Determining the Relationship between the Influenza Vaccination and Disease Control in Children with Asthma

Astımlı Çocuklarda İnfluenza Aşısı İle Hastalık Kontrolü Arasındaki İlişkinin Belirlenmesi

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ABSTRACT

Objective: The influenza vaccine's effect on the control of asthma is debatable. The purpose of this study was to investigate the effect of the influenza vaccine on disease control in children with asthma.

Material and Methods: Children with a diagnosis of asthma were prospectively included in this study. The socio-demographic characteristics of the patients, the status of influenza vaccination within the previous year, the use of bronchodilators and systemic steroid therapy, the frequency of hospitalization, risk factors which may affect the disease's control status, and the effects of vaccination status were investigated.

Results: A total of 187 asthmatic children with a median age of 11 years were included in this study. Almost half of the patients (47.6%) did not have their asthma under control. In the last year, 14.4% had one asthma attack, 14.4% had two attacks, 19.3% had ≥3 attacks, while 51.9% had no asthma attack. In the previous year, 52.4% of the patients received an influenza vaccination. Influenza vaccination was equally common in those patients with controlled and uncontrolled asthma (54.1% vs 50.6%), and vaccination had no effect on disease control (p=0.662). Those patients with allergic rhinitis and atopy had a significantly higher uncontrolled asthma status than those without allergic rhinitis (p=0.027 and p=0.041, respectively). Children with uncontrolled asthma used less prophylactic drugs than those with controlled asthma (p<0.001).

Conclusion: The influenza vaccine has no effect on disease control in children with asthma. Having allergic rhinitis and atopy reduces the control of this disease.

Key Words: Asthma, Allergic rhinitis, Child, Influenza, Vaccine

ÖZ

Amaç: İnfluenza aşısının astım kontrolü üzerindeki etkisi tartışmalıdır. Bu çalışmanın amacı astımlı çocuklarda influenza aşısının hastalık kontrolüne etkisini araştırmaktır.

Gereç ve Yöntemler: Astım tanısı alan çocuklar prospektif olarak çalışmaya dahil edildi. Hastaların sosyo-demografik özellikleri, bir önceki yılda influenza aşısı olma durumu, bronkodilatatör kullanımı ve sistemik steroid tedavisi, hastaneye yatış sıklığı, aşılam durumunu ve hastalığın kontrol durumunu etkileyecek risk faktörleri araştırıldı.

Bulgular: Çalışmaya ortanca yaşı 11 olan toplam 187 astımlı çocuk dahil edildi. Hastaların yaklaşık yarısında (%47.6) astım kontrol altında değildi. Son bir yılda %14.4'ü, %14.4'ü iki, %19.3'ü ≥3 atağı geçirirken, %51.9'u astım atağı

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geçirmedi. Bir önceki yılda hastaların %52.4'ü grip aşısı olmuştu. İnfluenza aşılaması, kontrollü ve kontrolsüz astımı olan hastalarda eşit oranda yaygındı (%54.1'e karşı %50.6) ve aşılamanın hastalık kontrolü üzerinde etkisi yoktu (p=0.662). Alerjik riniti ve atopisi olan hastalarda, alerjik riniti olmayan hastalara göre anlamlı olarak daha yüksek kontrolsüz astım durumu vardı (sırasıyla p=0.027 ve p=0.041). Kontrolsüz astımı olan çocuklar kontrol grubuna göre daha az profilaktik ilaç kullanmışlardı (p<0.001).

Sonuç: İnfluenza aşısının astımlı çocuklarda hastalık kontrolüne etkisi yoktur. Alerjik rinit ve atopiye sahip olmak hastalığın kontrolünü azaltır.

Anahtar Sözcükler: Astım, Allerjik rinit, Çocuk, İnfluenza, Aşı

INTRODUCTION

Asthma is the most common chronic disease in children in developed countries, and it is one of the leading causes of paediatric hospitalization (1,2). Although its prevalence varies by country, it has been reported to occur at a rate of 1-18% (3-5). Acute asthma attacks are a clinical picture which has a significant impact on both children and their parents. In children, asthma is usually diagnosed after the first attack, and these attacks account for the vast majority of subsequent hospitalizations (6). Poor asthma control can lead to severe asthma exacerbations (7). In terms of asthma control, Peters S.P. et al. (8) reported in a study with 1.003 patients in the United States that the rates of unplanned physician and emergency department visits in children with uncontrolled and controlled asthma were 70%-43% and 36%-10%, respectively.

