Curr Pediatr Res 2013; 17 (1): 21-26 ISSN 0971-9032

Association between allergic rhinitis and lung function in school children with asthma.

Riikka Leskelä[1], Minna Ruokonen[1], Matti Korppi[1], Heidi Kainulainen[2] and Marita Paassilta[3]

[1]Pediatric Research Center, Tampere University and University Hospital, Tampere, Finland
[2]Tampere School of Public Health, Tampere University, Tampere, Finland
[3]Allergy Centre, University Hospital, Tampere, Finland

Abstract

Allergic rhinitis (AR) and asthma are considered as manifestations of a common inflammatory process rather than separate diseases. In our earlier study, AR was under-diagnosed and under-treated in children with asthma, and when present, AR was associated with severe asthma. The aim of the present study was to evaluate if concomitant AR has an influence on lung function in school-aged children with asthma. Data on AR and lung function, measured by flow-volume spirometry (FVS), were retrospectively collected from hospital records of 252 school-aged children with doctor-diagnosed asthma. The limits of abnormal airflow values were 80% of predicted for FEV_1, 88% for FEV% (FEV_1/FCV) and 62% of predicted for FEF_{50}. At least one parameter in FVS was abnormal in 50.4 % of the study subjects. There were no statistically significant differences between any lung function parameter and the AR status or the medication used for AR. The result was similar regardless of whether FVS parameters were analyzed as dichotomized or continuous variables. The present retrospective hospital chart review was not able to reveal any significant associations between the presence, treatment or severity of AR and lung function in school-aged children with asthma.

Keywords: Airflow limitation, Allergic rhinitis, Asthma therapy, Childhood asthma, Lung function tests

Accepted October 2012

Introduction

Allergic rhinitis (AR) and asthma are considered as manifestations of a common inflammatory process rather than separate diseases [1]. The prevalence of AR among school-aged children with asthma is approximately 75%, and conversely, asthma has been diagnosed in 10-40% of patients with AR [2]. Studies in both adults and children have shown that AR may be associated with bronchial hyper-reactivity (BHR) [3-5]. In a recent study, BHR was documented in 33.2% of the children who had AR but not asthma [5]. In both adults and children, AR is a significant risk factor for emerging asthma [1], and AR may deteriorate asthma balance and increase asthma severity [6-10].

Measurement of lung function by flow-volume spirometry (FVS) is an objective way to demonstrate bronchial obstruction, to estimate asthma severity and to monitor asthma balance and asthma therapy in patients aged $\geq$5 years [11]. Despite this, no studies have been published on the influence of allergic rhinitis to lung function in children with asthma.

In our recent study, AR was both under-diagnosed and under-treated in school-aged children with doctor-diagnosed asthma, and those with AR presented with more severe asthma requiring inhaled steroids combined with long-acting beta-agonists more often than asthma patients with no AR [12]. The aim of the present study was to evaluate the association between AR and lung function in the same group of school-aged children with doctor-asthma.

Material and Methods

This paper belongs to our retrospective study series on allergic rhinitis (AR) in school-aged patients with doctor-diagnosed asthma [12]. In brief, 903 children aged 7-15 years attended at least one regular control visit for asthma in the Department of Pediatrics, Tampere University Hospital, during the year 2002. The hospital provides secondary-level care for a population of about 90,000 children. All Children had asthma diagnosis J45* according to the international classification of diseases (ICD-10). A random sample of 400 children with proportional allocation by age and gender was taken from the eligible children. After checking of hospital records,

28 children were excluded since they did not fulfill the inclusion criteria (doctor-diagnosed asthma, regular control visit) and so, the study group consisted of 372 children with asthma. The presence or absence of AR was actively recorded in hospital cards for 266(71.5%) children. As published earlier [12], AR diagnosis was considered if the doctors had recorded the diagnostic code 4779A (ICD-9), or J30* (ICD-10), or the diagnosis "allergic rhinitis", or the synonyms "seasonal rhinitis" or "hay fever". If the AR diagnosis was not recorded but nasal symptoms suggestive for AR were recorded, such as runny nose, stuffy nose, itching or sneezing during pollen seasons or animal contacts, the children were considered to have AR symptoms only.

