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Original article

THE ASSESSMENT OF PATIENTS WITH NON-EROSIVE GASTROESOPHAGEAL REFLUX DISEASE BY USING THE BRAVO® PH MONITORING SYSTEM

Gök Mehmet,[1] Gencdal Genco[2]

[1] Istanbul Okan University, Department of Gastroenterology, İstanbul, Turkiye
[2] Koc University, School of Medicine, Department of Gastroenterology, İstanbul, Turkiye

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Abstract: **Background and aim:** Gastroesophageal reflux disease (GERD) is a common disease in the world. GERD is always treated with drugs. The Bravo® wireless pH monitoring system is a good technique. The Bravo® may affect increasing the specificity and sensitivity in the diagnosis of GERD with its 48-hour recording feature. In this study, we aimed to assess the diagnostic performance of the Bravo® pH monitoring system in patients with non-erosive GERD.

Materials and Methods: Patients with non-erosive reflux disease (normal endoscopy) whose symptoms persisted after PPI treatment (at least two months) were included in the study. All patients had upper gastrointestinal system endoscopies performed in our clinic between January 2013 and December 2019. All patients had a 48-hour Bravo® wireless pH monitoring record.

Results: Twenty-three patients (M: 18 (78.3%; Age: 35.7 ± 11) were included in the study. All patients completed the 2-day recording protocol. During and after the procedure, no patient showed any adverse effects of the Bravo® procedure. We diagnosed GERD in 13 of 23 patients by Bravo® capsule. According to the Bravo® pH-meter recordings; Total time pH < 4 (minute) was 187 ± 190, the total number of refluxes was 90 ± 61, the percentage of time with pH < 4 was 7.1 ± 7.22, the number of long reflux events were 8.1 ± 8, the duration of the longest reflux episode during pH < 4 (minute) was 31 ± 49, the Demeester score was 20.8 ± 19.3 detected.

Conclusion: Based on the results of the current study, the Bravo® pH monitoring system is a practical and effective diagnostic technique for non-erosive GERD. Further prospective studies would be useful for comparing the differences between 24-hour and 48-hour pH recording results.

Keywords: Gastroesophageal Reflux, Esophagus, Reflux.

INTRODUCTION

The leakage of gastric acidic juice or alkaline secretions into the esophagus is named gastroesophageal reflux. Gastroesophageal reflux, which is a physiological event, is defined as gastroesophageal reflux disease (GERD) when it causes symptoms. The most important preventive factor in the pathological transformation of gastroesophageal reflux in physiological conditions is the mechanical barrier at the lower esophageal sphincter (LES). GERD can occur when this mechanical barrier is weakened by LES insufficiency, hiatus hernia, or temporary LES relaxation. The prevalence of GERD has been reported in 10-29% in the western world. In the GORHEN study (3214 cases in 20 provinces in Turkey) the frequency of GERD has been reported as 23% (1, 2, 3). One or both of the classic GERD symptoms (pyrosis, regurgitation), once a week or more often, is sufficient for diagnosing GERD. GERD is always classified into two groups according to endoscopy. Erosive reflux disease (ERD) is defined in cases with erosion or ulceration in the endoscopic examination. Non-erosive reflux disease (NERD) is defined by determining acid exposure for 24 hours or more with new diagnostic methods such as pH-meter, impedance, and Bravo® pH measurement. In NERD cases, response to proton pump inhibitor (PPI) therapy is low (3, 4, 5).

GERD should be investigated with intraesophageal monitoring in cases that has no response to PPI treatment, in cases with extraesophageal symptoms, or in cases where an operation is planned for GERD, especially if there is no evidence of upper GI endoscopic

examination (non-erosive reflux disease) because objective evidence is needed. For this purpose, conventional catheter-based pH-meters and the Bravo® wireless intraesophageal capsule pH-meter can be used. The conventional method may restrict the patient's diet and physical activity, and the catheter may migrate. Patients with Bravo® wireless intraesophageal capsule pH-meter do not experience such problems with its 48-hour recording feature (6-10).

