Seropositivity for Chlamydia Pneumoniae and Mycoplasma Pneumoniae in Asthmatic Children

Bronşiyal Astımlı Çocuklarda Chlamydia Pneumoniae ve Mycoplasma Pneumoniae Seropozitifliği

Astımlı Çocuklarda Chlamydia Pneumoniae ve Mycoplasma Pneumonia /
Chlamydia Pneumoniae and Mycoplasma Pneumoniae in Asthmatic Children

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Özet

Akut solunum yolu enfeksiyonları astımlı çocuk hastalarda akut astım atağını tetikleyebilir ve etyopatogenezde sorumlu tutulabilir. Bakteriyel enfeksiyonlar daha az dikkati çekmekle beraber son zamanlarda özellikle Chlamydia pneumoniae (CP) ve Mycoplasma pneumoniae (MP) olası etken olarak bildirilmektedir. Bronşiyal astımlı (3-14 yaş arası) 66 çocuk hastada CP ve Mycoplasma pneumoniae IgM ve IgG seroprevalansı araştırıldı. Toplam 66 olgunun 18'inde (%27.2) CP IgG, 27'sinde (%40.9) MP IgG pozitifliği saptandı. Kontrol grubunun 6'sında (%13.0) CP IgG, 6'sında (%10.8) MP IgG pozitifliği saptandı. Astım hastalarında MP IgG seropozitifliği olanların oranı kontrol grubunun 4 katı fazlaydı. Daha sık atak geçirenlerde CP IgG antikoru seropozitifliğinin daha fazla olduğu görüldü. M. pneumaniae IgG antikoru seropozitifliği açısından böyle bir farklılığa rastlanmadı. CP ve MP enfeksiyonlarının çocuklarda bronşiyal astım ve astım atağı etyolojisinde önemli yer tuttuğuna dair pek çok çalışma vardır. Sonuçlarımız her iki mikroorganizmanın bronşiyal astım etyopatogenezinde ve astım atağı sayısının artışında etkili olduğunu ortaya koymaktadır.

Anahtar Kelimeler

Bronşiyal Astım; Chlamydia Pneumoniae; Mycoplasma Pneumoniae; Çocuk

Abstract

Acute respiratory tract infections may trigger acute asthma attacks and may be held responsible for etiopathogenesis in children with asthma. Although bacterial infections attract a limited amount of attention, recently Chlamydia pneumoniae (CP) and Mycoplasma pneumoniae (MP), in particular, are reported to be the possible factors. IgM and IgG seroprevalence was investigated in 66 children patients with bronchial asthma (between the ages of 3 and 14) for CP and Mycoplasma pneumoniae. In a total of 66 cases, 18 (27.2%) patients were detected with IgG positivity for CP whereas 27 of them (40.9%) were detected with IgG positivity for MP. IgG positivity was determined in 6 patients (13.0%) in the control group for CP, and in 6 patients (10.8%) in the control group for MP. The rate of the asthma patients with IgG seropositivity for MP was 4 times higher than that of the control group. It was seen that IgG antibody seropositivity for CP was higher in those with more frequent attacks. No such difference was observed in terms of IgG antibody seropositivity for M. pneumoniae. There are many studies indicating that CP and MP infections take an importance place in the etiology of bronchial asthma and asthma attacks in children. The results obtained reveal the effect of both microorganisms on the etiopathogenesis of the bronchial asthma and the increased number of asthma attacks.

Keywords

Bronchial Asthma; Chlamydia Pneumoniae; Mycoplasma Pneumonia; Children

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Introduction

Bronchial asthma is a chronic disease characterized by bronchial hypersensitivity, increased responsiveness of the airway and variable airway obstruction as a result of chronic airway inflammation [1-3]. Paroxysmal coughing, dyspnea, wheezing and chest tightness occur as a result of this inflammation in the airways of sensitive people. These symptoms are accompanied by diffuse yet variable respiratory tract obstruction which is reversible spontaneously or by treatment [3]. The resulting histopathological changes are related with the persistent airway inflammation and hypersensitivity and are responsible for the chronic base of the disease [4]. The frequency of asthma varies from 13 to 15% in the studies conducted with ISAAC method in our country.