For asthmatic patients of all ages, viral upper respiratory tract infections (URTIs) are accepted as the primary trigger (>80%) factors (9,10). In children aged 6-17 years (55%) and infants/pre-schoolers (33%), rhinovirus was the most common virus identified in asthma exacerbations of proven viral origin. However, influenza is only responsible for 0-7% of virus-induced asthma exacerbations, and there is insufficient evidence that it poses an additional risk in asthmatic children (12). Although the influenza vaccination is recommended in many countries in order to reduce asthma exacerbations in children, most children do not get vaccinated (13,14). Furthermore, the effect of the influenza vaccine on the frequency of attacks in children with asthma throughout the year is controversial. Although there are some studies that demonstrate that the influenza vaccine reduces the number of attacks in children with asthma, there are also other studies which have shown that it has no effect (15,16).

Our primary aim in this study was to examine the effects of the influenza vaccine on attack frequency and asthma control in children with asthma.

MATERIALS and METHODS

This study included all asthma patients who had been followed up at a paediatric allergy outpatient clinic for at least one year. The patients were contacted by phone, and after providing the parents with verbal information about this study, written/verbal consent was obtained from those parents who agreed to participate in this study. Those patients who could not be reached by phone or who provided incomplete data were excluded from this study. The hospital's ethics committee granted approval for this study.

The patients' socio-demographic data were recorded and included in this study. The patients were called and asked questions from questionnaire forms. The patients contacted by phone were asked about their influenza vaccination status in the previous year, their use of bronchodilator and systemic steroid therapy, any emergency service admissions, their frequency of hospitalizations, and any risk factors (atopy, smoking, crowded environment, school situation) affecting disease control. All data were recorded by a paediatric allergist.

Statistical Analysis

The data were analysed using the program SPSS 25.0 (IBM, Armonk, NY: IBM Corp.). Mean ± standard deviation for parametric tests, as well as median and categorical variables for non-parametric tests are expressed as numbers and percentages in the presentation of continuous variables. The Kolmogorov-Smirnov test was used to determine whether the data conformed to the normal distribution. To assess the relationship between two variables, a simple correlation test was used. To examine the differences between categorical variables, chi-square analysis was used. In all analyses, p<0.050 was considered statistically significant.

RESULTS

203 patients were included in this study. This study excluded 14 patients who could not be reached by phone and two patients who had missing data (Figure 1). In this study, which was completed with a total of 187 patients, the M/F ratio was 1.5/1, the median age was 11.0 years (min 5.0 - max 19.0, IQR 9.0-14.0), and 61.5% (n=115) of the patients were in the 5-12 years old age range (Table I). Almost half of the patients (47.6%) did not have their asthma under control. Having only one asthma attack in the previous year was observed with a frequency of 14.4%, two attacks with a frequency of 14.4%, and ≥3 attacks with a frequency of 19.3%, while 51.9% of the patients had no asthma attack with the previous 12 months (Table I). Furthermore, when the patients' asthma attacks during influenza infections were examined, 58.8% had no

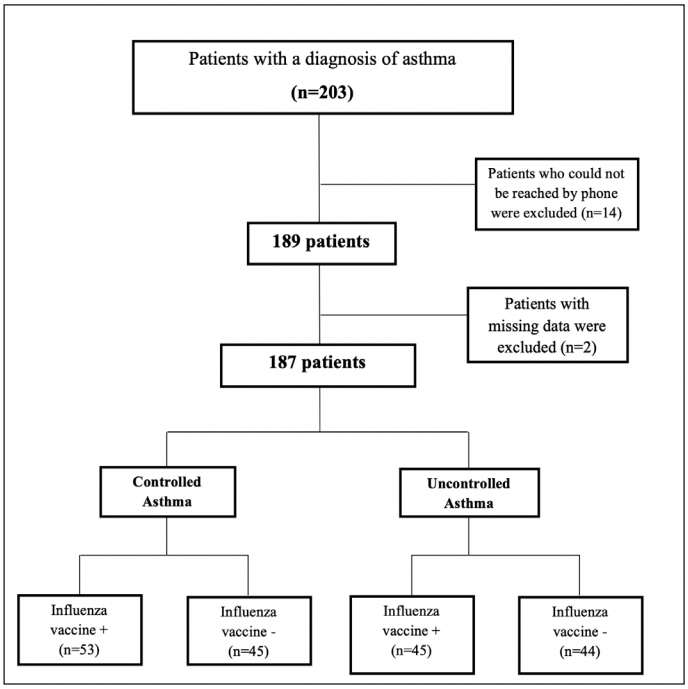

Figure 1: Distribution of patients included in the study.

