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Reflux Mechanisms in Gerd : Analysis of the role of transient lower esophageal sphincter relaxations

Straathof, J.W.A.

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COMPARISON OF TWO TECHNIQUES FOR LOWER ESOPHAGEAL SPHINCTER MANOMETRY: SLEEVE AND SPHINCTOMETER

J.W.A. Straathof, M. Lüchtenborg, A.A.M. Masclee

Department of Gastroenterology-Hepatology
Leiden University Medical Center, The Netherlands

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ABSTRACT

Background and methods: We have compared the sphinctometer with the water-perfused sleeve (gold standard) for measurement of lower esophageal sphincter (LES) characteristics by simultaneous recording.

Results: LES pressure and transient LES relaxations (TLESR) measured by sleeve and sphinctometer in eleven healthy volunteers showed identical patterns. However, output of the sphinctometer was significantly ($p < 0.01$) lower than output of the sleeve. A total of 249 TLESR were recorded. Of these, 176 TLESR were identified by both sleeve and sphinctometer, 50 TLESR were identified by sleeve alone and 23 TLESR by sphinctometer alone. Due to the lower pressure output of the sphinctometer, 29 LES relaxations did not reach amplitude criteria to qualify as TLESRs. When TLESR criteria were adjusted for sphinctometer pressure measurements, the number of TLESRs identified by both sleeve and sphinctometer increased from 176 to 205.

Conclusions: In healthy volunteers the sphinctometer registers TLESR with results comparable to sleeve recording. However at low LES pressures, the number of TLESR is underscored by the sphinctometer.

INTRODUCTION

In patients with reflux disease and in healthy subjects transient lower esophageal sphincter relaxations (TLESR) are the major reflux mechanism(1). The water-perfused sleeve designed by Dent (2) is used to record TLESR during stationary or ambulatory studies. Gotley et al. described the sphinctometer, an oil-filled cylinder containing a pressure microtransducer incorporated into an ambulatory esophageal solid state catheter. In vitro studies have shown that the sphinctometer adequately records LES pressure (3,4) However, when the length of the sphinctometer is only partially exposed to pressure, the absolute pressure recorded by the sphinctometer is lower than the applied pressure. In vivo, catheters incorporating a sphinctometer have been used for ambulatory LES pressure recording (5). However, until recently ambulatory recording of TLESR by the sphinctometer has not been performed. In one study with the sphinctometer, LES characteristics during acid reflux events were consistent with the concept of TLESR (4).

The aim of our study was to compare water-perfused sleeve manometry and solid state sphinctometer manometry for recording TLESRs during simultaneous measurements.

METHODS

Eleven healthy subjects (age 19-24 years; 6 females) without a history of gastrointestinal disease or surgery participated in the study. Informed consent was obtained and the study had been approved by the local Ethics Committee.

Manometric and pH technique

Water-perfusion manometry (sleeve) was performed as described previously (6), using a multilumen silicone rubber tube (outer diameter 5.0mm) with 7 side-holes at 29, 23,

18, 13, 8, 3 and -4 cm from the mid-point of the 6 cm long sleeve sensor (Dentsleeve Pty Ltd, Belair, South Australia). Solid-state manometry (sphinctometer) was performed with a electronic catheter (Sentron, Medtronic, Roden, the Netherlands) with five solid-state pressure microtransducers at 30, 18, 8, 0 and -4 cm from the mid-point of the sphinctometer. The sphinctometer is an oil-filled silicone rubber cylinder around a solid-state pressure microtransducer, 6cm long and a diameter of 0.4 cm. The sphinctometer had been calibrated at 0 mmHg and at 50 mmHg. Data of sleeve catheter and sphinctometer were displayed continuously on a monitor and stored on a personal computer system (Polygram Upper GI 6.30, Gastrosoft Inc., Medtronic, Denmark).

In vitro studies were performed in triplicate to test the sphinctometer susceptibility to pressure reading drifts during 24 hour recordings. The sphinctometer was calibrated at 20 °C and thereafter submerged into a warm water bath of 37 °C for recording. Changes in pressure reading of the sphinctometer and microtransducers were recorded on a portable recorder (µdigitrapper, Medtronic, Denmark) and processed afterwards. In vitro studies with the sphinctometer showed that during 24 hours at a constant temperature of 37°C the drift in output of the sphinctometer was <1 mmHg.

