ADHERENCE TO AND EFFICACY OF AN EVIDENCE-BASED MANAGEMENT ALGORITHM FOR ACUTE ASTHMA IN THE EMERGENCY DEPARTMENT

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NATIONAL UNIVERSITY OF SINGAPORE

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Summary of the Thesis

Objectives: To evaluate the adherence to and the outcome of an evidence-based treatment algorithm for asthma in an emergency department (ED). Design: A non-randomized, controlled trial. Subjects were adults aged > 14 years with a diagnosis of acute asthma exacerbation. We compared treatment and outcome before (n= 330, 2000) and after (n=344, 2001) the introduction of a simple but evidence based treatment algorithm. The algorithm included: 1) a combination of nebulized salbutamol and ipratropium as first line treatment; 2) intravenous hydrocortisone and magnesium sulfate with repeat nebulizations as second line treatment and 3) oral prednisolone on admission to ED & upon discharge. Results: The use of oral prednisolone at ED admission increased from 42% to 65% ($p<0.001$), combination of salbutamol and ipratropium bromide in 1st line treatment increased from 55% to 94% ($p<0.001$), oral prednisolone on ED discharge increased from 72% to 90 %($p<0.001$), and an increase in intravenous hydrocortisone when admitted from 52% to 69% ($p=0.009$). The admission rates (38% Vs 35%) and mean of length of stay (LOS) in hospital (5.21 days Vs 4.49 days) were not significantly reduced. Conclusion: We found that introduction of a simple treatment algorithm in the ED resulted in (1) a significantly improved compliance with evidence based treatment but (2) no significant reductions in admission rates or LOS.

Chapter 1 Background

1.1 Current views on asthma

1.1.1 Definition

Asthma is not caused by a single factor, but by many cells and cellular elements playing a role in it, in particular, mast cells, eosinophils, T Lymphocytes, macrophages, neutrophils, and epithelial cells. As the mechanism of asthma has not been completely uncovered, the definition of this disease is not unified. Here, we introduce the one from the expert panel report 2, published by National Heart, Lung, and Blood Institute of the National Institutes of Health from the USA (EXPERT PANEL REPORT 2). Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role, in particular, mast cells, eosinophils, T lymphocytes, macrophages, neutrophils, and epithelial cells. In susceptible individuals, this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment. The inflammation also causes an associated increase in the existing bronchial hyper responsiveness to a variety of stimuli.

1.1.2 Classification

Asthma can be classified into two categories: atopic and non-atopic. The classification is based on whether specific IgE antibodies to environmental allergens are identified.

Asthma is a chronic relapsing and remitting disorder involving episodic reversible airway obstruction due to bronchospasms, increased mucus secretion and mucosal cell edema. This makes breathing more difficult and may result in respiratory failure. Asthma may occur due to an allergy (atopic/extrinsic) or because of other factors (non-atopic/intrinsic). Both causes are equally common. Asthma attacks vary in duration, intensity and frequency. Attacks may be mild to life threatening, occur suddenly or with premonitory symptoms, and may occur at any time, even in sleep. Symptoms of airway obstruction can persist between acute episodes.

If allergic, the best treatment to control symptoms and decrease relapse, if possible, is prevention by elimination of the causative agent from the person's environment.

1.1.3 Risk and trigger factors

Although we may not know the real causative agents for many patients with asthma, many risk factors are found, which increase the probability of asthma development, increase tendency to asthma attacks by inducing airway inflammation and /or acute bronchoconstriction. Accordingly, patients are advised to avoid exposure to some factors, such as smoking, air pollution, aspirin, pollens and molds.

Common triggers of asthma attacks include inhaled irritants, inhaled allergens, and viral infections of the respiratory tract. Most viral infections that could be associated with asthma attacks are difficult to document by commonly available means, so the diagnosis is often presumptive, made on the basis of history and physical examination findings.

Airway inflammation may be induced by viruses, which produce a variety of inflammatory mediators both directly and indirectly. The mediators cause bronchoconstriction and airway edema.

1.1.4 Further understanding of the pathogenesis

As mentioned before, asthma is not a single disease entity but rather a syndrome with a multitude of presentations and, most likely, a multitude of causes. Traditionally, asthma has been regarded as a manifestation of an underlying abnormality of airway smooth muscle and its neural control systems. However, more recent and current evidence suggests that in many patients, asthma is an inflammatory disease of the airways. Pathologic evidence shows that many inflammatory cells and mediators take part in it, for example, eosinophils, lymphocytes, mast cells (Rowe, 2001). Each cell has an important contribution and a specific relation to the development of airway inflammation.

Consequently, these cells have become an important target of treatment in the clinical management of asthma. Understanding how these cells participate in allergic inflammatory events and how their function can be regulated by therapeutics has provided insights into asthma pathogenesis and mechanisms of drug action.

1.1.5 Emphasis on anti-inflammation in asthma treatment

Since the definition of inflammation has been proven by biopsies, treatment by anti-inflammatory drug has been emphasized recently. Studies have shown that improvement in asthma control achieved by inhaled corticosteroids is associated with improvement in markers of airway inflammation. These observations indicate that a strong link may exist

between features of airway inflammation, bronchial hyper responsiveness, and asthma symptoms and severity. Corticosteroids affect inflammatory cells through several mechanisms described below: corticosteroids decrease airway mast cell numbers, and through this diminish the immediate response to antigen (Barnes,1992); corticosteroids induce eosinophil apoptosis and in this way it can not release inflammatory mediators (Goldie,1995); corticosteroids decrease expression and generation of proinflammatory cytokines (Horwitz,1995), which are generated principally by the T-lymphocyte.