Table I: Demographic data of patients, disease and vaccination status

Gender (M/F)	1.5 / 1
Age (Year) [median (min-max)]	11.0 (5.0 – 19.0)
Age groups(year)*	
5-12	115 (61.5)
≥12	72 (38.5)
Asthma control status*	
Under control	98 (52.4)
Uncontrolled	89 (47.6)
Frequency of asthma attacks*	
0	97 (51.9)
1	27 (14.4)
2	27 (14.4)
≥3	36 (19.2)
Frequency of asthma attacks during influenza infection*	
0	110 (58.8)
1	23 (12.3)
2	25 (13.4)
≥3	29 (15.5)
Influenza vaccination in the last 1 year*	
No	89 (47.6)
Yes	98 (52.4)

M: *male,* ***F:*** *female,* ***max:*** *maximum,* ***min:*** *minimum,* *******: (n,%)*

attack, 12.3% had only one attack, 13.4% had two attacks, and 15.5% had at least 3 asthma attacks. Furthermore, when the risk factors which may cause an asthma attack were investigated, 44.9% of the patients had risk factors such as cigarette smoke exposure, 54.0% had allergic rhinitis, 70.0% had school-age siblings, and 41.2% had risk factors such as living in a crowded environment (Table II). While 47.1% (n=88) of the patients received prophylactic treatment, only 26.7% (n=50) of them were receiving it on a regular basis.

Table II: Asthma attack risk factors in patients

Risk factors	n (%)
Cigarette smoke exposure	
Yes	84 (44.9)
No	103 (55.1)
Allergic rhinitis	
Yes	101 (54)
No	86 (46)
Siblings attending school	
Yes	131 (70)
No	56 (30)
Living in a crowded environment	
Yes	77 (41.2)
No	110 (58.8)

Table III: Comparison of patients' influenza vaccination with asthma status, exacerbation and hospitalization frequency

	influenza vaccine		p
	-	+	
Asthma control status*			
Under control	45 (50.6)	53 (54.1)	0.662
Uncontrolled	44 (49.4)	45 (45.9)	
Having an asthma attack during an influenza infection*			
No	51 (57.3)	59 (60.2)	0.766
Yes	38 (42.7)	39 (39.8)	
Hospitalization*			
No	3 (3.4)	3 (3.1)	0.841
Yes	86 (96.6)	95 (96.9)	

***** *n(%)*

It was observed that 52.4% (n=98) of the patients in this study had received an influenza vaccination within the previous year (Table I). The rate of influenza vaccination was 54.1% in those patients with controlled asthma and 50.6% in those with uncontrolled asthma, and it was determined that the influenza vaccination had no effect on disease control (Table III) (p=0.662). In terms of having an asthma attack during an influenza infection, there was no significant difference between the groups of patients with or without the influenza vaccine (39.8% vs 42.7%, respectively) (Table III) (p=0.766). The influenza vaccine had no effect on the annual number of attacks, absenteeism from school, or hospitalization rates due to asthma attacks in the children with asthma (Table III).

When the risk factors for asthma attacks were examined, those patients with allergic rhinitis were statistically significantly more likely than those without allergic rhinitis to have uncontrolled asthma (55.4% vs 38.3%, respectively) (p=0.027) (Table IV). Furthermore, uncontrolled asthma was observed to be more prevalent in those patients with atopy than in the asthmatic patients without atopy (55.7% vs 40.4%, respectively) (p=0.041) (Table IV). There was no statistically significant difference in cigarette smoke exposure between those with controlled asthma and those with uncontrolled asthma (p=0.244).

