk). It is the practice of the authors to prescribe bronchodilator nebulisers on a regular basis *throughout the night,* rather than falling into more traditional 'drug-round' times that may allow a 6-8 hour break in administration during night hours. The diurnal variability of asthma and cyclical endogenous production of corticosteroid would suggest night time events in asthma as particularly important. A combination of nebulised ipratropium and β_2-agonist has been shown to produce greater bronchodilatation in severe asthma, but the same effect has not been demonstrated in milder asthma.[15-17] Therefore the addition of nebulised anticholinergic e.g. ipratropium bromide 500 microgrammes, is only recommended in severe asthma exacerbations.[8,18]

Intravenous Salbutamol

Inhaled or nebulised β_2-agonist deposition in the small airways may be impaired in severe bronchoconstriction with gas trapping. This has led to interest in the use of intravenous (IV) salbutamol during an acute exacerbation. A meta-analysis of 15 studies, comprising 582 adults with acute asthma, failed to demonstrate statistically significant changes in PEFR, recovery time or hospital outcome when using IV β_2-agonists in comparison to inhaled β_2-agonists or IV methylxanthines (theophyllines).[19] There was, however, a higher incidence of side effects including tachycardia, palpitations, hypertension, nausea

and tremor in patients who received IV β_2-agonists. Thus the use of IV β_2-agonist is not recommended routinely.[8,18] Their use may be considered in patients where nebulised or inhaled β_2-agonists cannot be administered such as in the critical care setting in a mechanically intubated patient. Outside of this setting, the risk of side effects remains higher than any statistically significant benefit in outcome.

Corticosteroids

Corticosteroid administration during an asthma exacerbation reduces mortality, relapses and hospital readmissions.[20,21] The benefit is greater the earlier they are administered in an exacerbation. There is no benefit in prescription of IV steroids over that of oral steroids, provided the oral route is viable i.e. patients can swallow the tablets. The current recommendation for prednisolone dose is 40-50 mg to be given for at least 5 days, or until recovery.[8,18] Longer courses of oral steroids should be considered if patients have frequent exacerbations or if they are on a maintenance dose of oral steroids. Inhaled steroids should be continued during an acute exacerbation, but there is no strong evidence that increasing the dose of the inhaled corticosteroid has any benefit over concurrent administration of oral corticosteroids.[8,18,22-24] If a patient is admitted who is not taking inhaled corticosteroids, these should be commenced as soon as possible as part of their chronic asthma management. Continuing or increasing the regular medication could reduce the risk of prescription error on discharge, and could help short-term compliance and consistency of therapy.

Methylxanthines

Methylxanthines (IV or oral theophyllines) have been used for the treatment of asthma for many decades. Methylxanthines act as weak bronchodilators but their use in acute asthma exacerbations remains controversial. Despite numerous studies and 2 large meta-analyses, there has been no clinical benefit demonstrated in the use of IV theophylline over and above conventional bronchodilatation and corticosteroids.[25,26] National guidelines however recognise that there may be individuals with near fatal or life threatening asthma who will benefit from IV theophylline.[8]

Intravenous theophylline use will result in increased side effects such as palpitations, nausea, vomiting and tremor.[26] Its use should be overseen by senior specialist medical staff, and blood levels should be checked daily. If patients are taking oral theophyllines at the time of admission, a loading dose should be omitted. Patients should be monitored in a controlled environment. However cardiac monitoring is not routinely required, unless treating those at risk of cardiac side effects. Special precautions should be taken with co-administration of drugs known to interact with theophyllines such as macrolide antibiotics and warfarin.

