The characteristics of salivary pepsin in patients with severe motor and intellectual disabilities

Naoki Hashizume\textsuperscript{a,*,} Suguru Fukahori\textsuperscript{a}, Kímio Asagiri\textsuperscript{a}, Shinji Ishii\textsuperscript{a}, Nobuyuki Saikusa\textsuperscript{a}, Naruki Higashidate\textsuperscript{a}, Motomu Yoshida\textsuperscript{a}, Daisuke Masui\textsuperscript{a}, Saki Sakamoto\textsuperscript{a}, Yoshiaki Tanaka\textsuperscript{a,\textsuperscript{c}}, Minoru Yagi\textsuperscript{a}, Yushiro Yamashita\textsuperscript{b}

\textsuperscript{a}Department of Pediatric Surgery, Kurume University School of Medicine, Kurume, Fukuoka, Japan
\textsuperscript{b}Department of Pediatrics and Child Health, Kurume University School of Medicine, Kurume, Fukuoka, Japan
\textsuperscript{c}Division of Medical Safety Management, Kurume University School of Medicine, Kurume, Fukuoka, Japan

Received 31 January 2017; received in revised form 8 April 2017; accepted 11 April 2017

Abstract

\textit{Purpose:} The aim of the present study was to determine the utility of measuring the salivary pepsin level (SPL) as an objective assessment of gastroesophageal reflux disease (GERD) in severe motor and intellectual disabilities (SMID) patients.

\textit{Subjects and methods:} This prospective study included 26 SMID patients who underwent simultaneous 24-h multichannel intraluminal impedance pH measurement (pH/MII) and SPL evaluation. The enrolled patients were divided into GERD (+) or GERD (−) groups according to the pH/MII findings. The age, gender and pH/MII parameters were compared between the two groups. A correlation analysis was also conducted for the SPL following early-morning fasting and post-enteral feeding and the age, gender, presence of gastrostomy and tracheostomy and pH/MII parameters. The SPL was compared between the two sampling groups.

\textit{Results:} Fifteen patients were classified as GERD (+), and 11 patients were classified as GERD (−). The mean SPL following early-morning fasting and post-enteral feeding among all patients were 104.3 (median: 38, 25th and 75th percentile: 12, 361) ng/ml and 222.2 (median: 152, 500) ng/ml, respectively. Regarding positivity, 76.9\% and 73.1\% of SPL values in early-morning fasting and post-enteral feeding SMID patients, respectively, were positive (≥16 ng/ml). The SPL following early-morning fasting demonstrated a weak but significant positive correlation with age. In contrast, we noted no correlation between the pH/MII parameters and the SPL for either the early-morning fasting or post-enteral feeding patients, and no significant difference in the SPL was observed between the GERD (+) and (−) patients.

\textit{Conclusions:} The present study showed that a high proportion of SMID patients had a relatively high SPL, regardless of the presence of GERD. The SPL in SMID patients might be affected by several distinctive factors in addition to gastroesophageal reflux.

© 2017 The Japanese Society of Child Neurology. Published by Elsevier B.V. All rights reserved.

\textit{Keywords:} Salivary pepsin; Severe motor and intellectual disabilities; Gastroesophageal reflux disease

1. Introduction

Severe motor and intellectual disabilities (SMID) patients account for the majority of patients suffering from gastroesophageal reflux disease (GERD) who require anti-reflux surgery [1]. While 24-h pH monitor-
ing is widely used as the gold-standard method for evaluating GERD, this conventional examination is unable to detect non-acidic refluxes, and false-negative results have been reported at rates of 15–30% [2]. Recently, 24-h multichannel intraluminal impedance pH measurement (pH/MII) has been established as a pH-independent measurement tool [3–6]. The main advantage of this novel technique is that the pH of both acidic and non-acidic reflux episodes can be simultaneously detected using a multiple-impedance catheter with integrated pH sensors. There is also a good correlation between the pH/MII and manometry or videofluoroscopy in healthy subjects as well as in patients with GERD [3]. There have been previous reports evaluating pH/MII in SMID patients. In 2006, Del Buono et al. reported that in 16 SMID children with 12-h impedance recordings, more than half of the reflux events were non-acidic and would have gone undetected by conventional pH measurement [4]. We previously reported on the utility of pH/MII for detecting GERD subtypes that could not be detected by 24-h pH monitoring and suggested that pH/MII be considered the go-to tool for GERD testing, especially in SMID patients [5,6]. Moreover, Tanaka et al. were reported that the postoperative reflux parameters such as pH reflux index, acid clearance time, bolus exposure index, and the number of acid reflux episodes significantly decreased ($P < 0.05$) compared with the preoperative ones in SMID patients using 24-h pH/MII [7]. Evaluating pH/MII were also effective tool for detecting GERD in SMID patients. However, despite the usefulness of pH/MII for diagnosing GERD, this technique is often invasive and expensive due to the requirement of nasogastric intubation for a long time, which is uncomfortable and inconvenient, especially for SMID patients.