Prophylactic drug use was found to be significantly lower in those children with uncontrolled asthma than in those with

Table IV: The effect of risk factors on patients' asthma status

Risk factors	Asthma control status		Total*	p
	Under control*	Uncontrolled*		
Allergic rhinitis				
No	53 (61.7)	33 (38.3)	86 (100)	0.027
Yes	45 (44.6)	56 (55.4)	101 (100)	
Atopy				
No	59 (59.6)	40 (40.4)	99 (100)	0.041
Yes	39 (44.3)	49 (55.7)	88 (100)	
Exposure to cigarette smoke				
No	58 (3.4)	45 (3.1)	103 (100)	0.244
Yes	40 (96.6)	44 (96.9)	84 (100)	
Prophylactic drug use				
No	67 (67.7)	32 (32.3)	99 (100)	<0.001
Yes	31 (35.2)	57 (64.8)	88 (100)	

***** *n(%)*

controlled asthma (p<0.001) (Table IV). It was observed that the influenza vaccine had no effect on prophylactic drug use (p=0.187).

DISCUSSION

Asthma is the most common chronic respiratory disease in children and adolescents around the world (1,2,17). Despite its high prevalence, poor results are still obtained in cases of childhood asthma, and even child death is reported each year, despite the fact that it is preventable (17). Asthma management's main goals are to provide good control of asthma-related symptoms while minimizing the risk of exacerbations and/or complications (18). The World Health Organization (WHO), the United States of America (USA), and some European countries (19,20) recommend the influenza vaccination for aetiology to ensure asthma control. In addition, influenza infections may lead to severe asthma attacks, which usually require hospitalization (11). On the other hand, the rate of influenza vaccination in high-risk groups, such as those with asthma, remained far below the 75% target (58.6% between the ages of 6 months and 17 years in 2020-2021) (21,22). Parental and physician confusion about the benefits of the influenza vaccination and the role of immunization in preventing asthma attacks in this population is one of the barriers to compliance (23). The effect of the influenza vaccine on disease control and attack frequency in children with asthma was investigated in this study.

While asthma is more common in males in childhood, it is more common in females in adulthood. The reversal of this gender disparity in prevalence suggests that pubertal hormones may be involved in the aetiology of asthma (24). As in the literature, patients with asthma were found to be males more frequently in our study. According to the Centres for Disease Control and Prevention (CDC), half of all children with asthma (50.3%) do not have the disease under control (25). In our study, asthma was not under control in almost half of the patients (47.6%). This result supported the literature.

Many guidelines recommend an annual influenza vaccination for children with asthma, but there is insufficient clinical evidence to support this (26,27). In recent years, the findings of studies investigating the effect of the influenza vaccine on the number of attacks and disease control in children with asthma have remained contentious. Although there are some publications stating that the influenza vaccine reduces asthma attacks, health-care utilization, other respiratory diseases, and the number of asthma medications used, the fact that the majority of these are observational studies with low-quality evidence has led to biased and controversial results (28-31). Watanabe S. et al. (31) identified that the influenza vaccine reduced the incidence, frequency, and duration of attacks in 201 asthmatic children aged 1-15 years compared to a control group in a randomized controlled study. Additionally, Smitz et al. (32) reported in their retrospective study of preschool children with asthma that the influenza vaccine reduced the number of lower respiratory tract infections and acute otitis media. According to Ong et al. (33), the influenza vaccine reduced the use of oral steroids in children with asthma. In our study, asthmatic children who received or did not receive the influenza vaccine had similar attack frequencies and disease control. In contrast to the literature, our study showed that the influenza vaccine had no effect on the frequency of attacks in children with asthma. This can be attributed to the fact that our study was based on a questionnaire which obtained information from the families about the past, which may have resulted in insufficiently accurate information.

Aside from viral infections, atopic structure and allergic rhinitis have been identified as risk factors for asthma attacks in children, making the disease difficult to control (34,35). Uncontrolled disease was more common in those children with allergic rhinitis and atopic structure according to our study, which supports the literature. Additionally, it was discovered in the study conducted by JR DiFranza et al. (36) that exposure to cigarette smoke may trigger asthma attacks in children, making it challenging to control this disease. In our study, it was observed that exposure to cigarette smoke had no effect on the control of asthma or the frequency of attacks. The failure of families in our study to adequately explain their smoking/child exposure may have contributed to this result.

Limitations of this study include: (1) the single-centre nature of our study, which limits the generalizability of our findings; and (2) being a survey study with no face-to-face interviews resulting in concerns regarding the proficiency of our data.

In conclusion, it was observed in our study that the influenza vaccine had no effect on attack frequency or disease control in

children with asthma. However, based only on the data of our study, we cannot generalize that children with asthma do not need to be vaccinated against influenza. Larger, multicentre, and randomized controlled studies on this subject are needed.

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