



ARAŞTIRMA / RESEARCH

Seasonal differences in the treatment of childhood asthma

Çocukluk çağı astım tedavisinde mevsimsel farklılıklar

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Cukurova Medical Journal 2019;44(4):1357-1363.

Abstract

Purpose: The purpose of the current study was to examine the frequency of respiratory symptoms in children with asthma who were off their medication during summer season.

Materials and Methods: The records of 212 children with mild and moderate asthma were retrospectively analyzed between June and September 2017 at the pediatric pulmonary section, Mersin City Training & Research Hospital. Demographic characteristics, severity of asthma symptoms, current treatment, summer and fall season asthma attacks were compared among groups.

Results: Data for a total 212 children at ages between 31/2 and 18 years were analyzed. Most patients did not report any asthma exacerbations (77.7% in preschool group and 87.0% in school-aged group) during summer. Approximately 42.6% of patients in preschool group and 32.6% of patients in school group showed variable asthma symptoms at the time of their fall clinic visit. Most patients did not report any asthma exacerbations (72.0% in preschool group and 70.9% in school-aged group) during summer. Approximately 44.0% of patients in preschool group and 56.2 % of patients in school group showed variable asthma symptoms at the time of their fall clinic visit.

Conclusion: Most children with mild persistent asthma and moderate persistent asthma did not show any exacerbation in the absence of asthma controller treatment during summer. However, such a practice resulted an increase of asthma exacerbations during the subsequent fall season.

Keywords: Childhood asthma; compliance; exacerbation; summer season

Öz

Amaç: Çalışmamızın amacı, yaz sezonunda astım koruyucu tedavisi almayan çocuklarda astım atak sıklığını araştırmaktır.

Gereç ve Yöntem: Haziran 2017-Eylül 2017 tarihleri arasında Çocuk Göğüs Polikliniğinde hafif ve orta persistan astım tanısı ile takip edilen 212 hastanın dosyası retrospektif olarak incelendi. Hastaların demografik özellikleri, astım şiddeti ve almakta oldukları tedavi, yaz ve sonbahar döneminde atak sıklığı kayıt edildi.

Bulgular: Yaşları 3,5 ile 18 arası toplam 212 çocuğun verileri analiz edilmiştir. Çoğu hasta astım ile ilgili probleminin yaz sezonunda olmadığını bildirmiştir (%77.7 okul öncesi grup ve %87.0 okul dönemi grup).Yaklaşık olarak okul öncesi gruptan %42.6hasta ve okul döneminden %32.6 hastanın sonbahar poliklinik başvurularında değişken astımla ilgili şikayetleri gözlenmiştir. Çoğu hasta astım ile ilgili probleminin yaz sezonunda olmadığını bildirmiştir (%72.0 okul öncesi grup ve %70.9 okul dönemi grup).Yaklaşık olarak okul öncesi gruptan %44.0 hasta ve okul döneminden %56.2 hastada sonbahar poliklinik başvurularında değişken astımla ilgili şikayetleri gözlenmiştir.

Sonuç: Yaz sezonunda hafif ve orta persistan astımlı çocukların çoğunda astım profilaksi tedavisi almamasına rağmen şikayetleri olmamıştır. Ancak ardından gelen sonbahar dönemi hastalarda artmış astım şikayetleri ile ilgili başvurulara neden olmuştur.

Anahtar kelimeler: Çocukluk astımı, uyum, alevlenme, yaz sezonu

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Geliş tarihi/Received: 22.02.2019 Kabul tarihi/Accepted: 26.04.2019 Çevrimiçi yayın/Published online: 15.09.2019

INTRODUCTION

Asthma is the leading cause of chronic inflammatory lung disease in children. The prevalence of childhood asthma has increased over the past several decades affecting as much as 20% of children in some countries¹. It is characterized by reversible small airway obstruction with variable symptoms of wheeze, shortness of breath, chest tightness and/or cough. The symptoms are often triggered by different factors such as allergen or irritant exposure, viral respiratory infections, exercise or change in weather conditions.

The severity or intensity of asthma for each patient is variable. Asthma is classified as intermittent, mild persistent, moderate persistent or severe persistent depending of the magnitude of airflow limitation and frequency of exacerbations². Treatment with regular use of asthma controller medications is highly effective in the management of childhood asthma.

