Risk Factors of Relapse within Eight Weeks After an Acute Asthma Exacerbation in Thai Children

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Abstract

Background : Acute asthma relapse following treatment and discharge from hospital remains a substantial problem. Various potential risk factors for relapse have been reported including age, sex, frequency of hospitalization and emergency medications. All these factors, however, may not be generalized for all patients because of difference in prevalence, trigger factors, types of allergens, medical accessibility and psychosocial problems.

Objective : To identify factors associated with relapse following treatment for acute asthma within the next 8 weeks in Thai children.

Material and method : The authors prospectively followed 91 children discharged from Ramathibodi Hospital after treatment of an asthma attack from June 1999 to December 2000. Parents were surveyed concerning their child's medical history, trigger factors, psychosocial and economic variables. Data on severity of the attack, asthma scores, emergency treatment, and response to treatment were recorded. Investigations included eosinophil count, total IgE, serum eosinophil cationic protein (ECP), skin test, methacholine bronchial challenge test, and IQ test were performed and recorded.

Results : Within the first week, only 6.6 per cent had relapsed and increased to 29.7 per cent by 8 weeks. Patients who suffered relapse were more likely associated with age at asthma diagnosis (OR, 2.90; 95% CI, 1.1-7.5) and 6 years of age or under (OR 4.49, CI 1.22-16.54). From the investigation results including eosinophil count, total IgE, serum ECP, skin test, methacholine bronchial challenge test, and IQ test, there was no significant difference in the factors between patients who suffered relapse and those who did not. From the psychosocial evaluation, 18 out 39 (46.2%) studied cases had significant psychosocial disorders. They were 4 cases with delayed development and mental retardation, 9 cases with parent-child relation problems, and 2 cases with serious intrafamilial disorders. Most of these patients were non-relapse cases. However, the relationship between asthma relapse and psychosocial disorders could not be ascertained since psychosocial evaluation was only performed in one-third of the study population.

Conclusion : Among patients following acute asthma therapy, 29.7 per cent will have a relapse. The authors identified the age at onset of asthma before the age of 6 years as an important risk factor. This may help to decrease the relapse rate by more intensive and comprehensive management among patients at high risk.

Key word : Acute Asthma, Relapse Asthma

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In recent years the morbidity and mortality of asthma has increased, although the etiology is still poorly understood[1,2]. Most patients with asthma suffer from acute attacks that are commonly treated in a hospital emergency room (ER). Acute asthma relapse after treatment and discharge from the ER remains a substantial problem. Moreover, the rate of relapse after ER treatment for acute asthma is difficult to ascertain, because the reported rate varies from 10 per cent to 31 per cent in the days to weeks after ER discharge[3-6]. Identifying patients at risk of asthma relapse is a vital aspect of patient care if the objective of reducing asthma morbidity and mortality is to be achieved. A number of potential risk factors for relapse have been identified including age, female sex, parental smoking, previous hospitalization for asthma, the number of ER visits in the previous year, and current medication use[7]. All these factors, however, may not be generalized for all patients because of differences in prevalence, triggering factors, types of local allergens, medical accessibility, and psychosocial problems.

The purpose of this study was to evaluate the incidence of relapse and the factors associated with relapse following treatment for acute asthma. Identifying patients with high risk of relapse could be useful in designing more aggressive asthma therapy programs to reduce the relapse rate. The present study design differs from previous investigations of this issue in two important respects. First, the authors sought to evaluate relapse following treatment for acute asthma over a longer period. Most of the previous studies followed the patients for 10 or fewer days[3-6]. The authors considered relapse over a period of eight weeks, since little is known about the incidence of relapse over this time in asthmatic children. Second, both clinical characteristics and psychological aspects of patients with asthma and their families were evaluated.

MATERIAL AND METHOD

Study population

The study was conducted at Ramathibodi Hospital, Bangkok, Thailand, a medical school setting. From June 1999 to December 2000, children aged 1-15 years, treated in the ER for acute asthma, were eligible for enrollment. The diagnosis of asthma was made by clinical grounds (a previous history of asthma, response to β_2-agonist therapy, recurrent wheezing of at least 3 episodes in the previous year, and worsening symptoms necessitating treatment in the ER). Patients were excluded if they had any of the following: a diagnosis of pneumonia, congestive heart failure, bronchopulmonary dysplasia or chronic lung diseases prior to eligibility assessment; had neurological disorders or were unable to communicate in data collection and investigations; had a history of upper or lower respiratory tract infection within 6 weeks at the time of patient recruitment.

