

Published in final edited form as:

J Craniofac Surg. 2013 March ; 24(2): 380–383. doi:10.1097/SCS.0b013e31827feb08.

CLINICAL PRESENTATION OF GASTROESOPHAGEAL REFLUX DISEASE IN CHILDREN WITH CHRONIC OTITIS MEDIA WITH EFFUSION

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Introduction

Otitis media with effusion (OME) is characterized by a middle ear effusion lasting for more than 3 months and the most common cause of hearing loss in children. It generally has no clinical signs and symptoms of active infection. Principal etiopathological factors of OME are infections of the upper respiratory tract, insufficiency of ciliary clearance and drainage of the eustachian tube. Reflux of the gastric content into the larynx, nasopharynx and the eustachian tube, called as gastroesophageal reflux (GER), may be an inflammatory cofactor and can result in upper respiratory tract disorders, including OME in adult and pediatric age group.^{1,2} The angle of the immature eustachian tube in children may allow reflux of gastric contents from the nasopharynx into the middle ear. Tasker et al., had a study on 54 children aged between 2–8 years old. They took samples from middle ear effusions of these children who were undergoing myringotomy and analysed the Pepsin concentrations with ELISA and enzyme activity assays. They found a pepsin/pepsinogen concentrations of up to 1000-fold greater than those in serum in eighty three percent of the samples. This study gave an idea that the reflux of gastric content could be a major factor in glue ear in children.³ The results of animal studies demonstrated that multiple middle ear exposure to pepsin, led to eustachian tube and mucociliary clearance dysfunctions.^{2,3,4} It is very difficult to prove any relation between middle ear infections and gastroesophageal reflux disease due to their common condition in population. Gastroesophageal reflux disease is thought to have an important role in upper respiratory tract complaints, like vomiting, regurgitation, sore throat, bitter taste in the mouth, and respiratory symptoms.⁵ Except the typical symptoms of gastroesophageal reflux disease, such as emesis, burping, gagging, failure to grow, chest or

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We have no conflict of interest that we should disclose

abdominal pain, or dysphagia, children sometimes present with atypical symptoms like aerodigestive problems which is the most important one for otolaryngologists.⁶ The aim of this study was to establish the frequency of gastroesophageal reflux disease and gastroesophageal reflux disease symptoms as a risk factor in the development of chronic otitis media with effusion in the pediatric age group.

Method

Children who came to ENT department with the symptoms of hearing loss or aural fullness and diagnosed as OME which lasted more than 4 month by examination and tympanometry (Tip B curve) were included into the study. Children who have congenital or acquired abnormalities of upper gastrointestinal (GI) tract, neurological disorders, craniofacial anomalies and allergic rhinitis were excluded from the study. An informed consent was obtained from the patients and their families.

Radionuclide gastroesophageal scintigraphy was performed on all of the patients. Following a minimum of a 4-hour fasting, 100 cc 0,1 N HCL and 200 ml orange juice mixed with 300 mikroCi 99mTc DTPA was given to the patient in the upright position. All patients were placed supine position and dynamic images (64X64 byte mode matrix, 15 s/frames, total 240 image) were carried out with using a gamma camera (Toshiba GCA 602 A/SA, Japan) fitted with a low energy, general purpose collimator. Regions of interest (ROI) were drawn from the oesophagus and time-activity curve (TAC) were generated. Scintigraphic evaluation classified by TAC: become flat and below of initial activity; reflux negative, TAC increased 10% or more of initial activity; reflux positive.

Patients had undergone a prolonged ambulatory 24-h esophageal pH monitoring. The Synetics pH 1.07 and 7.01 buffer solutions were used in the calibration of the pH-electrodes. The distal pH-probe was placed at the level of the distal 1/3 of the esophagus and the proximal probe was placed in the hypopharynx. The correct position of the naso-esophageal catheter was controlled by Chest X-ray. The probe was connected to a Digitraper MK III (Synetics Medical AB, Stockholm Sweden). All cases kept their routine life style and took the routine diet but only the very hot and cold drinks were forbidden. Data were analyzed using Software Synetics. A decrease in esophageal pH to less than 4 for at least 15 seconds was defined as acid reflux. We used some variables; the reflux index (RI; the percentage of time when pH was lower than 4), the number of reflux episodes, the number of reflux episodes longer than 5 minutes, and the longest episode of reflux. An RI greater than 5% was considered to be reflux positive.^{7,8} Results of gastric scintiscan and 24 hour pH probe were examined, and at least one positive test resulted in inclusion in the gastroesophageal reflux disease positive group.