1.2 Summary of guidelines

1.2.1 Guidelines arise in need

In recent decades there have been striking advances in the clinical treatment of asthma, but morbidity and mortality for the disease are still high. That is due mainly to under-detection of disease severity and inappropriate therapy. The National Asthma Education and Prevention Program (NAEPP) comprised of the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH) in the USA initially published guidelines for the diagnosis and management of asthma in 1991.The guidelines were based on expert opinion and experience. The purpose of the guidelines was to provide assistance to clinicians in the diagnosis and treatment of asthma when they encounter different conditions, to help public health officials, and program planners take action to control asthma and reduce its personal, social, and economic burdens.

1.2.2 Concept of containment at Emergency Departments

Meanwhile, management for acute exacerbation at Emergency Departments (ED) is a crucial opportunity to minimize these burdens. Because with appropriate treatment at ED, there are three ways to decrease cost: 1) first it can lessen cost at ED, only using drugs in need, no more unnecessary ones (Suh, 2001); 2) with appropriate methods of assessment and intensive use of therapy, excess hospitalization can be avoided (Suh, 2001; Akerman, 1999); 3) giving patients a good action plan and follow-up schedule can decrease asthma relapse and repeat attendance to ED (Bolton, 1991; ED Manag, 2001);

1.2.3 Guidelines in USA

With understanding of the importance of management in the emergency room, numerous clinical guidelines on acute exacerbation of asthma have been disseminated. In November 1997, the National Asthma Education and Prevention Program (NAEPP) released the final version of its comprehensive second Expert Panel Report. This is revision of the one published in 1991. In 1995 the NAEPP convened a second expert panel to update the guidelines to reflect important scientific and clinical advances, through critical review of evidence based literature.

The panel's recommendations for acute asthma care stressed the use of aggressive inhaled ß2-agonist therapy, early systemic corticosteroid administration, anticholinergics as add-on drugs to ß2-agonist in those with severe attack, and oral systemic corticosteroids for 3 to 10 days after discharge (Wiliam, 1998).

1.2.4 Guidelines in Canada

In Canada, guidelines for the emergency management of asthma were set up by members of the Canadian Association of Emergency Physicians (CAEP) and the Canadian Thoracic Society (Guidelines for Canadian Clinical Practice Guidelines). Recommendations are similar to the ones in the United States: Beta2-agonists are the first-line therapy for the management of acute asthma in the emergency department; anticholinergic therapy should be added to ß2-agonist in severe and life-threatening cases and may be considered in cases of mild to moderate asthma; all patients should be considered candidates for systemic corticosteroid therapy at discharge. The different point in the Canadian guidelines is that adrenaline is recommended as an alternative to conventional therapy in unresponsive life-threatening cases (Evans, 1993).

1.2.5 Common features in guidelines

There are other guidelines generated by some organizations, such as British asthma guidelines coordinating committee, Thoracic Society of Australia and New Zealand, and the Singapore Ministry of Health in 2002. Though some specific steps are different among these guidelines, the outline of the main points is the same, containing four sections: Measures of assessment and monitoring, Control of factors contributing to asthma severity, Pharmacologic therapy, and Education for a partnership in asthma care.

Making the correct diagnosis of asthma is extremely important. Clinical judgment is required because signs and symptoms vary widely from patient to patient as well as within

each patient over time. During therapy, periodic assessment is also required, to establish whether the goals of asthma therapy have been achieved.

Exposure of sensitive patients to inhalant allergens has been shown to increase airway inflammation, airway hyper responsiveness, asthma symptoms, need for medication, and death due to asthma (Vervloet 1991; Kuehr, 1995; Leung, 2002). Substantially reducing exposures significantly reduces these outcomes.

Observations into the basic mechanisms of asthma have had a tremendous influence on therapy. Because inflammation is considered an early and persistent component of asthma, therapy for persistent asthma must be directed toward long-term suppression of the inflammation. Inhaled corticosteroids are the preferred first-hand medication for suppression of asthmatic inflammation.

Education remains the cornerstone of asthma management and should be carried out by health care providers delivering asthma care. Education should start at the time of asthma diagnosis and should be integrated into every step of clinical asthma care. Asthma self-management education should be tailored to the needs of each patient, maintaining sensitivity to cultural beliefs and practices.

2.2.6 Evaluation of clinical practice guidelines

Although many asthma practical guidelines have been published in the past decade, the morbidity and mortality for the disease are still high. In 1995, there were an estimated 1.9 million ED visits for asthma in the United States. Hence, some programs were carried out to help bridge the gap between practice guidelines and the reality of current asthma

management. Despite advances in drug treatment, outcomes of patients with asthma remain largely unsatisfactory. Low rates of patient compliance to the prescribed treatment regimen, inadequate physician-patient communication, and inconsistent implementation of evidence-based treatment guidelines are the most important causes for the poor outcomes. Physician and patient adherence to the guidelines is an important factor in the control of asthma. Recently in several articles, researchers have suggested that the under utilization of the asthma guidelines may in part be related to a lack of understanding (Courtney, 2000; Wan, 2002).

1.3 Use of guidelines in routine practice

1.3.1 Chicago-area survey

A cross-sectional, self-administered survey of ED asthma care was conducted in 1996 to 1997. Sixty-four EDs took part in the study, with a response rate of 71.9%. Systemic steroids (either IV or po) were estimated to be given to 73.2 ± 3.9% of patients during their ED visits. Systemic steroids were prescribed for 55.9 ± 3.5% of patients at time of discharge. Only 57.0 ± 5.4% of patients were estimated to have received any type of written asthma educational material (Michael, 1999).

The medical directors reported that many of the Chicago-area EDs provided asthma care that was consistent with key aspects of national guidelines. However, in certain critical areas of care, the EDs demonstrated a high degree of variation. In view of this, we are unable to declare that guideline compliance was poor in the Chicago area, because this study has several limitations. First, the study was based on self-reported perceptions of the

medical directors of the EDs. Some physicians liked the way questionnaire was asked, while others did not, therefore certain bias might have existed between respondents and non-respondents; Secondly, the responses were not verified by direct observation or chart audit, so accuracy of recall was doubtful.