Although the exact reason of childhood asthma has not been indicated, the recent investigations have emphasized the interaction between the environmental and genetic factors[4]. The correlation between the childhood asthma and allergy has revealed that the environmental factors are responsible for the differentiation of the immune system of the sensitive individuals towards the asthma phenotype [4]. The studies performed have demonstrated that the infants treated for respiratory tract more frequently experience asthma, and that the patients with asthma more frequently suffer from respiratory tract infections [5].

The incidence of Mycoplasma Pneumoniae (MP) is considered as 20-30% [6, 7], whereas that of Chlamydia Pneumoniae (CP) is regarded as 15-20% [7, 8] in children population.

The data obtained from epidemiological and experimental animal studies have demonstrated that the viruses, particularly Adenovirus [9] and Respiratory Syncytial Virus [9] and MP [10] and CP [11, 12] as well as two atypical bacteria may result in persistent infection and play a part in the pathogenesis of asthma. The discussions are still ongoing whether the correlation between MP or CP and asthma is causal or accidental. The persistent chlamydial infections usually remain untreated since they progress silently and slowly. Serious sequelae are not common. Additionally, MP exhibits growth characteristics in mucosal epithelial cells and endothelial cells whereas CP exhibits growth characteristics in alveolar macrophages and smooth muscle cells that are related to asthma [8, 13]. The presence of the significant correlation between the indicators of asthma severity and extent of the antibody titers against MP and CP has not been established for the other common respiratory tract agents [14]. This is regarded as a strong evidence in support of CP. CP has been found to inhibit the ciliary activity in ciliated epithelial cells in vitro [15]. CP stimulates proinflammatory cytokine synthesis in human peripheral mononuclear cells and alveolar macrophages[16, 17]. Although seroepidemiological studies espouse the judgment that the essential role of MP and CP is to increase the inflammation and stimulate the disease status, [14, 18] the possibility that the disease is occasionally developed due to these agents can not be excluded. There are actual data regarding that it may be applicable in certain cases [18,19].

Sabato has monitored 108 children between the ages of 1.1 and 15.8 who were determined to suffer from MP infection as specified with complement fixation test throughout the acute disease period and the following 3 years and determined the rate of development of wheezing [20]. The incidence of development of wheezing with acute infection was found higher (40%) than expected with respect to normal children population. The findings have shown that MP affects motor tonus even in non-asthmatic children and that bronchodilator therapy provides benefit. This study suggests that MP results in pulmonary damage or may affect the pulmonary development even after years following infection.

Our aim is to determine the seropositivity for MP and CP and to examine the correlations between them and pathogenesis of asthma, asthma attack and asthma treatment.

Material and Method

A total of 66 patients between the ages of 3-14, of whom 17 were female and 49 were male, with chronic persistent asthma monitored with the diagnosis of bronchial asthma in Dicle University Faculty of Medicine Pediatric Chest Diseases Unit were enrolled in our investigation. The patients were subjected to a follow-up period of 1-3 months. The other reasons of bronchial obstruction were excluded by the history, physical examination, laboratory and imaging methods. Sixteen female and 30 male healthy children of similar ages without recurrent symptoms of asthma and without family and personal history of doctor-diagnosed asthma and atopy were enrolled in the study as the control group. All the patients enrolled in the study were examined in terms of antibody positivity for MP and CP by conducting Indirect Immunofluorescent Antibody Method. This method was applied via EUROIMMUN device. Reaction positivity was considered affirmative in 1/10 titers for MP antibodies and in 1/100 titers for CP [21, 22].

Statistics

The comparison of IgM and IgG antibody seropositivity for MP and CP between the patients with asthma and control group as well as the correlation between the rate of attack/year and seropositivity was evaluated by Chi-square methods using SPSS Software 10 program.

Findings

In this study, a total of 66 cases between the ages of 3 and 14, of whom 17 were female (25.7%) and 49 were male (74.2%), were assessed to examine the correlation between MP and CM infections and the etiology of Bronchial asthma and asthma attack. A total of 46 healthy children, of whom 16 (34.7%) were female and 30 (65.2%) were male, of similar ages without doctor-diagnosed asthma and presenting with a history devoid of recurrent symptoms of coughing, dyspnea and wheezing were enrolled in the study as the control group (Table 1).