Salivary pepsin, which is produced in the stomach, was recently introduced as a new biomarker for the diagnosis of GERD in healthy subjects [8–10]. In a single adult study evaluating proximal oesophageal reflux by conducting simultaneous salivary pepsin and pH measurements, the sensitivity and specificity of salivary pepsin for predicting proximal oesophageal reflux was reported to be 75% and 91%, respectively [10]. Furthermore, in a similar study, the sensitivity and the specificity of a positive salivary pepsin value for the diagnosis of GERD-related symptoms was reported to be 77.6% and 63.2%, respectively [8]. However, no reports have yet described the relationship between the presence of salivary pepsin and GERD in SMID patients.

The aim of the present study was to determine the utility of measuring the salivary pepsin level (SPL) as an objective assessment of GERD in SMID patients.

2. Patients and methods

2.1. Patients

This prospective study included 26 SMID patients (male/female: 17/9; mean age: 15.0 years, median: 14.0 years, 25th and 75th percentile: 4, 19.5 years). Regarding the causal disorders of SMID, 3 patients had a genetic anomaly, 1 had a chromosomal anomaly, 2 had adrenoleukodystrophy, 8 had suffered cerebral damage in the neonatal period, 11 had suffered cerebral damage in infancy or later and 1 was unknown. Nineteen patients were fed via a nasogastric tube, and seven were fed via a gastrostomy tube. Fourteen patients underwent tracheostomy. Pharmacotherapies for GERD, such as the administrations of prokinetics, laxatives and Japanese herbal medicine, were discontinued at least three days before the patients entered the study. The study protocol was approved by the Kurume University Ethical Committee (No. 13179). Informed consent was obtained from the families before the participants were enrolled in the study.

2.2. 24-h multichannel intraluminal impedance pH measurements

A multiple intraluminal impedance catheter (outer diameter, 2 mm) with 2 pH antimony electrodes and 7 impedance electrodes (Sandhill Scientific, Inc., Highlands Ranch, CO, USA) was used. The catheter was inserted transnasally through the oesophagus, and the pH sensor placement was confirmed by radiography. The impedance data were automatically evaluated using the BioVIEW analysis software program, and each tracing was manually reviewed by the same author (SF).

Liquid reflux was defined by pH/MII as a fall in the impedance ≥50% from baseline in at least two consecutive channels in an aboral direction. Each type of reflux was defined as follows: acidic reflux was diagnosed in cases associated with a pH drop to ≤4, non-acid reflux was diagnosed in cases associated with a nadir pH value >4. The pH index (pHI) was defined as the percentage of time that the pH was <4.0. We defined 4.0% as the upper cut-off value in accordance with the definition outlined in the NICE guidance 2015 [11]. The bolus exposure index (BEI) was defined as the percentage of time with retrograde movement of intraluminal oesophageal material. We defined 1.4% as the upper cut-off value [12]. Pathological GERD was defined as a case in which the pHI exceeded 4.0% or the BEI exceeded 1.4%. The numbers of total reflux episodes (TRE) (total/acid/non-acid) and proximal reflux episodes (PRE) (total/acid/non-acid) were also evaluated. GERD in all patients was evaluated and diagnosed in accordance with the above pH/MII measurement abilities. Brain Dev (2017), http://dx.doi.org/10.1016/j.braindev.2017.04.008
دریافت فوری
متن کامل مقاله

امکان دانلود نسخه تمام متن مقالات انگلیسی
امکان دانلود نسخه ترجمه شده مقالات
پذیرش سفارش ترجمه تخصصی
امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
امکان دانلود رایگان ۲ صفحه اول هر مقاله
امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
دانلود فوری مقاله پس از پرداخت آنلاین
پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات