

Pepsinogen Assay as a Marker of Reflux in Children with Otitis Media with Effusion

Abstract

Background: Otitis media with effusion remains the most common cause of deafness in childhood. Reflux of gastric contents into the nasopharynx and then into the middle ear cleft has been reported as a contributing factor in the development of OME.

Objective: To investigate the relationship between gastro esophageal reflux diseases (GERD) and Otitis media with effusion (OME) by evaluation of the presence of gastric pepsinogen in middle ear fluid of children with OME.

Materials and Methods: In this prospective study, middle ear effusions as well as blood samples were collected from 25 patients suffering from OME and undergoing bilateral myringotomy with ventilation tube insertion. Total pepsinogen concentrations of effusions and serum samples were measured with an enzyme-linked immuno sorbent assay (ELISA) using Human Pepsinogen I ELISA Kit.

Results: 64% (16 cases) of the study sample (25 children) were found with pepsinogen in the middle ear effusions while 36% (9 cases) were not found to have pepsinogen in the middle ear. The concentrations of pepsinogen measured in the effusions were found to be higher than the levels found in the serum of the same patients as detected in each case separately.

Conclusion: GERD should be considered one of the contributing factors in the etiopathogenesis of OME.

Keywords: Gastro esophageal reflux disease; Otitis media with effusion; Pepsinogen

Research Article

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Abbreviations: OME: Otitis Media with Effusion; GER: Gastro Esophageal Reflux; ELISA: Enzyme-Linked Immuno Sorbent Assay; GERD: Gastro Esophageal Reflux Diseases

Introduction

Otitis media with effusion (OME) is defined as chronic inflammation of the middle ear mucosa characterized by the retention of fluid within the middle ear space without signs or symptoms of an acute ear infection. It is highly prevalent during childhood, with more than 50% of children experiencing OME in the first year of life. Although most episodes resolve spontaneously, 5 to 10% of cases will persist for over 1 year [1]. The role of gastro esophageal reflux (GER) or extra esophageal reflux in this disease has only been recognized recently as one of the risk factors for OME in children [2]. GER disease (GERD) occurs when gastric contents reflux into the esophagus or oropharynx and produce symptoms. It has been linked to the development of many airway disorders: croup, chronic cough, laryngospasm, laryngomalacia, vocal cord nodules, asthma, reactive broncho constriction, apnea, sudden infant death syndrome, rhinitis, sinusitis, subglottic stenosis, and glottic granuloma. The possible relationship between GER and OME has been studied over recent years. GER is thought to cause inflammation of the nasopharynx, dysfunction of the Eustachian tube, and impairment of the mucociliary clearance, thus

increasing in the incidence of OME [3]. The repeated exposure of the ciliated respiratory epithelium to pH 4 or less blocks ciliary movement and mucus clearance, HCl and pepsin cause local inflammation, edema, and ulceration of the respiratory mucosa, leading to loss of tube ventilatory function and this leads to impaired pressure equalization with persistent negative pressure, resulting in middle ear effusions [4].

Materials and Methods

This study includes 25 patients suffering from otitis media with effusion (clinically diagnosed). The patients were chosen from outpatient clinic of Otorhinolaryngology, Menoufia University Hospital with mean age 6.44 ± 1.72 years the minimum was 4 years and maximum was 9 years. Male represent 56% (14) of the studied group and female 44% (11). A written consent was taken from the parents of all patients. We excluded children reviving treatment for gastric disorders and patients with allergic diseases. Tympanometry and pure tone audiometry were done to confirm the diagnosis of OME and to evaluate the condition of hearing. All patients were prepared for myringotomy with insertion of ventilation tube and then middle ear effusions as well as blood samples were collected. The effusion fluid samples were centrifuged to separate cellular components and were stored at -20°C for later pepsinogen assay. The blood samples were allowed to clot for 30 min at room

temperature and centrifuged for 5 min to separate the serum, the separated serum was stored at -20°C . Then pepsinogen concentrations of all effusions as well as serum samples were measured by use enzyme-linked immuno sorbent assay (ELISA) using Human pepsinogen 1 ELISA Kit, (Epitope Diagnostics, Inc, USA). The normal serum pepsinogen level is 49.8–86.6 ng/ml. All pepsinogen levels in middle ear effusion above 90 ng/ml were considered as a significant mark for presence of gastric pepsinogen rather than pepsinogen transudation from the patient's own plasma.

Results

The study shows no significant difference between group with & without pepsinogen in the middle ear regarding Age & Sex (Table 1). There were high significant differences between pepsinogen level in serum & middle ear (Table 2). There were no significant differences between group with and without pepsinogen in the middle ear regarding upper respiratory disorder except recurrent OM (Table 3). There were significant differences between group with and group without pepsinogen in the middle ear regarding gastro-esophageal reflux disorder (Table 4).

Table 1: Age and sex distribution in group with and without pepsinogen in the middle ear.

