Measurement of upper esophageal sphincter tone and relaxation during swallowing in premature infants

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Measurement of upper esophageal sphincter tone and relaxation during swallowing in premature infants. Am. J. Physiol. 277 (Gastrointest. Liver Physiol. 40): G862–G866, 1999.—Upper esophageal sphincter (UES) motor function has not been previously evaluated in premature infants. The motor patterns associated with tonic activity and swallowing-related relaxation of the UES were recorded for 1 h after completion of gavage feeding in 11 healthy preterm neonates (postmenstrual age 33–37 wk) with a micromanometric assembly, which included a sleeve sensor specifically adapted for UES recordings. A clearly defined UES high-pressure zone was observed in all premature infants studied. Resting UES pressure ranged from 2.3 to 26.2 mmHg and was higher during periods of irritability and apparent discomfort. During dry swallows, UES pressure relaxed from a resting pressure of 28.2 ± 4.0 mmHg to a nadir of 1.1 ± 3.3 mmHg. The mean UES relaxation interval (the time from relaxation onset to relaxation offset) was 0.31 ± 0.11 s. We conclude that in premature infants ≥33 wk postmenstrual age the motor mechanisms regulating UES resting pressure and the onset of UES relaxation are well developed.

NORMAL SWALLOWING REQUIRES the precise coordination of lingual propulsion and pharyngeal contraction with relaxation and opening of the upper esophageal sphincter (UES). This mechanism facilitates the passage of a food bolus and is also the major mechanism of pharyngeal clearance. UES resting pressure is generated predominantly by tonic contraction of the cricopharyngeus muscle. With swallowing, the cricopharyngeus muscle is inhibited and the UES is opened by a combination of intrabolus pressure and the superior relaxation in response to swallowing (5, 18, 19). In addition, basal UES pressure is highly dependent on state of arousal, varying from 18 mmHg during rest to 56 mmHg when crying. Abrupt changes in the level of arousal are similarly associated with abrupt changes in UES pressure (5).

The function of the UES of the premature neonate has not been documented until now because of the lack of suitable micromanometric sleeve assemblies for evaluation of UES tone and relaxation. Such assemblies have now been made, and the aim of this study was to use these to characterize UES motor function for the first time in premature infants.

MATERIALS AND METHODS

Subjects. The study protocol was approved by the Ethics Research Committee of the Women's and Children's Hospital, and written informed parental consent was obtained before each study. Studies were performed in 11 (5 male and 6 female) healthy preterm infants with a mean postmenstrual age of 35 wk (range 33–37 wk). All infants were well at the time of the study, were considered not to have reflux disease, had no evidence of neurological dysfunction, and were not on prokinetic medication. Mean infant weight was 1,840 g (range 1,600–2,290 g). Four infants were receiving either theophylline or caffeine treatment because of previous episodes of apnea and bradycardia. All 11 infants were being gavage (tube) fed, 7 with nonfortified expressed breast milk and 4 with infant formula (S26 low birth weight formula, Wyeth Australia, Parramatta, NSW, Australia).

Manometric technique. The manometric technique used allowed monitoring of pressures from the pharynx, UES, and esophageal body with an assembly that could also be used to feed the infants. The intraluminal portion of the manometric assembly consisted of a 2.0-mm diameter 10-lumen extrusion that incorporated a 2-cm-long sleeve sensor for UES pressure measurement. The UES sleeve was ovalized in cross section (Fig. 1) by “shaving” the extrusion and building it up laterally (OD 1.8 × 4 mm) to enable consistent antero-posterior self-orientation of the sleeve within the radially asymmetric pressure profile of the UES high-pressure zone (6, 8). Six side-hole sensors recorded pressures from the pharynx (two), UES (one), and esophageal body (three) (Fig. 1). The assembly was long enough to ensure reliable delivery of feeds to the stomach via the large central lumen. Pharyngeal side holes were air-perfused at 4 ml/min; all other side holes were perfused with sterile degassed water at 0.04 ml/min. The UES sleeve was perfused at 0.08 ml/min to ensure that the rate of pressure rise at the distal margin of the sleeve was 20 mmHg/s, sufficient for reliable recording of the onset of UES tone after relaxation. Air/water flow rates were controlled by hydraulic resistors (Dentsleeve, Wayville, SA, Australia). Bubble entrapment was minimized by preflushing of manometric lines and catheters with carbon dioxide (15).

Analog pressure transducer and pH probe signals were amplified and filtered with a Synectics polygraph (Synectics, Stockholm, Sweden). Data acquisition and analysis were performed on a Macintosh Quadra 700 with software based on National Instruments' Labview (M.A.D. Software, Royal Adelaide Hospital, C. Malbert).