Data on lung function measured by flow-volume spirometry (FVS) were collected for the period of 12 months before or after the control visit for asthma in 2002. Adequate lung function data were available in 252(94.7%) of the 266 children, and these asthma patients (154 boys and 98 girls) form the subjects of the present study. Their basic data, including asthma and AR treatments, are presented in Table 1. In our hospital, lung function tests are not performed during acute respiratory symptoms, whether caused by infection or allergy.

FVS was studied by VMAX 20c 4.0 (SensorMedics, Milwaukee, Wisconsin, USA). At least two graphically cceptable curves had to be present, and the curve with the highest sum of forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) was chosen to the analyses. Lung function parameters were expressed both as absolute values and as percentages of the gender-specific and height-related reference values (% of predicted) for Finnish children [13]. The parameters registered were FVC, FEV_1, peak expiratory flow (PEF) and forced expiratory flow at 50% of vital capacity (FEF_{50}). FEV% was calculated from FEV_1 and FVC using the following formula: FEV_1 / FVC x 100. The limits of abnormal airflow values were 80% of predicted for FEV_1, 88% for FEV% and 62% of predicted for FEF_{50} [14]. If one or more of these three parameters were below these limits, the child was defined to have reduced lung function.

Since only hospital charts were retrieved and data registered during routine control visits were used, with no new contact with the subjects, the study was performed by the permission of the Chief Doctor of the Tampere University Hospital.

Statistical analyses were carried out by SPSS Statistics 17.0 software (SPSS Inc, Chicago, Illinois, USA). The results by categorized variables are expressed as frequencies and percentages, and the significances of the differences between the groups were tested by Pearson`s Chi-square and Fischer´s exact tests. The results by quantitative variables are expressed mainly as medians and ranges. The significances of the differences between the groups were tested by Kruskal-Wallis and Mann-Whitney tests. When FVS parameters were analyzed in relation to the presence of AR and asthma severity, the differences were tested with one-way analysis of variance. Logistic regression adjusted for asthma treatment was used to analyze the association between the AR status (diagnosis, symptoms only, no AR) and reduced lung function.

Results

In all, 127(50.4%) asthma patients had reduced lung function that is an abnormal value in FEV_1 of predicted, FEV% or FEF_{50} of predicted. FEV% revealed 97.6%, FEV_1 8.7% and FEF_{50} 13.4% of the reduced lung function cases. There were no statistically significant differences in lung function between the three groups based on AR diagnosis and symptoms (Table 2).

Table 1. *Clinical profile of the study group*

	N	%
Gender		
Boy	154	61.1
Girl	98	38.9
Allergic rhinitis		
Diagnosis	82	32.5
Symptoms only	146	57.9
No	24	9.5
Asthma treatment		
Steroids combined with long-acting beta-agonists	65	25.8
Steroids only	131	52.0
No steroids	56	22.2
*Treatment for allergic rhinitis**		
Nasal steroids only	24	10.5
Antihistamines only	63	27.6
Nasal steroids and antihistamines	54	23.7
No treatment	87	38.2

**Data available in 228 cases*

The severity of asthma, assessed by required maintenance medication, had no association with reduced FEV% or FEF_{50} of predicted (Data not shown). FEV_1 was abnormal in 9.2% of the patients treated with inhaled steroids combined with long-acting beta agonists, compared with 1.5% and 5.4% in the other two groups (p=0.028).