We recorded age, gender, main complaint, and symptoms. We divided the symptoms into two groups (A and B): (A) the airway symptoms including stertor, stridor, frequent cough, recurrent croup, wheezing, obstructive apnea, cyanotic spells, hoarseness, nasal congestion, and throat clearing; (B) the feeding symptoms including wet burps, globus sensation, frequent emesis, dysphagia, choking/gagging, sore throat, halitosis, food refusal, stomach aches, arching, drooling, chest pain, irritability, and failure to thrive. Two symptom groups were evaluated by pooling variables: airway (included stridor, frequent cough, throat clearing), and feeding (included irritability, pyrosis, failure to thrive). These variables were used due to their relatively common frequency in the group and their possible relation to gastroesophageal reflux disease. We accept the results as positive if the case had at least one of the symptoms contained in the group.

Data were analysed using the SPSS 15.0 computed statistical software. Data were defined by “mean \pm sd” and percent (%). The chi-squared test and Fisher’s exact test were used to test for the importance between the data. A p-value <0.05 was considered to indicate significance.

Results

Of the patients 40 (56,3%) girls and 31 (43,7%) boys with a mean age of 6.3 ± 3.2 year (minimum, 1 year; maximum, 13 years). There were 39 (54.9%) patients in gastroesophageal reflux disease positive group, and 34 patients (45.1 %) in gastroesophageal reflux disease negative group. There was no statistical difference between the gastroesophageal reflux disease positive and negative groups from the point of age, sex, duration of complaints ($p>0.05$) (Table 1).

Stertor(12,8%), dysphagia (20,5%), pyrosis (25,6%), irritability (20,5%) and choking: gagging (12,8%) were the more frequent symptoms in the gastroesophageal reflux disease positive group when both the gastroesophageal reflux disease positive and gastroesophageal reflux disease negative groups were compared. The gastroesophageal reflux disease negative group showed a higher incidence of throat clearing (28,1%) and Failure to thrive (21,9%). There was no statistical difference between the gastroesophageal reflux disease positive and negative groups from the frequencies of symptoms ($p>0.05$). Some symptoms including: stertor, recurrent croup, wet burps, globus sensation, halitosis, food refusal, stomach aches, arching, drooling and chest pain were not found in children. These results are shown in (Table 2).

No significant difference was seen when we compared the gastroesophageal reflux disease positive and negative groups according to total number of symptoms (Table 3). gastroesophageal reflux disease positive group had a tendency to have more symptoms.

Thirty four percent of the gastroesophageal reflux disease negative group did not show any findings in the symptom complexes, but the gastroesophageal reflux disease positive group had a percentage of 25,6% (Table 4). 74,4% of the gastroesophageal reflux disease positive group had one or more positive symptom complexes. Percentage of positive symptom complexes for gastroesophageal reflux disease positive and gastroesophageal reflux disease negative groups was statistically no different ($>0,05$).

All of the ENT disorders were found more frequent in gastroesophageal reflux disease positive group (Table 5). Between the gastroesophageal reflux disease positive and gastroesophageal reflux disease negative groups tonsillitis/pharyngitis was significantly more frequent in gastroesophageal reflux disease positive group ($<0,05$).

Discussion

Otitis media with effusion (OME) is the most common cause of hearing problems and it affects pediatric age group.⁹ The pathogenesis of middle ear effusion in children is multifactorial. Infections, anatomical problems, impaired immunologic status, allergic history, familial predisposition, male gender, feeding method and environmental factors have role in pathogenesis. Gastroesophageal reflux is another frequent problem in the newborn and preschool ages. It was suggested in recent researches that the gastroesophageal reflux disease may be related to eustachian tube dysfunction and otitis media.

Reflux of gastric contents into the nasopharynx can cause inflammation of the nasopharynx and eustachian tube. And these contents can arrive into the middle ear due to the angle of the immature eustachian tube and can cause to lay the groundwork for bacterial infections.^{1,10}

Several studies, aimed to prove the relationship between GER and OME, demonstrated that the intermittent application of gastric contents to the middle ear mucosa led to the eustachian tube and mucociliary clearance dysfunctions.^{2,4} In the middle ear fluid samples, which was collected after the myringotomy, it was determined that pepsin/pepsinogen concentrations up to 1000-fold greater than in those serum and no evidence of pepsin production in the middle ear biopsy specimens.³ Gastroesophageal reflux disease has been found in 55,6 to 64 percent of the children with OME and OME frequency has increased in children with GER reported by clinical studies.^{11,12,13} In our study, similar with the literature, gastroesophageal reflux disease were demonstrated in 39 (54,9%) of 71 children with OME.