In this study, we aimed to assess the diagnostic performance of the Bravo®pH monitoring system in patients with non-erosive GERD.

MATERIAL AND METHOD

Study population

In this study, patients with NERD whose symptoms persisted after PPI treatment (at least two months), were included. All patients had undergone upper gastrointestinal system endoscopy in our clinic between January 2013 and December 2019. All patients had undergone a 48-hour Bravo® wireless pH monitoring. Since the study was retrospective, patient data were obtained from the digital database of our hospital.

Cases under the age of 18, presence of malignancy in the upper gastrointestinal system endoscopy or presence of reflux due to gastric outlet obstruction, cases with motility disorder, cases who underwent Nissen fundoplication, and cases with connective tissue disease (scleroderma, etc.), were not included in the study. The local Ethics Committee approval was obtained (2021.371.IRB1.161).

Bravo® (Esophageal capsule Ph meter) (Medtronic, Shoreview, MN, USA)

The Bravo® pH monitoring system has several items: pH receiver kit; capsule with a delivery system, an internal battery, and transmitter; vacuum pump; suction tubes; calibration stand, buffer solution; infrared receiver device; and software. Drugs (proton pump inhibitors and H2-blockers) must be discontinued for 14 days. Antacids should be stopped at least 24 hours before the operation. Patients must fast (at least 8 hours). The capsule-shaped probe (6 mm × 5.5 mm × 25 mm) that will measure pH is attached to the 6 cm proximal of the LES during the endoscopic examination performed while the patient is sedated. The main parameters measured are listed as percent of the total time of pH < 4; the total number of reflux periods in both positions; duration of reflux period; the number of long reflux periods (longer than 5 minutes); symptom score; and the mean duration of reflux period. A reflux period is defined as a drop in pH below 4, lasting for ≥ 10 seconds. In addition to the possibility of measuring in more physiological conditions due to its catheter-free nature, it provides the opportunity to measure intraesophageal pH-meter until it falls. The capsule always detaches from the esophagus spontaneously (2 days to 2 weeks). It measures 2-5 days until the capsule falls. The day in which reflux is detected the most is taken into account. For this reason, it has been shown that the sensitivity has increased by 30% with the concept of "worst day". Complications such as chest pain (3%-5%), failure of the capsule to hold, and premature or no fall (0-3%) may develop. The contraindications for Bravo® are known as pregnancy, history of bleeding diathesis, the presence of esophageal strictures, esophageal varices, diverticula of the esophagus, and severe esophagitis with metaplasia. For patients with a history of previous upper GI surgery, Zollinger-Ellison syndrome, active malignancy, or Crohn's disease, the Bravo®pH monitoring system was not recommended (11-14).

Statistical Analysis

The data distribution characteristics were reviewed before the statistical analysis. Non-parametric group data were listed as the median (interquartile range). The Wilcoxon signed-rank test is used for comparing paired data. The statistical significance is defined as a P value of less than 0.05.

RESULTS

All twenty-three patients had undergone the 2-day recording protocol. No side effects were observed after or during the Bravo® procedure (chest pain, dysphagia, bleeding, etc.). The indications for pH testing were PPI responsiveness symptoms such as chest pain, refractory heartburn, and laryngeal symptoms. We diagnosed GERD in 13 of 23 patients by Bravo® capsule. According to Bravo® pH-meter records; Total time pH < 4 (minute) was 187 ± 190, the total number of reflexes was 90 ± 61, the percentage of time with pH < 4 was 7.1 ± 7.22, the number of long reflux events was 8.1 ± 8, the duration of the longest reflux episode during pH < 4 (minute) was 31 ± 49, the Demeester score was 20.8 ± 19.3 detected.

The demographics of the patients and results of Bravo® capsule presented in Table 1.

We also compared Day 1 and Day 2 results and found no statistically significant difference between the two days (Table 2).