Study protocol

Experiments were started at 8.30 a.m. with subjects fasted overnight. The sleeve catheter was positioned so that the sleeve sensor straddled the LES. Side holes were used for recording pharyngeal swallow signals, esophageal body motility, and intragastric pressure. The sphinctometer was placed at exactly the same position as the sleeve. A glass pH electrode (Ingold LOT 440; Ingold Messtechnik AG, Urdorf, Germany; calibrated at pH 4.0 and pH 7.0) was positioned 5 cm above the upper margin of the LES. Esophageal pH and motility were recorded simultaneously for one hour under fasting conditions (time -60 to 0min) and for three hours (0 to 180min) after ingestion of a 400 ml liquid meal (Nutridrink; Numico, Zoetermeer, The Netherlands) containing 20g protein, 26g fat and 72g carbohydrates (2520 kJ).

Data analysis

Lower esophageal sphincter tracings were analyzed for LES resting pressure and TLESR. The TLESR were defined according to Holloway et al.(1,7) Gastro-esophageal reflux episodes and reflux mechanisms were scored using criteria described previously(6). Data are expressed as mean \pm SEM. The Wilcoxon signed ranks test was used to compare results between sleeve and sphinctometer. Data were analyzed using MANOVA. When this indicated a probability of less than 0.05 for the null hypothesis, Student-Newman-Keuls analyses were performed to determine which values between or within the experiments differed significantly ($p < 0.05$).

RESULTS

Lower esophageal sphincter pressure

LES pressure and LES relaxations measured by sleeve and sphinctometer showed an identical pattern (Figure 1, tracing A). However, the output of the sphinctometer was significantly ($p < 0.01$) lower than the output of the sleeve (Figure 2) from 15 to 180 minutes after meal ingestion LES pressure decreased significantly ($p < 0.01$) compared to basal level, and this was identified with both recording techniques.

Transient lower esophageal sphincter relaxations

In total 249 TLESRs were identified by the sleeve and/or the sphinctometer. Of these, 176 TLESRs (71%) were identified by both sleeve and sphinctometer, 50 by sleeve alone (20%) TLESRs, and 23 by sphinctometer alone (9%) TLESRs. Recordings were analyzed in detail (Table 1). Twenty-nine LES relaxations not detected by the sphinctometer had the typical characteristics of a TLESR except for one or two criteria: relaxation rate and absolute fall in pressure did not fulfill the strict criteria of TLESR described by Holloway *et al* (7) especially when LES pressure was low (< 5 mmHg). Adjustment of the criteria for TLESR improved identification of TLESR by the sphinctometer. Thus, with minimum LESP decrease set at ≥ 4 mmHg and relaxation rate at ≥ 0.4 mmHg/s, 195 TLESRs were scored by both sleeve and sphinctometer. Four episodes were identified by sphinctometer as 'drift of LES pressure' instead of TLESR because the rate of LES pressure decrease was less than 1.0 mmHg/sec (recorded value 0.4 mmHg/sec.) With minimum LES pressure decrease set at ≥ 3 mmHg and relaxation rate of ≥ 0.3 mmHg/s, 205 TLESRs were scored by both sleeve and sphinctometer. With other cut-offs, the number of identified TLESR was not higher, and visual identification became more difficult.

The duration of TLESR measured by the two different catheters correlated significantly (r_s ; $p < 0.001$) and was slightly longer as measured by sleeve (16.5 ± 0.4 s) compared to sphinctometer (14.9 ± 0.4 s, $p < 0.05$).

Table 1. The tracings at time of a TLESR, identified by either sleeve or sphinctometer, were analyzed in detail to determine the criteria on which proper qualification had failed by sleeve or sphinctometer. The main characteristics of each LES relaxation that was not identified as TLESR by sleeve or sphinctometer are described (results in numbers).

| | Sleeve | Sphinctometer |
|-------------------------------|--------|---------------|
| failed to qualify as TLESR | 23 | 50 |
| Relaxation rate < 1 mmHg/s | 3 | 22 |
| LESP decrease < 5 mmHg | 0 | 7 |
| LES nadir pressure > 2 mmHg | 10 | 12 |
| Swallow related LESR | 8 | 9 |
| Refill water container | 2 | 0 |

Figure 1. Transient lower esophageal sphincter relaxations (arrows) during simultaneous measurement by water-perfused sleeve and sphinctometer in healthy subjects. The tracings consist of esophageal pH (1), pharyngeal pressure (2), esophageal body pressure (3,4), LES pressure (5-sleeve, 6-sphinctometer) and intragastric pressure (7).