Protocol. The assembly was passed transnasally and positioned with the UES sleeve straddling the UES high-pressure zone and the UES side hole just proximal to the UES high-pressure zone on the basis of observed pressure patterns.

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and depth of insertion. After positioning and with the infant in the right lateral position, the feed was administered into the stomach over 10–15 min via the core channel of the assembly. Patterns of UES motor function were then recorded during the gavage feed and then for 1 h postprandially. No boluses were administered orally. The assembly was well tolerated by infants with no adverse effects related to the procedure.

In addition to motility, infant behavioral patterns were observed. Behavioral patterns were characterized according to criteria established by Davidson et al. (5) and consisted of the following: A, resting/eyes open; B, resting/eyes closed; C, moving/comfortable; D, restless/uncomfortable; and E, irritable/crying. Patterns were scored continuously at 30-s intervals for the duration of the study period (i.e., 120 times over 60 min).

Analysis of manometric tracings. The postprandial manometric recordings were analyzed to determine resting UES pressure and the characteristics of UES relaxation during spontaneous “dry” swallowing.

Resting UES pressure was determined for the whole study in periods of 30 s and expressed relative to basal hypopharyngeal pressure. UES pressure drops that occurred in association with swallowing were excluded from the analysis.

For each swallow-induced UES relaxation, the resting pressure before relaxation, the nadir pressure at maximal relaxation, and the relaxation interval were determined. The relaxation interval was defined as the time from relaxation onset, recorded by the sleeve, to relaxation offset, recorded by the side hole located just proximal to the UES (Fig. 2). This measurement provides the best manometrically determinable estimate of physiological UES opening and closing compared with video fluoroscopy (10). UES relaxations that were suboptimally recorded (because of incorrect sleeve position or movement/straining artifact) or occurred in response to multiple swallowing (a sequence of two or more swallows with an interswallow interval of <5 s) were excluded from the analyses.

Statistical analysis. Grouped data were compared with an ANOVA technique (F-test and Scheffé’s test). Correlation was determined by simple regression analysis. P < 0.05 was considered statistically significant. Data are expressed as means ± SD.

RESULTS

UES motor function. All infants exhibited a manometrically identifiable UES high-pressure zone that relaxed in response to pharyngeal swallow. The mean resting UES pressure of all infants was 15.2 ± 6.9 mmHg and ranged from 2.3 ± 5.9 to 26.2 ± 6.2 mmHg. Resting UES pressure did not correlate with postmenstrual age (r = 0.036; not significant (ns)) or postnatal age (r = 0.045; ns). Resting UES pressure in infants having theophylline/caffeine therapy did not differ from those not receiving this treatment (12.8 ± 3.8 mmHg vs. 16.5 ± 8.1 mmHg, respectively; ns). Infants receiving breast milk feeds had similar UES pressures to

Fig. 1. Schematic diagram of upper esophageal sphincter (UES) sleeve assembly in situ alongside a manometric recording of pharyngeal, UES, and esophageal pressures during pharyngeal swallow (sw). A diagram of UES sleeve sensor oval cross section is also shown.
those receiving formula feeds (14.8 ± 8.2 mmHg vs. 15.9 ± 4.8 mmHg). UES relaxation characteristics were analyzed for a total of 326 dry swallows (mean of 36 swallows per study, range 7–118). The mean resting UES pressure at the onset of relaxation ranged from 21.5 to 32.3 mmHg (overall mean 28.2 ± 4.0 mmHg). Nadir UES pressure ranged from −4.4 to 5.4 mmHg (overall mean 1.1 ± 3.3 mmHg). The time from relaxation onset to maximum relaxation ranged from 0.22 to 0.34 s (overall mean 0.28 ± 0.04 s). The time from relaxation onset to relaxation offset ranged from 0.45 to 0.78 s (overall mean 0.59 ± 0.10 s), and the relaxation interval ranged from 0.14 to 0.49 s (overall mean 0.31 ± 0.11 s). None of these characteristics were altered by the presence of theophylline/caffeine therapy or feed type, nor were these parameters influenced by postmenstrual age. Postnatal age did not correlate with the resting pressure at relaxation onset, the time from onset to maximal relaxation, or the nadir pressure. However, a significant correlation was observed between older postnatal age and a shorter time interval from UES relaxation onset to relaxation offset (r = 0.828; P < 0.01) and shorter UES relaxation intervals (r = 0.785; P < 0.05). The number of oral feeds per day that individual infants were receiving (ranging from 1 to 5, mean 1.5) was not significantly associated with the UES relaxation interval (r = 0.253 and 0.171, respectively; ns) or postnatal age (r = 0.476 and 0.418, respectively; ns) but did correlate with postmenstrual age (r = 0.641; P < 0.05).