Table 2. *Reduced lung function in relation to allergic rhinitis*

Lung function parameters	Allergic rhinitis			P-value
	Diagnosis (N=82)	Symptoms only (N=146)	No (N=24)	
Reduced lung function^	44 (53.7 %)	70 (47.9 %)	13 (54.2 %)	0.658
FEV_1 < 80*	6 (7.3 %)	3 (2.1 %)	2 (8.3 %)	0.066
FEV % < 88	42 (51.2 %)	69 (47.3 %)	13 (54.2 %)	0.744
FEF_{50} < 62*	6 (7.3 %)	7 (4.8 %)	4 (16.7 %)	0.096

** % of predicted*
^FEV1 < 80 or FEV% < 88 or FEF_{50} < 62

Table 3. *Lung function in relation to allergic rhinitis*

Parameter	Median (range) Allergic rhinitis			P-value
	Diagnosis	Symptoms only	No	
	(N=82)	(N=146)	(N=24)	
FEV_1*	98.0 (62-129)	97.0 (71-130)	97.0 (68-122)	0.586
FEV %	87.0 (63-100)	88.0 (53-100)	87.0 (71-110)	0.735
FEF_{50}*	89.5 (51-182)	91.5 (51-187)	82.0 (51-174)	0.308
FVC*	99.0 (76-133)	101.0 (74-128)	98.0 (72-124)	0.547
PEF*	108.0 (77-179)	112.0 (77-170)	108.5 (85-145)	0.286

** % of predicted*

Table 4. *Logistic regression: Reduced lung function in relation to the diagnosis of allergic rhinitis adjusted for asthma treatment*

Lung function parameter	Diagnosis (N=82)
Reduced lung function^	44 (53.7 %)
Odds ratio (95% CI)*	0.96 (0.38-2.41)
FEV_1 < 80	6 (7.3 %)
Odds ratio (95% CI)*	0.59 (0.10-3.43)
FEV% < 88	42 (51.2 %)
Odds ratio (95% CI)*	0.87 (0.35-2.19)
FEF_{50} < 62	6 (7.3 %)
Odds ratio (95% CI)*	0.28 (0.07-1.16)

^FEV_1 < 80 or FEV% < 88 or FEF_{50} < 62
**Vs. the group of no allergic rhinitis*

When the lung function parameters were analyzed as continuous variables, the main result of the study remained negative (Table 3). None of the individual parameters had a significant association with the presence of AR diagnosis or AR symptoms (Data not shown). Again, FEV_1 of predicted was significantly lower in the group treated with inhaled steroids combined with long-acting beta agonists (median 94.7%, range 62-129) than in the two other groups (median 99.1% and 97.3% respectively) (p=0.046). Data on the use of AR treatment were available in 228 cases and the medication had no significant association with lung function results (Data not shown).

All analyses were repeated separately in boys and girls, and the results remained as negative (Data not shown). Likewise, the results remained as negative when the association between AR and reduced lung function was analyzed by logistic regression adjusted for asthma treatment (Table 4).

Among the original 372 children, lung function data were available in 94 cases with no AR data available. When these 94 children were compared with the 252 children of the present study, there were no significant differences in age, gender or reduced lung function between the groups. Instead, the groups differed for asthma maintenance medication; the included children with data on allergic rhinitis available used more often inhaled steroids combined with long-acting beta-agonists (25.8% vs. 12.8%) and were less often without inhaled steroids (22.2% vs. 35.1%) (p=0.008).

Discussion

The main result of the present study was that the presence or severity of AR had no significant association with lung function measured by FVS in school-aged children with asthma. The result was similar in the analyses by continuous and categorized FVS parameters. An alarming result was that over half of the patients had reduced lung function, though only <10% of the findings were based on reduced FEV_1. However, post-bronchodilator values eliminating temporarily reduced results were not available. As expected, the severity of asthma, when assessed by the requirement of inhaled steroids with or without long-acting beta-agonists as maintenance medication, had some association with reduced FEV_1 in FVS. The main result remained negative when analyses were repeated as adjusted for asthma treatment.

