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Key Words

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Association of Asthma with Gastroesophageal Reflux Disease in Children

Background. The objective in this study was to assess the association of gastroesophageal reflux disease (GERD) with asthma in pediatric patients.

Methods. Thirty-six pediatric patients who were diagnosed as having bronchial asthma were included in the study. The male-to-female ratio was 2 to 1. The diagnosis of GER was made by 24-hour pH monitoring.

Results. GER was present in 27 of 36 (75%) patients, of whom 19 (70%) were male and 8 (30%) were female patients. The GER frequency was found to be different between the supine and upright positions ($p < 0.05$). GER was more frequent in the upright position. However, duration of GER was longer in the supine position than the upright position ($p < 0.05$). Overall reflux duration was similar in both positions ($p > 0.05$).

Conclusions. Demonstration of the relationship between asthma and GER suggests that GER is involved substantially in the pathogenesis and/or symptomatology of asthma. The patients with asthma should be evaluated for the presence of GER even in the absence of GER-related symptoms.

Gastroesophageal reflux disease (GERD), which is caused by the reflux of gastric contents into the esophagus, is a common clinical problem. A close relationship between GERD and asthma has been described in children. GERD is considered to be involved in a variety of pulmonary diseases, such as intractable asthma, chronic bronchiolitis, and recurrent pneumonia. Pulmonary symptoms may be the initial complaint of patients with GERD. However, pulmonary disease, particularly asthma, may lead to GERD as well. Children with GERD-related asthma may not always present with the common symptoms of reflux like regurgitation and vomiting. But they may present with nocturnal pulmonary symptoms due to chronic aspiration.

Prevalence of GERD is reported to range from 47% to 64% in children with asthma. The mechanisms by which GERD induces bronchoconstriction may be microaspiration of the gastric contents and a vagally mediated reflex, though the exact mechanism remains unclear.¹⁻⁶

In this study, we aimed to assess association of body position with GERD in children who were diagnosed as having bronchial asthma.

METHODS

Thirty-six children who had bronchial asthma were included in the study. Their ages ranged between 13 months and 15 years (mean, 8.6 ± 4.5 years). Normal children could not be included as a control group, because an informed consent could not be obtained from the families. The diagnosis of asthma was based on the symptoms of wheezing, dyspnea, recurrent cough, and observation of 20% improvement in FEV1 (the volume exhaled in the first second of a forced expiration) after bronchodilator inhalation on pulmonary function testing in the cooperable children.

All patients had mild asthma as far as frequency of the attacks and lengths of the symptom free periods were concerned. The frequency of the asthmatic attacks was less than 2 per week in all children. No patient had nocturnal pulmonary symptoms, and all were asymptomatic between the asthmatic attacks. The symptoms of the patients were not consistent with GERD or neurological disorders. Twenty-four hour intraesophageal pH moni-

Table 1. Results of 24 hour pH monitoring in the asthmatic children with gastroesophageal reflux (n = 27)

Parameter	Total	Position of patient		Statistics
		Upright	Supine	
Total reflux number in 24 hour	254.7 ± 200.8	162.1 ± 139.2	101.7 ± 86.6	<i>p</i> < 0.05
Number of reflux lasting more than 5 minutes	3 ± 2.4	1 ± 1.18	2.2 ± 2.2	<i>p</i> < 0.05
Total reflux time in 24 hours (minutes)	120 ± 61.9	60.6 ± 39.1	55.1 ± 36.1	<i>p</i> > 0.05

toring was performed in all patients in an effort to diagnose GER

Also, skin prick test (Alk Abello, ALK Diagnostic Laboratory, Denmark) and specific IgE testing by ELISA (CLA Hitachi, USA) was performed.

pH monitoring

A semidisposable glass pH probe with internal reference electrode was used (Lot 440 M3 internal reference glass pH with Lemo plug, MIC AG, Solothurn, Switzerland). Prior to pH monitoring, calibration was performed using solutions with pH 7.0, 4.0 and 1.7. The nasal cavity and pharynx were anesthetized with topical Xylocaine preceding the insertion of the probe through the nasal cavity. The esophageal length was estimated as described previously.² The tip of the probe was placed just proximal to the lower esophageal sphincter. Plain chest x-ray was obtained to control the position of the probe. The probe was connected to a 24-hour recording device (Gastrograph Mark III, MIC AG, Solothurn, Switzerland). During 24-hour monitoring, the patient was hospitalized. The families were informed about the use of the device in detail, and instructed to record the activity of the child by pressing on certain buttons of the device and noting on a specified chart. These data were loaded into a personal computer, and analyzed by using the "Pack II" program (MIC Inc., Switzerland).

On pH monitoring, GER diagnosis was made according to reflux index (a decrease in pH below 4 for a period longer than 4% of 24 hour).⁷ The physical examination of the patients was normal during monitoring, and none of them had asthmatic complaints.

Statistical analyses

SPSS 6.0 for Windows (SPSS, Inc, Chicago, IL) was used and chi-square test was applied. A *p* value < 0.05 was considered significant.

