

Idiopathic Chest Pain in Children: Is it Gastroesophageal Reflux Disease?

Çocuklarda İdiyopatik Göğüs Ağrısı: Gastroözofageal Reflü Hastalığı mı?

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ABSTRACT Objective: Causes of chest pain in children, rarely due to cardiac disease and usually described as idiopathic, account for 20% to 45% of all cases. In this study, we investigated the frequency of gastroesophageal reflux in children with noncardiac chest pain and the characteristics of the pain. **Material and Methods:** Children with at least two episodes per month of chest pain for a maximum of six months were enrolled in the study. After diagnostic evaluation excluded a cardiac source of chest pain, all patients underwent 24-hour pH monitoring. Characteristics of chest pain and other symptoms were recorded daily by the patients or their parents using the symptom diary. Lansoprazole treatment was administered to patients diagnosed as having gastroesophageal reflux disease. Then, the results of the lansoprazole treatment were evaluated on the basis of the presence of chest pain and other symptoms at the second month after the completion of therapy. **Results:** Thirty-one children (17 boys and 14 girls) aged between eight and 18 years (11.6±2.4 years) with the primary complaint of chest pain were studied. Based on the 24-hour pH monitoring test results, eight patients (25.8%) for distal sensor and six patients (19.4%) for proximal sensor were defined as Gastroesophageal Reflux Disease (GERD)-positive. No significant difference was noted for characteristics of chest pain and other symptoms between the GERD-positive and GERD-negative groups. All GERD-positive children became symptom-free after the two-month lansoprazole therapy. **Conclusion:** The symptoms of GERD-induced chest pain are often non-specific, and can be determined with certainty only by 24-hour pH monitoring, so 24-hour pH monitoring may be proposed to all children with idiopathic chest pain.

Key Words: Chest pain; gastroesophageal reflux; esophageal pH monitoring

ÖZET Amaç: Çocuklarda göğüs ağrısının nedeni nadiren kardiyak kökenli olur ve nedeni çoğunlukla saptanamaz. İdiyopatik göğüs ağrısı olarak tanımlanan bu durum göğüs ağrısı olgularının %20-45'ini oluşturmaktadır. Bu çalışmada göğüs ağrısı olan çocuklarda kalp kökenli nedenler dışlandıktan sonra, idiyopatik göğüs ağrısı olarak değerlendirilen çocuklarda gastroözofageal reflü sıklığını ve bu ağrının karakteristik özelliklerini araştırdık. **Gereç ve Yöntemler:** Altı aydan uzun süre ve ayda en az iki kez göğüs ağrısı atağı olan çocukların dahil edildiği çalışmada, kardiyak nedenler dışlandıktan sonra tüm hastalara 24 saat pH monitörizasyon uygulandı. Hastalar veya ebeveynler tarafından göğüs ağrısının karakteristik özellikleri ve diğer semptomlar günlük olarak kaydedildi. Gastroözofageal reflü saptanmış olan hastaların göğüs ağrısı ve diğer semptomları iki ay süren Lansoprazol tedavisi sonrası tekrar değerlendirildi. **Bulgular:** Çalışmaya alınan çocukların (14 kız, 17 erkek) yaş aralığı 8 ile 18 yıl, yaş ortalaması ise 11,6±2,4 yıl bulundu. Çalışmada 24 saatlik pH monitörizasyon sonuçlarına bakıldığında proksimal sensör ölçümlerine göre 8 (%25,8), distal sensör ölçümlerine göre 6 (%19,4) hastada Gastroözofageal Reflü (GÖR) saptandı. Göğüs ağrısının karakteristik özellikleri açısından değerlendirildiğinde GÖR saptanan ve saptanmayan hastalar arasında anlamlı farklılık bulunmadı. Benzer şekilde bildirilen diğer semptomlar açısından da iki grup arasında anlamlı farklılık yoktu. Lansoprazol tedavisi verilen GÖR saptanmış tüm hastalarda iki aylık tedavi sonrası tüm yakınmalar düzeldi. **Sonuç:** Gastroözofageal reflüsü olan çocuklarda GÖR'e bağlı ortaya çıkan göğüs ağrısının karakteristik özellikleri ve diğer semptomlar hastalığa özgü değildir, bu nedenle idiyopatik göğüs ağrısı olan tüm hastalarda 24 saat pH monitörizasyonu yapılması önerilmelidir.