The present study is the first one on the association between lung function and AR in children with asthma. In two retrospective American studies including 2031 and 488 adults with asthma, AR was reported by >70% of the participants [15]. Against expectations, patients with AR had better baseline lung function than those without AR, when measured by PEF [15]. In a small prospective cross-sectional study, 20 adults with asthma were classified into 2 groups: 12 with AR and 8 without AR. Asthma patients without AR had more severe airflow obstruction when measured by FEV% [16]. The presence of an association between AR and less severe airflow obstruction may be understandable, if patients with asthma and concomitant AR have more seasonal and less non-seasonal permanent symptoms. Most children with asthma have seasonal symptoms, and although concomitant AR increases BHR and worsens asthma balance, AR does not necessarily reduce lung function, as seen also in the present study.

There are only two pediatric studies on the association between AR and lung function. FEF_{25-75} was reduced in 20-30%, but FEV_1 or FEV% only in <10% of children with AR [17, 18]. Lung function was studied in 50 children with allergic rhinitis and house dust mite sensitization, and 11(22%) had reduced FEF_{25-75}, but only one (2%) had reduced FEV_1 [17]. During a 3-month treatment by nasal steroids, FEF_{25-75} increased to normal in two-thirds of the cases. In a more recent study in 200 children with AR, 31% had reduced FEF_{25-75}, and 11% had both reduced FEF_{25-75} and reduced FEV_1 [18]. Long AR duration and sensitization to house dust mites increased the risk of lung function reduction. Both findings are understandable, since sensitization to house dust mites is rare in young children and when present, it is associated with permanent symptoms. Over 250 children with asthma were included in the present study, and there were no significant associations between the presence of AR or required treatment for AR and lung function by FVS. Due to the retrospective design of the study, the negative results should be interpreted with caution, and analyses based on allergen-specific sensitization or the duration of AR, for example were not possible.

Studies both in adults [3, 4, 19] and in children [5, 20] have shown that AR may be associated with BHR even in the absence of asthma. In addition, an introduction of nasal steroids has improved BHR to metacholine [12] and to exercise [22] in patients with AR, and use of antihistamines has improved BHR in children with AR and asthma [23]. In line, treatment of AR with intranasal corticosteroids in 25 asthmatic adolescents aged 12-17 years reduced BHR to exercise and tended to improve quality of life [24]. One-hundred adults with seasonal AR with no asthma were examined during and outside pollen seasons [25]. FEF_{25-75} was decreased in 17% during and in 11% outside the season. FEV_1 was decreased in 5% during the pollen season, and metacholine inhalation challenge was pathological in 54% both during and outside the pollen season [25]. The newest study included 190 children with AR and with no asthma [5]. FEV1 was normal (>80% of predicted) in all included cases. Eighteen (9.5%) children had marked and 45(23.7%) had mild BHR in methacholine inhalation challenge [5]. Thus, BHR seems to be associated with long AR duration and sensitization to seasonal pollens [22, 25]. In the present study, bronchial reactivity was not systemically studied and therefore not included in the analyses.

In both adults and children, AR is a significant risk factor for the later emergence of asthma [1, 26, 27], and there is indirect evidence that insufficiently treated AR may deteriorate asthma balance [6-10]. In the German birth cohort study, allergic rhinitis at 5 years of age predicted developing wheezing between 5 and 13 years of age, with an adjusted relative risk of 3.8 [27]. In the Danish birth cohort, 7-year-old children with allergic and non-allergic rhinitis had both a 4-fold asthma risk [28]. In the present group of school-aged children with doctor-diagnosed asthma, AR was both under-diagnosed and under-treated, and children with AR diagnosis or AR symptoms had more severe asthma when assessed by the needed maintenance medication [12]. Though AR increased the severity of asthma, we were not able to confirm any association between reduced lung function and presence AR.