There are seasonal differences in the symptoms of children with asthma. Most of them experience few exacerbations in summer probably due to atopic status and less respiratory viral illnesses^{3,4}. While not recommended in the childhood asthma guidelines, there is a clinical practice among pediatric physicians to temporarily discontinue asthma controller medications in the summer season. Generally they also restart in the fall in most children with asthma in Turkey. There have been no studies yet investigating such a practice in these patients' clinical status when free of asthma controller medications in summer season.

The aim of the current study was to evaluate the seasonal clinical status in children with asthma in the absence of asthma controller medications during summer, clinic visit at fall, and evaluate if such a current practice is appropriate.

MATERIALS AND METHODS

The study was conducted among regularly followed and treated children with asthma (at least a year) at the pediatric pulmonology section of Mersin City Training & Research Hospital. The records of children between ages 3¹/₂ and 17 years diagnosed with mild persistent and moderate persistent asthma whose controller medications were stopped at the beginning of the summer season in the year 2017 were included. The records of 212 children with mild

and moderate asthma were retrospectively analyzed between June and September 2017. The parents were informed that the medications of their children would be temporarily stopped during summer and given clinic appointments to restart their treatments at the beginning of fall. They were also told to record any self rescue β -agonist treatment, or clinic and/or emergency department visits due to asthma symptoms during the summer season. Compliance with fall clinical appointment, any symptoms related to asthma or need for admission to the hospital of the child at the fall visit were included in the study analysis.

Additional study variables were age, male sex, MD-diagnosed parental asthma, age of first asthma symptoms, severity of the illness, atopic status confirmed by laboratory tests, current asthma medications, number of asthma symptoms and hospitalization in the previous year.

The study was reviewed and approved by the Human Subjects Committee of the University Cukurova (Approval No: 16), and that participation involved by informed parental consent.

Statistical analysis

All analysis were performed using IBM SPSS Statistics Version 19.0 statistical software package. Categorical variables were expressed as numbers and percentages, whereas continuous variables were summarized as mean and standard deviation, and as median and minimum-maximum where appropriate. Chi-square test was used to compare categorical variables among groups. For comparison of continuous variables between two groups, the Student's t-test or Mann-Whitney U test was used depending on the statistical hypothesis. Ratios between two groups were compared using z test. The statistical level of significance for all tests was considered to be $p < 0.05$.

RESULTS

The study subjects were classified into two groups as preschool children (aged 3¹/₂-7 years) or school-aged children (aged ≥ 7 years). A total of 118 children were in the preschool group and 94 children in the school-aged group. Table 1 summarizes the characteristics of the patients. The mean age was 5.22 ± 0.90 years [median: 5.5 years (3.5-7)] for preschool children and 10.20 ± 2.67 years [median: 9 years (7-18)] for school-aged children. Male sex, history of parental asthma,

atopic dermatitis defined by a physician, frequency of asthma symptoms and hospitalization in the previous year were similar among groups ($p > 0.05$). Age of first asthma symptoms was reported earlier in preschool children [mean: 1.43 ± 1.06 years; median: 1 year (0.4-4)] than in the school-aged children [mean: 2.44 ± 1.74 years; median: 2 years (1-8)] ($p < 0.001$). There were more mild persistent asthma patients than moderate persistent asthma patients in the preschool group (78.8% versus 21.2%). In contrast, the severity of asthma was almost equally distributed among school-aged children (mild persistent: 48.9% versus moderate persistent: 51.1%).

Atopic status measured by serum Ig E [normal level is < 100 IU; < 7 years; mean: 250.7 ± 285.7 IU and median: 198 IU (17-2100) versus ≥ 7 years; mean: 370.1 ± 430.4 IU and median: 290 IU (17-3610)]

($p = 0.001$) and any inhalant allergen positivity [< 7 years; 54 subjects (45.8%) versus ≥ 7 years; 61 subjects (64.9%)] ($p < 0.001$), and physician diagnosed allergic rhinitis [< 7 years; 29 subjects (24.6%) versus ≥ 7 years; 39 subjects (41.5%)] ($p = 0.013$) was significantly higher in school-aged children than preschool children.