Anahtar Kelimeler: Göğüs ağrısı; gastroözofageal reflü; özofageal pH izlemi

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Chest pain during childhood is a common complaint in general medical practice that often presents a difficult diagnostic problem for the physician. Causes of chest pain in children, rarely due to cardiac disease and usually described as idiopathic, account for 20% to 45% of all cases.¹⁻⁴ The most common noncardiac causes of chest pain include idiopathic, chest wall or musculoskeletal, psychogenic, respiratory, and gastrointestinal.¹⁻⁴ Gastrointestinal disorders are thought to be responsible for only 4-6% of children with chest pain.³ However, it has been reported that about 80% of patients previously labeled with “idiopathic chest pain” actually suffer from a gastrointestinal cause.⁴ A diagnosis of idiopathic chest pain is established if no cause can be found after a thorough history, physical examination and appropriate laboratory investigations.³ The esophagus is one of the most common sources of noncardiac chest pain with gastroesophageal reflux disease (GERD).⁴ However, there are only a few studies in the literature that focused on the relationship between chest pain and GERD in children. In this study, we investigated the frequency of gastroesophageal reflux in children with noncardiac chest pain and the characteristics of the pain.

MATERIAL AND METHODS

PATIENTS

Children with at least two episodes of chest pain per month for a maximum of six months were enrolled in the study. After admission to our pediatrics outpatient clinic for chest pain, the attending pediatrician ruled out the possible noncardiac causes of the pain on the basis of a normal history and physical examination along with a laboratory study. Patients were then referred to a pediatric cardiologist. After a diagnostic evaluation excluded a cardiac source for their chest pain (normal electrocardiography, no abnormalities of cardiac enzymes, normal telecardiography and normal two dimensional and color Doppler echocardiography), all patients underwent 24-hour pH monitoring. Following the 24-hour pH study, all patients diagnosed as having GERD received four-week PPI treatment (lansoprazole, 1 mg/kg/day, 2 h before

meals for two months). All the children and families were informed about conservative measures of GER control.

All patients were asked to provide a clinical history of digestive (epigastric or abdominal pain, pyrosis, regurgitation, dysphagia, and emesis) and respiratory symptoms (chronic cough, hoarseness, and wheezing) for GERD.

Characteristics of chest pain and other symptoms were recorded daily by the patients or their parents using the symptom diary. The results of this treatment were then evaluated on the basis of the presence of chest pain and other symptoms in the second month after the completion of therapy.

Exclusion criteria

1) Presence of history of congenital cardiac pathology, asthma, pneumonia, pleural fluid collection and chest trauma, and had costochondritis, cardiac pathology on physical examination.

2) Presence of an underlying disease (e.g. psychogenic, pulmonary and musculoskeletal disorders) or were taking medication that might affect pH monitoring results, as well as those who were unwilling to complete the pH monitoring examination.

3) Patients who had a body mass index above 20 to avoid the GER-provoking influence of obesity.

24-HOUR pH MONITORING

All cases underwent 24-hour pH monitoring according to a standard protocol. None of the subjects had received anti-reflux treatment during the previous month.

Then an antimony pH probe (ComforTec PLUS, Sandhill Scientific Inc., Highlands Ranch, USA) with a diameter of 2.13 mm/6.4 FR, 10 cm spacing and dual pH channel was placed nasally following an overnight fast.

Ambulatory pH monitoring was effected by placing nasally following a pH probe 5 cm above the upper border determined manometrically. The pH probes were calibrated at pH 7.0 and 1.0 using buffer solutions (Reagecon Diagnostics Limited,

Shannon Free Zone, Shannon, Co. Clare, Ireland) before each study. Measurements of pH were stored in a digital data logger (Orion II, MMS, Enschede, Netherlands). Patients received regular feeds during recording and daily activities resumed as normal. Parents recorded the meal times and position of the patients using the buttons on the recorder. Recorded pH data were downloaded to an IBM compatible computer and analyzed by Orion Medical Measurement Systems Software Version 8.3, Build 1147 (MMS, Enschede, Netherlands). The number of episodes under pH 4, the total duration of these 'acid' periods, the reflux index (RI: mean percentage of time <pH 4), the number of reflux episodes longer than 5 min, and the longest episode of all refluxes were calculated. When reflux percentages for proximal and distal probes were over 1% and 4%, respectively the diagnosis was accepted as GER. The study was approved by the Ethics Committee of Celal Bayar University Medical Faculty, Manisa. Informed consent was obtained from the parents of all participating children.

