The impact of continuous positive airway pressure on the lower esophageal sphincter

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Continuous positive airway pressure (CPAP) has been shown to reduce reflux in individuals with and without sleep apnea, by an unknown mechanism. The aim of this study was to determine the effect of CPAP on swallow-induced LES relaxation. Measurements were made in 10 healthy, awake, supine individuals. Esophageal (Pes), LES (Ples), gastric (Pg), and barrier pressure to reflux (Pb) were recorded using a sleeve catheter during five swallows of 5 ml of water. This was repeated at four levels of CPAP (0, 5, 10, and 15 cmH2O). Pressures were measured during quiet breathing and during the LES relaxation associated with a swallow. Duration of LES relaxation was also recorded. During quiet breathing, CPAP significantly increased end-expiratory Pes, Ples, Pg, and Pb (P < 0.05). The increase in Pb was due to a disproportionate increase in Ples compared with Pg (P < 0.05). During a swallow, CPAP increased nadir Pes, Pg, and Pb and decreased the duration of LES relaxation (4.1 s with 0-cmH2O CPAP to 1.6 s on 15-cmH2O CPAP, P < 0.001). Pb increased with CPAP by virtue of a disproportionate increase in Ples compared with Pg. This may be due to either reflex activation of LES smooth muscle, or nonspecific transmission of pressure to the LES. The findings suggest CPAP may make the LES less susceptible to reflux by increasing Pb and decreasing the duration of LES relaxation.

Lower esophageal sphincter relaxation; esophageal function; gastroesophageal reflux

GASTROESOPHAGEAL REFLUX is common, with ~20% of the general community reporting reflux symptoms on a weekly basis (19). Nocturnal reflux has been reported to occur in 9–11% of the population (9) and may be particularly harmful to the esophagus because of the associated prolonged acid clearance time (5). Obstructive sleep apnea (OSA) is an aggravating factor for nocturnal reflux, presumably because of the development of obstructive events of pressure gradients across the lower esophageal sphincter (LES) that favor reflux.

The LES is a high-pressure zone located between the esophagus and stomach, which acts as a barrier to reflux. Pressure within the sphincter is generated by contraction of esophageal smooth muscle and of the crural diaphragm during inspiration.

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were to determine whether varying levels of CPAP influenced Ples during periods of swallow-induced LES relaxation and to examine the possible mechanisms underlying any such change.

METHODS

Subjects

Studies were performed on 10 normal (5 men, 5 women) healthy volunteers, with no history of gastroesophageal or pulmonary disease. Subjects were 31 yr (SD 7) of age, with a body mass index of 24 kg/m² (SD 3). Written, informed consent was obtained before participation in the study, which was approved by the Human Research Ethics Committee of Sir Charles Gairdner Hospital.

Measurements

Manometry. A purpose-built multilumen silicone manometry catheter (outer diameter 2.5 mm) (Dentsleeve) was passed via the nares into the esophagus to simultaneously record pressure changes within the esophagus, LES, and stomach. The catheter incorporated a 6-cm sleeve sensor for measuring Ples, five side holes above the sleeve to measure esophageal pressure (Pes), and two side holes below the sleeve to measure gastric pressure (Pg). Side holes were spaced at 4-cm intervals. All manometric channels were continuously infused with distilled water at a rate of 0.15 ml/min using a low-compliance capillary infusion pump (Dentsleeve). The infusion system was connected to pressure transducers (Abbott Australasia) that were calibrated before each study. The sleeve was positioned across the LES using a slow pull-through technique (14). Absolute pressures for the sleeve and side holes were referenced to atmospheric pressure.

Airway pressure. Subjects breathed via a tight-fitting nasal mask (Sullivan Mirage, ResMed, North Ryde, NSW, Australia) for the duration of the study. Pressure was measured at the mask via a side port (model 143 PC, microswitch, Honeywell, Morristown, NJ). Before each study, the pressure transducer was calibrated against a water manometer.