Magnesium – intravenous and nebulised

Magnesium is a weak smooth muscle relaxant and there is evidence that when magnesium is infused into asthmatic patients, it can provide additional bronchodilatation. This effect is weaker than salbutamol, and shorter lasting.[27,28] There is some evidence that IV magnesium can improve PEFR in patients with severe asthma without a desirable response to initial treatment.[29] It is not recommended in mild and moderate asthma exacerbations.[8,18] In the US it is only recommended in life-threatening asthma.[30]

We believe the overall evidence is weak, and there is an urgent need for well-designed randomised controlled trials to confirm the effects of parenteral magnesium in acute asthma and to determine which patients are most likely to benefit, a view shared by others.[31]

A recent Cochrane review of the use of *nebulised* magnesium in combination with salbutamol demonstrated an increased PEFR in patients presenting with severe asthma.[32] Nebulised magnesium appears safe to administer with few adverse effects, and could be a promising adjunct to treatment. Currently however, the utilisation of nebulised magnesium is not endorsed by the National and International bodies and its use is not widespread.

Non-Invasive Ventilation

Non invasive ventilation (NIV) in acute severe asthma remains contentious, with a lack of randomised controlled trial (RCT) evidence to support its routine use. A small RCT of 30 patients has suggested there may be some clinical benefit in the Emergency Department setting,[33] however larger robust RCTs are required to further validate this finding. At present, in a patient with life threatening asthma who has not responded to usual medical management, early intensive care involvement is mandatory and this is the only environment that NIV in asthma may be considered. Such patients may require prompt intubation if this treatment fails.

Heliox

Heliox (a gaseous mix of helium and oxygen, available in differing proportions) has a lower density than air. This theoretically leads to improved gas flow in the distal airways with a reduction in airway resistance. It has been used successfully in cases of airway obstruction and bronchiolitis, though its use in acute asthma is unproven. A recent meta-analysis of 10 studies comprising 544 patients demonstrated variable results and no clear benefit in patients with acute severe asthma.[34] Further evidence of clinical benefit is lacking, and the treatment cost is high, thus the routine use of heliox in acute severe asthma is currently not recommended.

Antibiotics

About 80% of asthma exacerbations in children are due to viral infection and about 50% in adults.[35] In the absence of clinical or radiographic signs of bacterial infection, the routine use of antibiotics is not currently recommended.[8,18] However, a recent trial of 10 days of oral telithromycin or

placebo in 278 adults with acute asthma led to significantly greater reductions in symptoms (but not improvement in PEF) at 10 days.[36] This may in part be due to the anti-inflammatory effects of macrolide antibiotics, and this requires further study before this should be part of routine practice.

Process of care

The use of a structured acute asthma algorithm has been shown to improve patient outcomes and provide a basis for audit and quality control.[38,39] An example of a local acute asthma management protocol is provided in Figure 1. Patient education prior to discharge has been shown to reduce morbidity and relapse.[40] It is thus strongly recommended that every asthma patient admitted to hospital should have a review with a specialist respiratory nurse to ensure appropriate understanding and concordance with treatment, and agree a personalised action plan in the event of recurrent exacerbation. Additional follow up in primary care or by a respiratory nurse or physician 1 month after discharge is also recommended.[8]

Discharge

It is beyond the remit of this article to give recommendations as to when it is safe to discharge a patient. It is desirable that a patient should be stable clinically for 24 hours off nebulisers and oxygen, on their normal asthma treatments. Additionally, a decision about discharge should also take into account the severity of the asthma exacerbation, any previous life threatening attacks, any repeated need for oral steroids, and social and psychological circumstances. It has been demonstrated that patients with PEF <75% best or predicted or with diurnal variation >25% are at increased risk of relapse and readmission.[37]

Summary

Early recognition of the severity of acute asthma will provide a basis for its subsequent management. Areas of controversy in treatments only exist in the management of severe and life threatening asthma: an overall summary is given in Table 3. In many of these cases any such treatments should take place under senior specialist supervision, ideally in level 2 or 3 facilities (HDU/ICU) with appropriate additional monitoring and healthcare resources.