Tracing A: Both tracings reveal identical patterns, however, the output of the sphinctometer is significantly lower than the output of the sleeve sensor.

Tracing B: Although the tracings reveal identical patterns, the output of the sphinctometer does not fulfill the criteria of a TLESR because the rate of relaxation is less than 1.0 mmHg/s. This TLESR is associated with acid reflux.

Tracing C: After a peristaltic wave in response to multiple wet swallows (S) a prolonged LES relaxation is registered by the sphinctometer. The sphinctometer output is scored as a TLESR, but the tracing of the sleeve does not fulfill the criteria of TLESR. The nadir pressure is > 2 mmHg above intragastric pressure.

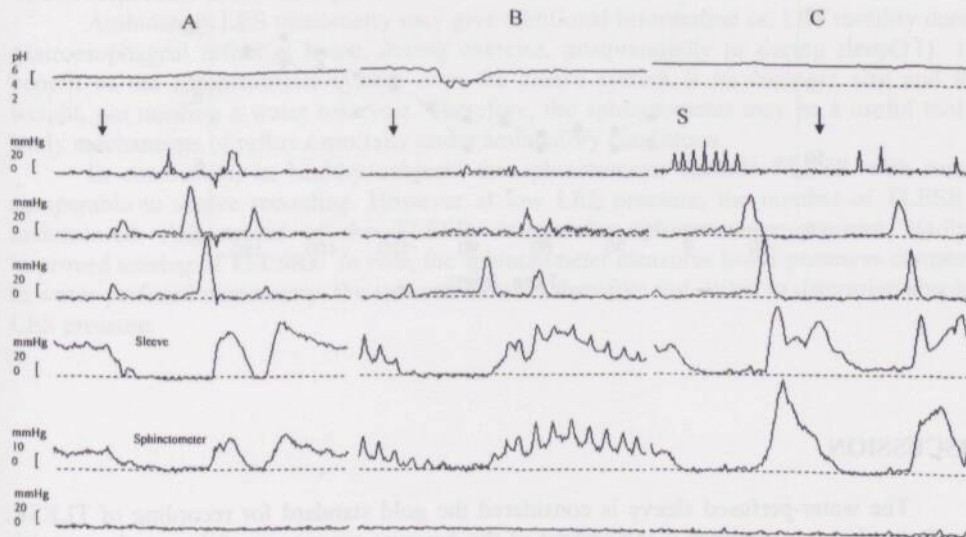
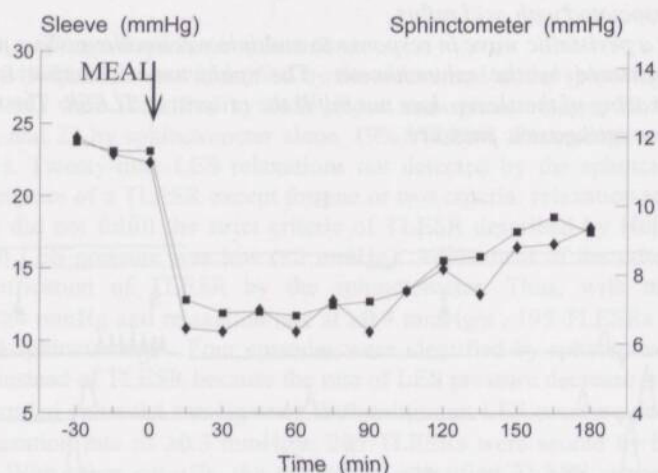


Figure 2. Lower esophageal sphincter pressure (mean \pm SEM) in eleven healthy volunteers under fasting conditions and after ingestion of a meal (2520 kJ) at $t=0$ min. The output of the sphinctometer (diamonds) is significantly lower than the output of the sleeve (squares). The output of sleeve and sphinctometer are plotted on different scales to show an identical postprandial decrease.



