

Esophagogastroduodenoscopy with conscious sedation does not interfere with catheter-based 24-h pH monitoring

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Abstract

AIM: To investigate the impact of esophagogastroduodenoscopy with conscious sedation on the subsequent 24-h catheter-based pH monitoring.

METHODS: Fifty patients with extra-esophageal symptoms of gastroesophageal reflux disease undergoing ambulatory dual-probe 24-h pH monitoring were enrolled from March 2010 to August 2011. All of the data were collected prospectively and analyzed retrospectively. Thirty-six patients (72%, group A) underwent pH monitoring shortly after esophagogastroduodenoscopy (EGD) with conscious sedation, and 14 patients (28%, group B) underwent pH monitoring without conscious

sedation. The 24-h pH data from two time periods were analyzed: the first 4 h (Period I) and the remaining time of the study (Period II).

RESULTS: The mean age of the patients was 49.6 ± 12.5 years; 20 patients (40%) were men. The baseline data, including age, sex, body mass index, reflux esophagitis, the Reflux Symptom Index, and the Reflux Findings Score, were comparable between the two groups. The percentage of total time with a pH < 4 and the frequency of acid reflux during Period I were not significantly different between the two groups, as measured using both pharyngeal ($0.03\% \pm 0.10\%$ vs $0.07\% \pm 0.16\%$, $P = 0.32$; and 0.07 ± 0.23 episodes/h vs 0.18 ± 0.47 episodes/h, $P = 0.33$, respectively) and esophageal probes ($0.96\% \pm 1.89\%$ vs $0.42\% \pm 0.81\%$, $P = 0.59$; and 0.74 ± 1.51 episodes/h vs 0.63 ± 0.97 episodes/h, $P = 0.49$, respectively). The percentage of total time with a pH < 4 and the frequency of acid reflux were also not significantly different between Periods I and II in group A patients, as measured using both pharyngeal ($0.03\% \pm 0.10\%$ vs $0.23\% \pm 0.85\%$, $P = 0.21$; and 0.07 ± 0.23 episodes/h vs 0.29 ± 0.98 episodes/h, $P = 0.22$, respectively) and esophageal probes ($0.96\% \pm 1.89\%$ vs $1.11\% \pm 2.57\%$, $P = 0.55$; and 0.74 ± 1.51 episodes/h vs 0.81 ± 1.76 episodes/h, $P = 0.55$, respectively).

CONCLUSION: EGD with conscious sedation does not interfere with the results of subsequent 24-h pH monitoring in patients with extra-esophageal symptoms of gastroesophageal reflux disease.

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Key words: Esophagogastroduodenoscopy; Conscious sedation; pH monitoring; Gastroesophageal reflux disease; Extraesophageal symptoms

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INTRODUCTION

The manifestation of gastroesophageal reflux disease (GERD) can be either esophageal or extra-esophageal^[1]. Extra-esophageal reflux, or laryngopharyngeal reflux (LPR), refers to the backflow of gastric contents into the larynx and pharynx^[1,2]. Ambulatory dual-probe 24-h pH monitoring is currently considered the gold-standard diagnostic modality for the evaluation of patients with LPR^[2-4]. This catheter-based pH measurement is performed with a pH sensor located within 2 cm above the proximal border of the upper esophageal sphincter (UES)^[5]. Prior manometry-guided localization is required to determine UES positioning relative to the nostril. The two trans-nasal procedures are usually performed without intravenous sedation. Therefore, they are unpleasant and uncomfortable tests for patients^[6,7].

Conscious sedation improves the quality of the test and increases the patient's willingness to undergo a gastrointestinal examination^[8]. Benzodiazepine administration and opiate-based sedation are the most common practices for conscious sedation^[9]. Meperidine causes a reduction in the LES pressure in animal and human studies^[10,11]. It may induce or exacerbate gastroesophageal reflux (GER), causing interference with pH studies^[11]. However, capsule-based (Bravo) wireless pH measuring system is usually performed during or shortly after an esophagogastroduodenoscopy (EGD) with conscious sedation^[12]. Therefore, it is unclear whether conscious sedation during EGD has an impact on the results of the subsequent esophageal pH test. To increase patient willingness to undergo 24-h pH monitoring, we attempted to perform a catheter-based pH study in a manner similar to the Bravo system in our patients. The aim of this study was to investigate whether EGD with conscious sedation interfered with subsequent catheter-based 24-h pH monitoring in patients with extra-esophageal symptoms of GERD.