Topic	Grade of asthma	Recommendation/Best practice
Oxygen	All	All patients should receive high flow oxygen. Aim for saturations of at least 92%.
Nebulisers	Severe & Life threatening	Continuous "back-to-back" nebulisers recommended for those who do not respond to initial therapy. The addition of ipratropium to salbutamol nebuliser is only validated in acute severe asthma.
IV Salbutamol	Severe & Life threatening	Evidence supporting the use of IV salbutamol is lacking. Its use is discouraged outside of the critical care setting.
Corticosteroids	All	There is no additional benefit in administering steroids IV over orally.
IV Methylxanthines	Severe & Life threatening	Evidence for the use of IV aminophylline in acute severe asthma is lacking. Its routine use should be discouraged unless under specialist care.
Magnesium	Severe & Life threatening	The use of IV magnesium is only validated in acute severe asthma. Nebulised magnesium, in addition to salbutamol, may improve PEFR, but its use via this route is not currently endorsed.
Non-Invasive Ventilation (NIV)	Severe & Life threatening	At present, reliable evidence supporting the use of NIV in acute severe and life threatening asthma is lacking, and its use in this context is strongly discouraged.
Heliox	Severe & Life threatening	Evidence is lacking to support the use of heliox in acute asthma.
Antibiotics	All	Unless there is clinical or radiographic evidence of bacterial infection, the routine use of antibiotics is discouraged.
Process of Care	All	All patients should be treated in accordance with a locally endorsed protocol. All patients should have a consultation prior to discharge with a respiratory specialist and agree a personalised action plan.

Table 3. Summary of topics covered and recommendations.