Predominant symptoms seen in GER are related to GIS such as nausea, vomiting or pyrosis, regurgitation, emesis, sore throat, sour or bitter taste in the mouth. But extra-GI symptoms like chronic cough, hoarseness, pharyngitis, recurrent bronchitis, reflex apnea are also common in childhood. Their frequency is not well known and they are not limitative. The symptoms of GER seen in pediatric age group have been investigated and known in recent studies. Feranchuk et al evaluated infants with pH probes and video and found that irritability, regurgitation: burping, yawning, stridor, arching or mouthing were related to reflux episodes.¹⁴ Cough and stridor can be the only symptoms of gastroesophageal reflux disease.^{15,16} Krishnamoorthy et al. determined the most common respiratory symptoms in infants with gastroesophageal reflux disease as apnea/bradycardia, pneumonia, cyanosis, cough, and stridor, and found that the most of the patients were misdiagnosed before gastroesophageal reflux disease was discovered.¹⁷ Altman et al. found that 28% of children requiring hospitalization for congenital airway abnormalities have gastroesophageal reflux disease and the most common presenting symptom was stridor with the most common location as the larynx.¹⁸ Our most common symptoms were stertor (12,8%), dysphagia (20,5%), pyrosis (25,6%), irritability (20,5%) and choking: gagging (12,8%). Throat clearing (28,1%) and failure to thrive (21,9%) were more common in gastroesophageal reflux disease negative group. These symptoms were no significantly different between two groups. To be able to use a symptom in gastroesophageal reflux disease diagnosis, it must be seen relatively frequently in the gastroesophageal reflux disease positive group and relatively infrequently in the gastroesophageal reflux disease negative group. None of these symptoms evaluated here are enough to be diagnostic by itself, therefore the pooling of symptoms are used to perform symptom groups. Typical gastroesophageal reflux disease symptoms were not common in patient group, even in many cases they were less common in the gastroesophageal reflux disease patients than in the gastroesophageal reflux disease negative patients. The types of gastroesophageal reflux disease symptoms we evaluated in our study are similar to those reported in the literature. Clinical history alone is probably not sufficient to diagnose the gastroesophageal reflux disease, but it can be useful to guide the clinician. History is important in suspicion of gastroesophageal reflux disease. The tests used for diagnosis still have some insufficiencies and may be falsely negative in some cases; therefore medical therapy for gastroesophageal reflux disease can be tried because of the symptoms in these cases. Shaw and Searl demonstrated the importance of symptomatology in treatment of laryngeal reflux in a group of adult patients. There was statistically significant improvement in symptoms such as throat clearing, globus sensation, and hoarseness in their group of adult patients who were undergone a reflux treatment.¹⁹ ENT disorders such as chronic rhinitis/sinusitis, laryngitis (and hoarseness, vocal cord granulomas, vocal cord ulcers), otitis/otalgia, tonsillitis/pharyngitis, adenoid hypertrophy thought to be caused by gastroesophageal reflux disease.

El-Serag compared 1980 children with gastroesophageal reflux disease (age: 2–8 years) to 7920 controls and found that children with gastroesophageal reflux disease were significantly more likely to have the diagnosis as sinusitis and laryngitis and less likely to have the diagnosis as otitis media.²⁰ Phipps et al. used 24-hour pH monitorization and

