British Journal of Medicine & Medical Research
20(9): 1-6, 2017; Article no.BJMMR.31845
ISSN: 2231-0614, NLM ID: 101570965

SCIENCEDOMAIN *international*
www.sciencedomain.org

Role of Laryngopharyngeal Reflux in Eustachian Tube Dysfunction in Adults

Ugo Cesari[1*], Pasqualina Apisa[1], Simona Ruggiero[2], Arturo Armone Caruso[1], Teresa Russo[2], Donato Alessandro Telesca[2], Cesare Formisano[2] and Luigi Sivero[2]

[1]Department of Head and Neck, Federico II University Hospital, Naples, Italy.
[2]Department of Gastroenterology, Endocrinology and Surgery, Federico II University Hospital, Naples, Italy.

Authors' contributions

This work was carried out in collaboration between all authors. Authors UC, LS and PA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors SR, AAC and DAT managed the analyses of the study. Authors TR and CF managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2017/31845
Editor(s):
(1) Domenico Lapenna, Associate Professor of Internal Medicine, Department of Medicine and Aging Sciences, University "G. d'Annunzio" Chieti-Pescara, Chieti, Italy.
Reviewers:
(1) Shawki Mahmoud Elmoursi, Mansoura university, Egypt.
(2) Natasa Kovac, University Hospital Centre Zagreb, Zagreb, Croatia.
(3) Karol Zelenik, University Hospital, Czech Republic.
Complete Peer review History: http://www.sciencedomain.org/abstract/18501

Original Research Article

Received 27th January 2017
Accepted 28th March 2017
Published 4th April 2017

ABSTRACT

We have here studied the relationship between Eustachian tube dysfunction and laryngopharyngeal reflux, evaluating also the results of medical therapy in patients with such problems. Based on clinical, endoscopic and cytological investigations, we found that acid laryngopharyngeal reflux was the basis of audiological symptoms and chronic dysfunction of the Eustachian tube.

Keywords: Eustachian tube dysfunction; laryngopharyngeal reflux; gastro-esophageal reflux.

**Corresponding author: E-mail: ugo.cesari@unina.it;*
Communication id: sivero@unina.it;

1. INTRODUCTION

In recent years, gastroesophageal reflux has been found to involve a large number of people; indeed, its incidence in developed countries is about 20-40% for patients between 45 and 65 years of age, a percentage that is growing up to the range of 65-75 [1]. Half of children in the range of 0-3 months of age, presents at the least an episode of regurgitation during the day, but this kind of event trends to disappear later due to the psychomotor development.

The wrong food and behavior habits (huge meals, fat rich food, caffeine, clinostat position), smoking, pregnancy and obesity may increase the expression of disease [1].

Gastroesophageal reflux (GER), in particular extra-esophageal reflux, has been associated with a variety of upper aerodigestive tract symptoms or diseases, such as sinusitis and otits [2].

Many Studies show the role of reflux in chronic otitis media in children [2-5].

Middle ear effusions (MEE) is characterized by the presence of hypersecretion of mucous in the middle ear space for 3 months or longer. Children with persisting MEE also frequently have recurrent acute otitis media (OM).

MEE often interferes with hearing and can lead to speech and developmental delay [3].

Furthermore, it is a chronic inflammatory condition, of which the causes are thought to be multifactorial. Bacterial infections, obstruction of the Eustachian tube, respiratory tract viruses, and formation of bacterial biofilms have all been suggested to play a role in the development of this condition.

Besides, in recent years, extra-esophageal reflux (EER) is supposed to be as a possible associated factor in the pathogenesis of OM and Eustachian tube dysfunction [4-7].

EER in young children and infants is a common phenomenon, and reflux into the middle ear in children is possible through an immature Eustachian tube.

As a matter of fact, reflux of gastric acid and pepsin into the middle ear and Eustachian tube has the potential to cause mucosal inflammation and result in Eustachian tube dysfunction. It is more accurately defined as failure of the functional valve of the Eustachian tube to open and/or close properly. The symptoms involve aural fullness or popping discomfort/ pain for a period of less than three months in case of acute Eustachian tube dysfunction and more than 3 months in case of chronic dysfunction [6-8].