MATERIALS AND METHODS

From March 2010 to August 2011, 53 patients with LPR-like complaints underwent ambulatory 24-h pH monitoring at the Chang Gung Memorial Hospital. These complaints included globus ($n = 27$), sore throat ($n = 13$), chronic cough ($n = 9$), hoarseness ($n = 3$), and dysphagia ($n = 1$). Three patients were excluded from the analysis because of numerous artifacts (pH out of range) on their pH records ($n = 2$) and intolerance of the procedure ($n = 1$). All of the patients were instructed to discontinue any

medications that affect gastric acid secretion and esophageal motility at least 7 d prior to the 24-h pH monitoring. This cohort study was incorporated into a prospective study (CMRPG390591) that was originally designed to evaluate the effects of different doses of proton pump inhibitors on the treatment of LPR. All of the data were collected prospectively and analyzed retrospectively. The study protocol was approved by the ethics committee at Chang Gung Memorial Hospital (IRB No: 99-3494C).

A total of 50 patients were enrolled in the current study. The mean patient age was 49.6 ± 12.5 years (range, 20-76 years). There were 20 (40%) men and 30 (60%) women. The mean body mass index (BMI) was 23.0 ± 3.2 kg/m² (range, 18.1-30.0 kg/m²). Group A included 36 patients (72%) who underwent EGD with conscious sedation 30 min prior to pH monitoring. Group B included the remaining 14 patients (28%) who did not undergo EGD or conscious sedation on the same day.

EGD with conscious sedation

All of the patients in group A underwent EGD with intravenous sedation using meperidine and midazolam on the same day prior to their 24-h pH monitoring study. The dosage of meperidine was 0.52 ± 0.10 mg/kg (range, 0.32-0.81 mg/kg), and the dosage of midazolam was 33.1 ± 7.1 g/kg (range, 16.1-53.6 g/kg). Hyoscine butylbromide was not given before or during the endoscopy in any of the participants.

Esophageal manometry and 24-h pH monitoring

All of the patients underwent esophageal manometry using a station pull-through technique to locate the UES in reference to the nostril. Subsequently, 24-h pH monitoring was performed using antimony electrodes and fitting recorders (Orion II, Medical Measurement Systems, The Netherlands). The pH catheter had two or four sensors that were 15 cm or 5 cm apart. The pH electrodes were calibrated before and after the test using reference buffer solutions with a pH of 4 or 7. The most proximal electrode (pharyngeal probe) was placed in the hypopharynx 2 cm above the manometry-defined proximal border of the UES. Each patient wore a data-logger with a sampling frequency of 1 Hz during the test period. Symptom occurrence, meal times and body positions (supine or upright) were written down in a diary and recorded in a data log. The patients were advised to eat their usual meals and engage in their usual activities on the day of the test. After a period of 24 h, they returned the data log, and the data were downloaded onto a computer using software provided by the manufacturer. The data from the diaries were extracted for interpretation.

A single pharyngeal event (pH < 4) preceded by a precipitous pH drop of the same magnitude in the esophageal probe was defined as a positive result for LPR. The most distal pH sensor in the esophagus (esophageal probe) was 15 cm away from the pharyngeal probe. Pathologic GER was defined as a percentage of total time with a pH < 4 greater than 4.2% as measured

Table 1 Comparisons of baseline data and data obtained during the first 4 h between patients in group A and group B

Variables	Group A (n = 36)	Group B (n = 14)	P value ¹
Baseline data			
Age (yr)	49.5 ± 13.2	49.9 ± 11.0	0.91
Sex (F)	15 (41.7)	5 (35.7)	0.70
Body mass index	22.8 ± 3.2	23.3 ± 3.4	0.75
Presence of heartburn or regurgitation	13 (36.1)	7 (50)	0.37
Erosive esophagitis on EGD	6 (16.7)	2 (14.3)	1
Reflux symptom index	15.9 ± 7.5	16.8 ± 9.2	0.62
Reflux findings score	8.1 ± 3.7	6.4 ± 2.4	0.19
Positive for LPR	12 (33.3)	5 (35.7)	0.87
Positive for pathologic GER	3 (8.3)	1 (7.1)	1
Data obtained during the first 4 h			
Frequency of symptoms onset (episodes/h)	0.04 ± 0.1	0.14 ± 0.22	0.08
Pharyngeal probe			
Total time of pH < 4 (%)	0.03 ± 0.10	0.07 ± 0.16	0.32
Mean frequency of reflux (episodes/h)	0.07 ± 0.23	0.18 ± 0.47	0.33
Patients with long reflux	0	0	1
Esophageal probe			
Total time of pH < 4 (%)	0.96 ± 1.89	0.42 ± 0.81	0.59
Mean frequency of reflux (episodes/h)	0.74 ± 1.51	0.63 ± 0.97	0.49
Patients with long reflux	1 (2.8)	0	1

Data are expressed as absolute numbers (percentage) or mean ± SD.