Protocol

Subjects were asked to limit fluid intake for 2 h before the study, abstain from caffeine and high-fat foods, and to have only a light meal 2–3 h beforehand. All measurements were made in the supine position during wakefulness. CPAP of 0, 5, 10, and 15 cmH₂O were applied in random order via a nasal mask (BiPAP, Respironics). At each level of CPAP, subjects were asked to perform five swallows of 5 ml of water. Each swallow was preceded by at least 30 s of stable Ples, which was monitored continuously. The time at which each swallow was initiated was recorded using an event marker. Double swallows were excluded from subsequent analysis. Throughout each study, all signals were recorded continuously on a computerized data-acquisition and analysis system (Powerlab 16S, ADInstruments, Castle Hill, NSW, Australia).

Analysis

Data analysis. End-expiratory Pes, Ples, Pg, transdiaphragmatic pressure (Pdi = Pg – Pes), and barrier pressure (Pb = Ples – Pg) were measured for each of the five breaths preceding a swallow. During each swallow-induced LES relaxation, measurements of nadir Ples, Pg, and nadir Pb were obtained. Duration of LES relaxation was defined as the time the LES was <20% of baseline pressure (12). Peristaltic wave amplitude was defined as the peak Pes in each Pes channel referenced to basal intraesophageal pressure. Peristaltic wave velocity was calculated by measuring the time between the onset of contractions, taking into account the distance between the most proximal esophageal side hole and the most distal esophageal side hole (i.e., a total distance of 16 cm). Intrabolus pressure (the pressure within the water bolus) was defined as the average of the plateau/ramp pressure before the onset of the peristaltic contraction wave referenced to basal intraesophageal pressure (1, 20). The border between these pressure regions was visually determined by the investigators.

Statistical analysis. Differences in Pes, Ples, Pg, Pdi, and Pb among levels of CPAP were compared using one-way repeated-measures ANOVA. Differences in intrabolus pressure, peristaltic wave amplitude, and velocity and duration of LES relaxation were also compared.
using one-way repeated-measures ANOVA. A two-way repeated-measures ANOVA was used to compare the magnitude of changes in Pes, Pg, and Ples with CPAP application. Post hoc analyses were performed using the Student-Newman-Keuls test. Results are presented as means (SD). A P value < 0.05 was considered statistically significant.

RESULTS

Effect of CPAP on Basal Ples

Application of increasing levels of CPAP systematically increased Pes, Ples, Pg, and Pb (Figs. 1 and 2). Compared with breathing at atmospheric pressure (0 cmH2O), a CPAP of 15 cmH2O increased Pes, Ples, Pg, and Pb by 10.1, 7.9, 3.4, and 4.1 cmH2O, respectively (P < 0.05 for all). The absolute values are summarized in Table 1. At each level of CPAP, the magnitude of increase in Pes was greater than the magnitude of increase in Ples (P < 0.05), which in turn was greater than the magnitude of increase in Pg (P < 0.05). A CPAP of 15 cmH2O significantly decreased Pdi by 6.7 cmH2O (P < 0.05).

Effect of CPAP During Swallow-induced LES Relaxation

Progressively increasing CPAP also systematically increased the nadir Ples, Pg, and Pb during a swallow-induced LES relaxation (Table 1, Figs. 1 and 3). Compared with a swallow performed at atmospheric pressure, a CPAP of 15 cmH2O significantly increased nadir Ples, Pg, and Pb during swallow-induced LES relaxation by 7.3, 3.9, and 4.6 cmH2O, respectively (P < 0.05). At a CPAP of 15 cmH2O, the magnitude of increase in nadir Ples was greater than the increase in nadir Pg (P < 0.05). A CPAP of 15 cmH2O significantly decreased the duration of LES relaxation by 2.5 s (P < 0.001, Table 1, Fig. 4).