The most common treatment in preschool children was montelukast [80 subjects (67.8%) in < 7 years and 32 (34.1%) in ≥ 7 years; $p < 0.001$]. In contrast, montelukast or inhaled corticosteroid/long acting β agonist combinations (ICS/LABA) were more common in school-aged children (inhaled steroids & montelukast: $p = 0.023$; ICS/LABA: $p = 0.002$) than preschool children. It should be noted that inhaled corticosteroid/LABA combination is not approved in preschool ages.

Table 1. Demographic characteristics of children with asthma

	<7 years n=118	≥ 7 years n=94	p value
Age			
mean*	5.22 \pm 0.90	10.20 \pm 2.67	NA**
median*	5.5 (3.5-7)	9 (7-18)	
Male sex	73 (61.9%)	56 (59.6%)	0.778
Parental asthma	26 (22.0%)	22 (23.4%)	0.869
First asthma symptom*			
mean	1.43 \pm 1.06	2.44 \pm 1.74	< 0.001
median	1 (0.4-4)	2 (1-8)	
Severity of asthma			
mild persistent	93 (78.8%)	46 (48.9%)	NA
moderate	25 (21.2%)	48 (51.1%)	NA
Ig E levels (IU)			
mean	250.7 \pm 285.7	370.1 \pm 430.4	0.001
median	198 (17-2100)	290 (17-3610)	
Inhalen allergen positivity	54 (45.8%)	61 (64.9%)	< 0.001
Allergic rhinitis	29 (24.6%)	39 (41.5%)	0.013
Atopic dermatitis	16 (13.6%)	6 (6.4%)	0.114
Asthma symptoms***			
mean	2.24 \pm 1.16	2.05 \pm 1.33	0.276
median	2 (0-5)	2 (0-6)	
Hospitalization****	21 (17.8%)	13 (13.8%)	0.572
Treatment			
montelukast	80 (67.8%)	32 (34.1%)	< 0.001
inhaled steroids	27 (22.9%)	33 (35.1%)	0.071
inhaled steroids & montelukast	11 (9.3%)	20 (21.3%)	0.023
inhaled steroids & LABA	0 (0.0%)	9 (9.5%)	0.002

*Given in years.

**Statistics not applicable.

**Number of asthma symptoms required treatment in previous year.

***Patients admitted to hospital for asthma in previous year.

Summer and fall seasonal clinical characteristics in children with mild persistent asthma are given in Table 2. Treatment cessation was 3.50 ± 0.61 months [median: 3.5 months (2-4.5)] in preschool children and 3.61 ± 0.68 months [median: 4 months (2-5)] in school-aged children. There were no statistical significance in treatment cessation, self reported asthma symptom, physician and emergency visit for asthma, short acting β agonist use during the summer season, compliance with the fall appointment, asthma symptoms at appointment, or hospitalization for asthma during the fall season among preschool and school children. ($p > 0.05$) Most children in both groups were free of symptoms (preschool group:

77.7% and school children: 87%) and had less need for asthma care (Physician visit; preschool group: 14.9% versus school group: 6.5%. Emergency visit; preschool group: 5.3% versus school group: 2.2%. Reliever medication use; preschool group: 22.3% versus school group 13%) during the summer. However, compliance to fall appointment was 35.1% in preschool children and 45.7% in school-aged children and a significant number of patients had some degree of asthma symptoms (preschool group: 42.6% and school group: 32.6%) and a few hospitalizations (preschool group: 7.4% and school group: 2.2%) at the fall appointment.