¹Statistical significance was defined as a $P < 0.05$. EGD: Esophagogastro duodenoscopy; LPR: Laryngopharyngeal reflux; GER: Gastroesophageal reflux.

by the esophageal probe^[13].

Analysis of the pH data

The elimination half-life of meperidine is 3.2–3.7 h, and the half-life of midazolam is approximately 3 h^[14,15]. To analyze the effect of conscious sedation on 24-h pH monitoring, computer software provided by MMS was used to analyze the 24-h pH data of each patient during two periods: the first 4 h (Period I) and the remaining time of the study (Period II). Meal times and sleep h were excluded from the analysis. Thus, only data recorded when the patients assumed an upright position were used for the comparisons. The mean duration of each period was 3.5 ± 0.5 h for Period I and 10.1 ± 2.1 h for Period II.

An acid reflux event was defined as an episode of pH < 4 detected on the pharyngeal or esophageal probe. Long reflux was defined as a reflux event lasting more than 5 min. The variables used for the comparisons were percentage of total time with a pH < 4, frequency of acid reflux events (episodes/h), and presence of long reflux.

Statistical analysis

Continuous variables are expressed as the mean ± SD in the text and tables. The differences in the variables between patients in group A and B were compared using a t test for age and a Mann-Whitney U test for BMI, Reflux Symptom Index (RSI), Reflux Finding Score (RFS),

percentage of total time with a pH < 4, and frequency of acid reflux. Either a χ^2 or Fisher's exact test (when χ^2 test was inappropriate) was used to analyze differences in sex, presence of heartburn and regurgitation, erosive esophagitis, LPR, pathologic GER, and long reflux. The differences in the variables between Period I and Period II in group A patients were compared using a Wilcoxon Signed Rank test for the percentage of total time with a pH < 4, frequency of symptoms, and the presence of acid reflux. A McNemar's test was used to analyze differences in the presence of long reflux. Statistical significance was defined as $P < 0.05$. The statistical analyses were performed using the SPSS version 17.0 for Windows.

RESULTS

Comparisons between patients with and without sedated EGD

The demographic, clinical, and endoscopic data from the patients in groups A and B were compared (Table 1). There were no significant differences between the two groups. Characteristic symptoms of GERD, heartburn and acid regurgitation were present in both groups (13/36 vs 7/14, $P = 0.37$). Six patients (16.7%) in group A and 2 (14.3%) in group B had erosive esophagitis (all were grade A, except one patient in group A who was grade B based on the Los Angeles classification) on the EGD ($P = 1$). The RSI is a validated patient-administered questionnaire for the diagnosis of LPR^[16]. A total score greater than 13 is regarded as a positive result. The patients in group A scored 15.9 ± 7.5 , and the patients in group B score 16.8 ± 9.2 ($P = 0.62$). The RFS is an 8-item scale listing common physical findings in LPR patients^[17]. A total score of greater than 7 is regarded as a positive result. The RFS was 8.1 ± 3.7 in group A and 6.4 ± 2.4 in group B ($P = 0.19$). Twelve patients (33.3%) in group A and 5 (35.7%) in group B met the pH criteria for LPR ($P = 0.87$). There were three (8.3%) patients in group A and one (7.1%) in group B who had pathologic GER ($P = 1.00$).

The pH data obtained from Period I were compared between the two groups (Table 1). Using the pharyngeal probe, the percentage of total time with a pH < 4 was $0.03\% \pm 0.10\%$ (range, 0%–0.4%) in group A and $0.07\% \pm 0.16\%$ (range, 0%–0.5%) in group B ($P = 0.32$). The frequency of acid reflux events was 0.07 ± 0.23 episodes/h (range, 0–1.1 episodes/h) in group A and 0.18 ± 0.47 episodes/h (range, 0–1.7 episodes/h) in group B ($P = 0.33$). None of the patients in either group had long reflux events. Using the esophageal probe, the mean percentage of total time with a pH < 4 was $0.96\% \pm 1.89\%$ (range, 0%–7%) in group A and $0.42\% \pm 0.81\%$ (range, 0%–2.9%) in group B ($P = 0.59$). The frequency of acid reflux events was 0.74 ± 1.51 episodes/h (range, 0–6.3 episodes/h) in group A and 0.63 ± 0.97 episodes/h (range, 0–3.1 episodes/h) in group B ($P = 0.49$). One patient in group A and no patients in group B had long reflux ($P = 1$).