Emergency room (ER) treatment protocol

The studied population had treatment initiated in the ER setting. The dosage, method of administration, and frequency of medication were determined

by ER physicians. In this setting, patients were treated with nebulized β_2-agonist (salbutamol) every 20 minutes for the first hour, and supplemental oxygen. The decision to discharge patients after ER therapy was made at the discretion of the treating physician. All physicians were provided with asthma score assessment check and pulse oxymetry for measurement of oxygen saturation.

Data collection

After signing the consent form, patients or parents were interviewed to assess the patients' demographic characteristics, asthma history, symptoms, treatment and details of the current asthma exacerbation. Severity of asthma was assessed by using the asthma score before the initial treatment. Data on ER management and disposition were obtained by chart review. Laboratory investigations included complete blood count for total eosinophil enumeration, serum eosinophil cationic protein (ECP), serum total IgE, and paranasal sinuses X-ray. All patients were appointed to follow-up at 1, 4 and 8 weeks after an ER discharge. They were contacted by telephone if they were lost to follow-up. Follow-up data were collected by a structural interview in detail regarding history of smoker exposure, home environment, and family income. Additional investigations included allergy skin test with common allergens (house dust mites, grass pollen, mold, cockroach, and animal dander), and methacholine bronchial challenge test in children older than 6 years of age. Psychosocial evaluation was assessed by psychiatrist (A.B.) and using the global assessment of psychosocial disability questionnaire. IQ test and developmental assessment were performed by psychologist (K.S.).

Relapse was defined as any urgent or unscheduled visit to any physician (ER or clinic) for worsening asthma symptoms during the 8-week follow-up period.

Statistical analysis

Continuous variables were reported as means and SDs for normal distributed data, median and range for skewed results. Univariate analyses of the relation of various factors to risk for relapse employed χ^2 test, student's t-test, and Wilcoxon rank sum test where appropriate. Variables that were assessed with relapse at a two-tailed $p<0.1$ in univariate analysis were evaluated for inclusion in a multivariate logistic regression model. All results were considered to have significant difference at $p<0.05$.

RESULTS

Demographic factors and the risk of relapse

The overall study results were based on 91 appropriately enrolled patients. Table 1 shows that the mean ages were 3.8 ± 2.1 and 5.4 ± 3.4 years in the relapse and non-relapse groups, respectively. The majority of subjects were male (63% and 64% respectively). A substantial proportion reported an allergy history (68.4% and 76%), family history of allergic disorders (76% and 74.6%), exposure to cigarette smoke (45.8% and 63.6%) and using non-synthetic mattress (47.6% and 37.5%). Among the 91 study patients, 27 subjects (29.7%) reported at least one relapse for acute asthma during the prospective 8-week follow-up period. Six children (6.6%) had a relapse within the first week after ER discharge. Of the demographic characteristics, age at asthma diagnosis (OR, 2.9; 95% CI, 1.1-7.5) was associated with a greater risk of relapse for acute asthma during the 8-week follow-up. Previous number of ER visits (median 3, range 0-12) and urgent clinic visits (median 5, range 0-12) in the past 12 months had an increased likelihood of relapse, although the confidence interval did not exclude no association. Patient's allergy history, family history of allergy, family income and environmental triggers and allergens did not appear related to risk of acute asthma relapse. The authors examined the relation between age and relapse in more detail. Children under 6 years of age were associated with an increased risk of relapse (OR, 4.49; 95% CI, 1.22-16.54).

Clinical and laboratory risk factors for relapse

Several index factors of acute asthma characteristics were not associated with relapse such as systemic steroid prescribed during an attack, presence of sinusitis, asthma score, and duration of symptoms before ER visit (Table 1). Furthermore, in terms of the laboratory tests, there was no difference between the relapse and non-relapse groups in skin test reactivity, methacholine bronchial challenge test, IQ test, total white blood cell count, eosinophil count, total IgE and serum ECP (Table 2).

On multivariate analyses, age, sex, and history of ER and clinic visits were not significantly associated with relapse of acute asthma.

Psychosocial evaluation

Upon conclusion of the study, 39 children were eligible to complete the psychosocial and developmental assessment. Of those evaluated according

Table 1. Patient characteristics, according to relapse within 8 weeks after ER discharge.