The symptoms at the time of first application were found as coughing in 61 (92.4%) patients, dyspnea in 55 (83.3%) pa-

Table 1. Gender distribution in patient and control groups

	Female		Male		Total	
	n	%	n	%	n	%
Asthma	17	25.7	49	74.2	66	58.9
Control	16	34.7	30	65.2	46	41.1
Total	33	29.4	79	70.5	112	100

tients, wheezing in 55 (83.3%) patients and fever in 11 (16.6%) patients with asthma. Family history of atopic disease was found positive in 28 (42.4%) patients (Figure 1).

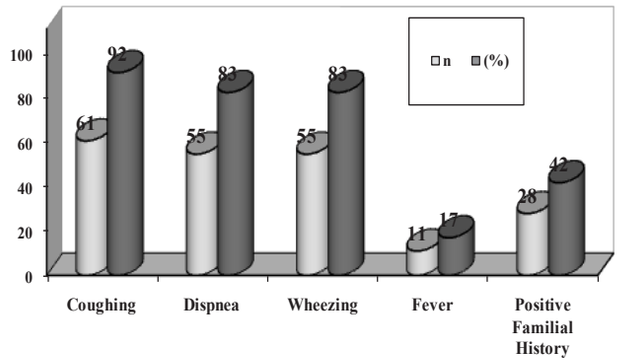


Figure 1. Complaints of patients at the time of application

Among a total of 66 cases, 18 (27.2%) patients were detected with IgG seropositivity for CP whereas 1 (1.5%) patient was detected with IgM seropositivity for CP. CP IgG (x^2=3.26, p=0.056) was reported in 6 (13.0%) patients while CP IgM was reported in 1 (2.1%) patient out of a total of 46 individuals in the control group. IgG seropositivity for CP was found 2 times higher in asthmatic patients than that of the control group; however, it was not found as statistically significant by a narrow margin (x^2=3.26, p=0.056). Among a total of 66 cases, 27 (40.9%) patients were detected with IgG seropositivity for MP whereas 6 (9.1%) patients were detected with IgM seropositivity for MP. In the control group of 46 people, 6 (10.8%) individuals were detected with IgG seropositivity for MP whereas IgM seropositivity for MP was determined in 2 (4.3%) patients. IgG seropositivity for MP was found statistically significantly higher in asthmatic patients with respect to the control group (x^2=11.986, p=<0.001). IgG and IgM values are shown in Table 2 and Table 3, respectively.

Table 2. IgG seropositivity for CP and MP

	CP					MP				
	Negative		Positive		Total	Negative		Positive		Total
	n	%	n	%	(n)	n	%	n	%	(n)
Asthma	48	72.7	18	27.2	66	39	59.0	66	40.9	66
Control	40	86.9	6	13.1	46	41	89.1	46	10.9	46
Total	88	78.5	24	21.5	112	80	71.4	112	28.5	112
	x^2=3.26,p=0.056					x^2=11.986; p=<0.001				

Table 3. IgM seropositivity CP and MP

	CP					MP				
	Negative		Positive		Total	Negative		Positive		Total
	n	%	n	%	(n)	n	%	n	%	(n)
Asthma	65	98.4	1	1.5	66	60	9.1	6	90.9	66
Control	45	97.8	1	2.1	46	44	95.6	2	4.3	46
Total	110	98.2	2	1.7	112	104	92.8	8	7.1	112
	insignificant					x^2=0.919p=0.285				

IgG antibody seropositivity for CP was found higher in the group with more frequent attacks when examined in 2 groups with the number of attacks <4 and ≥4 (x^2=13.917, p<0.001). No such difference was determined in terms of IgG antibody seropositivity for MP (x^2=0.991, P=0.229) (Figure 2).

IgG antibody seropositivity for CP and MP did not differ between the female and male gender (for CP: x^2=0.296, p=0.520; for MP: x^2=0.001, p=0.683). With respect to the age groups, antibody seropositivity for both MP (59.2%) and CP (55.5%) was found higher in the age group of 7-10.

Discussion

Although asthma has been well established and can be treated efficiently in the recent years, increased prevalence and increased rates of emergency department application are noted. It is important to specify the underlying pathogenetic mechanisms and to conduct the treatment accordingly as a worldwide health problem of great importance.

On the one hand there is a discussion to determine which factors contribute to the development of asthma [23], on the other hand the importance of genetic in the development of asthma, particularly atopic asthma has been understood (24, 25) and a close link has been established between the environmental stimulants and development of asthma [23, 26, 27]. Further, epidemiological studies indicate the potential role of infection in the development of airway inflammation. Viral infections are the most common trigger of the asthma attacks[28]. No significant correlation was established between the viral respiratory infections and wheezing in adult patients with asthma [29].