reported that 19 (63%) of 30 children with chronic sinusitis had gastroesophageal reflux disease. In 15 (79%) of these 19 patients, sinus symptoms healed after treatment of GRD.²¹ In another retrospective study with 155 children underwent laryngoscopy and bronchoscopy, gastroesophageal reflux disease as defined by upper gastrointestinal contrast series, pH probe, gastric scintiscan, or esophageal biopsy was found in 130 cases (84%). 90% of these patients was seen to have a laryngotracheal abnormality.²² Barbero²³ showed in his study that 68% of children with chronic sinusitis who did not recover with appropriate medical treatment and candidates for endoscopic sinus surgery had a remission of symptoms after 3 months of antireflux treatment. After 2 years, the percentage was 89% who had remission of symptoms. Halstead²⁴ had similar results in children with upper respiratory tract symptoms, 96% of whom had pathologic pHmetry. Of these, 90% responded to antireflux treatment. Phipps et al.²⁵ had a study about the relation between gastroesophageal reflux disease, nasopharyngeal reflux and chronic sinus disease and he has demonstrated that 79% of patients showed remission of symptoms after treatment of gastroesophageal reflux disease. Silvia et al.²⁶ detected a 68.88% incidence of chronic nasal obstruction, while Carr et al.²⁷ reported a 45% incidence in 214 children with gastroesophageal reflux disease and a 47% incidence in 81 controls. Parlier et al.²⁸ reported the high frequency of gastroesophageal reflux disease in 22 of 33 infants (66.6%) with the complaint of subchronic otitis, whereas in 19 of that 22 patients, they also reported the presence of “silent” GER.

Relations between gastroesophageal reflux disease and tonsillitis/pharyngitis or adenoid hypertrophy highly reported in literature. Silvia et al.²⁶ 24.44% had recurrent tonsillitis and to a 90.90% cure rate in patients with recurrent tonsillitis. Keles et al. revealed that children with adenoid hyperplasia had a higher frequency of pharyngeal reflux than the healthy group at the same age.²⁹ In our study all of the ENT disorders were found more frequent in gastroesophageal reflux disease positive group (Table 5). Between the gastroesophageal reflux disease positive and gastroesophageal reflux disease negative groups only tonsillitis/pharyngitis (33,3%) was significantly more frequent in gastroesophageal reflux disease positive group ($P<0,05$).

Conclusion

Gastroesophageal reflux disease should be considered in the patients with OME or other upper respiratory tract infections. No concordance may be found between the complaints and gastroesophageal reflux disease findings. For this reason, a decision about gastroesophageal reflux disease; should not only be made by looking to complaints, diagnostic tests must also be performed.

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Table 1

Demographic data of the patients

	GERD positive	GERD negative	P
Number of patients	39 (%54,9)	32 (%45,1)	
Age (year)	6,1 ± 3,5	6,5 ± 2,9	>0,05
Gender male	15 (%40,5)	16 (%47,1)	>0,05
female	22 (%59,5)	18 (%52,9)	
Duration of complaints (month)	25±19,5	20,8±14,5	>0,05

Table 2

Frequencies of symptoms in GERD positive versus GERD negative children

Chief complaint positive	% GERD negative N=39	% GERD N=32	P
Airway complex	61,5	59,4	>0,05
Stridor	12,8	6,3	>0,05
Wheezing	5,1	00	>0,05
Apnea/ cyanosis	5,1	00	>0,05
Frequent cough	53,8	53,1	>0,05
Recurrent croup	10,3	6,3	>0,05
Throat clearing	12,8	28,1	>0,05
Hoarseness	7,7	3,1	>0,05
Feeding complex	43,6	34,4	>0,05
Regurjitation	15,4	12,5	>0,05
Dysphagia	20,5	9,4	>0,05
Frequent emesis	7,7	6,3	>0,05
Failure to thrive	17,9	21,9	>0,05
Choking/gagging	12,8	3,1	>0,05
Pyrosis	25,6	15,6	>0,05
Irritability	20,5	9,4	>0,05
Anemia	2,6	3,1	>0,05

Table 3

Total number of symptoms for GERD positive and GERD negative children (%)

% with Symptoms	GERD positive N=39	GERD negative N=32	P
0-2 Symptoms	64,1	75,0	>0,05
3-5 Symptoms	30,8	25,0	>0,05
6+ Symptoms	5,1	0	>0,05

Table 4

Percentage of positive symptom complexes for GERD positive and GERD negative children

No. positive Symptom complexes	% GERD positive N=39	% GERD negative N=32	P
0	25,6	34,4	>0,05
1	43,6	37,5	>0,05
2	30,8	28,1	>0,05

Table 5

Percentages of ENT findings for GERD positive versus GERD negative groups

ENT findings	% GERD Positive N=39	% GERD negative N=32	P
Rhinitis/sinusitis	38,5	34,4	>0,05
Adenoid hypertrophy	35,9	18,8	>0,05
Tonsillitis/pharyngitis	33,3	12,5	<0,05
Laryngitis (Hoarseness)	7,7	3,1	>0,05