	Relapse (n = 27)	Non-relapse (n = 64)	P-value
Age (yr), mean ± SD	3.8 ± 2.1	5.4 ± 3.4	0.06
Male, %	63	64	0.92
Age at asthma diagnosis, median (range)	1 (0.3-4.8)	2 (0.2-12)	0.01
Ever taken steroid medication for asthma, %	25.9	26.7	0.95
Taken β_2-agonist regularly, %	7.4	7.8	0.66
Patient's allergy history, %	68.4	7.6	0.36
Family history of allergic diseases, %	76	74.6	0.89
No. of ER visits in the past 12 months, median (range)	3 (0-12)	2 (0-10)	0.05
No. of urgent clinic visits in the past 12 months, median (range)	5 (0-12)	3.5 (0-10)	0.06
No. of admission for asthma in the past 12 months, median (range)	1 (0-5)	0 (0-5)	0.41
Family income/month, median (range), Baht	13,650 (3,000-38,000)	13,750 (4,000-40,000)	0.43
Acute asthma characteristics			
Systemic steroid during attack (%)	55.6	72.6	0.12
Presence of sinusitis (%)	68	58	0.42
Asthma score, median (range)	9 (5-11)	9 (5-11)	0.44
Duration of symptoms before ER visit, median (range)	12 (2-48)	12 (0.5-48)	0.73
Environmental status			
Exposed to cigarette smoke, %	45.8	63.6	0.14
Household pets, %	25	29	0.71
Allergen loaded bedroom, %	18	7.4	0.17
Non-synthetic mattress, %	47.6	37.5	0.42
Furry toy, %	31.6	30.6	0.94
Polluted environment, %	50	42	0.53

Table 2. Investigation data, according to relapse within 8 weeks after ER discharge.

	Relapse (n = 27)	Non-relapse (n = 64)	P-value
Positive skin test, %	62.5	65.2	0.85
Methacholine bronchial challenge test (PD20), median (range)*	165.5 (22.6-201)	135.5 (1.1-201)	0.71
IQ test, median (range)**	107 (89-124)	99 (66-137)	0.22
Total WBC, mean ± SD, per µl	12,103.1 ± 4283.5	13,207.2 ± 4643.5	0.35
Eosinophil count, median (range), per µl	185 (0-2613)	168 (0-2352)	0.76
Total IgE (IU/ml), median (range)	221 (17.2-3145.6)	338.5 (6.9-2475)	0.15
Serum ECP (mg/L), median (range)	8.7 (0-26.9)	6.9 (0-61)	0.7

* n = 4 in relapse group, n = 17 in non-relapse group

** n = 9 in relapse group, n = 24 in non-relapse group

PD20 = provocative dose of methacholine which causes a reduction in force expiratory volume in one second (FEV_1) 20% less than the baseline value

WBC = white blood cell counts

ECP = eosinophil cationic protein

to the World Health Oganization ICD-10 classification[8], 18 out of 39 cases (46.5%) were found to have psychosocial disorders. Of these, 14 out of 18 cases were found in the non-relapse group. There were 3 cases with significant clinical psychiatric disorders including attention deficit/hyperactivity disorder in 1 case, and phonological disorder in 2 cases. Specific disorders of psychosocial development were detected in 4 cases, who were all mentally retarded. A high proportion of parent-child relation problems was found in 9 cases. Seven of 9 cases were parental overprotection, 1 case with inappropriate parental pressure and another case with inadequate intrafamilial communication. Lastly, the authors found a serious

intrafamilial disorder among adults such as divorce in 2 cases of children with asthma. Although the majority of the problematic psychiatric and developmental disorders were found in the non-relapse group, the authors could not demonstrate the association between psychosocial problems and the occurrence of acute asthma because of the small sample number of studied subjects.

DISCUSSION

Asthma related morbidity and mortality have risen substantially worldwide including Thailand[1, 2]. Hospitalization or ER visits for acute asthma, a potentially avoidable outcome, is a specific index of asthma severity and burdens. In this prospective study of children with asthma who had been discharged from ER after emergency treatment, the authors identified an association between the age of onset of asthma and relapse. Furthermore, in the present study, younger children had a higher relapse risk than older children. This result is in contrast to a previous report of a lower relapse rate in the younger age group[6]. In a similar manner, Henry RL et al[9] found that older children are at increased risk of recurrent admission. The reason for the difference may be due to differences in compliance, recognition of asthma, and ability of using inhaled medication between preschool and older children. The relationship between age of onset of asthma and severity of asthma that leads to increased morbidity and mortality has many potential explanations. It has been observed that the mean age of hospitalized children with asthma is likely to be the younger age group [10]. In addition, from a prospective study of asthma children with chronic symptoms, their lung functions are irreversible if the therapy begins after the onset of asthma for more than 5 years. While the poor outcome of pulmonary function test is significantly found in the non-steroid treated group compared to the steroid-treated group[11]. This delayed treatment may be vulnerable to asthmatic airways to develop the remodelling process which causes a poor lung function with chronic asthma symptoms[12].