The present study was a retrospective retrieve of hospital records. There are two obvious strengths in the study. First, the study group was a random sample from a large group of over 900 eligible children, and data on lung function were present in over 90% of the included children. However, only baseline FVS results were available. Lung function was measured during the maintenance medication, but post-bronchodilation FVS values which reflect permanent changes in lung function, were not available. Second, the sample of 252 children with complete data on allergic rhinitis and lung function available was large enough to minimize statistical errors allowing *e.g.* adjusted analyses. An obvious shortcoming of the study was that the data on the presence or absence of allergic rhinitis were not recorded in a fourth of the eligible cases. When these drop-outs were compared with included children, the groups did not differ for age, gender or lung function results. The included children used more often inhaled steroids with long-acting beta-agonists which means that severe cases were over-represented in the study cohort. This suggest that the negative result of the study was not due to mild asthma cases, and when the main analyses were repeated as adjusted for asthma treatment, the results did not change.

In conclusion, we were not able to confirm any significant associations between the presence or treatment of allergic rhinitis and lung function in school-aged children with asthma. Our study is the first one published on that specific problem. Due to the retrospective design, the

results are only preliminary and should be interpreted with caution, and prospective studies are needed to solve this important question.

References

1. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008; 63 (Suppl 86): 8-160.
2. Bousquet J, Van Cauwenberge P, Khaltaev N and Aria Workshop Group (World Health Organization). Allergic rhinitis and its impact on asthma. Review. J Allergy Clin Immunol. 2001; 108 (Suppl 5): 147-334.
3. Kateralis CH. Allergic rhinitis and asthma: epidemiological evidence for the link. Review. Clin Exp Allergy Rev. 2003; 3: 5-8.
4. Cirillo I, Pistorio A, Tosca M, Ciprandi G. Impact of allergic rhinitis on asthma: effects on bronchial hyperreactivity. Allergy. 2009; 64: 439-444.
5. Ciprandi G, Tosca MA, Cirillo I, Capasso M. Impact of allergic rhinitis on asthma in children: effects on bronchial hyperreactivity. Allergy. 2010; 65: 1199-1201.
6. Bousquet J, Gaugris S, Kocevar VS, Zhang Q, Yin DD, Polos PG. Increased risk of asthma attacks and emergency visits among asthma patients with allergic rhinitis: a subgroup analysis of the improving asthma control trial. Clin Exp Allergy. 2005; 35: 723-27.
7. Price D, Zhang Q, Kocevar V S, Yin D D, Thomas M. Effect of a concomitant diagnosis of allergic rhinitis on asthma-related health care use by adults. Clin Exp Allergy. 2005; 35: 282-87.
8. Crystal-Peters J, Neslusan C, Crown W H, Torres A. Treating allergic rhinitis in patients with comorbid asthma: The risk of asthma-related hospitalizations and emergency department visits. J Allergy Clin Immunol. 2002; 109: 57-62.
9. Adams R J, Fuhlbrigge A L, Finkelstein J A, Weiss S T. Intranasal steroids and the risk of emergency department visits for asthma. J All Clin Immunol. 2002; 109: 636-42.
10. Corren J. The impact of allergic rhinitis on bronchial asthma. Review. J Allergy Clin Immunol. 1998; 101 (Suppl 3): 52-6.
11. Expert Panel Report (EPR-3): Guidelines for the diagnosisand management of asthma – summary report 2007. J Allergy Clin Immunol. 2007; 120 (Suppl 5): 94-S138.