Mean peristaltic wave amplitude over all five recording sites was 102.0 cmH2O (SD 48.8) and was unaffected by CPAP application (data not shown). In contrast, peristaltic wave velocity progressively increased with increasing levels of CPAP, with a 15 cmH2O CPAP increasing peristaltic wave velocity by 1.2 cm/s compared with a CPAP of 0 cmH2O. CPAP decreased intrabolus pressure by 3.6 cmH2O with 15 cmH2O CPAP compared with a CPAP of 0 cmH2O (P < 0.05) (Table 1).

DISCUSSION

The major findings of this study in healthy, asymptomatic individuals were that nasal CPAP 1) systematically increased both basal end-expiratory Pb during quiet breathing and nadir Pb during swallow-induced LES relaxation; 2) systematically increased the velocity of swallow-induced esophageal peristalsis; and 3) decreased the duration for which the LES was relaxed following a swallow. To the extent that these findings reflect physiological function in individuals with gastroesophageal reflux, they suggest that the beneficial effects of CPAP on reflux (11, 15, 16, 27) may be mediated by an increased gastroesophageal antireflux barrier during swallow-induced relaxation and decreased time of LES relaxation.

The Effect of CPAP on the LES

The strength of the LES to act as a barrier to reflux is reflected in the difference in pressure between the pressure generated within the LES (Ples) and the pressure generated below it (Pg), the LES Pb (Pb = Ples − Pg). Accordingly, an increase in Pb, indicative of an increased capacity of the LES to act as a barrier to reflux, could occur as a result of either a decrease in Pg in excess of Ples or by a greater increase in Ples.
than Pg. The present study shows that increasing levels of CPAP systematically increases end-expiratory Ples, Pg, and Pb during quiet breathing and nadir Ples and Pb during swallow-induced LES relaxation. In both circumstances, the increase in Pb was the result of a disproportionate increase in Ples compared with Pg.

There are several potential mechanisms for the effect of CPAP on Ples. Contraction of the crural diaphragm during inspiration has been shown to contribute to Ples (21). It is, therefore, possible that the CPAP-induced increases in Ples and Pb may relate to CPAP-induced shortening of the crural diaphragm (26). However, we believe this to be unlikely, given that all measurements were obtained at end-expiration when the diaphragm is electrically and mechanically quiet (24). Furthermore, end-expiratory Pdi, which reflects passive tension within the diaphragm, decreased rather than increased with increasing levels of CPAP.

The CPAP-induced increases in Ples and Pb may be a consequence of the increase in Pg, which occurs as a result of downward displacement of the diaphragm and compression of the stomach (17). Several studies have shown that an increase in Pg can result in a reflex increase in LES tone (4, 13, 18, 22).

Other potential mechanisms for the CPAP-induced increases in Ples and Pb relate to the effect of CPAP on intraesophageal pressure and esophageal shortening and peristalsis. Nonspecific transmission of positive pressure from the esophagus to the LES could increase Ples, for example via esophageal compression (10). Supporting this hypothesis is the finding that, at all levels of CPAP, Pes increased more than Ples. CPAP may also affect esophageal shortening during swallow-induced LES relaxation by preventing axial movement of the LES and, therefore, inhibiting complete sphincter opening, increasing nadir Ples and Pb. Last, nadir Pb could also be increased as a result of an increase in intrabolus pressure, which would impose a pressure on the Ples sensor during LES relaxation. However, this is unlikely, given that intrabolus pressure decreased rather than increased during CPAP.

While the present study is the first to examine the effect of CPAP on LES function during swallow-induced relaxation, several earlier studies have examined the effect of CPAP on basal Ples. In normal, healthy individuals during wakefulness, Fournier et al. (10) reported a small (2 cmH2O) but nonsignificant increase in Ples with a CPAP of 8 cmH2O CPAP. Kerr et al. (16) reported a 13.2 cmH2O increase in basal Ples at a CPAP of 8 cmH2O in sleeping individuals with reflux disease. In the present study, we recorded a 3 cmH2O increase in Ples with 5 cmH2O CPAP, and a 5.5 cmH2O increase in Ples with 10 cmH2O CPAP. The reason for the differences between the findings of these studies is not immediately clear but may relate to differences in the phase of respiratory cycle at which Ples was measured, whether changes in Ples were expressed relative to Pg, differences in patient groups, and whether the study was performed during wakefulness or sleep.