In this prospective study, the authors found that 29.7 per cent of children, who were discharged from ER after treatment of acute asthma, had a relapse over an 8-week follow-up period. The relapse rate was reported with estimates of 31 per cent in children [5,7]. In contrast, other investigators have reported very low relapse rates in children treated with either intramuscular or oral corticosteroids after an ER visit for acute asthma[6,13,14]. These studies differ in some ways from the present study including : definition of relapse over a 10-day period[5], using intramuscular corticosteroid after an ER visit[13], and severity of asthma in each study.

Although other studies have reported an association between clinical acute asthma characteristics, environmental and triggering factors, and relapse of acute asthma[3,5,15,16], these factors did not appear to predict relapse in the present study. Furthermore, the authors found no difference in the type of treatment prescribed for these patients in the ER, which is similar to a recent study in children[6]. The authors also explored some potential laboratory tests, which could be risk factors of relapse[17-21]. The results of skin test, methacholine bronchial challenge test, IQ test, total white blood count, eosinophil count, total IgE, serum ECP and sinusitis showed no relationship with relapse of acute asthma. Butz et al[7] found a number of factors associated with relapse including female sex, maternal smoking, increased number of asthma attacks in the previous year and duration of medication use. Duchrame and Kramer[5] found that children with a history of repeated ER visits relapsed more frequently. In the present study there was a tendency of the association between the number of ER visit and relapse ($p=0.05$). This may be due to the differences in number of the population study and the definition of relapse.

ECP has been suggested to be a marker of allergic or eosinophilic inflammation, which reflects disease severity[22]. Unfortunately, other studies in confirmation of the present study, have found that a high level of serum ECP is not associated with asthma severity[23]. Recent studies also showed that the measurement of serum ECP or ECP/eosinophil ratio is a poor marker in asthmatic children[24, 25].

The authors have demonstrated that children with asthma have significant psychosocial and psychiatric problems. The statistical analyses were not feasible to differentiate these children due to the inadequate sample size. An increased prevalence of psychiatric complications of pediatric asthma has been shown associated with severely asthmatic children [26,27], but little evidence is known to suggest that the disorders are risk factors for asthma relapse. The authors found 46.2 per cent of children with asthma associated with psychosocial problems. The results may be difficult to ascertain the true relationship because only one-third of the study population were evaluated. There were several reasons of why the

psychiatric interview could not be performed in some subjects including: parents were not interested in participating in this part of the project, refused because the parents thought that their children and families were in good mental health. Hence, they were lost to follow-up. The authors suggest that further studies are needed to elaborate the problems. However, it is important to note that the psychosocial disorders are not uncommon in pediatric asthma such as psychiatric disorders, intrafamilial stress and inappropriate child caring.

There are several limitations to the present study. First, the ER management was not standardized. It is possible that some differences in patient management may have masked factors associated with relapse, for example the treatment with systemic corticosteroids may reduce the relapse rate and hospitalization in acute asthma[28,29]. Second, the study patients were recruited from an ER in a medical school setting. This may not be generalized to the overall population. The study may be confounded by population bias, differences in accessibility to medical care for asthma and higher median household income. Thus, the authors found no significant difference in family income between the relapse and non-relapse group, unlike Ray NF, et al[30] and Gottlieb DJ, et al[31] who reported that a low income family was strongly associated with a higher rate of relapse and hospitalization for asthma. Third, the enrolled patients could not be fully investigated during the follow-up period. This caused inadequate data for the interpretation of psychosocial assessment.

SUMMARY

Acute asthma relapse following treatment and discharge from ER remains a substantial problem. The authors reported a relapse rate of 29.7 per cent among children with acute asthma exacerbation during an 8-week follow-up period. The age at onset of asthma before 6 years old as an important risk factor was identified. This may help to decrease the relapse rate by more intensive and comprehensive management of patients at risk.

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ปัจจัยเสี่ยงของการจับหืดซ้ำ ภายใน 8 สัปดาห์หลังการจับหืดเฉียบพลันในเด็กไทย

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การจับหืดซ้ำในผู้ป่วยเด็กโรคหืดยังเป็นปัญหาที่สำคัญที่มีผลกระทบต่อผู้ป่วย ครอบครัว และระบบการดูแลรักษา มีการศึกษาถึงปัจจัยต่าง ๆ ที่อาจจะสัมพันธ์กับภาวะการจับหืดซ้ำ เช่น อายุ เพศ อัตราการเข้ารักษาในโรงพยาบาล และการใช้ยารักษาในห้องฉุกเฉิน เนื่องจากอุบัติการณ์ของโรคหืด สิ่งกระตุ้น สารก่อภูมิแพ้ ระบบการดูแลรักษาผู้ป่วย และปัญหาทางจิตสังคมในผู้ป่วยโรคหืด มีความแตกต่างกันมากในแต่ละกลุ่มประชากร ดังนั้นจึงควรที่จะศึกษาถึงปัจจัยเสี่ยงของการจับหืดซ้ำในเด็กไทย เพื่อเป็นประโยชน์ในการรักษาผู้ป่วยต่อไป