DISCUSSION

The water-perfused sleeve is considered the gold standard for recording of TLESR. The 6 cm sleeve overcomes displacement of the pressure sensor out of the esophagogastric junction during respiration, peristalsis etc. The catheter incorporating the sphinctometer was constructed according to the same specifications as the water-perfused sleeve catheter: a 6 cm long sensor, with a pressure sensor for swallow signals and an intragastric pressure sensor necessary for identification of TLESR (1). LES pressures recorded with the sphinctometer were lower than those with the sleeve. This difference did not result from the position of the catheter in the LES. A catheter in the left lateral position measures higher pressures because of the radial asymmetry of the LES (8). In our study positioning of the catheters occurred randomly. The differences in LES pressure appear more likely to be related to the techniques themselves. The sleeve records the highest external pressure at any point along the sensor (2,9), whereas the sphinctometer accurately records pressure only when the whole surface of the sphinctometer is exposed to an external pressure (3,4). Partial exposure of the sphinctometer reduces the output depending on the length of the sphinctometer exposed in a linear way. The sphinctometer is calibrated during total (6 cm) surface exposure in a water

column. However, the length of the LES segment covering the sphinctometer *in vivo* is usually less than 6 cm. It therefore appears inherent that the output of this sphinctometer will be lower than the exposed pressure.

LES relaxations were recognized by both sleeve and sphinctometer. Using the sleeve criteria (7) for analysis of the sphinctometer recording, 50 spontaneous LES relaxations were not classified as TLESR, and this was most apparent in subjects with low postprandial spontaneous LES relaxations. Adjustment of two of the criteria postulated by Holloway *et al* (7) markedly improved TLESR identification by the sphinctometer: 1) abrupt falls of LES pressure within 10 sec reaching a pressure of ≤ 3 mmHg above intragastric pressure and 2) a relaxation rate ≥ 0.3 mmHg/s. With these criteria, over 90% of TLESR measured by sleeve were also classified as TLESR by the sphinctometer. Trudgill *et al* (10) compared sleeve and sphinctometer during simultaneous manometry. Based upon a small number of TLESR analyzed (N=28), they also concluded that the sphinctometer has a low capacity to register TLESR especially at low LES pressures.

Ambulatory LES manometry may give additional information on LES motility during gastroesophageal reflux at home, during exercise, postprandially or during sleep(11). The benefit of the sphinctometer system over the sleeve system is its compact size and low weight, not needing a water reservoir. Therefore, the sphinctometer may be a useful tool to study mechanisms of reflux especially under ambulatory conditions.

In conclusion, in healthy subjects the sphinctometer records TLESR with results comparable to sleeve recording. However at low LES pressure, the number of TLESR is underscored. Adjustment of the TLESR criteria for sphinctometer pressure readings improved scoring of TLESRs. *In vivo*, the sphinctometer measures lower pressures compared to water-perfused manometry, the sphinctometer is therefore not suited to determine absolute LES pressure.

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DISCUSSION

The water-perfused sleeve is considered the gold standard for recording of LESN. The 0.5 mm radius overcomes disadvantages of the pressure sensor end of the esophago-gastric junction during inspiration, peristalsis etc. The catheter incorporating the sphinctometer was constructed according to the same specifications as the water-perfused sleeve, although a 6 mm long sensor, with a diameter chosen for swallow safety and an inflatable reservoir within necessary for identification of LESN (1). LES pressure recorded with the sphinctometer were lower than those with the sleeve. This difference did not result from the position of the catheter in the LES. A catheter in the left lateral position increases LES pressure because of the basal curvature of the LES (6). In our study positioning of the catheter occurred randomly. The difference in LES pressure appears more likely to be related to the technique employed. The sleeve records the highest internal pressure at any point along the sensor (2,7), whereas the sphinctometer accurately records pressure only when the whole surface of the sphinctometer is exposed to an external pressure (1,4). Partial exposure of the sphinctometer reduced the output depending on the length of the sphinctometer exposed in a lateral way. The sphinctometer is calibrated during void (6) and surface exposure in a water