STATISTICAL ANALYSIS

Statistical analyses were performed by SPSS 13.0 (Chicago, IL) computer program. Statistics were calculated using Chi-square test, Fisher's exact test or the Mann-Whitney U test for nonparametric distributions where appropriate. P values less than 0.05 were regarded as statistically significant.

RESULTS

Thirty-one children (17 boys and 14 girls) aged between eight and 18 years (11.6±2.4 years) with the primary complaint of chest pain were studied. The mean age for the girls was 10.66±2.25 years and the mean age for the boys was 10.75±2.51 years. Based on the 24-hour pH monitoring test results, eight patients (25.8%) and six patients (19.4%) were classified as GERD-positive for distal and proximal sensors, respectively. There were no statistically significant differences between the GERD-positive and GERD-negative groups regarding demographic variables (Table 1). As expected, 24-hour pH monitoring results were significantly different between

TABLE 1: Comparison of demographic characteristics between GERD-positive and GERD-negative children with idiopathic chest pain.

	GERD-Positive	GERD-Negative	P
Distal Sensor	n=8	n=23	
Mean age±SEM (yrs)	10.65±0.52	10.87±0.69	0.59
Age range	8-14	8-17	
Gender (male/female)	4/4	12/11	1.00*
Proximal Sensor	n = 6	n = 25	
Mean age±SEM (yrs)	10.50±0.92	10.76±0.48	0.81
Age range	8-14	8-17	
Gender (male/female)	3/3	13/12	1.00*

GERD: Gastroesophageal reflux disease.

* Fisher's Exact Test.

the two groups for each sensor. Percentages of total time pH less than four (reflux time), mean time of reflux episodes and mean time of reflux episodes >5 min were significantly higher in the GERD-positive group compared to those in the GERD-negative group for both sensors (distal sensor p=0.000, p=0.000 and p=0.000; proximal sensor p=0.000, p=0.000 and p=0.003, respectively) (Table 2). None of the patients in either group reported chest pain during the 24-h pH test.

Eleven patients (35.5%) experienced chest pain daily, 13 (41.9%) had at least two episodes weekly, and seven (22.6%) had at least two monthly events. In all cases, the time course of the pain was longer than 48 hours and the duration of the pain was between 1-60 minutes except for one patient. There was no radiation from the original site in 14 patients (45.16%). There was no relation with meals in 22 patients (70.96%). No significant difference was noted for characteristics of chest pain between the GERD-positive and GERD-negative groups (Table 3). Other symptoms reported in addition to chest pain were not significantly different between the two groups (Table 4). All GERD-positive children became symptom-free after the two-month lansoprazole therapy.

DISCUSSION

Chest pain is a common complaint in pediatric patients. The incidence among children is unknown, but chest pain accounts for 0.2% to 0.6% of patient

TABLE 2: Comparison of results obtained from distal and proximal pH probes between GERD-positive and GERD-negative groups (mean \pm SEM).

	GERD-Positive	GERD-Negative	P
Distal Sensor	n=8	n=23	
Reflux index (%)	11.83 \pm 3.44	1.82 \pm 0.25	0.000
Mean time of reflux episodes >5 min	6.00 \pm 1.11	0.56 \pm 0.25	0.000
Total number of reflux episodes >5 min	48	13	
Mean time of reflux episodes (min)	191.75 \pm 37.68	40.04 \pm 5.46	0.000
Total number of reflux episodes	1534	921	
Proximal Sensor	n=6	n=25	
Reflux index (%)	1.66 \pm 0.18	0.33 \pm 0.06	0.000
Mean time of reflux episodes >5 min	0.83 \pm 0.40	0.08 \pm 0.08	0.003
Total number of reflux episodes >5 min	5	2	
Mean time of reflux episodes (min)	37.33 \pm 4.81	7.44 \pm 1.54	0.000
Total number of reflux episodes	224	186	

GERD: Gastroesophageal reflux disease.