Table 2. Features of mild persistent asthma patients

	<7 years n=93	≥ 7 years n=46	p value
Treatment cessation in summer (months)			
mean	3.50 \pm 0.61	3.61 \pm 0.68	0.175
median	3.5 (2-4.5)	4 (2-5)	
Self-reported asthma symptom at summer			
none	73 (77.7%)	40 (87.0%)	0.278
once	14 (14.9%)	4 (8.7%)	0.447
more than once	7 (7.4%)	2 (4.3%)	0.736
Physician visit for asthma at summer			
none	80 (85.1%)	43 (93.5%)	0.248
once	11 (11.7%)	2 (4.3%)	0.267
more than once	3 (3.2%)	1 (2.2%)	0.836
Emergency visit for asthma at summer	5 (5.3%)	1 (2.2%)	0.664
Reliever asthma medication use at summer	21 (22.3%)	6 (13.0%)	0.255
Compliance to clinic appointment at fall	34 (35.1%)	21 (45.7%)	0.359
Asthma symptom at fall appointment			
none	54 (57.4%)	31 (67.4%)	0.340
mild	21 (22.3%)	8 (17.4%)	0.652
moderate	14 (15.0%)	7 (15.2%)	0.825
severe	5 (5.3%)	0 (0.0%)	0.269
Hospitalization at fall	7 (7.4%)	1 (2.2%)	0.272

Summer and fall seasonal clinical characteristics in children with moderate persistent asthma are given in Table 3. Treatment cessation was 3.36 ± 0.77 months [median: 3.5 months (2-4.5)] in preschool children and 3.29 ± 0.79 months [median: 3 months (2-5)] in school-aged children. Similar to children with mild persistent asthma, there were no statistical significances in treatment cessation, self reported asthma symptoms, physician and emergency visits for asthma, short acting β agonist use during the summer season, compliance to the fall appointment, asthma symptoms at the fall appointment, or hospitalization

for asthma during the fall season between preschool and school-aged children ($p > 0.05$). Most children in both groups were free of symptoms (preschool group: 72% and school children: 70.9%). However, in contrast to the mild persistent group, a greater number of school-aged children sought asthma care (Physician visit; preschool group: 20% versus school group: 25%. Emergency visit; preschool group: 4% versus school group: 10.4%. Reliever medication use; preschool group: 28% versus school group 31.3%) during the summer. Compliance to the fall appointment was 32% in preschool children and

54.2% in school-aged children, and similar to mild persistent children a significant number of patients had some degree of asthma symptoms (preschool

group: 44% and school group: 56.2%) and hospitalizations (preschool group: none and school-aged group: 14.6%) at the fall appointment.

Table 3. Features of moderate persistent asthma patients

	<7 years n=25	≥7 years n=48	p value
Treatment cessation in summer (months)			
mean	3.36±0.77	3.29±0.79	0.765
median	3.5 (2-4.5)	3 (2-5)	
Self-reported asthma symptom at summer			
none	18 (72.0%)	34 (70.9%)	0.861
once	5 (20.0%)	10 (20.8%)	0.822
more than once	2 (8.0%)	4 (8.3%)	0.685
Physician visit for asthma at summer			
none	20 (80.0%)	36 (75.0%)	0.851
once	5 (20.0%)	9 (18.7%)	0.857
more than once	0 (0.0%)	3 (6.3%)	0.517
Emergency visit for asthma at summer	1 (4.0%)	5 (10.4%)	0.657
Reliever asthma medication use at summer	7 (28.0%)	15 (31.3%)	0.999
Compliance to clinic appointment at fall	8 (32.0%)	26 (54.2%)	0.087
Asthma symptom at fall appointment			
none	14 (56.0%)	21 (43.8%)	0.457
mild	8 (32.0%)	13 (27.1%)	0.867
moderate	3 (12.0%)	14 (29.1%)	0.177
severe	0	0	
Hospitalization at fall	0 (0.0%)	7 (14.6%)	0.087

DISCUSSION

Seasonal and geographic variations in childhood asthma are well recognized with the lowest incidence during summer, highest in fall, and fluctuations through winter and spring^{5,6}. The fall peak in childhood asthma exacerbation is thought to be related to an increase in viral infections and allergen exposure when children return to school or spend more time indoors. After summer break, the fall season is associated with an increase in scheduled or unscheduled visits to physicians, prescriptions of asthma medications and even hospitalization in children with asthma⁷⁻⁹. This evidence has prompted a practice among most pediatric specialist and subspecialist (pediatric allergists and pediatric pulmonologists) in our country to advise cessation of asthma controller medications in most children with asthma over the summer if they are free of symptoms in the previous summer break, and restart early in the fall season. However, to our knowledge, this practice

has never been recommended in the pediatric asthma guidelines and we aimed to investigate if such advice was appropriate.