Table 2 Comparisons between Period I and Period II in group A patients (mean \pm SD)

Variables	Period I	Period II	P value ¹
Frequency of symptom (episodes/h)	0.04 \pm 0.10	0.03 \pm 0.06	0.29
Pharyngeal probe			
Total time of pH < 4 (%)	0.03 \pm 0.10	0.23 \pm 0.85	0.21
Mean frequency of reflux (episodes/h)	0.07 \pm 0.23	0.29 \pm 0.98	0.22
Patients with long reflux	0	0	1
Esophageal probe			
Total time of pH < 4 (%)	0.96 \pm 1.89	1.11 \pm 2.57	0.55
Mean frequency of reflux (episodes/h)	0.74 \pm 1.51	0.81 \pm 1.76	0.55
Patients with long reflux	1 (2.8%)	5 (13.9%)	0.22

¹Statistical significance was defined as a $P < 0.05$.

Comparisons between different periods in patients who underwent EGD with conscious sedation

The pH data for Period I and Period II from the group A patients are shown in Table 2. The frequency of symptom occurrence was 0.04 ± 0.10 episodes/h (range, 0-0.3 episodes/h) during Period I and 0.03 ± 0.06 episodes/h (range, 0-0.3 episodes/h) during Period II ($P = 0.29$). Based on the pharyngeal probe measurements, the percentage of total time with a pH < 4 was $0.03\% \pm 0.10\%$ (range, 0%-0.4%) in Period I and $0.23\% \pm 0.85\%$ (range, 0%-5%) in Period II ($P = 0.21$, Figure 1A). The frequency of acid reflux was 0.07 ± 0.23 episodes/h (range, 0-1.1 episodes/h) in Period I and 0.29 ± 0.98 episodes/h (range, 0-5.7 episodes/h) in Period II ($P = 0.22$). None of the patients had a long reflux event. Based on the esophageal probe measurements, the percentage of total time with a pH < 4 was $0.96\% \pm 1.89\%$ (range, 0%-7%) in Period I and $1.11\% \pm 2.57\%$ (range, 0%-13.6%) in Period II ($P = 0.55$, Figure 1B). The frequency of acid reflux was 0.74 ± 1.51 episodes/h (range, 0-6.29 episodes/h) in Period I and 0.81 ± 1.76 episodes/h (range, 0-9.78 episodes/h) in Period II ($P = 0.55$). One patient had a long reflux event during Period I and five had a long reflux event during Period II ($P = 0.22$).

DISCUSSION

EGD is usually performed without conscious sedation in Taiwan. Some of our patients reported that nasally passed procedures for esophageal manometry and 24-h pH monitoring were less tolerable than EGD without conscious sedation. Because moderate conscious sedation may be helpful to facilitate gastrointestinal procedures, we performed a catheter-based pH study in a manner similar to the Bravo system in our patients^[8,12]. Our study results showed that EGD with conscious sedation does not have an immediate effect on subsequent catheter-based pH monitoring with regard to the relevant parameters assessed with pH monitoring techniques^[6,18].

The Bravo capsule is usually placed during an EGD with conscious sedation^[19-23]. The Bravo pH system allows for the measurement of esophageal acid exposure