1.3.2 Canadian survey

From July 1, 1997 to November 18, 1997 a retrospective chart collection and review was conducted in Canada, to compare the results with accepted management guidelines for the emergency department treatment of asthma. In contrast to management guidelines, only 59% of patients received treatment in the emergency departments with inhaled or systemic corticosteroids. Furthermore, specific follow-up plans were infrequently documented in the emergency department charts (37%) (Reid, 2000). Adherence with published Canadian guidelines for the emergency department management of acute asthma exacerbations was suboptimal. Corticosteroid use in the emergency department was significantly less than recommended.

1.3.4 Hypothesis on poor compliance

Why does poor compliance with guidelines exist universally for so many years after their introduction? Some surveys show that the reason is partly due to a lack of understanding of the guidelines. There are too many guidelines, and each one seems as huge as a book. Working in busy EDs, it is difficultfor medical staff to devote toomuch time to read lengthy guidelines. So we feel that, simple treatment steps may be easier to teach, learn and practice.

Asthma management evolves with the advance in knowledge of its pathogenesis, and significant progress has been made. But an update of guidelines takes several years, and the dissemination after a new version has been published also takes more time. (Guidelines were issued by the expert panel's review of the literature, experience and opinion). Compliance with guidelines is not adequate in many aspects.

1.3.5 Asthma surveillance in Singapore

Ng et al have conducted a series of studies on adult asthma in Singapore that describe the prevalence, morbidity and mortality and their relationships with environmental and medical care factors. These studies showed that there was no evidence of a temporal increase of mortality from 1976 to 1995 for adults and there is considerable morbidity among asthmatics, corticosteroids are under-used, and patients' knowledge and self-management skills are poor (Ng,1999; Tan, 2000).

The latest survey on asthma in the primary care was conducted in late 2001. A group of family physicians were investigated with regards to their asthma management using a self-administered questionnaire. There was much disparity between the recommendations by international guidelines on asthma management and current practice in reality. This was attributed to both patient's and doctor's factors (Tan, 2001). From previous studies, we can find that similar problems do exist in Singapore, like inappropriate asthma management and variation in compliance with guidelines.

To reduce the inappropriate management of asthma, the Singapore Ministry of Health (MOH) published clinical practice guidelines----management of asthma in January, 2002,

to work towards the goal of reducing asthma morbidity and mortality (MOH Clinical Practice Guidelines 1/2002).

1.4 Specific aims

1.4.1 Asthma mortality and morbidity trends

Asthma is a common chronic inflammatory disease, which affects quality of life in patients and even threatens many people's lives. Despite more understanding in the pathobiology of asthma and advancement in drug therapy over recent years, most well-conducted studies suggest that the prevalence of asthma has been increasing in children and young adults for the last several decades by approximately 5% to 6% per year worldwide. In the United States, asthma affected between 9 and 12 million persons in 1987, 14 million to 15 million persons in 1995 (Evans,1987). Asthmatics have 470,000 hospitalizations annually. More than 5,000 people die of asthma annually. In Singapore, it is estimated that 140,000 individuals have current asthma and more than 100 individuals die of this disease annually (Chew, 1999).

1.4.2 Economic burden

These increases have laid the economic burden to the whole society. The cost of illness related to asthma in 1990 in the United States was estimated to be $6.2 billion. Inpatient hospital services represented the largest single direct medical expenditure for this chronic condition, approaching $1.6 billion. Forty-three percentage of its economic impact was associated with emergency room use, hospitalization, and death. (Weiss, 1992) In Canada, the total cost of asthma was estimated to be between $504 million and $648 million. The

single largest component of direct costs was the cost of drugs ($124 million) (Krahn, 1996). Acute asthma (emergency department visits and hospitalization) accounted for approximately 25% of the total cost associated with asthma care (Bloch, 1995). In Singapore, the total cost of asthma was estimated to be US$33.93 million per annum. Inpatient hospitalization accounted for the largest proportion of direct medical expenditure, approximately US$8.55 million (Chew, 1999).

Chapter 2 Methodology

2.1 Study setting and design

In 2001, we conducted a Hospital-based retrospective chart review with the ED electronic records and medical treatment cards of all adult patients who had an ED ID code of asthma (493.9).

The objective of this study was to evaluate the adherence to and efficacy of a management algorithm for acute asthma in the ED, with focus on evidence-based treatment steps rather than documentation and patient classification.

The study was performed at National University Hospital, Singapore, a large community-based teaching hospital that provides tedious health care. Research targets were patients who were admitted to ED with a diagnosis of asthma.

This is a retrospectively controlled study of all adult patients admitted for the treatment of acute asthma in the same ED over two epochs (February to May inclusive) in consecutive years 2000 and 2001. We compared the treatment intensity and clinical outcomes of patients managed in the usual manner before our intervention and following the intervention program which was instituted in January 2001.