The correlation between the bacterial infections and asthma attacks was less remarkable as compared to the viral infections. MP and CP are possible cofactors accused of the development and exacerbation of asthma [10, 30].

Although childhood infections have been proven to provide protection against atopy and asthma development [26], it has been shown that the extended presence of certain microorganisms in the bronchi may be associated with the development of asthma. CP and MP infections are held responsible for the pathogenesis of asthma also in children. Emre et al. [31] examined CP-positive cases with asthma to investigate whether they produce CP specific IgE antibody. CP specific IgE was determined in 12 of 14 subjects with culture positive asthma, 1 of 11 subjects with culture positive pneumonia, 2 of 11 asthmatic culture negative children presenting with wheezing and 2 of 9 culture-negative children without symptoms in the study; however, atopic condition of the asthmatic patients and control group was not reported. There are limited studies to demonstrate the effects of previous infection on the frequent asthma episodes in children. Based on the findings obtained from our study, the rate of IgG seropositivity for CP was found higher in patients with more frequent asthma attacks as compared to those undergoing fewer episodes.

Hahn et al. [32] have reported the correlation between CP infection and the attack and probable persistency of asthma. They also reported that 9 of 19 patients with CP infection clinically presented with symptoms of bronchospasm, and that only 2 of them were known to have chronic obstructive pulmonary disease. The asthma group also demonstrated significant IgG positivity in our study. Although

insignificant, there were numerically more cases of IgM positivity than the control group.

Viral chlamydial and mycoplasmal respiratory tract infections are known to result in over-responsiveness of the airway via certain mechanisms such as virus specific IgE production, epithelial damage, granulocyte dependent inflammation and increased mediator release, and to have an important part in the etiology of bronchial asthma [5, 29]. Therefore, determining the previous viral or mycoplasmal respiratory tract infection is essential in describing the etiology of asthma in patients with bronchial asthma. As particularly IgG antibody level remains high following the infection for years, (+) test result also indicates the previous MP and CP infections [30]. In 1986, Korppi et al. [33] conducted a study in 127 children with wheezing under the age of 2, and determined the rate of infection agents as 56%. The highest rate was found for RSV (71%), whereas MP was seen only with a rate of 4%. The findings of our study also support the role of previous mycoplasmal and chlamydial infections in asthma. IgG seropositivity for CP was found two times higher in the asthmatic patients as compared to the control group, and IgG seropositivity for MP was determined as statistically significantly high.

Generally, MP and CP infections are slightly more common in male subjects in the age group of children [34]. In our particular study, the antibody positivity was found higher in male children as compared to female children in terms of the frequency of occurrence of MP and CP antibody when compared between the female and male children in asthmatic and control groups. However, this difference was not found statistically significant (x^2 =0.001, p=0.520, x^2=0.296, p=0.683, respectively).

MP and CP infections are known to be most common between the ages of 5 and 15 [35]. Our study has shown that the rate of antibody seropositivity for both MP (59.2%) and CP (55.5%) was higher in children between the ages of 7 and 10.

In order to understand the causal relationship between the infectious agents and chronic diseases, either the agent should stimulate the abnormal immunopathological host response sensitive individuals [15-17, 36], or all of the following three conditions should be provided: 1- the agent should be determined more frequently in patients as compared to normal individuals [13, 30, 32]; 2- the presence of the agent should be associated with the severity of the disease [12, 30], 3- successful treatment for the agent should provide clinical benefit for the disease [37]. Our study has determined a higher rate of previous chlamydial and mycoplasmal seropositivity in asthmatic patients as compared to the healthy controls (x^2=3.26,p=0.056, x^2=11.986, p<0.001, respectively); and has established an association between the chlamydial seropositivity, particularly, and the number of asthma episodes (x^2=13.917, p<0.001).

Along with the factors supportive of the abovementioned hypothesis that MP and CP infections take part in the pathogenesis of asthma [10, 12, 14, 29, 30, 32, 38], the available data indicates both the correlation between this organism and asthma episodes and its role in the development of asthma. Although the role of the viral respiratory tract infections is evident in the occurrence of asthma attacks and wheezing, it is concluded that extensive studies should be conducted regarding the role and efficacy of MP and CP.

Competing interests

The authors declare that they have no competing interests.

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