วัตถุประสงค์ : เพื่อหาปัจจัยเสี่ยงที่สัมพันธ์กับภาวะการจับหืดซ้ำภายใน 8 สัปดาห์ หลังจากเกิดการจับหืดเฉียบพลันในเด็กไทย

วิธีการศึกษา : ได้ติดตามผู้ป่วยเด็กจำนวน 91 ราย ที่ป่วยด้วยการจับหืดเฉียบพลันจนต้องมารับการรักษาที่โรงพยาบาลรามาธิบดี ตั้งแต่เดือน มิถุนายน 2542 ถึงธันวาคม 2543 โดยได้ทำการรวบรวมข้อมูลที่อาจจะเป็นปัจจัยเสี่ยงที่ทำให้เกิดการจับหืดซ้ำได้ เช่น ประวัติการเจ็บป่วย สิ่งกระตุ้นให้หอบ ปัญหาทางจิตสังคม เศรษฐฐานะ ระดับความรุนแรงของการจับหืด การดูแลรักษาที่ห้องฉุกเฉินและการตอบสนองต่อการรักษา นอกจากนี้ได้ทำการตรวจพิเศษเพิ่มเติมดังต่อไปนี้ eosinophil count, total IgE, serum eosinophil cationic protein (ECP), skin test, methacholine bronchial challenge test และ IQ test เพื่อนำมาหาความสัมพันธ์กับการจับหืดซ้ำ

ผลการศึกษา : พบอัตราการจับหืดซ้ำร้อยละ 6.6 ในสัปดาห์แรกและเพิ่มเป็นร้อยละ 29.7 ภายใน 8 สัปดาห์หลังจากการจับหืดเฉียบพลัน ปัจจัยเสี่ยงที่สัมพันธ์กับการจับหืดซ้ำคือ อายุที่ได้รับการวินิจฉัยว่าเป็นโรคหืด (OR, 2.90; 95% CI, 1.1–7.5) โดยเฉพาะผู้ป่วยที่อายุน้อยกว่าหรือเท่ากับ 6 ปี (OR, 4.49; CI, 1.22–16.54) นอกจากนี้แล้วไม่พบความสัมพันธ์อย่างมีนัยสำคัญทางสถิติระหว่างกลุ่มผู้ป่วยที่มีการจับหืดซ้ำเปรียบเทียบกับกลุ่มที่ไม่มี ในปัจจัยอื่น ๆ ที่ทำการศึกษาคือ eosinophil count, total IgE, ECP, skin test, methacholine bronchial challenge test และ IQ test พบปัญหาทางด้านจิตสังคมในผู้ป่วย 18 จาก 39 ราย (ร้อยละ 46.2) ที่ได้รับการประเมิน โดยเป็นผู้ป่วยที่มีปัญหาทางด้านพัฒนาการและปัญญาอ่อน 4 ราย การเลี้ยงดูไม่เหมาะสม 9 ราย และภาวะเครียดมากในครอบครัว 2 ราย โดยรวมแล้วผู้ป่วยส่วนใหญ่ที่มีปัญหาทางจิตสังคมจะเป็นกลุ่มที่ไม่มีการจับหืดซ้ำ จึงยังไม่สามารถบอกถึงความสัมพันธ์ของการจับหืดซ้ำกับปัญหาทางด้านจิตสังคม เพราะสามารถทำการประเมินทางด้านจิตสังคมได้เพียงหนึ่งในสามของผู้ป่วยทั้งหมด

สรุป : พบอัตราการจับหืดซ้ำภายใน 8 สัปดาห์ ร้อยละ 29.7 ปัจจัยเสี่ยงที่สำคัญคือ อายุที่ได้รับการวินิจฉัยว่าเป็นโรคหืด โดยเฉพาะผู้ป่วยอายุน้อยกว่าหรือเท่ากับ 6 ปี ดังนั้นควรที่จะมีการวางแผนการรักษาให้ผู้ป่วยกลุ่มนี้อย่างเป็นระบบ เพื่อที่จะได้ลดหรือป้องกันอัตราการป่วยในผู้ป่วยกลุ่มนี้ได้มากขึ้น

คำสำคัญ : การจัดหืดเฉียบพลัน, การจับหืดซ้ำ

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