### Effect of CPAP on the Esophageal Body

CPAP also caused an increase in the velocity of the swallow-induced esophageal peristaltic wave. Such a finding is consistent with those of Fournier et al. (10). We also noted a decrease in the duration of LES relaxation. This change may be related to the increase in peristaltic wave velocity, as the swallow-induced LES relaxation will persist for as long as the peristaltic contraction takes to reach the distal esophageal segment (2, 7, 8).

The mechanism underlying the effect of CPAP on peristaltic wave velocity is unclear. It may be that increased Pes resulting from CPAP application are responsible for the increase in peristaltic wave velocity. It may also be related to its effect on esophageal smooth muscle and/or Pg. In much the same way that the force-velocity relationship of circular esophageal smooth muscle is dependent on the preload, or the amount the muscle is stretched (bolus size) (3), it is possible that the CPAP-related increase in lung volume and associated downward displacement of the diaphragm and mediastinal contents (17) exerts a longitudinal stretching force on the esophagus, increasing preload on longitudinal muscle fibers and increasing the velocity of force propagation along the esophagus. Alternatively, application of CPAP effectively leads to increased esophageal outflow resistance (18). Based on previous studies.

### Table 1. Absolute pressures with CPAP application

<table>
<thead>
<tr>
<th>CPAP, cmH2O</th>
<th>0</th>
<th>5</th>
<th>10</th>
<th>15</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline LES function</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Ples, cmH2O</td>
<td>15.4 (5.3)</td>
<td>18.5 (4.8)</td>
<td>20.9 (4.3)</td>
<td>23.3 (5.8)</td>
</tr>
<tr>
<td>Pg, cmH2O</td>
<td>6.4 (4.4)</td>
<td>7.6 (4.3)</td>
<td>8.4 (4.4)</td>
<td>9.8 (4.8)</td>
</tr>
<tr>
<td>Pb, cmH2O</td>
<td>8.5 (4.0)</td>
<td>10.7 (4.5)</td>
<td>11.9 (4.6)</td>
<td>12.6 (5.9)</td>
</tr>
<tr>
<td><strong>Swallow-induced LES relaxation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ples, cmH2O</td>
<td>8.3 (4.7)</td>
<td>10.8 (4.6)</td>
<td>12.4 (3.1)</td>
<td>15.6 (4.9)</td>
</tr>
<tr>
<td>Pg, cmH2O</td>
<td>6.7 (4.1)</td>
<td>8.1 (4.1)</td>
<td>8.7 (3.7)</td>
<td>10.6 (4.2)</td>
</tr>
<tr>
<td>Pb, cmH2O</td>
<td>-0.6 (4.2)</td>
<td>1.2 (5.2)</td>
<td>2.4 (5.0)</td>
<td>4.0 (6.0)</td>
</tr>
<tr>
<td>Duration of LES relaxation, s</td>
<td>4.1 (1.1)</td>
<td>2.6 (1.2)</td>
<td>1.9 (1.1)</td>
<td>1.6 (1.7)</td>
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<tr>
<td><strong>Esophageal body</strong></td>
<td></td>
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<tr>
<td>Pes (basal), cmH2O</td>
<td>-1.3 (2.1)</td>
<td>2.9 (3.1)</td>
<td>5.7 (3.8)</td>
<td>8.8 (4.4)</td>
</tr>
<tr>
<td>Intrabolus pressure (distal), cmH2O</td>
<td>10.1 (3.2)</td>
<td>7.8 (3.1)</td>
<td>7.1 (2.1)</td>
<td>6.5 (2.1)</td>
</tr>
<tr>
<td>Peristaltic wave amplitude, cmH2O</td>
<td>102.0 (48.8)</td>
<td>100 (49.8)</td>
<td>99.2 (41.3)</td>
<td>98.7 (40.6)</td>
</tr>
<tr>
<td>Peristaltic wave velocity, cm/s</td>
<td>2.5 (0.5)</td>
<td>3.0 (0.6)</td>
<td>3.5 (0.9)</td>
<td>3.7 (0.9)</td>
</tr>
<tr>
<td><strong>Diaphragm</strong></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Diaphragm (Pdi), cmH2O</td>
<td>7.7 (5.4)</td>
<td>4.7 (4.4)</td>
<td>2.7 (4.4)</td>
<td>1.0 (4.4)</td>
</tr>
</tbody>
</table>

