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2 REVIEW

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Pediatric middle ear infections and gastroesophageal reflux

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KEYWORDS

Children; Gastroesophageal; Laryngopharyngeal; Reflux; Otitis media

Summary

Objectives: The pathogenesis of middle ear infections in children is multifactorial and includes infection, anatomical factors, impaired immunologic status, allergy, familial predisposition, male sex, method of feeding and environmental factors. Glue ear remains the commonest cause of deafness in childhood. Gastroesophageal reflux (GOR) is a common problem in the newborn and preschool periods. Recent research suggests that it may be related to eustachian tube dysfunction and otitis media. Methods: We review the literature and discuss the possible relationship between Gastroesophageal reflux and otitis media in children.

Conclusions: The current data are not enough to support antireflux treatment in children with refractory middle ear infections. More prospective randomised placebocontrolled studies are needed.

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Gastroesophageal reflux (GOR) is believed to be an important inflammatory cofactor in many adult and

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1. Introduction

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paediatric disorders of the upper aerodigestive tract. A connection between chronic otitis media and GOR is recognised, but the underlying mechanism remains unclear. Vagal reflexes from the lower part of the oesophagus might contribute. Another possible mechanism is thought to be the microaspiration of gastric contents into the throat with resultant damage to the eustachian tube. The size and shape of the immature eustachian tube in children can be blamed for the reflux of acid and pepsin from the nasopharynx into the middle ear [2].

2. Animal studies

Several animal studies have proven the relationship between GOR and laryngeal disorders. Delahunty and Cherry, in 1968, have demonstrated that the intermittent application of gastric acid to the mucosa of the vocal process in dogs can produce vocal cord granulomas [5]. The relationship between GOR and middle ear pathology has also been explored in animal studies. Heavner et al., investigated the relationship between simulated GOR and eustachian tube dysfunction. In their study, rat middle ears were exposed to acid or phosphatebuffered saline solution. The rats exposed to pepsin had an impaired ability to clear positive and negative pressure from the middle ear compared to the rats exposed to saline. Their results demonstrated that multiple middle ear exposure to pepsin led to eustachian tube dysfunction [7]. In a similar randomised controlled trial study, mucociliary clearance of middle ear contents was measured in rats exposed to acid and was found to be disabled [20].

3. Clinical studies

Otitis media with effusion is a multifactorial condition and remains the commonest cause of deafness in children. Causes include eustachian tube obstruction, upper respiratory tract infections or a dysfunctional mucociliary clearance. GOR is a common physiological occurrence in neonates and decreases in frequency during the first year of life [14]. Reflux of acid and pepsin into the middle ear from the nasopharynx is possible due to the angle of immature tube in children. This would cause inflammation of the nasopharynx and the eustachian tube leading to eustachian tube dysfunction. On the other hand, Ayanoglu et al. in a recent prospective trial studied the possibility of nasopharyngeal content passing into the middle ear. During the recovery phase of general anaesthesia a radionuclide substance was administered intranasally and pressure

changes reflected to the nasopharynx were recorded. The patients were extubated 10 min after the radionuclide was applied. Passage of nasopharyngeal contents into the middle ear was not a statistically significant observation, therefore this study does not support the hypothesis that reflux of nasopharyngeal contents can happen directly through the eustachian tube into the middle ear and cause deleterious effects [1]. Of course, this study involved adults alone.

Velepic et al. examined 30 children (aged 2-13) with secretory otitis media or recurrent otitis media and tried to establish a possible relationship between GOR, allergy and chronic tubotympanal disorders [17]. The method used involved 24-hour double probe pH monitoring. Sixty percent of the subjects had pathological GOR. In a recent study by Tasker et al., middle ear effusions were taken from 54 children aged 2-8 years who were undergoing myringotomy. Pepsin concentrations were measured using ELISA and enzyme activity assays. Eighty three percent of the effusions contained pepsin/pepsinogen at concentrations of up to 1000-fold greater than those in serum. The data suggested that reflux of gastric juice could be a major cause of glue ear in children [15].

