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LETTER TO THE EDITOR

Laryngopharyngeal reflux disease, digestive enzymes and otitis media in pediatric populations

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Dear Editor,

We read the paper of Yan et al.. investigating the role of laryngopharyngeal reflux disease (LPRD) in the etiology of otitis media with effusion (OME) in children [1]. Authors measured pepsin and trypsin concentrations in adenoid tissues and glue ear of 30 pediatric patients with otitis media with effusion (OME) requiring tympanostomy/tubes placement and compared their findings with a control group of 30 children with adenoid hypertrophy without OME. The concentrations of pepsin and trypsin were similar across groups, while both enzymes were detected in all adenoid specimen. Authors also tested for pepsin and trypsin in middle ear effusion (MEE) finding higher concentrations of trypsin thus concluding that complicated OME may be caused by LPRD and trypsin may have a greater destructive effect on the middle ear [1]. We congratulate the authors for this study, which is one of the first study investigating multiple digestive enzyme measurements in MEE. However, we would like to draw attention to some methodological points that can affect the results of the study.

In epidemiology, association is not causality. The causal relationship between two phenomenon requires mechanistic investigations in subjects with a confirmed disease diagnosis [2]. In that way, based on a simple trypsin detection in the middle ear, the evidence presented is insufficient to support that this enzyme may have a greater destructive effect on the middle ear structure. The involvement of digestive enzymes in the pathogenesis of OME may require the comparison of adenoid and middle ear anatomical structures between a group of children with a demonstrated LPRD and a control group composed on children with negative LPRD diagnosis. Current worldwide [3] and European [4] LPRD guidelines support the use of 24-hour hypopharyngeal-esophageal multichannel intraluminal impedance-pH testing (HEMII-pH) for the LPRD diagnosis regarding the non-specificity of symptoms and findings, and the false positive pepsin detection rates. Yan et al. did not base the diagnosis on HEMII-pH, while they did not evaluate the presence of LPRD symptoms and findings, which are both mandated to confirm the diagnosis. HEMII-pH use remains critical because both pepsin and trypsin can be detected in upper aerodigestive tract of asymptomatic individuals [5, 6], which limits their values for the LPRD diagnosis. The lack of confirmation of the diagnosis, despite positive detections of trypsin and pepsin into the MEE of children is therefore insufficient to consider a causative relationship between LPRD and MEE.

Finally, the investigation of gastroduodenal enzymes in the development of OME should consider other digestive enzymes, such as elastase or bile salts, which demonstrated a potential involvement in upper aerodigestive tract LPRD-associated disorders, including OME or chronic cough [7,

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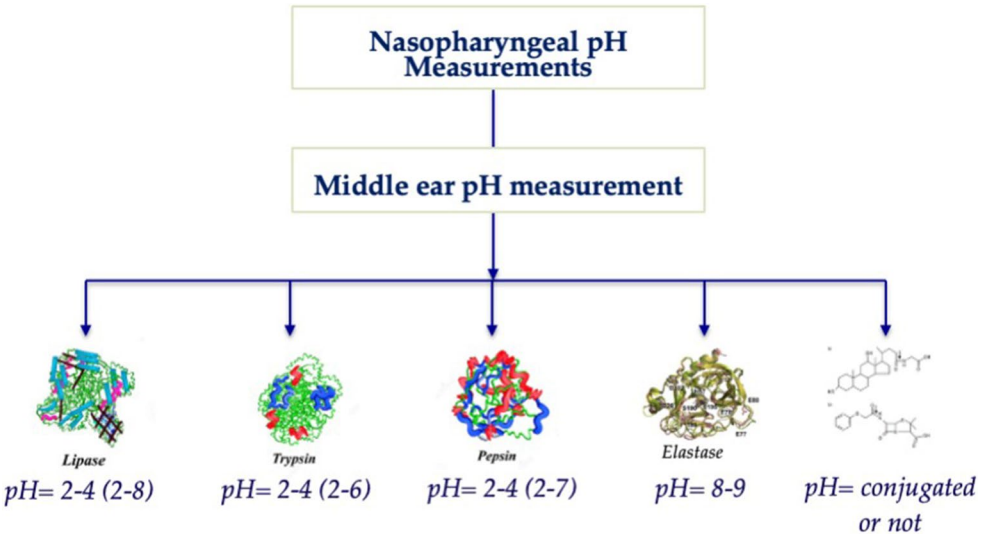

Fig. 1 Methodological Approach of Reflux-Induced Otitis Media. The pH of activation of enzyme is highlighted under the enzyme description

8]. Future studies need to consider the pH of MEE that influences the enzyme activity (Fig. 1). Considering that more than 90% of LPRD are alkaline, the OME pepsin can be inactivated, and, consequently, poorly involved in the pathogenesis of OME.

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Declarations

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Conflict of interest The author had no conflict of interest.

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