As previously reported in the literature, the current study confirms children with mild persistent and moderate persistent asthma have less symptoms of their illness during the summer season. Furthermore, most of these children experienced fewer exacerbations in the absence of any asthma controller medication during summer break. Unfortunately, this was associated in our patient population with subsequent missed appointment for clinic visits in approximately 2/3 of children with mild persistent and 1/2 of children with moderate persistent asthma even though parents had been informed that the asthma controller medications would be restarted at fall. Not surprisingly, a considerable number of patients presented with variable degree of asthma exacerbations at fall season.

A large retrospective longitudinal observational analysis using US health care claims investigated

pharmacy based dispensing of fluticasone propionate plus salmeterol in a single inhaler (FSC) between June and November in patients with asthma¹⁰. The patients were categorized as children (4-11 years), adolescents (12-18 years) and adults (19-55 years). Summertime dispensings of FSC were associated with a significantly lower risk of asthma exacerbations or hospitalization than nondispensings in all age groups. This protective effect also persisted for all patient groups with fall dispensings of FSC and decreased the risk of serious asthma-related outcomes in the fall season. It would be ideal if the current study had a group of children with mild persistent and moderate persistent asthma who were on the controller medications during the summer season to compare the features of children who were off the medications. Unfortunately, there were only a limited number of patients on the controller medications at the summertime (especially in the mild persistent group) and thus, a comparison with the current nonmedicated groups was not possible.

Obviously, the major limitation of our study is the relatively small number of participants. Thus, it may not be appropriate to recommend or advise against cessation of asthma controller medications generally in children with asthma during summer break based on our data. Our findings should be supported with additional studies in large group of children in our country. It should also be noted that children with asthma living in different geographic areas may show different variations in the exacerbation of symptoms. Therefore, physicians must be aware of seasonal trends in asthma exacerbations in their areas. In our study, few children with asthma had symptoms in summer season. Because of the limited number of participants, we were not able to identify any risk factors (e.g., atopic status, indoor smoking, crowded living conditions) in the development of their exacerbations. This might be important to determine who is at risk of developing asthma exacerbation during summer season. Such a practice should not be recommended in these subsets of patients. In a study investigating seasonal risk factors for asthma exacerbations among inner city children in the US, impaired pulmonary function, as measured by FEV₁/FVC ratio; allergic sensitivity to *Alternaria*; elevated blood eosinophils; requirement for higher levels of ICS to maintain control; and an exacerbation in the previous season were determinants of asthma symptoms during summer season¹¹.

The results of our study also indicate the importance

of the fall clinic appointment to reduce the fall exacerbation rate in children with asthma. Additional efforts (e.g., reminder post cards, phone calls) need to be used to improve compliance in these patients.

In conclusion, the current study has shown cessation of asthma controller medications during summer break with mild persistent and moderate persistent asthma appears to be safe in the majority of children. However, such a practice is associated with missed fall appointments with variable asthma exacerbations in patients during the fall season. The parents of children with asthma should be sufficiently informed to restart asthma controller medications early in the fall to avoid any illness problems.

Yazar Katkıları: Çalışma konsepti/Tasarımı: AÖ, DD; Veri toplama: DD; Veri analizi ve yorumlama: AÖ; Yazı taslağı: AÖ; İçeriğin eleştirel incelenmesi: DD; Son onay ve sorumluluk: AÖ, DD; Teknik ve malzeme desteği: AÖ; Süpervizyon: AÖ, DD; Fon sağlama (mevcut ise): yok.

Bilgilendirilmiş Onam: Katılımcılardan yazılı onam alınmıştır.

Hakem Değerlendirmesi: Dış bağımsız.

Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.

Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.

Author Contributions: Concept/Design : AÖ, DD; Data acquisition: DD; Data analysis and interpretation: AÖ; Drafting manuscript: AÖ; Critical revision of manuscript: DD; Final approval and accountability: AÖ, DD; Technical or material support: AÖ; Supervision: AÖ, DD; Securing funding (if available): n/a.

Informed Consent: Written consent was obtained from the participants.

Peer-review: Externally peer-reviewed.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support

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