visits to pediatric outpatient clinics or emergency departments. A diagnosis of idiopathic chest pain is established if no cause can be found after a thorough history, physical examination and appropriate laboratory investigations.¹⁻³ Fyfe and Moodie considered 55% of their patients with normal physical examinations, chest roentgenograms and electrocardiograms as having idiopathic chest pain.⁵ In another study, Berezin et al. diagnosed gastrointestinal causes in 21 of 27 children (78%) with chest pain who had previously been assumed to be idiopathic.⁴

Gastroesophageal Reflux Disease was defined as total distal RI >4 in distal esophagus and total proximal RI >1 in proximal esophagus determined by the most suitable diagnostic tool for GERD that is the 24-hour pH monitoring with a sensitivity and specificity above 90%.^{6,7} In this study, eight of 31 patients (25.8%) for distal sensor and six of 31 patients (19.4%) for proximal sensor had abnormal results for pH-monitoring. Wang et al. showed that GERD positivity was 58.3% in children with non-cardiac chest pain.⁸ Although the exact mechanism that caused this discrepancy in the GERD rates between our study and that of Wang et al. is not fully understood, it might be related to the patient selection criteria.

In children with chest pain, the most important part of the assessment is a careful history and physical examination. The causes of chest pain in

children can be diagnosed from the history and by examination. However, it has been reported that the type of pain, its position, radiation, and relieving and exacerbating factors might be less useful in defining the etiology of chest pain in children.¹⁻³ In accordance with previous studies, in this study a comparison of the characteristics of chest pain among GERD-positive and GERD-negative groups revealed that time course, duration, frequency, localization, radiation and association with meals of chest pain were not significantly different between GERD-positive and GERD-negative groups for distal and proximal sensors.

Gastroesophageal Reflux Disease, which is the retrograde passive regurgitation of gastric contents into the esophagus, is termed as pathological GERD when it results in gastrointestinal and respiratory symptoms.⁶ Gastroesophageal reflux with esophagitis is the most common gastrointestinal disorder associated with chest pain.⁴ The pain can be described as a retrosternal burning sensation (heartburn), which is aggravated by increased intra-abdominal pressure or assuming a recumbent position. Respiratory symptoms associated with GERD mainly include cough, dyspnea and wheezing.⁶ However, some studies found that even in the absence of the characteristic symptoms of GER such as heartburn, regurgitation, pain on swallowing, dysphagia, hemorrhage, or 'water brash', chil-

TABLE 3: Comparison of chest pain characteristics between GERD-positive and GERD-negative children with idiopathic chest pain.

Distal Sensor	GERD-Positive n = 8	GERD-Negative n = 23	P
Time course			
48 hours-1 week	7 (87.5%)	14 (60.9%)	0.165
1 week-6 months	1 (12.5%)	9 (39.1%)	0.222 *
Duration (min)			
1-5	4 (50%)	10 (43.5%)	0.938
5-30	3 (37.5%)	9 (39.1%)	
30-60	1 (12.5%)	3 (13.0%)	
> 60	0	1 (4.3%)	
Frequency			
1/day	4 (50%)	7 (30.4%)	0.555
2-7/week	3 (37.5%)	10 (43.5%)	
2-7/month	1 (12.5%)	6 (26.1%)	
Localization			
Left precordium	6 (75%)	18 (78.3%)	0.208
Right precordium	1 (12.5%)	0	
Sternum	1 (12.5%)	5 (21.7%)	
Radiation			
None	6 (75%)	8 (34.8%)	0.244
Right precordium	1 (12.5%)	5 (21.7%)	
Back	1 (12.5%)	7 (30.4%)	
Epigastrium	0	3 (13%)	
Increasing after meals	3 (37.5%)	6 (26%)	0.540
Proximal Sensor			
Time course			
< 1 week	5 (83.3%)	16 (64%)	0.363
> 1 week-6 months	1 (16.7%)	9 (36%)	0.634 *
Duration (min)			
< 5	2 (33.3%)	12 (48%)	0.850
5-30	3 (50%)	9 (36%)	
30-60	1 (16.7%)	3 (12%)	
> 60	0	1 (4%)	
Frequency			
1/day	3 (50%)	8 (32%)	0.709
2-7/week	2 (33.3%)	11 (44%)	
2-7/month	1 (16.7%)	6 (24%)	
Localization			
Left precordium	4 (66.6%)	20 (80%)	0.116
Right precordium	1 (16.7%)	0	
Sternum	1 (16.7%)	5 (20%)	
Radiation			
None	4 (66.6%)	10 (40%)	0.626
Right precordium	1 (16.7%)	5 (20%)	
Back	1 (16.7%)	7 (28%)	
Epigastrium	0	3 (12%)	
Increasing after meals	1 (16.7%)	8 (32%)	0.457

GERD; gastroesophageal reflux disease.