Values are means (SD). Subjects were awake and supine. CPAP, continuous positive airway pressure; LES, lower esophageal sphincter; Ples, LES pressure; Pg, gastric pressure; Pb, barrier pressure; Pes, esophageal pressure; Pdi, transdiaphragmatic pressure.
one might, therefore, have expected peristaltic velocity to slow rather than increase (7, 23). The reason for the increase in velocity observed in our study and the discrepancy with the previous findings remain unclear.

**Implications for Gastroesophageal Reflux**

This study suggests that CPAP may decrease reflux by two mechanisms: 1) by increasing the mechanical barrier to reflux, and 2) by decreasing the length of time the LES is relaxed and, therefore, susceptible to being breached by abdominal contents. It is also possible that the increase in Pes limits proximal acid migration and accelerates esophageal clearance. Considering that the majority of reflux events occur during periods of transient relaxation, it appeared important to investigate the effect of CPAP under such a condition. Our data show that CPAP increased Pb and decreased relaxation duration in a dose-dependent fashion. This implies that a greater reduction in reflux might be expected with a higher level of CPAP. Consistent with this hypothesis, the findings of Green et al. (11) in 189 subjects with OSA and nocturnal reflux showed a strong correlation between improvements in reflux symptoms and the magnitude of applied CPAP.

Several potential limitations exist when extrapolating the observations from the present study to the circumstances surrounding spontaneous reflux events. First, we studied healthy, asymptomatic individuals, not individuals with reflux disease. While this may be an important distinction, it is notable that Kerr et al. (16) reported a similar effect of CPAP on baseline Ples in individuals with and without reflux disease. However, this may not be the case for all patient groups, as Shoenum et al. (27) have previously shown that CPAP reduces reflux in individuals with achalasia but not with scleroderma. Second, we investigated the effect of CPAP on swallow-induced LES relaxation, not during transient LES relaxations, which usually accompany reflux events. While transient LES relaxations share elements of the swallow-induced relaxation neural pathway, specific studies on transient LES relaxations are needed to confirm the observations on swallow-induced LES relaxation. Finally, we studied our subjects during wakefulness rather than at night during sleep when CPAP is usually applied. However, it is notable that the pressure changes surrounding reflux events during wakefulness and sleep have previously been shown to be similar (6), suggesting that the findings from the present study may indeed be directly referable to any changes that may occur during sleep.

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**Fig. 3.** Change in nadir Ples, Pg, and Pb (Pb = Ples − Pg) with increasing levels of Pm (cmH2O) during swallow-induced LES relaxation. Mean of 5 trials is shown. Values are means ± SD; n = 10. P < 0.05 vs. Pm = ⋅0 cmH2O, †5 cmH2O, and ‡10 cmH2O.

**Fig. 4.** Change in peristaltic wave velocity and change in duration of LES relaxation with increasing levels of Pm. Mean of 5 trials is shown. Values are means ± SD; n = 10. P < 0.05 vs. Pm = ⋅0 cmH2O and †5 cmH2O.
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REFERENCES