4. Discussion

Middle ear infections are still prevalent around the world despite advances in public health and medical care. Risk factors that have been attributed to the high rates of chronic middle ear in certain populations are: lack of breast feeding, overcrowding, poor hygiene, poor nutrition, passive smoking, high rates of nasopharyngeal colonization with potentially pathogenic bacteria and inadequate and unavailable health [3]. The possible relationship between GOR and otitis media has also been studied over recent years.

GOR occurs throughout the day in healthy infants, children, adolescents as well as adults. However laryngopharyngeal reflux is more common in infants and this places the infant at particular risk for potential supraoesophageal complications of GOR [13]. Pediatric GOR usually manifests as regurgitation or vomiting. Recurrent vomiting occurs in up to 70% of infants aged 3–4 months but decreases gradually so that by 18 months of age, vomiting is infrequent [9]. In a follow-up symptom survey results showed that there was no increase in the frequency of ear nose and throat symptoms in infants with GOR compared with controls [10].

GOR is thought to cause inflammation of the nasopharynx with secondary obstruction of the

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eustachian tube leading possibly to an increase in the incidence of otitis media. Unfortunately, both middle ear infections and GOR are extremely common conditions in the general population and it is very difficult to prove any link between the two. Epidemiologic studies showed no difference in the incidence of otitis media between children with GOR and controls [10]. Rozmanic et al. studied 27 children with chronic tubotympanal disorders by means of 24-hour dual probe pH monitoring. The pH was less than 4 for more than 5% in 55.6%. Based on their results the authors recommended that pH monitoring be performed in children with chronic tubotympanal disorders when standard treatment is ineffective [12]. In a smaller study of six children with otalgia, the symptom was reported to improve with antireflux treatment [6].

The gold standard test for diagnosis of laryngo-pharyngeal reflux in adults and children is dual probe 24-hour pH monitoring. It is superior to endo-scopy, single probe pH monitoring, barium studies or any other diagnostic modality and, more importantly, it reveals the pattern of reflux, so that subsequent treatment can be custom-tailored to each patient [18]. Yet, there is no consensus with respect to the number of probes, the positioning of the proximal probe or the interpretation of results. The establishment of a normative database for LPR is controversial and ongoing and remains a topic of debate in all international and national gastroenterological and other "reflux related" congresses [18].

Little at al in a large study of 222 children demonstrated, by means of pH monitoring, naso- or hypopharyngeal reflux of gastric acid in patients with otorhinolaryngological symptoms [8]. The positioning of the proximal probe is also somewhat contro-Loss of mucosal contact, displacement, pH changes caused by oral intake and intermittent drying are few of the problems blamed for spurious results. The presence of the proximal probe in the posterior pharynx has been speculated to precipitate acid reflux secondary to irritation, possibly resulting in false-positive results [19].

Successful empiric antireflux treatment is another positive argument for the contribution of GOR in the pathogenesis of otorhinolaryngological problems. The efficacy of this medical treatment has been shown in a few studies and reaches up to 80–85% of patients involved [11,16]. The duration of treatment is not known, but overall an aggressive antireflux therapy can dramatically reduce the number of surgical procedures [4].

The current data are not enough to support antireflux treatment in children with refractory middle ear infections. More prospective randomised placebo-controlled studies are needed. On the other hand, studies like the one from Tasker et al., opened new horizons in the associations between pepsin and common middle ear conditions [15]. It is perhaps the role of pepsin that needs to be addressed and the search for an objective diagnostic tool, both clinical and/or immunological, which will give answer to these questions.