* Fisher's Exact Test.

dren with chest pain could be diagnosed as GERD.^{4,9} Dekel et al. also indicated that the symptom index provided very little improvement in diagnosing GERD-related noncardiac chest pain in adults.¹⁰ Similarly in our study, except for the respiratory associated symptoms for proximal sensor (Table 4), GERD symptom positivity (frequency of characteristic symptoms of GERD) was not significantly different between GERD-positive and GERD-negative groups for both sensors. Our data suggest that the evaluation of children with idiopathic chest pain should include pH monitoring, even in the absence of other symptoms of GERD.

In childhood, the peak incidence of chest pain is between 12 and 14 years old and chest pain affects children of all ages regardless of gender.¹⁻³ Similarly, in our study the mean age was 11.6±2.4 years and no significant difference was found between GERD-positive and GERD-negative groups according to the age and gender.

Esophageal acid exposure from GER is the most important pathophysiologic mechanism shown to play a role in the etiology of idiopathic chest pain. Although ambulatory pH monitoring can be useful in correlating chest pain with either specific GERD episodes or abnormal esophageal acid exposure, individual episodes of reflux in pH study are not consistently associated with chest pain. Therefore, making a diagnosis of reflux-related chest pain is not always easy.¹¹ Moreover, the patients were not selected for daily chest pain in our study. All patients were asymptomatic during 24-hour pH monitoring in this study and the association between chest pain and GER episodes was not established. This has been accepted as a limitation of our study. A second limitation of this study is the small number of patients. On the other hand, because these unselected children with idiopathic chest pain were consecutively referred after physical examination and laboratory tests proved negative, our study population best reflects usual medical practice.

Acid reflux is a common and potentially treatable cause of noncardiac chest pain.^{1,3} Lansoprazole has been shown in clinical trials to provide a faster

TABLE 4: Comparison of respiratory and gastrointestinal symptoms between GERD-positive and GERD-negative children with idiopathic chest pain.

	GERD-Positive n=8	GERD-Negative n=23	P
Distal Sensor			
Respiratory symptoms	4 (50%)	5 (21.7%)	0.18
Vomiting	1 (12.5%)	3 (13.0%)	1.00
Regurgitation	3 (37.5%)	6 (26.0%)	0.66
Retrosternal pyrosis	5 (62.5%)	8 (34.8%)	0.22
Abdominal pain (epigastric)	4 (50%)	9 (39.1%)	0.68
Proximal Sensor	n=6	n=25	
Respiratory symptoms	4 (66.7%)	5 (20%)	0.043
Vomiting	0	4 (16%)	0.56
Regurgitation	3 (50%)	6 (24%)	0.32
Retrosternal pyrosis	5 (62.5%)	8 (32%)	0.059
Abdominal pain	3 (50 %)	10 (40%)	0.67

GERD: Gastroesophageal reflux disease.

Fisher's Exact test was used to comparison of the study groups.

onset of action, faster control of gastric pH and, therefore, more rapid control of GERD symptoms

in patients with erosive esophagitis. Results of adult studies indicate that using treatment response to lansoprazole has a high sensitivity and specificity for the diagnosis of GERD-related non-cardiac chest pain.¹² Therefore, not only frequency of GERD but also response of chest pain to anti-reflux treatment was evaluated in this study. In the GERD-positive group, all patients reported elimination of chest pain symptoms by day thirty. Therefore, we believe that children with GERD-related idiopathic chest pain are also likely to demonstrate a good response to the lansoprazole empirical trial. However, future studies are needed to support this statement.

In conclusion, the result of this study indicates that idiopathic chest pain in children should be investigated. The symptoms of GERD-induced chest pain are often non-specific, and can be determined with certainty only by 24-hour pH monitoring, so 24-hour pH monitoring may proposed to all children with idiopathic chest pain.

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