Effect of infant behavior on resting UES pressure. Behavioral patterns A (resting/eyes open), B (resting/eyes closed), and C (moving/comfortable) were observed for 96% of the total time recorded (65%, 7%, and 24%, respectively). In contrast, behavioral patterns D (restless/uncomfortable) or E (irritable/crying) were less frequently observed (3% and 1% of total time recorded), suggesting that the manometric technique used in this study was well tolerated by the infants. Infant behavioral patterns greatly influenced resting UES pressure, with higher UES pressures recorded during periods when behavioral patterns indicated a heightened state of arousal (Fig. 3). Mean resting UES pressure increased from 13.5 ± 11.0 mmHg for behavioral pattern A to 33.8 ± 16.7 mmHg for behavioral pattern E (P < 0.0001). Abdominal straining was also observed to transiently augment UES pressure, although the de-
degree of increase in UES pressure during straining was not quantified.

**DISCUSSION**

This study examines, for the first time, UES motor function in premature infants by micromanometric recording techniques. In these babies, UES motor patterns are almost identical to those recorded previously in older infants, children, and adults with similar techniques (4, 5, 7, 8, 10).

Premature infants exhibit UES resting tone and UES relaxation in response to dry swallow. The magnitude of UES resting pressure is greatly dependent on the behavioral state of the infants. The scoring of infant behavioral patterns in real time was relatively easy to perform. In practice, continuous behavioral scoring at 30-s intervals proved to be sufficiently frequent to effectively monitor changes in patterns of general behavior. Periods of apparent comfort were associated with significantly lower UES pressures than periods of activity and apparent discomfort or abdominal straining. These findings are consistent with those reported in older infants and children with the same behavioral scoring system (5, 19). Studies in adults have shown that resting UES pressure is low during sleep and increases during arousal (9), whereas factors such as emotional stress and straining considerably augment UES pressure (3, 19).

On average, UES relaxation intervals associated with dry swallows in premature infants were similar to those recorded in healthy adult subjects. Kahrilas and colleagues (10) showed that the relaxation interval corresponds closely to the physiological opening and closing of the UES and that the presence of a food bolus during swallowing prolongs both the UES relaxation interval and the duration of UES opening. The UES relaxation interval in premature infants varied considerably, from 0.14 to 0.49 s, and our data suggest that this parameter became shorter as postnatal age increased. An important distinction between the current study and previous adult studies, however, is that we examined spontaneous swallows and not swallows initiated on command. The variation in the UES relaxation interval may therefore be due to differences in the volume of saliva accumulated during the interswallow period. In addition, more premature infants may swallow less frequently, leading to greater accumulation of saliva and longer relaxation intervals.

Our data suggest that premature infants have manometrically normal patterns of UES tone and dry-swallow-related UES relaxation. Previous studies in premature infants have also shown that dry-swallow-related esophageal body peristalsis and lower esophageal sphincter relaxation are also manometrically normal (16, 17). Premature infants still, however, experience difficulty with feeding, requiring gavage feeding despite their apparently normal sphincter motility. One explanation for this may be that effective passage of a food bolus past the UES depends on the generation of sufficient intrabolus pressure to open the UES, even though it is relaxed. Intrabolus pressure is not generated by pharyngeal contraction, but is instead generated by the piston-like posterior movement of the base of the tongue (7). Hypopharyngeal contractions follow the passage of the bolus and function to clear the pharynx of feed residues (11). This characterization of the swallowing mechanism of adults shows clearly that, although the manometrically recorded patterns of pharyngeal and UES function during dry swallowing in premature babies may resemble those seen in adults, these infants may nevertheless experience feeding difficulties if they have a diminished capacity to generate the intrabolus pressures required to propel the bolus beyond the UES. These pressures were not evaluated in this study. It is certainly the case that lingual coordination and feeding capacity is impaired in premature infants and improves as they approach term (2).

Premature infants also generate 40% lower intraoral pressures when sucking compared with full-term infants (1, 13). Synchronization of breathing with swallowing is also usually rare in prematurity, probably explaining the episodes of apnea, bradycardia, and oxygen desaturation that occur during swallowing (12, 14). These additional factors may also contribute to feeding difficulties.

This study shows that the manometric determinants of UES motor function, such as UES tone and relaxation characteristics, can be measured in premature infants by miniaturization of established techniques developed for use in adult humans. In premature infants, the esophageal motor mechanisms that generate and modify UES tone appear well developed. Pharyngeal dry swallows are well coordinated with the onset of appropriate relaxation of the UES. Our data suggest that the oral feeding difficulties experienced by premature infants may be due to factors other than immaturity of the neuroregulatory mechanisms of UES motility.

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