References

- [1] E. Ayanoglu, C. Uneri, T. Turoglu, V. Dogan, Reflux of nasopharyngeal content into the middle ear through the eustachian tube, Eur. Arch. Otorhinolaryngol. (2003) [Epub. ahead of print].
- [2] C.D. Bluestone, Epidemiology and pathogenesis of chronic suppurative otitis media: implications for prevention and treatment, Int. J. Pediatr. Otorhinolaryngol. 42 (1998) 207— 223.
- [3] C.D. Bluestone, Q.C. Beery, W.S. Andrus, Mechanics of the eustachian tube as it influences susceptibility to and persistence of middle ear effusions in children, Ann. Otol. Rhinol. Laryngol. 83 (Suppl.) (1974) 27–34.
- [4] M.R. Bothwell, D.S. Parsons, G.J. Talbot, B. Barbero, B. Wilder, Outcome of reflux therapy on pediatric chronic sinusitis, Otolaryngol. Head Neck Surg. 121 (1999) 255—261.
- [5] J.E. Delahunty, J. Cherry, Experimentally produced vocal cord granulomas, Laryngosope 78 (1968) 1941–1947.
- [6] W.S. Gibson Jr., W. Cochran, Otalgia in infants and children a manifestation of gastroesophageal reflux, Int. J. Pediatr. Otorhinolaryngol. 28 (1994) 213–218.
- [7] S.B. Heavner, S.M. Hardy, D.R. White, J. Prazma, H.C. Pills-bury 3rd, Transient inflammation and dysfunction of the eustachian tube secondary to multiple exposure of simulated gastroesophageal refluxant, Ann. Otol. Rhinol. Laryngol. 110 (10) (2001) 928–934.
- [8] J.P. Little, B.L. Matthews, M.S. Glock, Extraesophageal pediatric reflux: 24-hour double probe pH monitoring of 222 children, Ann. Otol. Rhinol. Laryngol. 106 (Suppl. 169) (1997) 1—16.
- [9] S.P. Nelson, E.H. Chen, G.M. Syniar, K.K. Christoffel, Pediatric Practice Research Group, Prevalence of symptoms of gastroesophageal reflux during infancy, Arch. Pediatr. Adolesc. Med. 151 (1997) 569–572.
- [10] S.P. Nelson, E.H. Chen, G.M. Syniar, K.K. Christoffel, Pediatric Practice Research Group, One-year follow-up symptoms of gastroesophageal reflux during infancy, Pediatrics 102 (1998) 67.
- [11] C.D. Phillips, C.E. Wood, W.J. Gibson, W.J. Cochran, Gastroesophageal reflux contributing to chronic sinus disease in children A prospective analysis, Arch. Otolaryngol. Head Neck Surg. 126 (2000) 831–836.
- [12] V. Rozmanic, M. Velepic, M. Ahel, M. Velepic, D. Bonifacic, M. Velepic, Prolonged esophageal pH monitoring in the evaluation of gastroesophageal reflux in children with chronic tubotympanal disorders, J. Pediatr. Gastroenterol. Nutr. 34 (2002) 278–280.
- [13] C.D. Rudolph, Supraesophageal complications of gastroesophageal reflux in children: challenges in diagnosis and treatment, Am. J. Med. 115 (3A) (2003) 150–156.

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- [14] R.W. Sheperd, J. Wren, J.W. Evans, M. Lander, T.H. Ong, Gastroesophageal Reflux in children: clinical profile, course and outcome with active therapy in 126 cases, Clin. Pediatr. 26 (1987) 55–60.
- [15] A. Tasker, P.W. Dettmar, M. Panetti, J.A. Koufman, J.P. Birchall, J.P. Pearson, Reflux of gastric juice and glue ear in children, The Lancet 359 (2002) 493.
- [16] T. Van Den Abbeele, V. Couloigner, C. Faure, P. Narcy, The role of 24-h pH recording in pediatric otolaryngologic gastroesophageal reflux disease, Intl. Congress Ser. 1254 (2003) 123–130.
- [17] M. Velepic, V. Rozmanic, M. Velepic, D. Bonifacic, Gastroesophageal reflux, allergy and chronic tubotympanal disor-

- ders in children, Int. J. Pediatr. Otorhinolaryngol. 55 (2000) 187–190.
- [18] D.A. Vincent Jr., J.D. Garrett, S.L. Radionoff, L.A. Reussner, C.R. Stasney, The proximal probe in esophageal pH monitoring: development of a normative database, J. Voice 14 (2000) 247–254.
- [19] G.J. Weiner, J.A. Koufman, W.C. Wu, J.B. Cooper, J.E. Richter, D.O. Castell, Chronic hoarseness secondary to gastroesophageal reflux disease: documentation with 24-hour pH monitoring, Am. J. Gastroenterol. 84 (1989).
- [20] D.R. White, S.B. Heavner, S.M. Hardy, J. Prazma, Gastroesophageal reflux and eustachian tube dysfunction in rats: an animal model, Laryngoscope 112 (6) (2002) 955–961.

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