Table 1. *Demographics of patients and Bravo capsule pH results*

Age	35.7 ± 11
Gender (Male)	18 (78.3%)
Patients with extraesophageal symptoms	9 (39.1%)
Total time pH < 4 (minute)	187 ± 190
Total number of refluxes	90 ± 61
Percentage of time with pH < 4	7.1 ± 7.22
Number of long reflux events	8.1 ± 8
Duration of longest reflux episode during Ph < 4 (minute)	31 ± 49
Demeester score	20.8 ± 19.3

Table 2*. The comparison of Day 1 and Day 2 results of the Bravo Capsule pH Meter*

	Day 1	**Day 2**	**P Value**
Total time pH < 4 (minute)	88.09 ± 74	103 ± 138	0.9
Total number of refluxes	50.6 ± 32	45.6 ± 29	0.58
Percentage of time with pH < 4	6.7 ± 5.5	7.9 ± 10	1
Number of long reflux events	4.1 ± 4	3.8 ± 4.6	0.72
Duration of longest reflux episode during pH < 4 (minute)	17.5 ± 14	20.8 ± 48	0.21
Demeester score	18.4 ± 13.6	19.5 ± 21.8	0.7

DISCUSSION

Conventional pH-meter limits the daily life activities, diets, and physical activities of the patients, thus causing a decrease in their quality of life. Bravo® allows the patient to continue his daily activities and does not reduce his quality of life. Bravo® is better tolerated, longer records can be undertaken, and this can increase the diagnostic sensitivity. Because the conventional catheter pH meters may cause discomfort in patients, it may lead them to eat less and behave differently in their daily lives during the process. Patients with Bravo® wireless intraesophageal capsule pH-meter do not experience such problems, so the Bravo® procedure provides "real" measurement. On the other hand, it is important to stay in place because it has been shown that conventional catheter pH meters can be displaced within hours. Measurement differences may be in conventional catheter pH meter and Bravo® capsule pH meter because recording intervals are different in these two methods. The recording interval is 4 seconds for a conventional pH meter and 6 seconds for Bravo® pH-meter. In a study, Azzam et al. compared the conventional and capsule pH monitoring, reported as no significant difference was detected between the two methods for the diagnosis of GERD, and they also reported as they detected longer reflux durations in the capsule group. Hakanson et al. reported as the esophageal acid exposure time detected in capsule pH was approximately half of the value that was found with the catheter ($p < 0.05$)in a study. According to the current medical literature, catheter pH monitoring has 79%-96% sensitivity and 85%-100% specificity. Bravo's endoscopic application is easy, and it stands out with its long-term recording capability. Pandolfino et al. reported 78.3%-100% sensitivity and 84.5%-94.8% specificity for this method. Bravo® has advantages over conventional catheters in these respects, but Bravo® is expensive, and the number of applications remains low compared to other methods. Rare complications such as chest pain, failure of the capsule to hold, and premature or no fall may develop (8-18). In our study, patients tolerated the Bravo® procedure well, consistent with the literature.

Several studies in the medical literature had presented the positive effect of extended 48h pH monitoring for the diagnosis of GERD. Many studies are comparing the results of days one and two of the Bravo® procedure, but the results of these studies are contradictory. Pandolfino et al., in a study that included 37 patients with GERD and 39 controls, stated no significant difference between the 1st and 2nd day data in terms of acid exposure (11). Bechtold et al. reported that they detected higher acid reflux in Day 1 recordings compared to Day 2 recordings (19). In some studies, more reflux was detected in the 2nd day measurements (20-22). According to our study, no significant difference was found for acid reflux and Bravo® capsule parameters in the 1st and 2nd day recordings.

After the procedure, some patients may have throat discomfort, bleeding, odynophagia, dysphagia, mild foreign body sensation, and eating and chest discomfort. If the patients have severe odynophagia and

chest pain (< 2% cases), a chest X-ray may be useful for excluding perforation. Sometimes, in up to 15% of cases, technical failure may occur (data transmission decrease, attachment problems, early capsule dislodgement, detachment failure). The need for capsule removal may be indicated in patients whose chest discomfort is intolerable and persistent (6%) (14, 21, 22). In our study no major complications or serious side effects were observed after the procedure, and all patients tolerated the Bravo® capsule well. It was not necessary to remove the capsule in any of the patients.