We hypothesize, with the support of the literature [6-9], that the Eustachian tube dysfunction and the resulting middle ear problems are related to the extra-esophageal reflux, when it occurs.

2. METHODS

52 subjects were exanimate, 32 females and 20 males (from 22 to 55 years). They were complaining aural fullness, popping discomfort/pain and extra-esophageal reflux symptoms such as dysphonia, dysphagia, pain on swallowing and raclage; however, only 10 subjects (six females and four males) have been found to fit for our study.

As a matter of fact, after physical examination, medical history, tonal audiometric examination and impedance examination, we excluded patients with: previous barotrauma which causes dysfunction of Eustachian tube, tinnitus persisting since more than six months, sensorineural and mixed hearing loss, otosclerosis, maxillofacial malformations, middle and internal ear malformations.

Preliminary tests:

- Tonal audiometric examination
- Impedance audiometry (tympanometry, Eustachian function test)
- Rhinopharingolaryngoscopy with flexible endoscope (to evaluate a possible obstruction of tubal margin).

    - Cytology study of nasal and salivary pH, (to assess possible indirect effects of acid on the nasal mucosa).

Before performing the determination of the pH of saliva it was determined nasal pH, by the insertion of a map indicator strips (Macherey-Nagel pH interval 1-14) previously moistened with distilled water directly into each nostril of the patient; was subsequently performed a

withdrawal of the nasal mucosa cells on the middle part of the inferior turbinate, bilaterally, with nasalscraping®, which have been placed on a cytology slide electrostatically charged, SuperFrost Plus Menzel - Gläser Thermo Scientific. It proceeded to the staining according to the method panoptic Pappenheim (3 min. In the May-Grunwald dye pure; 6 min. In the May-Grunwald to 50%; 1 min. In distilled water; 30 min. In Giemsa 1:10) in solution . The slide was then covered with a cover object the size of 24 x 50 mm # 1 and observed under an optical microscope Nikon Eclipse 200, at 100x magnification in oil-immersion. For the acquisition of microscope images has been used a Nikon DS FI1 camera with a program of acquisitions images NIS - Elements D Version 2.30. For the determination of salivary pH from each patient they were collected 2.5 ml of saliva in a glass, without any stimulation. A strip of pH 1-14 range Macherey-Nagel map has been dipped in saliva and after a few seconds was displayed the coloration of its pH value.

After such preliminary tests, patients underwent to practice an esophago-gastro-duodenoscopy with eventually biopsy, to find presence of gastro-esophageal reflux signs, like cardial incontinence, with or without hiatal hernia presence, esophagitis (classifies by Los Angeles score) or Barret's esophagus.

Of these 10 patients, 8 resulted positive for endoscopic diagnosis of gastro-esophageal reflux disease. Two patients had no evidence of endoscopic signs but were positive for reflux symptoms.

Eight patients positive to endoscopy had evidence of cardial incontinence, of which five had a simple incontinence while three had evidence of hiatal hernia (with a cardio-diaphragmatic inversion included between 2 and 4 cm).

Six patients had evidence of esophagitis, scored by Los Angeles classification like grade A (one or more mucosal break no longer than 5 mm) in three patients, grade B (one or more mucosal break more than 5 mm long) in two patients, and grade C (one or more mucosal break that is continuous between the tops of two or more mucosal folds but which involves less than 75% of the circumference) in a single patient.

No one had Barrett's esophagus evidence.

Patients were treated with the following therapeutic scheme:

- Omeprazole, 40 mg, taken twice daily per OS, for at least 6 weeks

Steroids and antihistamines were excluded from treatment.

3. RESULTS

The obtained data turned out as follows:

Audiometric examination shows conductive hearing loss (conductive gap between 25 and 35 dB for frequencies between 125 and 1000 hz) for six subjects, on the other hand hearing was in the normal range (20 dB for all frequencies) for the other four subjects.

- All Subjects examined showed pathological tympanometry and Eustachian tube function tests. The tympanograms were reduced in amplitude (AS type) in 40% of cases and deviated towards negative values (type C) in the remaining 60%. The functional Eustachian tube test confirmed dysfunction in 100% of cases. (The peak of the tympanogram made after Valsalva maneuver does not deflected towards the positive values).

At rhinopharyngolaryngoscopy all patients showed typical changes compatible with laryngopharyngeal reflux such as hyperemia and edema of the arytenoid and interarytenoid mucosa.