2.2 Description of intervention program

An evidence-based clinical algorithm which was easily understood and acceptable to doctors was developed. Both emergency and respiratory medicine specialists critically

reviewed a total of 169 articles, out of which 8 were Meta analyses on efficacy of corticosteroids, ipratropium bromide, magnesium sulfate and aminophylline in acute asthma. These articles were searched out in the literature for clinical evidence on the management of acute asthma by using MEDLINE (PUBMED) and COCHRANE electronic databases using the key words “acute asthma” and “randomized” and/or “meta analysis” dated to December 2000. Recommendations were introduced after review of the clinical evidence in the local context, with the following features:

1. Simple treatment algorithm rather than a complex clinical pathway
2. Emphasizing evidence-based treatment steps rather than precisely documenting disease severity and pulmonary function. Based on a study which aimed to assess the efficacy of a PEFR guided protocol in treating ED asthma. Data showed that in the management of acute asthma in the ED, a PEFR guided protocol neither improved overall PEFR response to treatment nor reduced admission rates when compared with current management as it is practiced in Singapore (Abisheganaden, 1998).
3. Enhancing second-line therapy to avoid inappropriate hospital admissions, patient disposition based upon symptoms and physical signs rather than pulmonary function testing, and
4. Initiating short and long-term preventive care at the ED. Short term aims to gain prompt control of inadequately controlled persistent asthma or severe acute exacerbations. Long term aims to reduce frequency and severity of asthma exacerbations.

2.3 Evidence for specific recommendations

2.3.1 Corticosteroid and ipratropium bromide in first line treatment

The recommendations are based on clinical evidence of a high quality. Corticosteroids are the most effective drugs in the treatment of asthma. They cause marked improvement in airway inflammation and lung function. Early use of corticosteroids at an ED significantly reduced the need for hospital admission in patients with acute asthma, and a short course of corticosteroids for follow-up significantly reduces the number of relapses to additional care (Rowe, 2002; Plotnick, 1998). Ipratropium bromide may relieve cholinergic bronchomotor tone and decrease mucosal edema and secretions (Aaron, 2001). The addition of ipratropium to beta2-agonists improves lung function and decreases hospitalizations without risk of adverse effects (Stoodley, 1999).

2.3.2 Magnesium sulfate and adrenaline in second line treatment

We noted that not all treatment options in the algorithm are strictly evidence-based. For example, there was no conclusive evidence for magnesium or adrenaline as second or third-line drugs in status asthmatics. They were included in the algorithm because we felt that, despite the lack of agreement on their application, a rapidly escalating intensity in bronchodilator treatment and thus a broad range of treatment options should be executed.

Some studies already have been conducted to determine whether magnesium sulfate (MgSO4) has a clinical effect in asthma and results have been conflicting, either in positive or in negative way. In Gustavo Rodrigo's study, a meta-analysis of randomized trials, pooled results revealed that MgSo4 did not decrease significantly admission rates

(Rodrigo, 2000); therefore, the addition of MgSo4 to ED patients with moderate to severe asthmatic exacerbations does not alter treatment outcomes. Nevertheless, the number and size of studies being pooled remains small, so further definitive controlled studies are needed to clarify its efficacy.

In research to demonstrate the impact of MgSo4 on expiratory flow in acute asthma exacerbations, Brian et al concluded that use of IV magnesium sulfate in addition to standard therapy does not provide clinically meaningful improvement of objective measures of expiratory flow in patients with moderate to severe asthma (Tiffany, 1993). But there is also evidence showing that intravenous MgSo4 decreased admission rate and improved FEV1 in patients with acute severe asthma (Bloch,1995) and it appears to be safe (Rowe,2000). A cellular mechanism for this bronchodilation effect has been proposed that it may involve smooth muscle relaxation via calcium antagonism (McLean, 1994). Mgso4 may also have a beneficial anti-inflammatory effect through affecting polymorphonuclear neutrophils by interfering with extracellular Ca2+ influx (Cairns, 1996).

Adrenaline is recommended as an alternative to conventional therapy in unresponsive life-threatening cases in Canada (Beveridge, 1996).

2.3.3 The key interventions in the asthma clinical algorithm

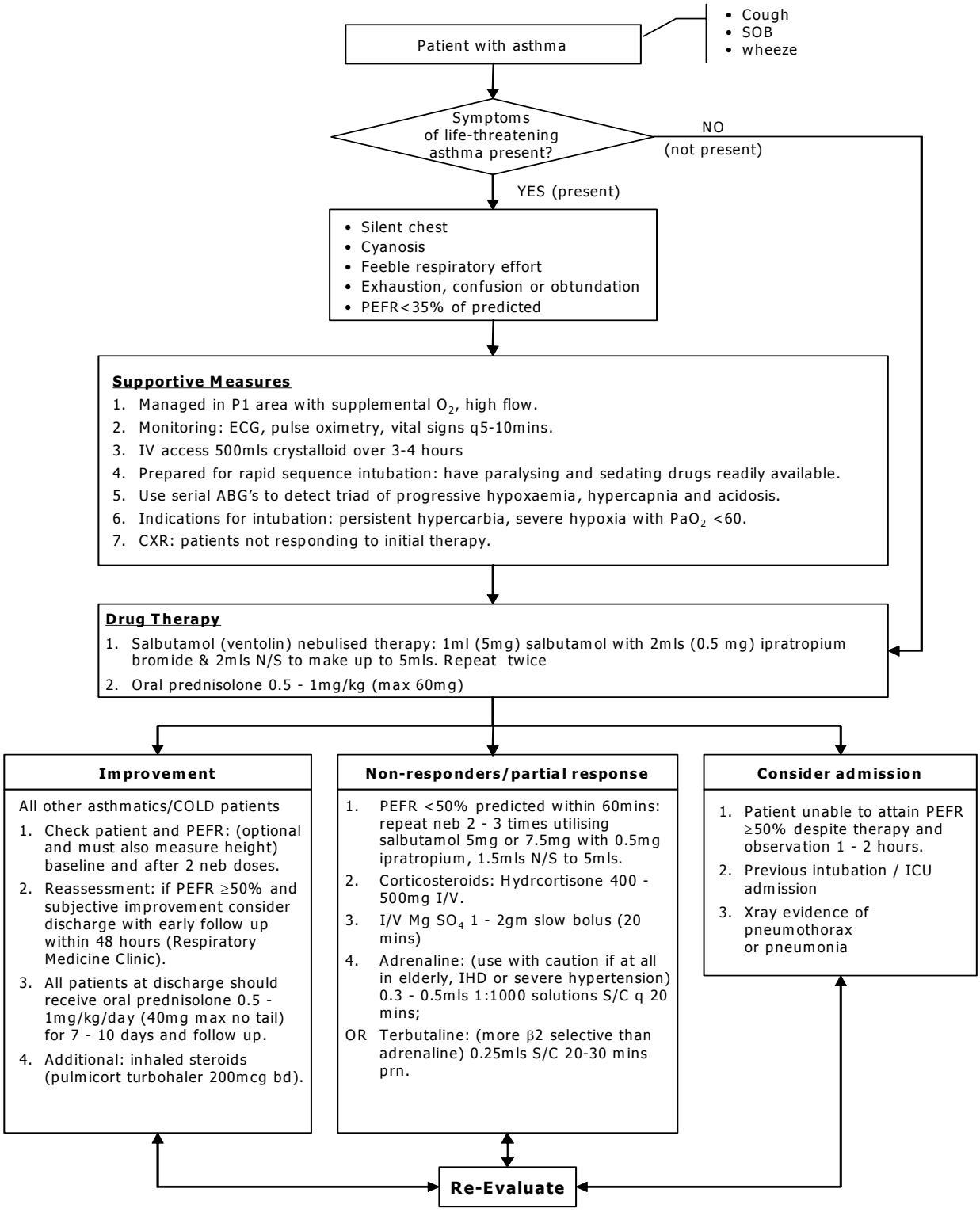
1) A combination of nebulized salbutamol and ipratropium as first line treatment;
2) Intravenous hydrocortisone and magnesium sulfate with repeat nebulizations in second line treatment
3) Early administration of a systemic corticosteroid