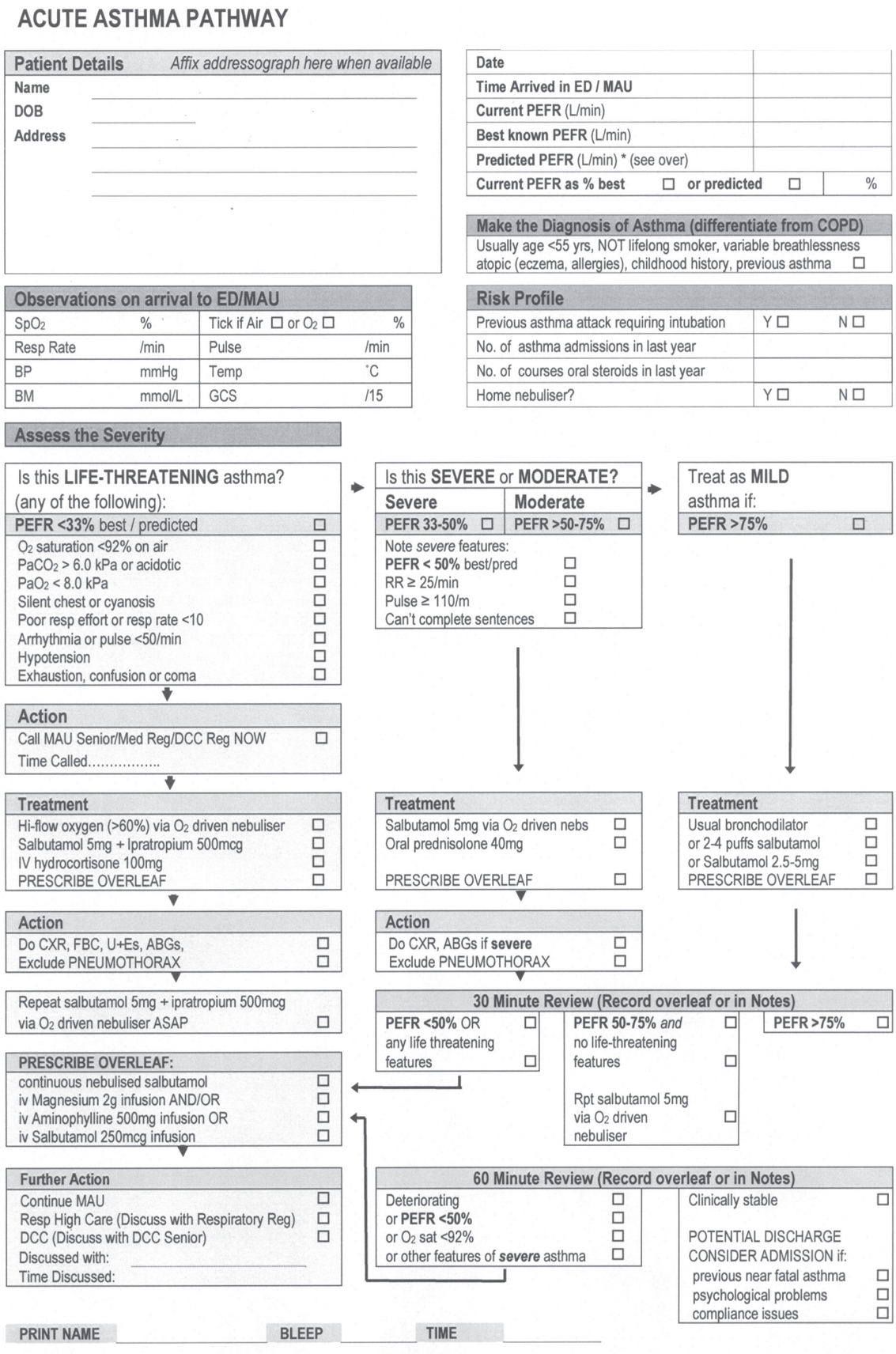

Figure 1

INITIAL DOSES OF DRUGS PRESCRIBED IN A&E and MAU (any other drugs should be prescribed on Prescription Chart and/or IV Chart)

Date	Drug	Dose	Time	Route	Signature	Given by	Time given
	High flow O_2			Mask			
	Salbutamol	5 mg		O_2 driven neb			
	Ipratropium Bromide	500 mcg		O_2 driven neb			
	Hydrocortisone	100mg		IV			
	Prednisolone	40mg		PO			
	Magnesium	2g		IV over 30min			
	Salbutamol	250 mcg		IV over 10min			
	Aminophylline*	500 mg		IV over 24 hrs			
	Salbutamol	5 mg		O_2 driven neb			
	CONTINUE ALL FURTHER AND REPEAT MEDICATIONS ON PRESCRIPTION CHART						

30 Minute Review and Management			
PEFR	L/min	PEFR (% best/pred)	%
SpO_2	%	State if Air or % O_2	
Resp Rate	/min	Pulse /min	
BP	mmHg		
Patient completes sentence in 1 breath?		Y ☐	N ☐

60 Minute Review and Management			
PEFR	L/min	PEFR (% best/pred)	%
SpO_2	%	State if Air or % O_2	
Resp Rate	/min	Pulse /min	
BP	mmHg		
Patient completes sentence in 1 breath?		Y ☐	N ☐

Record results in Notes e.g. ABGs ☐

Signed _____ Time _____

Record results in Notes e.g. ABGs ☐

Signed _____ Time _____

OUTCOME

ADMISSION (MAU Checklist)

Complete Drug Kardex:
- Nebulisers ☐
- Oral Prednisolone ☐
- Regular Medications ☐

Graphnet ☐
Enoxaparin ☐
Patient Handover completed ☐
Designate R1 for PTWR ☐

Signed _____ Time _____

DISCHARGE

Please do the following:
Leave message on ext 1389 or Bleep 1123
(Respiratory Nurse Specialists)
- Patient details ☐
- Date and Time of discharge ☐

PRESCRIPTION ADVICE:
- 5 days Prednisolone 40 mg if oral steroids given ☐
- Inhaled Beclomethasone 200µg 2 puffs BD if not on ICS ☐
- Double dose inhaled corticosteroid if already on ☐
- Inhaler technique checked ☐
- GP follow up advised within 2 **days** of discharge ☐
  - Write this on Discharge letter ☐
- Give copy of Discharge letter to patient ☐