12. Ruokonen M, Kaila M, Haataja R, Korppi M, Paassilta M. Allergic rhinitis in school-aged children with asthma – still under-diagnosed and undertreated? A retrospective study in a children´s hospital. Pediatr Allergy Immunol. 2010; 21: E149-E154.
13. Koillinen H, Wanne O, Niemi V, Laakkonen E. Reference values for spirometry and peak expiratory flow in healthy Finnish children [in Finnish]. Suomen Lääkärilehti. 1998; 39: 395-402.
14. Viljanen AA, Halttunen PK, Kreus KE, Viljanen BC. Spirometric studies in non-smoking, healthy adults. Scand J Clin Lab Invest Suppl. 1982; 159: 5-20.
15. Dixon AE, Kaminsky DA, Holbrook JT, Wise RA, Shade DM, Irvin CG. Allergic rhinitis and sinusitis in asthma: differential effects on symptoms and pulmonary function. Chest. 2006; 130: 429-435
16. Dixon AE, Raymond DM, Suratt BT, Bourassa LM, Irvin CG. Lower airway disease in asthmatics with and without rhinitis. Lung. 2008; 186: 361-368.
17. Kessel A, Halloun H, Bamberger E, Kugelman A, Toubi E. Abnormal spirometry in children with persistent allergic rhinitis due to mite sensitization: the benefit of nasal corticosteroids. Pediatr Allergy Immunol. 2008; 19: 61-66.
18. Ciprandi G, Capasso M. Association of childhood perennial allergic rhinitis with subclinical airflow obstruction. Clin Exp Allergy. 2010; 40: 398-402.
19. Frye C, Heinrich J, Wjst M, Wichmann HE; Bitterfeld Study Group. Increasing prevalence of bronchial hyperresponsiveness in three selected areas in East Germany. Eur Respir J. 2001; 18: 451-458.
20. Capasso M, Varricchio A, Ciprandi G. Impact of allergic rhitis on asthma in children: effects on bronchodilation test. Allergy. 2010; 65: 264-268.
21. Foresi A, Pelucchi A, Gherson G, Mastropasqua B, Chiapparino A, Testi R. Once daily intranasal fluticasone propionate (200 micrograms) reduces nasal symptoms and inflammation but also attenuates the increase in bronchial responsiveness during the pollen season in allergic rhinitis. J Allergy Clin Immunol. 1996; 98: 274-282.
22. Corren J, Manning B E, Thompson S F, Hennessy S, Strom B L. Rhinitis therapy and the prevention of hospital care for asthma: A case-control study. J Allergy Clin Immunol. 2004; 113: 415-419.
23. Aubier M, Neukirch C, Peiffer C, Melac M.Effect of cetirizine on bronchial hyper-responsiveness in patients with seasonal allergic rhinitis and asthma. Allergy. 2001; 56: 35-42.
24. Kersten ET, van Leeuwen JC, Brandt PL, Duiverman EJ, de Jongh FH, Thio BJ, et al. Effect of intranasal corticosteroid on exercise induced bronchoconstriction in asthmatic children. Pediatr Pulmonol. 2012; 47: 27-35.
25. Ciprandi G, Cirillo I, Tosca MA, Vizzaccaro A. Bronchial hyperreactivity and spirometric impairment in patients with seasonal allergic rhinitis. Respir Med. 2004; 98: 826-831.
26. Ferdousi HA, Zetterström O, Dreborg S. Bronchial hyper-responsiveness predicts the development of mild clinical asthma within 2 yr in school children with hayfever. Pediatr Allergy Immunol. 2005; 16: 478-486.
27. Rochat MK, Elli S, Ege MJ, Lau S, Keil T, Wahn U, et al. MAS study group. Allergic rhinitis as a predictor for wheezing onset in school-aged children. J Allergy Clin Immunol. 2010; 126: 1170-5.e2.
28. Chawes BL, Bönnelykke K, Kreiner-Möller E, Bisgaard H. Children with allergic and non-allergic rhinitis

have similar risk of asthma. J Allergy Clin Immunol. 2010; 126: 567-73.e1-8.

Ccorrespondence to:

Matti Korppi
Pediatric Research Center
Tampere University and University Hospital,
Tampere FM-3 building, Kauppi Campus
FIN-33013 Tampere University
Finland

None of the authors have any conflicts of interest