The nasal cytology has documented the presence of metaplastic epithelium with goblet cells, while the study found an alkaline pH of the nasal pH (mean 8) and salivary acid (average 5). After 3 weeks of treatment the following results were obtained:

All patients confirmed mild improvement in symptoms, no patients reported a total resolution of symptoms;

The audiometry examination was normal in all patients;

The Eustachian function tests confirmed tube dysfunction for all patients tested.

After 6 weeks:

Seven subjects reported resolution of symptoms, three substantial improvement;

Instrumental tests confirmed the data: audiometry, tympanograms and Eustachian tube function tests showed a resumption of tube activity. It is clear that the return to normality of the Eustachian tube function corresponds to the disappearance of the audiological symptoms in 70% of patients and a marked improvement in the remaining 30%.

Regarding cytological study, it was documented in all cases a clear improvement of metaplastic epithelium with goblet cells associated with a normalization of the nasal and salivary pH; however, in only three cases an optimization of results was not reached. The result is congruent with what was previously remarked.

4. DISCUSSION

In 1903 Coffin hypothesized that the “reflux of gas from the stomach” and “hyperacidity” were responsible for laryngeal and nasal symptoms in patients presenting hoarseness and posterior rhinorrhea [10].

Since then, other Authors have indicated reflux as a possible cause of laryngomalacia, subglottic stenosis, laryngospasm, reflex apnoea, bronchoconstriction, otitis and rhinosinusitis [11-16].

The typical symptoms of gastroesophageal reflux disease (GERD) are gastrointestinal, albeit are known also atypical symptoms of otorhinolaryngology interest related to two different pathophysiological pathways:

- Vagal stimulation of the esophageal wall (distal reflux): the refluxed gastric content causes irritation of esophageal receptors through vagal transmission causes persistent cough, ear pain, pharyngeal-laryngeal paresthesia, pain on swallowing;
- Direct injury to the refluxed acid on pharyngeal-laryngeal mucosa (proximal reflux): pharyngeal and laryngeal inflammatory processes with characteristic symptoms such as dysphonia, dysphagia, pain on swallowing, raclage, episodes of sleep apnea, otitis, which it is associated metaplastic epithelium with goblet cells and variation of pH [10-15].

Brunworth et al. [6] showed that nasopharyngeal reflux may have a role in the pathogenesis of Eustachian tube dysfunction; these authors, using a novel pH probe allowing detection of acidity in a non liquid environment, performed a comparison of nasopharyngeal pH between control patients and those with Eustachian tube dysfunction. Eustachian tube dysfunction was more likely to be associated with a higher number of nasopharyngeal reflux events and higher reflux finding score [6].

Formánek et al. [7] in a prospective study analyzed children 1-7 years of age who had been diagnosed with OME and underwent myringotomy with insertion of a ventilation tube. Middle ear fluid obtained during myringotomy was analyzed with Peptest to determine the presence of pepsin, and hence EER. Pepsin was detected in 1/3 of middle ear of patients with OME [7].

Doğru et al. [14] studied 31 children with OME. The pepsinogen levels in the middle ear fluid of all patients was measured and middle ear fluid of each patient was investigated for *Helicobacter pylori* (*H. pylori*).

The middle ear pepsinogen levels were compared with those in the serum. The correlation between the levels of pepsinogen and *H. pylori* positivity in the middle ear fluid was investigated. The study showed higher levels of pepsinogen and *H. pylori* positivity rates in middle ear fluid and serum of patients with otitis media with effusion. These results also support the role of laryngopharyngeal reflux in the pathogenesis of otitis media with effusion [14].

However, concerning otitis and reflux in adults, the literature is limited to case reports. Reflux is probably linked to many cases of otitis media in adults and may lead to Eustachian tube dysfunction in such subjects. Reflux in adult subjects with otitis media is potentially different from the physiologic events observed in children, but the causal link between them remains unclear. Evaluation of more cases that could be diagnosed as reflux-induced otitis media is

necessary for better understanding of the disease entity [9].

5. CONCLUSION

The purpose of our study was to investigate the relationship between ear fullness and laryngopharyngeal reflux, in order to focus medical therapy and improve therapeutic outcomes in this patient population.