RESULTS

Of 36 patients, 12 (33%) were girls and 24 (67%) were boys. The male-to-female ratio was 2 to 1. The ages ranged between 13 months and 15 years (mean, 8.6 ± 4.5 years). Both specific IgE testing and prick test were performed. These tests were positive only in 3 patients. One of them was sensitive to grass, and the others were sensitive to house dust.

GERD was diagnosed in 27 of 36 (75%) patients with asthma, of whom 19 (70%) were male and 8 (30%) were female. The positions of the children during pH monitoring influenced the frequency and duration of GER. In the boys, frequency of GER was higher in upright position (chi square = 2.546, *p* = 0.02), while duration of the reflux episodes was longer in supine position (chi square = 4.361, *p* = 0.01). However, total duration of the reflux episodes (24 hours) was not different between supine and upright positions (*p* > 0.05, Table 1). The same condition was also true for the girls; the frequency of GER was higher in upright position (chi square = 3.952, *p* = 0.03), while duration of the episodes was longer in supine position (chi square = 3.541, *p* = 0.02). Total duration of reflux episodes (24 hours) was not significantly different between upright and supine positions as well (*p* > 0.05).

In boys, the number of reflux episodes in 24 hours was significantly higher in upright position than in supine position (chi-square = 5.147, *p* = 0.01). The numbers of episodes longer than 5 minutes and total duration of reflux episodes were not different between both positions (*p* > 0.05).

DISCUSSION

GER can manifest atypically by apnea and cyanosis even in the absence of gastrointestinal symptoms like

vomiting or regurgitation. A close relationship between GER and asthma is evident.^{2,8,9} Despite the high incidence of esophageal dysfunction in the children and young adults with asthma, the incidence of GER in these patients is not known properly.¹⁰

In asthmatic patients, despite the absence of typical reflux symptoms like vomiting and regurgitation, chronic aspirations that are likely to occur during sleep may be the cause of the pulmonary symptoms. In addition to that, some autonomic reflex mechanisms triggered by the reflux may be involved in the bronchospasm. In children who have severe asthma or recurrent pneumonia, GER should be taken into consideration. The possibility of GER should be remembered when there is nocturnal cough of unknown etiology. GER appears to play a role in the occurrence of respiratory symptoms as well as perpetuation of the vicious cycle.^{4,11}

It was experimentally shown that acid reflux could cause bronchospasm with subsequent cough and asthma like symptoms.¹² Aspiration of the reflux material can impact on the airway resistance, which is referred to as reflux mechanism. It is evident that aspiration of even minor amount of gastric acid can lead to severe bronchospasm.¹³ Gastric acid in the reflux material can also stimulate the sensory afferents located in the distal portion of the esophagus, thereby initiating a neural response. This condition, in turn, leads to bronchospasm and alteration in the airway resistance. Inactivation of the pulmonary reflex mechanism during sleep leads to a decrease in the esophageal clearance and aspiration of the reflux material, which in turn results in reflex bronchoconstriction through vagal stimulation.^{14,15} On the contrary, asthma can also lead to reflux. This condition is attributable to a mechanical dysfunction in the lungs of the asthmatic patients as well as use of anti-asthmatic medications that decrease the lower esophageal sphincter pressure. Theophylline can cause GER in the normal adults, and increase the severity of GER in the patients with asthma, for example. Theophylline leads to GER by relaxing smooth muscle of the lower esophageal sphincter. Despite the fact that bronchodilator drugs used in the patients with asthma can exaggerate GER, particularly during sleep or after the meals, it should be remembered that occurrence of GER in these patients does not solely depend on the medication used.¹⁵⁻¹⁸ None of our patients

were using Theophylline or another bronchodilator during pH monitoring.

The incidence of GER in the children with asthma ranges from 25% to 80% in the literature.^{1,3,6,7} That wide range might have resulted from differences in the diagnostic work up (duration of pH monitoring, scintigraphy, endoscopy, radiologic options) and patient selection criteria in different studies. Thus it is not easy, and may be misleading, to compare the results of different studies. According to our results, GER was present in 75% of the patients with mild intermittent asthma. GER was present in 79% of boys and 67% of girls. These rates are comparable with the upper limits reported in the literature. In one study, the presence of GER was diagnosed in 75% of children with chronic asthma who were refractory to medical treatment and did not have findings suggestive of GER.⁶ Likewise, all patients included in our study had mild asthma, and none of them had the signs and symptoms of GER.

The majority of children with asthma complain of GER symptoms. It was reported that epigastric discomfort, regurgitation and dysphagia were the symptoms in 77%, 55% and 24% of adult patients with asthma, respectively, and these symptoms were significantly more frequent compared to those in healthy controls.¹⁹ However, the patients in our study did not have GER-related symptoms. This condition is likely to result from the fact that children are unable describe their symptoms as the adults do. Alternatively, GER symptoms may be less prevalent in the childhood than in the adulthood.

In a series of 27 adult patients with asthma in which 24-hour pH monitoring was performed using two electrodes, 44% of the patients had reflux in the distal esophagus.²⁰ In the same study, the total reflux time was not different between supine and upright position. This result is comparable to our findings that total duration of the reflux episodes in 24 hours was not different between either position.

In conclusion, GER may be involved in the pathogenesis of asthma.

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