The study has some limitations. The most important one is the retrospective nature of the study. The data of the patients (demographic, anthropometric, procedure history, treatment history, etc.) could not be obtained sufficiently. Another limitation is that the majority of the current study is male, and the study results may not be generalizable to the whole population.

In conclusion, the Bravo® pH monitoring system is an effective, practical, and safe diagnostic procedure. In our study, no significant difference was found between the first- and second-day values for acid reflux. Nowadays, few studies have compared the merits of 24 versus 48-hour wireless capsule pH monitoring. Many factors may affect the result, for example, the sedation given during endoscopy for capsule placement on the first day can increase the acid reflux in the distal esophagus. Further prospective studies would be useful for comparing the differences between 24-hour and 48- hour pH recording results and investigating the effects of sedation on 24-hour and 48-hour wireless pH monitoring.

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Licensing

Sažetak

ANALIZA PACIJENATA SA NEEROZIVNOM GASTROEZOFAGEALNOM REFLUKSNOM BOLEŠĆU KORIŠĆENJEM BRAVO® PH SISTEMA ZA MONITORING

Gök Mehmet,[1] Gencdal Genco[2]

[1] Istanbul Okan University, Department of Gastroenterology, İstanbul, Turkiye
[2] Koc University, School of Medicine, Department of Gastroenterology, İstanbul, Turkiye

Uvod i cilj: Gastroezofagealna refluksna bolest (GERB) je uobičajena bolest u svetu. GERB se uvek leči lekovima. Bravo® bežični sistem za praćenje pH vrednosti je dobra tehnika. Bravo® može uticati na povećanje specifičnosti i osetljivosti u dijagnozi GERB-a sa svojom funkcijom snimanja od 48 sati. U ovoj studiji, imali smo za cilj da procenimo dijagnostičke performanse Bravo®pH sistema za praćenje kod pacijenata sa neerozivnim GERB-om.

Materijali i metode: U studiju su uključeni pacijenti sa neerozivnom refluksnom bolešću (normalna endoskopija) čiji su simptomi perzistirali nakon tretmana PPI (najmanje dva meseca). Svim pacijentima je urađena endoskopija gornjeg gastrointestinalnog sistema u našoj klinici u periodu od januara 2013. do decembra 2019. Svi pacijenti su imali 48-časovni Bravo® bežični zapis o praćenju pH vrednosti.

Rezultati: U studiju su uključena 23 pacijenta (M: 18 (78,3%; Starost: 35,7 ± 11). Svi pacijenti su završili dvodnevni protokol snimanja. Tokom i nakon procedure, nijedan pacijent nije imao štetne efekte od Bravo® procedure. Dijagnostikovali smo GERB kod 13 od 23 pacijenta sa Bravo® kapsulom. Prema snimcima Bravo® pH metra, ukupno vreme pH < 4 (minuta) je 187 ± 190, ukupan broj refluksa bio 90 ± 61, procenat vremena sa pH < 4 je bio 7,1 ± 7,22, broj dugih refluksnih događaja je bio 8,1 ± 8, trajanje najduže epizode refluksa tokom pH < 4 (minuta) je bilo 31 ± 49, Demeester skor je bio 20,8 ± 19,3.

Zaključak: Na osnovu rezultata trenutne studije, Bravo® pH sistem za praćenje je praktična i efikasna dijagnostička tehnika za neerozivni GERB. Dalje prospektivne studije bi bile korisne za poređenje razlika između 24-časovnih i 48-časovnih rezultata pH snimanja.

***Ključne re**či:* gastroezofagealni refluks, jednjak, refluks.

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Correspondence to/Autor za korespondenciju

Assoc. prof Genco Gencdal

Koc University, School of Medicine, Department of Gastroenterology.

Topkapı, Koç Üniversitesi Hastanesi, Davutpaşa Cd. No:4, 34010 Zeytinburnu/İstanbul

Email:gencogencdal@yahoo.co.uk; Phone:090 506 3581760

ORCID numb: 0000-0002-5856-5384

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