Signed _____ Time _____

* Predicted PEFR Nomograms can be obtained in ED and MAU on the *back* of the PEFR Charts. ICS = Inhaled corticosteroid

Chauhan AJ,

References

1. Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy*. 2004; **59(5)**: 469–78.
2. Beasley R. The Global Burden of Asthma Report, Global Initiative for Asthma (GINA). 2004.
3. Yan DC, Ou LS, Tsai TL, *et al*. Prevalence and severity of symptoms of asthma, rhinitis, and eczema in 13- to 14-year-old children in Taipei, Taiwan. *Ann Allergy Asthma Immunol*. 2005; **95(6)**: 579–85.
4. Ko FW, Wang HY, Wong GW, *et al*. Wheezing in Chinese schoolchildren: disease severity distribution and management practices, a community-based study in Hong Kong and Guangzhou. *Clin Exp Allergy*. 2005; **35(11)**: 1449–56.
5. Carvajal-Uruena I, Garcia-Marcos L, Busquets-Monge R, *et al*. [Geographic variation in the prevalence of asthma symptoms in Spanish children and adolescents. International Study of Asthma and Allergies in Childhood (ISAAC) Phase 3, Spain]. *Arch Bronconeumol*. 2005; **41(12)**: 659–66.
6. BTS. The burden of lung disease: a statistical report from the British Thoracic Society. 2nd ed. London: British Thoracic Society, 2006.
7. European lung white book. Brussels, Belgium: Europe: European Respiratory Society and the European Lung Foundation., 2003.
8. BTS. British guideline on the management of asthma. *Thorax* 2009; **63(Suppl iv)**: iv1–iv121.
9. NICE. National Clinical Guideline on management of chronic obstructive pulmonary disease in adults in primary and secondary care. *Thorax* 2004; **59(Suppl I)**: 1–232.
10. Weber EJ, Silverman RA, Callaham ML, *et al*. A prospective multicenter study of factors associated with hospital admission among adults with acute asthma. *Am J Med*. 2002; **113(5)**: 371–8.
11. McFadden ER, Jr., Lyons HA. Arterial-blood gas tension in asthma. *N Engl J Med*. 1968; **278(19)**: 1027–32.
12. Rebuck AS, Read J. Assessment and management of severe asthma. *Am J Med*. 1971; **51(6)**: 788–98.
13. Group BTSEOG. Guideline for emergency oxygen use in adult patients. *Thorax* 2009; **63(Suppl VI)**: vi1–vi68.
14. Camargo CA, Jr., Spooner CH, Rowe BH. Continuous versus intermittent beta-agonists in the treatment of acute asthma. *Cochrane Database Syst Rev* 2003; 4.
15. Lanes SF, Garrett JE, Wentworth CE, *et al*. The effect of adding ipratropium bromide to salbutamol in the treatment of acute asthma: a pooled analysis of three trials. *Chest*. 1998; **114(2)**: 365–72.
16. Rodrigo G, Rodrigo C, Burschtin O. A meta-analysis of the effects of ipratropium bromide in adults with acute asthma. *Am J Med*. 1999; **107(4)**: 363–70.
17. Stoodley RG, Aaron SD, Dales RE. The role of ipratropium bromide in the emergency management of acute asthma exacerbation: a metaanalysis of randomized clinical trials. *Ann Emerg Med*. 1999; **34(1)**: 8–18.
18. Global Strategy for Asthma Management and Prevention. *NHLBI / WHO Workshop Report* 2005;NIH Publication No. 02-3659.
19. Travers AH, Rowe BH, Barker S, *et al*. The effectiveness of IV beta-agonists in treating patients with acute asthma in the emergency department: a meta-analysis. *Chest*. 2002; **122(4)**: 1200–7.