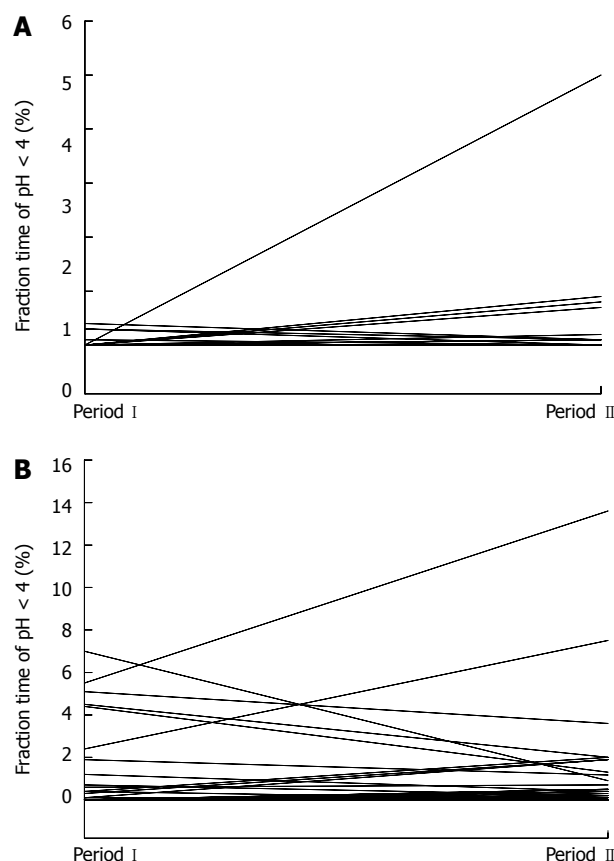


Figure 1 Individual comparison of the fraction of total time with a pH < 4 between Period I and Period II in group A patients. A: Using pharyngeal probe measurements; B: Using esophageal probe measurements.

over a 48-h period. Therefore, many studies have investigated whether there is day-to-day discrepancy during Bravo pH monitoring^[19-23]. The results are conflicting. Bechtold *et al.*^[19] and Bhat *et al.*^[20] reported more acid reflux events on day 1 than on day 2 using the Bravo system, suggesting that endoscopy and the associated sedatives may be responsible for the day-to-day discrepancy. Other studies showed that patients who underwent same-day EGD with intravenous sedation did not demonstrate any significant differences in reflux variables between day 1 and day 2 using Bravo pH monitoring^[21-23].

Bhat *et al.*^[20] further analyzed their pH data by dividing the study period into the first 6 h and the remaining 18 h on both day 1 and day 2. They found an increase in esophageal acid exposure during the first 6 h after capsule insertion on day 1 compared to the corresponding period on day 2. There was no such difference during the remaining 18 h on day 1 and day 2. They concluded that EGD with conscious sedation interferes with subsequent capsule-based Bravo pH measurements. In this study, we divided the study period into the first 4 h and the remaining 20 h because the elimination half-life is nearly 4 h for meperidine and approximately 3 h for midazolam^[14,15]. Our results showed no interference in patients who underwent EGD with sedation. Our data further revealed that three pH variables were not significantly different between the patients with and without prior sedation (us-

ing both the pharyngeal and laryngeal probes). Ayazi *et al.* observed a similar day-to-day discrepancy in patients receiving capsule-based Bravo pH monitoring without prior EGD and conscious sedation^[24]. Their results argue for an iatrogenic effect of sedated EGD on the pH monitoring.

There are some limitations in the present study. First, the study cohort had extra-esophageal symptoms (LPR) but not esophageal symptoms (classical GERD). The mechanism of LPR may be different from that of classical GERD^[2,25]. Therefore, whether the study results can be applied to pH monitoring in patients with characteristic symptoms of GERD needs further investigation. Second, the esophageal probe was placed at a variable distance above the proximal border of the LES of participants. The results of the pH parameters obtained from the esophageal probe may be suboptimal.

In conclusion, our results suggest that EGD with conscious sedation does not interfere with the results of subsequent catheter-based pH monitoring in patients with extra-esophageal manifestations of GERD. Catheter-based 24-h pH monitoring can be performed shortly after EGD with conscious sedation, especially for those patients who are intolerable to the procedures.

COMMENTS

Background

One of the limitations of catheter-based pH monitoring is discomfort. Whether it can be performed shortly after esophagogastroduodenoscopy (EGD) with conscious sedation like the performance of Bravo pH system is unknown. Authors aimed to investigate the impact of sedated EGD on the subsequent 24-h catheter-based pH monitoring.

Research frontiers

In order to increase patients' willingness to receive 24-h pH monitoring, authors have attempted to perform the catheter-based pH study in a similar way to Bravo system in our patients.

Innovations and breakthroughs

EGD with conscious sedation does not interfere with the results of the subsequent 24-h pH monitoring in patients with extraesophageal symptoms of gastroesophageal reflux disease.

Applications

Catheter-based 24-h pH monitoring can be performed shortly after sedated EGD especially for those patients who are intolerable to the procedures.

Terminology

Laryngopharyngeal reflux is backflow of gastric content into larynx and pharynx which has been widely used by otolaryngologists, while extraesophageal reflux is commonly used by gastroenterologist.

Peer review

The paper is well composed, documented. The results are interesting and suggest that EGD with conscious sedation does not interfere with the results of subsequent 24-h pH monitoring in patients with extra-esophageal symptoms of gastroesophageal reflux disease.

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