

# THE POSSIBLE ROLE OF GASTROESOPHAGEAL REFLUX DISEASE IN CHILDREN SUFFERING FROM CHRONIC OTITIS MEDIA WITH EFFUSION

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**Abstract-** The aim of this study was to compare the efficacy of antireflux therapy with both conventional management and those with no treatment in children with chronic otitis media with effusion (COME). In this prospective randomized clinical trial ninety children with COME which lasted more than 3 months or more, documented by physical examination and Type B tympanogram in at least one ear without clinical signs and symptoms of active infection that were refractory to 3 period of antibacterial treatment, were randomly allocated to receive a 3 month course in three groups of antireflux treatment (AR group, Cisapride 1 mg/kg/day), conventional antibacterial treatment (AB group, Co-amoxiclavate 40 mg/kg/day TID) and those with no treatment (Control group, no medication). All patients were followed every month. The favorable response was considered as complete resolution of effusion clinically and type A or more than -200 peak in tympanometry. Of the 30 patients assigned to AR group, 10 (33.3%) were judged to be clinically cured and in AB group 12 (40%) were cured while only 3 (10%) in control group were cured. The cure rate in AR and AB groups was significantly higher compared with control group but there was no significant difference between cure rates in AR and AB groups ( $P=0.59$ ). No subjects experienced complications during or after the study. There may be a possible role for GER medical management in patients with COME. Further investigations are necessary in order to confirm this hypothesis.

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**Key words:** Antireflux therapy, children, chronic otitis media with effusion, gastroesophageal reflux

## INTRODUCTION

Chronic otitis media with effusion (COME) or Glue ear remains the most common cause of deafness in childhood (1). There are various etiological factors, which can cause COME. Gastroesophageal reflux (GER) is a common problem in the newborn and preschool periods (1).

GER is believed to be an important contributing factor in many disorders of the upper respiratory tract as well as the developments of other phenomena such as otitis in children (2-7). Recently, Tasker et al. (8,9) reported high concentrations (up to a 1000-fold greater than serum levels) of pepsin/pepsinogen in 59 of 65 middle ear effusion samples from children with COME. The pepsin in middle ear effusions is almost certainly due to reflux of gastric contents.

It is possible to suppose on the basic of these findings that GER both, by local impact on the epipharynx area, or by reflex could emerge as the factor creating the conditions for the development of COME and there may be a role for antireflux therapy

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in the treatment of otitis media with effusion (8,9). It has been shown that in adults with chronic refractory secretory otitis media or chronic refractory feeling of pressure in the ear(s) medical management of GER accounts as an effective therapy (10).

The role of the antireflux therapy in the treatment of children with chronic otitis media with effusion (COME) is not clear and the aim of this study was to compare the efficacy of antireflux therapy with both conventional management and those with no treatment in children with COME.

## MATERIALS AND METHODS

In a prospective randomized clinical trial study, 90 children with chronic otitis media with effusion (secretory otitis media) which lasted more than 3 months or more, documented by physical examination and Type B tympanogram in at least one ear without clinical signs and symptoms of active infection that were refractory to 3 period of antibacterial treatment were included.

All patients underwent thorough examination for medical history and ENT examination. In all of the patients the presence of effusion were confirmed by clinical examinations by two separate ENT surgeons and the attendance of type B or C with peak less than -200 in tympanometry. Tympanometry was classified according to Jerger (11), while otitis media with effusion was classified according to the Maastrichts' Otitis Media With Effusion Study protocol (1,2).

Exclusion criteria were past medical history of disorders that are known to be associated with an increased prevalence of recurrent otitis media (ROM), otitis media with effusion (OME), with known etiology such as Down syndrome, cleft palate, neurodevelopmental delay, patients with genetic or congenital palate, craniofacial malformations or previously underwent VT or adenoidectomy operations, those with immunodeficiency, evidences of cholesteatoma, sensorineural hearing loss or other medical conditions (Renal, liver or cardiac illnesses).

The patients were randomly allocated to receive a 3 month course in three groups of antireflux

treatment (AR group, n=30), conventional antibacterial treatment (AB group, n=30) and those with no treatment (Control group, n=30) according to a computer-generated randomization schedule. All patients participated in the study only after the consent from parents had been obtained.

In AR group, patients were treated with Cisapride 1 mg/kg/day and patients in AB group received Co-amoxiclavate 40 mg/kg/day (maximum, 750 mg/day) in three divided doses (every 8 h without regard to meals) and the control group received no medication.

All patients were followed every month. The favorable response was considered as complete resolution of effusion clinically and type A or more than -200 peak in tympanometry by two unique independent ENT surgeons blinded to subject group assignment.

Data are expressed as mean  $\pm$  SD or number of patients. Parametric data were analyzed using one-way analysis of variance. When significant difference among groups was present, pair-wise multiple comparisons of mean testing (Tukey's method) were performed. For categorical data analysis Chi-squared test was utilized. Statistical calculations were performed utilizing SPSS version 12.0. Differences were considered significant at  $P < 0.05$ .

## RESULTS

No patients were excluded. Of the 90 children studied, 46 were males and 44 females, ranging in age from 2 to 12 years old, with a mean age of  $5.3 \pm 0.8$  years old. There were no significant differences among groups' demographic data with respect to age and sex (Table 1).