4) A course of oral prednisolone for all patients discharged from the ED

5) Fast track referral to a specialist clinic for all patients discharged from the ED

The management of Adult Acute Asthma is based on clinical evidence, as shown in the following flow chart (Thomas, 1995; Brenner, 1983; McFadden, 1989; Rodrigo, 1993).

ASTHMA CLINICAL ALGORITHM



The algorithm was disseminated to residents, fellows and consultants (total of 25 doctors) in January 2001 and the protocol, treatment steps and disposition of patients were briefly introduced.

2.4 Selection of patients

All adult patients (age≥14 years) with a discharged ICD code for asthma (493.9) admitted through the ED were included. Following individual chart review, patients who had diagnosis of chronic obstructive pulmonary disease, cardiac asthma, tumor, bronchiectasis, acute bronchitis or pneumonia were excluded. Patients in whom the clinical diagnosis of asthma was not made with confidence were also excluded. Clinical severity was categorized according to simple rules developed in the ED for triage and initial disposition. (See Table 5, it will be clarified later)

2.5 Data collection procedures

Data collection came from three sources: (1) Original paper-based data lodged at the Medical Record Office, (2) e-database at ED reservoir; information on in-patient at National University Hospital and, (3) In-hospital demographics and process measures were assessed by clinical chart review. Data collected included age, gender, ethnicity, hospital admission and discharge PEFR, pulse oximetry measurements, and arterial blood gases. In addition, length of stay (LOS), and possible antibiotic use were documented.

Cases were classified into two groups: patients admitted between February to May 2000, before introduction of the clinical algorithm; patients admitted during the same month in 2001, after dissemination of the clinical algorithm.

In the process of data collation, we used the paper-based as the primary data source. The paper records were the default in cases of in consistencies. In the vast majority of cases (over 95%) the hard copy records were used, in the rare case where case notes were not available we used the e-data source.

2.6 Statistical methods

Data was analyzed using SPSS software. The results were expressed and comparisons between the two study groups were made on the basis of acute asthma episodes rather than as individual patients. All values were expressed as mean $\pm$ SE and, where appropriate, 95%confidence interval. Comparison between the two groups was made using Student's unpaired t-test for parametric data and χ^2 tests for non-parametric data. P values of <0.05 were considered statistically significant.

Chapter 3 Results

3.1 Description of study patients

After reviewing the data from Icare (e-database at NUH), we found that, in 59 episodes,' the final diagnosis were not asthma. Examples of eventual diagnoses are “chronic airway obstruction, pneumonia, situs inversus, senile cataract, lumbago, congenital anomalies of spine" etc. This might have resulted from revision in the final diagnosis of patients who were wrongly diagnosed in the ED as having asthma. There episodes were excluded from our analysis.

From February to May 2000, a total of 364 episodes of adult asthmatics were identified from the ED register. Thirty-four were excluded from analysis: 18 had an uncertain diagnosis. Of the remaining eligible asthmatic episodes, 9 had no medications documented and 7 were missing records, therefore, a total of 330 episodes were included in the analysis (91%).

From February to May 2001, a total of 388 episodes of adult asthmatics were identified from the ED register. Twenty-one were excluded from analysis: 9 episodes which were not asthmatics and 12 which had an uncertain diagnosis. Of the remaining 367 eligible asthmatic episodes, 23 were excluded due to incomplete or missing data, leaving 344 asthmatic episodes for analysis (89%).

3.2 Tables and figures

There were a total of 330 episodes in 2000 and 344 episodes in 2001. Patient characteristics on ED admission are depicted for both groups in Table 1. These two groups were similar with respect to patient demographics. Severity of disease was defined by symptoms and physical signs, categorized according to simple rules developed in the ED for triage (Table 6). As noted in Table 5, significantly more patients in triage P1 in 2000 than in 2001 and respiratory rate much quicker in 2000 as well.