	Group without Pepsinogen in the Middle Ear (n= 9)		Group with Pepsinogen in the Middle Ear (n= 16)		Test of Significance	P value
Age Mean \pm SD Median Range	5.94 \pm 1.83 6.00 3.5-9.00		6.72 \pm 1.64 6.75 3.5-9.0		t= 1.08	>0.05 NS
Sex	No.	%	No.	%	FE=0.001	>0.05 NS
Male	5	55.6	9	56.2		
Female	4	44.4	7	43.8		

FE=Fisher Exact Test

Table 2: Correlation between pepsinogen level in serum and middle ear.

Pepsinogen Level In Middle Ear	Pepsinogen Level In Serum	
	r	P value
	0.69	<0.001**

**Highly Significant, r =Correlation Coefficient

Table 3: Frequency distribution of upper respiratory disorders in group with and without pepsinogen in the middle ear.

Upper Respiratory Disorders	Group without Pepsinogen in the Middle Ear (n= 9)		Group with Pepsinogen in the Middle Ear (n= 16)		Fisher's Exact Test	P value
	No.	%	No.	%		
Recurrent O.M.	3	33.3	4	25	7.6	0.02*
Otalgia	1	11.1	2	12.5	0.01	0.92 NS
Rhinorrhea	2	22.2	8	50	1.85	0.17 NS
Negative	3	33.3	2	12.5	1.56	0.21 NS

*Significant

Table 4: Frequency distribution of gastro-esophageal reflux disorder in group with and without pepsinogen in the middle ear.

GERD Disorders	Group without Pepsinogen in the Middle Ear (n= 9)		Group with Pepsinogen in the Middle Ear (n=16)		Fisher's Exact Test	P value
	No.	%	No.	%		
Vomiting & Regurgitation	1	11.1	11	68.8	7.7	0.006
Yes	8	88.9	5	31.2		
No						

Discussion

OME is the most common cause of deafness in children, and the etiology of OME is largely considered to be multi factorial, including factors such as infections, allergies, Eustachian tube dysfunction, adenoid hypertrophy, etc but recently, there is an increasing interest in GERD as one of the major contributing factors to this condition [5,6]. It has been demonstrated that the laryngeal epithelium is more sensitive than the esophagus to injury by gastric reflux. Based on pH monitoring studies, up to 50 reflux episodes per day into the esophagus (below pH 4) are considered normal. In contrast, it has been shown experimentally that as few as three reflux episodes per week can produce severe laryngeal damage [7]. O'Reilly et al. [6], as they made a study on a very large number of patients with OME, they found that the incidence of pepsinogen of the effusion samples was 14% (125/893). He et al. [8] also made a study on a large number of patients with OME and they found that 14.4% (22/152) of the patients had high pepsinogen level either in one ear sample or both, with no pepsinogen activity detected in their serum.

In this study our sample consisted of 25 children, regarding presence of pepsinogen in the middle ear 16 of the study sample are found with pepsinogen in the middle ear and 9 were not found to have pepsinogen in the middle ear, mean age was 6.44 ± 1.72 the minimum was 4 years and maximum was 9 years, and there was no significant difference regarding age between group with pepsinogen in middle ear (6.72 ± 1.64) and group without (5.94 ± 1.83). Male represent 56% (14) of the studied group and female 44% (11), with no significant difference between group with pepsin in middle ear and group without regarding age & sex.

Our finding about age was in contrary with Wilson [9] as he found Pepsin concentration in the middle ear of children younger than 1 year was significantly higher than in older age groups. In this study we found that there were high significant differences between pepsinogen level in serum & middle ear of the studied group.

And this was in agreement with Nair et al. [10], a prospective trial study, as they found that 65.63% (21 of 32) of patients with OME had high pepsinogen levels in their middle ear effusion samples, higher than 90 ng/ml.

This study showed that there were no significant differences between group with pepsinogen in the middle ear and group without regarding upper respiratory disorder except recurrent OM.

And these findings are in agreement with a study that investigated the causal relationship of GERD and OME by confirming the finding of pepsin/pepsinogen in the middle ear fluid of children undergoing myringotomy and tube placement for chronic or recurrent OM, and querying parents about symptoms that suggest the presence of GERD in these children [11]. Our study reported that there were significant

difference between group with pepsinogen in the middle ear and group without regarding GER disorders. And these findings are in agreement with Orenstein et al. [12] as they found a high significant association between GERD and presence of pepsinogen in the middle ear.

Conclusion

GER should be considered as one of the contributing factors in the etiopathogenesis of middle ear effusion, as gastric pepsin reaches the middle ear through the nasopharynx and the Eustachian tube to cause OME, and therefore, control of GER may play a role in the prophylaxis and management of OME and avoidance of tympanostomy. Also controlling GER may play a role in management of other reflux-related disorders e.g. persistent rhinorrhea, otalgia....etc.

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