Of the 30 patients assigned to AR group, 10 (33.3%) were judged to be clinically cured and in AB group 12 (40%) were cured while only 3 (10%) in control group were cured. The cure rate in AR and AB groups was significantly higher compared with control group but there was no significant difference between cure rates in AR and AB groups ( $P=0.59$ ). (Table 1) No subjects experienced complications during or after the study.

**Table 1.** The patients' characteristics and treatment response

	Control (n=30)	AB (n=30)	AR (n=30)
Age (yr)	5.1±0.5	5.8±0.3	5.3±0.1
Sex			
Male (no.)	15	14	17
Female (no.)	15	16	13
Response to treatment (no.)	3	12*	10**

NOTE. Data are represented as mean ± SD or numbers.

AR: Antireflux treatment group

AB: Antibacterial treatment group

\*: Significant difference with control group (Chi-square,  $P=0.007$ )

\*\* : Significant difference with control group (Chi-square,  $P=0.028$ )

## DISCUSSION

An increasing number of studies have indicated that GER is a potential factor in the development of chronic ear inflammation (3,6,13-15).

Gastroesophageal reflux is a common physiological occurrence in neonates and infants that decreases in frequency during the first year of life. Reflux of gastric content from the nasopharynx into the middle ear is, possibly, due to the angle of the immature Eustachian tube, a manifestation of skull anatomy in children (8). Controversial hypotheses exist regarding the manner of its effect. Possible mechanisms of GER-mediated damage to extraesophageal structures include direct-contact damage of mucosal surfaces by acid-pepsin exposure and a vagal reflex arc between the esophagus and the upper aerodigestive tract, triggered by acid reflux (4,16) or bacterial (eg, *Helicobacter pylori*) colonization of upper aerodigestive tract tissues (17-20).

Tasker et al. (8,9) found elements with a gastric content in middle ear secretion in chronic secretory otitis. The effect of elements from gastric juices on the structure of the mucous membrane of the ear has been described in numerous experimental studies (7,21). This would cause inflammation of the nasopharynx and Eustachian tube, making pressure equalization difficult and, possibly, inducing Eustachian tube dysfunction (1,7,8) and middle ear mucociliary clearance disturbances (22). Gastric juice that reflux into the middle ear will cause

transient damage to the Eustachian tube and the middle ear mucosa before it can be neutralized, resulting in inflammation and thus, ideal condition for secondary bacterial colonization, leading to the symptoms associated with glue ear (9).

The results of our study indicate that patients in AR group had a comparable cure rate with AB group that both were significantly higher than control group (33.3% vs. 40% compared to 10%). These findings were parallel with the results of earlier clinical trials which also utilized antireflux regimen in the treatment of refractory chronic sinus disease, (23-25) chronic laryngitis (26), and adult chronic ear complaints (10,27). Furthermore it was shown that antireflux surgery provided definitive and successful treatment of GER-induced otolaryngologic disease. However the authors clarified that medical management should remain the mainstay of GER therapy (28).

Based on reports in the literature and our own findings we hypothesize that medical management of GER can have a role in children with COME. Comparing our results with the control group makes the findings more reliable. But in this study we surprisingly found a high cure rate in AB group. It may be due to the definition of COME that was utilized. We enrolled cases that were refractory to three period of antibacterial treatment while these findings suggest that there may be a role for the forth period of antibacterial treatment which needs further investigations. Also we have no explanation for mysterious cure of 10% patients in control group. It should be partly depends on the mysteriously individual functional ability of the auditory tube, individual sensitivity to GER and other unidentified factors. In addition there is a considerable gap between the success rate of GER medical treatment in the present study and pervious reports. (about 80% van den Abbeele et al. (29) and 66.7% in Gibson et al. (3). It can be due to the lack of GER demonstration in this study. In the ideal form it would be better to detect patients with GER by the means of 24-hour esophageal pH monitoring as the 'golden standard' in assessment of GER in children prior to the treatment. But it is believed that children with ear, nose and throat disorders have a high incidence of pathologic GER (6,24,30-32). Tasker et

al. (8,9) showed that in the majority of children with COME, GER could be demonstrated. In another recent study, Rozmanic et al (6) found pathologic GER (defined as greater than 5% of time when pH was less than 4) by 24-hour pH monitoring in 55% of 27 patients with either ROM or OME. Lieu et al. (32) also replicated the finding of pepsin/pepsinogen in middle ear fluid of children with COME or ROM, but they did not find any increase in GER symptoms.

We are aware of the controversy concerning the connection between GER and inflammatory diseases of the middle ear. While it has been shown that pharyngeal reflux may play an important role in the etiology of COM with effusion, (30) some authors believe that the current data are not enough to support antireflux treatment in children with refractory middle ear infections (1). In this study we have attempted to justify our assumption regarding the possible role of GER medical management and the cure of COME by illustrating the difference in response rate between two treatment groups and control group patients. Further investigations are necessary in order to confirm the hypothesized significance of GER medical management as an efficient treatment modality in chronic inflammatory ear diseases. In conclusion, there may be a possible role for GER medical management in patients with COME. Further investigations are necessary in order to confirm this hypothesis.

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