Table 1 Characteristics of patients

(±SE)	Year 2000	Year 2001	
Total number of episodes	364	388	
Number studied	330 (91%)	344 (89%)	
M/F ratio	0.49	0.51	ns
Age (yrs)	43 (1)	44 (1)	ns
Chinese	44%	41%	ns

The average dose of medication for oral prednisolone and IV hydrocortisone in 2001 is significantly higher than in 2000 (Table 2).

Table 2 Corticosteroid dose

(±SE)	YEAR 2000	YEAR 2001	P
ORAL PRED (mg)	32(0.8)	43(0.8)	<0.001
Intra-venous hydrocortisone (mg)	195(3)	348(9)	<0.001

From Table 3, among patients who were admitted to the ward, there was a significantly higher dosage in 2001 than in 2000, in the medication of oral prednisolone, IV hydrocortisone, and atrovent. But length of stay at ward and expenditure at ward were not significantly decreased.

Table 3 Outcome & treatment when patients were admitted

(+SE)	Year 2000	Year 2001	p
Oral pred (mg)	33.51(1.2)	42.16(2.0)	0.001
IVhydrocort (mg)	196.0(4.0)	341.27(12.9)	<0.0001
Atrovent (ml)1ml/5mg	2.61(0.2)	5.6(0.2)	<0.0001
Length of stay (days)	4.79(0.7)	3.55(0.3)	0.11
Cost (s$)	1889.58	1562.21	0.3

Table 4 shows more intensive and aggressive treatment at ED in 2001 than in 2000. The total nebs used and dose of corticosteroids are much higher, and the P value is significant at less than 0.0001.

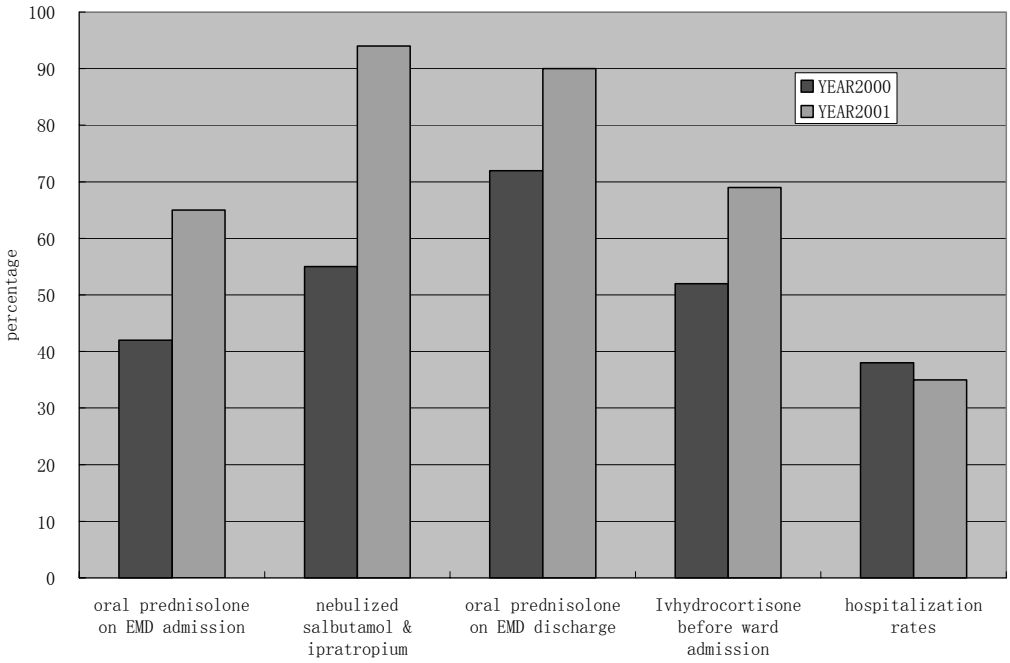
Table 4 Comparison of asthma treatment in 2000 versus 2001

(+SE)	Year 2000	Year 2001	P
Total neb (times)	1.97(0.07)	2.33(0.05)	<0.0001
Oral pred (mg)	32.17(0.8)	42.98(0.8)	<0.0001
IVhydrocort (mg)	195.0(3.0)	348.54(9.3)	<0.0001

Figure 1 summarizes the compliance with and outcome of the clinical algorithm. The use of oral prednisolone at ED admission & on discharge, combination of salbutamol and

ipratropium bromide as 1st line treatment, and intravenous hydrocortisone when admitted increased significantly in 2001 compared with 2000. However, the admission rate was reduced but not significantly.

Figure 1 Outcome & treatment



Chapter 4 Discussion

4.1 Summary of findings

There were three major findings in this study. First, following basic instructions on a set of simple recommendations for asthma treatment in the ED, the compliance with the algorithm in 2001, hadimproved significantly compared to that in 2000. Secondly however, the admission rate was not significantly decreased, with 38% in 2000 vs. 35% in 2001. Third, the length of stay (LOS) showed little difference between these two groups.

4.2 Comparison with previous studies

Following the implementation of the algorithm, the compliance of nebulized salbutamol & ipratropium was 94%, oral prednisolone on EMD discharge 90%, oral prednisolone on EMD admission 65%, and IV hydrocortisone before ward admission 69% respectively. These outcomes are much higher than the ones in a similar study conducted in France.

A 12-month cross-sectional observational cohort study in adult patients with acute asthma was carried out in France. The doctors used a formatted chart to describe information on asthma management. Initial treatment included nebulised ß2 agonists, anticholinergics, and systemic corticosteroids in 93%, 49% and 60%, respectively. The overall admission rate was 54.2% (Salmeron, 2001). In the report, Sergio et al mentioned that the high admission rate was mainly due to absence of standardized admission criteria. In our study, we encountered a similar problem (chapter 4.4).