Albeit our study is limited because of a small number of patients, nevertheless our results support the hypothesis that acid reflux can be the basis of audiological symptoms and that is involved in the genesis and chronic dysfunction of the Eustachian tube.

In our study, patients treated with proton pump inhibitors and antacids had a resolution of symptoms in 70% of cases, and in 30% there was a remarkable and progressive improvement.

CONSENT

All authors declare that 'written informed consent was obtained from the patient for publication of this paper.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Cesari U, Apisa P, Niri C, Ruggiero S, Telesca D. A, Cappello C, Sivero L. Dysphonia in pharyngolaryngeal reflux: Evaluation of acid lesions with video endoscopy. Otorinolaringologia. 2016; 66(1):1-4.
2. Abtahi SH, Kazerooni A, Brejis N, Abdeyazdan Z, Saneian H. Prevalence and characteristics of gastroesophageal reflux in children with otitis media in Isfahan, Iran. Adv Biomed Res. 2016;5:81. DOI: 10.4103/2277-9175.182212
3. Gorecka-Tuteja A, Jastrzebska I, Skladzien J, Fyderek K. Laryngopharyngeal reflux in children with chronic otitis media with effusion. J Neurogastroenterol Motil. 2016;22:452-458.
4. Crapko M, Kerschner JE, Syring M, Johnston N. Role of extra-esophageal reflux in chronic otitis media with effusion. Laryngoscope. 2007;117:1419-23.
5. Tasker A, Dettmar PW, Panetti M, Koufman JA, Birchall JP, Pearson JP. Is gastric reflux a cause of otitis media with effusion in children? Laryngoscope. 2002; 112:1930-1934.
6. Brunworth JD, Mahboubi H, Garg R, Brandon J, Bryan B, Djalilian HR. Nasopharyngeal acid reflux and eustachian tube dysfunction in adults. Ann Otol Rhinol Laryngol. 2014;6(123):415-419.
7. Formánek M, Zeleník K, Komínek P, Matoušek P. Diagnosis of extraesophageal reflux in children with chronic otitis media with effusion using Peptest. Int J Pediatr Otorhinolaryngol. 2015;79(5):677-67.
8. Schilder AGM, Bhutta MF, Butler CC, Holy C, Levine LH, Kvaerner KJ, et al. Eustachian tube dysfunction: Consensus statement on definition, types, clinical presentation and diagnosis. Clin Otolaryngol. 2015;40:407-411.
9. Sone M, Kato T, Nakashima T. Current concepts of otitis media in adults as a reflux-related disease. Otol Neurotol. 2013;34:1013-1017.
10. Koufman JA, Amin MR, Panetti M. Prevalence of reflux in 113 consecutive patients with laryngeal and voice disorders. Otolaryngol Head Neck Surg. 2000;123:385–8.
11. Little JP, Matthews BL, Glock MS, Koufman JA, Reboussin DM, Loughlin CJ, McGuirt WF. Extraesophageal pediatric reflux: 24-hour double-probe pH monitoring of 222 children. Ann Otol Rhinol Laryngol Suppl. 1997;169:1-16.
12. Koufman JA. The otolaryngologic manifestations of gastroesophageal reflux disease (GERD): A clinical investigation of 225 patients using ambulatory 24-hour pH monitoring and an experimental investigation of the role of acid and pepsin in the development of laryngeal injury. Laryngoscope. 1991;101(53):1-78.
13. Weaver EM. Association between gastroesophageal reflux and sinusitis, otitis

media, and laryngeal malignancy: A systematic review of the evidence. Am J Med. 2003;115(3A):81-89.

14. Dogru M, Kuran G, Haytoglu S, Dengiz R, Arikan OK. Role of laryngopharyngeal reflux in the pathogenesis of otitis media with effusion. J Int Adv Otol. 2015; 11(1):66–71.

15. Cesari U, Galli J, Ricciardiello F, Cavaliere M, Galli V. Dysphonia and laryngopharyngeal reflux. Acta Otorhinolaryngol Ital. 2004;24(1):13-9.

16. O'Reilly RC, He Z, Bloedon E. The role of extraesophageal reflux in otitis media in infants and children. Laryngoscope. 2008;118(7 pt 2 suppl 116):1-9.

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/18501