20. Rowe BH, Spooner C, Ducharme FM, *et al*. Early emergency department treatment of acute asthma with systemic corticosteroids. *Cochrane Database Syst Rev* 2001; 1.
21. Rowe BH, Spooner CH, Ducharme FM, *et al*. Corticosteroids for preventing relapse following acute exacerbations of asthma. *Cochrane Database Syst Rev* 2001; 1.
22. FitzGerald JM, Becker A, Sears MR, *et al*. Doubling the dose of budesonide versus maintenance treatment in asthma exacerbations. *Thorax*. 2004; **59(7)**: 550–6.
23. Harrison TW, Oborne J, Newton S, Tattersfield AE. Doubling the dose of inhaled corticosteroid to prevent asthma exacerbations: randomised controlled trial. *Lancet*. 2004; **363(9405)**: 271–5.
24. Rice-McDonald G, Bowler S, Staines G, Mitchell C. Doubling daily inhaled corticosteroid dose is ineffective in mild to moderately severe attacks of asthma in adults. *Intern Med J*. 2005; **35(12)**: 693–8.
25. Littenberg B. Aminophylline treatment in severe, acute asthma. A meta-analysis. *Jama*. 1988; **259(11)**: 1678–84.
26. Parameswaran K, Belda J, Rowe BH. Addition of intravenous aminophylline to beta2-agonists in adults with acute asthma. *Cochrane Database Syst Rev* 2000;4.
27. Okayama H, Aikawa T, Okayama M, *et al*. Bronchodilating effect of intravenous magnesium sulfate in bronchial asthma. *Jama*. 1987; **257(8)**: 1076–8.
28. Rolla G, Bucca C, Caria E, *et al*. Acute effect of intravenous magnesium sulfate on airway obstruction of asthmatic patients. *Ann Allergy*. 1988; **61(5)**: 388–91.
29. Rowe BH, Bretzlaff JA, Bourdon C, *et al*. Magnesium sulfate for treating exacerbations of acute asthma in the emergency department. *Cochrane Database Syst Rev* 2000; 2.
30. NHLBI. Guidelines for the Diagnosis and Management of Asthma: NHLBI, 2007.
31. Intravenous magnesium for acute asthma? *Drug Ther Bull*. 2003; **41(10)**: 79–80.
32. Blitz M, Blitz S, Beasely R, *et al*. Inhaled magnesium sulfate in the treatment of acute asthma. *Cochrane Database Syst Rev*. 2005(4): CD003898.
33. Soroksky A, Stav D, Shpirer I. A pilot prospective, randomized, placebo-controlled trial of bilevel positive airway pressure in acute asthmatic attack. *Chest*. 2003; **123(4)**: 1018–25.
34. Rodrigo G, Pollack C, Rodrigo C, Rowe BH. Heliox for nonintubated acute asthma patients. *Cochrane Database Syst Rev*. 2006(4): CD002884.
35. Friedlander SL, Busse WW. The role of rhinovirus in asthma exacerbations. *J Allergy Clin Immunol*. 2005; **116(2)**: 267–73.
36. Johnston SL, Blasi F, Black PN, ***et al***. The effect of telithromycin in acute exacerbations of asthma. *N Engl J Med*. 2006; **354(15)**: 1589–600.
37. Pearson M, Ryland I, Harrison B. National audit of acute severe asthma in adults admitted to hospital. Standards of Care Committee, British Thoracic Society. . *Qual Health Care* 1995; **4(1)**: 24–30.
38. McFadden ER, Jr., Elsanadi N, Dixon L, *et al*. Protocol therapy for acute asthma: therapeutic benefits and cost savings. *Am J Med*. 1995; **99(6)**: 651–61.
39. Goldberg R, Chan L, Haley P, *et al*. Critical pathway for the emergency department management of acute asthma: effect on resource utilization. *Ann Emerg Med*. 1998; **31(5)**: 562–7.
40. Cowie RL, Revitt SG, Underwood MF, Field SK. The effect of a peak flow-based action plan in the prevention of exacerbations of asthma. *Chest*. 1997; **112(6)**: 1534–8.