4.3 Length of stay in the wards

After excluding these patients who had inconsistent chart data, the average LOS was 4.79 days in 2000; average LOS was 3.55 days in 2001. Although LOS decreased, this was not statistically significant. The lower length of stay in 2001 might be explained by more intensive and aggressive treatment at the EMD. Among patients who were admitted to the ward, significantly higher dosage of medication was administered in 2001 than in 2000, in the use of oral prednisolone, IV hydrocortisone, and atrovent (Table 3). But there was no decrease in cost. With increase in drug used at EMD and decrease in LOS at ward, it did not lead to overall reduction of economic burden. So the question of how cost –effective more intensive asthma treatment in the ED really is needs to be resolved in further prospective studies.

Table 5 Clinical severity

(±SE)	Year 2000	Year 2001	P
SpO2 %	95 (0.002)	95 (0.002)	0.49
Pulse R/m	105 (1)	102 (1)	0.068
Resp R/m	23 (0.3)	22 (0.2)	0.005
Triage class P1 (see Table 6)	11%	6%	0.02

4.4 Weaknesses of the study

The limitations in this study may be categorized into patient factors, treatment factors and other confounding factors. Firstly, the patients were not prospectively randomized but

were only historically controlled in terms of their enrollment during February to May of two consecutive years. Also the sample is not a big one, and it was selected by four continual months definitively and not randomized, so the two groups of patients may not have been comparable. Indeed, as we can see from Table 5, respiratory rate of patients in 2000 is faster than the ones in 2001, and more patients in 2000 classified as triage P1. Since data collection is retrospective, some records were missing. However close to 90% of consecutive patients were included in the final analysis. Nevertheless, the patients in 2001, despite having less severe asthma than patients in 2000, actually received more intensive asthma treatment in the ED (Table 4). This is further confirmation that our simple treatment plan facilitated a high degree of compliance in 2001.

Secondly, the treatment during both study periods was not rigorously linked to a formal classification of asthma severity. Rather the emergency department in NUH classifies patients by a simple set of triage rules (Table 6). P1 marked as most severe asthmatics, and P3 as mild asthma attack. The treatment dose of an intensity was left to the judgment of the attending doctors in 2000 and guided by a simple treatment protocol in 2001(page 18). This resulted in some variation in treatment intensity but it is clear that patients in 2001 received more intensive and appropriate asthma treatment despite having overall less severe asthma than 2000.

The usual practice is for P1 patients to be admitted to the resuscitation ward, and P3 patients to routine waiting areas. Some of P2 were admitted, and part of P2 discharge, according to their response to therapy. But in this study, 7 patients categorized as P1 were also discharged. Thus, this triage classification system is also obviously not a reliable

predictor of the final decision on whether to admit or discharge patients after asthma treatment.

Table 6 Triage classification in ED

Priority 1 (P1)	Signs of life threatening asthma usually brought in by ambulance directly to the resuscitation area
Priority 2 (P2)	Walked in but presenting with active signs of asthma e.g. audible wheeze
Priority 3 (P3)	All other patients not in P1 or P2 categories

Traditionally, overall asthma severity has been defined by some combination of the following four features: symptoms, medication requirements, physiologic abnormalities, and morbidity. It is evident that most of these criteria (symptoms, beta2-agonist requirements, morbidity, and reduced flow rates) describe a lack of asthma control. Asthma severity and asthma control should be distinguished. Asthma severity should be defined by the minimum medication required to achieve adequate control rather than by symptoms and abnormal lung function (Cockcroft, 1996). A study was carried out to develop a simple and pragmatic procedure for applying the international consensus guidelines, to classify severity using information about symptoms, pulmonary function and asthma medication (Liard, 2000).

Thirdly, the outcomes of this study were confounded by a lack of pre- defined criteria for evaluation of the response to treatment during that acute period and for the eventual disposition of patients. One important outcome in evaluating the efficacy of a treatment algorithm for acute asthma is the hospitalization rate. However, the algorithm in this study

did not define the specific criteria for hospital admission but instead left it to the doctors in charge to decide subjectively. This may be the reason why there was no significant decrease in hospitalization rate in 2001 compared with 2000 despite less severe asthma and more intensive treatment regimens in the second year of the study. Because hospital admission was a clinical decision, it could have been biased by perceptions of either patients or doctors. However, the results of this study are an accurate reflection of the situation in current practice in the vast majority of EDs in the world where decisions on the patients' response to treatment and eventual disposition are based upon subjective decisions and not formal protocols. Further studies are needed on the impact of similar evidence based treatment plans with clear, prospectively defined objective criteria for hospital admissions.

Brenner et al suggest that several points should be taken into consideration as to whether to discharge patients, to continue treatment, or to admit to hospital: the duration of the bronchospasm, frequency of visits, history of previous endotracheal intubation, pulse rate, accessory muscle use, range of peak expiratory flow rate, pneumonia, lability, prominent psychiatric difficulties, poor access to medications, poor educability, fear of steroids, patients on glucocorticoids or those who have recently stopped glucocorticoids, and evening discharges of patients from the ED, of which all predispose to relapses of acute asthma. (Brenner, 1998) Medical doctors might be surprised to know that they should screen for so many items before making a decision, to discharge patients or to admit them and may be less likely to comply with such a complex method of evaluation.

However, this study was not designed to examine the impact of a treatment plan on hospital admission. Rather its main aim was to show the effect of a simple treatment plan

on compliance with evidence based management of acute severe asthma. In this regard, we have shown that following intervention, a significantly larger proportion of patients received the appropriate treatment steps even though overall they had less severe asthma than the control group of patients.

4.5 Secondary results and their implications

Though our main objective in this study was to compare the outcome and compliance of a clinical algorithm set at ED, between two groups before and after the introduction of this algorithm, when we combined these two groups as a whole, we found that:

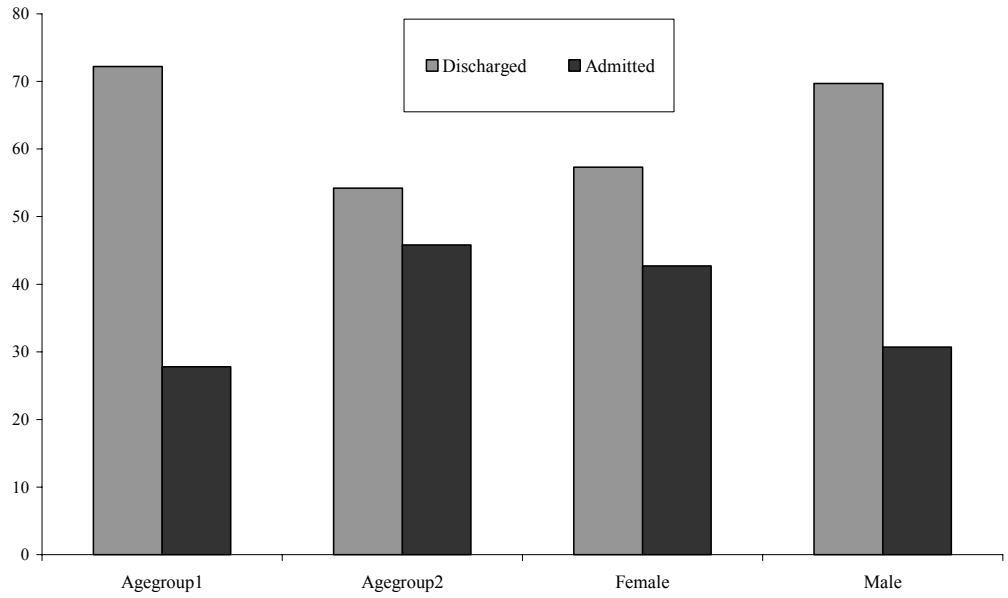
Overall, 674 episodes were analyzed. Of these, gender ratio is equally distributed, with female (49%) and male (51%). But in comparison to hospitalization, female (42.6%) is statistically higher than male (30.6%) (p=0.001) (Figure 2).

In Trawick DR's retrospective study, they compared the relative numbers and hospital course of men verses women admitted at least twice with asthma or status asthmatics to Yale-New Haven Hospital (YNHH) during the period from 1985 to 1994, and found that 68.6% of the admissions were women. After chart review, they point out that the mechanisms contributing to the gender differences in asthma admissions may include differences in the ventilatory response to hypercapnea or in the tolerance to airway obstruction.

From the figure below we can see that our results are very similar to Trawick's with regards to in gender differences in the admission rate. And in this study, we do find that

some other differences in treatment between women and men, like average dose of oral prednisolone used at ED is higher in men (39.79mg) than in women (37.90mg).

Figure 2 Hospitalization between gender and age group



The mean age of targets is 43 years old. Two age groups are set with 43 as cut-off point, group1 (age<43) and group2 (age>43), Therefore no age bias between them, with 51% and 49% respectively. The admission rate is 28% versus 45% in two groups (P<0.001). The observation that older patients have higher admission rates is consistent with another local study (Lee, 2000).

Table 7 shows the relationship between patient categorization according to triage rules in the EMD, admission rates and investigations.

Table 7 Triage classification, investigations and admission rate

Triage classification (%)	Admission (%)	Chest radiograph (%)	Arterial blood gas (%)
P1 8.3	89.3	83.9	39.3
P2 86.2	33.4	40.3	3.4
P3 5.5	5.4	35.1	0

With regards to investigations, chest radiograph appear to have been over-used while arterial blood gas measurements were under-used. All practice guidelines recommend objective measurement of asthma severity, but there have been few prospectively controlled studies to show how best to use this information to guide treatment.

Finally, I should point out that quite a few patients visited the emergency department several times within the four months of this study. In total there were 140 repeat cases among 674 (21%). Before introduction of this algorithm the number was 19%, and after the practice, it was 22%. This number is very high, and maybe it is in part the reason for the heavy economic burden. In Table 8, evidence showed that there were no obvious changes in ED repeat visits and relapse rates, despite the significant increasing use of oral prednisolone on discharge and more intensive therapy in ED, which were recommended in the clinical pathway. Some research on factors associated with repeat Emergency Department visits show that those not in possessions of a written asthma action plan were more likely to present frequently at the emergency department than those with such plans. (Adams, 2000) So we might consider a further study with more focus on action plan, follow-up plan and patient education, to show their association with asthma repeat ED visits and hospitalization.

Table 8 Comparison of ED relapse rates and repeat visits in 2000 versus 2001

Number	Year 2000	Year 2001
Total episodes	330	344
Repeat visits	63	77
Total patients	267	267
Relapse rates (<24 hours)	5	8

The plan should describe the signs, symptoms, and/or peak flow values that should prompt increases in self-medication, contact with a health care provider, or return for emergency care. Patient education is a powerful tool for helping patients gain the motivation, skill, and confidence to control their asthma. Research shows that asthma education can be cost-effective and can reduce morbidity, especially among high-risk patients (George, 1999).

4.6 Conclusions

We found that introduction of a simple treatment algorithm resulted in (1) significantly improved compliance with evidence based treatment but (2) no significant reductions in admission rates or LOS. (3) With regard to admission rate, some data suggested a lack of adequate assessment and decision on hospital admission partly influenced by patients' choice, and this might lead to the failure to evaluate the outcome of our clinical pathway. In view of this, we plan a formal examination of the effect of the algorithm on EMD length of stay and admission rates with regards to overall cost-effectiveness. The questions being considered are: (a) is it worth while to keep patients 60-90 minutes longer

in the EMD for more intensive treatment? And (b) what is the impact of a clinical judgment in deciding on hospital admission?

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