Pediatric gastroesophageal reflux and upper gastrointestinal tract motility: the use of multichannel intraluminal impedance and high resolution manometry

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Development of swallow physiology in the preterm infant

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ABSTRACT

Introduction: Poor feeding is a common cause of prolonged hospitalization of preterm infants. Pharyngeal and upper esophageal sphincter (UES) function of preterm infants has been technically difficult to assess and is therefore poorly characterised. This study aims to assess the development of pharyngeal motility, UES function and their coordination during nutritive sucking in preterm infants.

Patients and methods: Development of swallowing was assessed in 18 nasogastrically fed preterm infants. Eight channel manometry was performed at first oral feeding attempt (31-32 weeks) and then weekly for 4 weeks. The spatio-temporal relation of pharyngeal and UES pressure changes were characterised in 980 swallows.

Results: We observed an age-related increase in peak pharyngeal pressure during swallowing at the level of the laryngeal inlet (1cm above UES) but an age related decrease in the time required for the UES to fully relax to nadir. Analysis of the timing of proximal pharyngeal contractile peak and UES nadir showed that the UES was not completely relaxed when bolus propulsive forces were at their peak in the youngest infants.

Conclusions: Results show developmental changes in infant swallow physiology that can be clearly linked to the effectiveness of nutritive swallowing. Most premature infants demonstrated poor pharyngeal pressures in the region of the laryngeal inlet coupled with poor coordination of pharyngeal propulsion with UES relaxation. These pressure patterns were less efficient than those demonstrated by older infants who were more adept at feeding. These observations may explain why infants under 34 weeks are physiologically unable to feed effectively and experience frequent choking and fatigue during feeding.
INTRODUCTION

Early enteral feeding, particularly with expressed breast milk, assists in the development and normalisation of gut function and significantly reduces morbidities such as necrotising enterocolitis and sepsis. Oral feeding capacity is poor in the very preterm infant due to inadequate suck-swallow-breath coordination and leads to suboptimal nutrition and growth. With overall survival rates in these infants increasing, dysphagia is becoming the major clinical problem prolonging hospitalisation and increasing health care costs. It is standard clinical practise worldwide to delay oral feeding until the corrected age of 34 weeks. Development of swallow physiology has been studied in the human fetal model and in premature neonates, but studies have focused predominantly on the oral and preparatory stages of swallowing as well as the sensory-motor reflexes and function of pharynx and upper esophageal sphincter (UES) during non-nutritive swallowing. To date, the development of pharyngo-esophageal (PE) phase of nutritive swallowing remains poorly characterised. The present study uses a novel high-resolution manometry technique to assess the development of PE function in healthy preterm infants during the period of development of oral feeding competency. We hypothesize that the pharyngeal phase of swallowing as well as its coordination in relation to UES opening is impaired in very premature infants and matures with increasing gestational age.

PATIENTS AND METHODS

Subjects

Pharyngo-esophageal function during nutritive swallowing was evaluated weekly in 18 infants over a period of four weeks using high resolution manometry. Infants had no significant morbidity other than prematurity. Initial manometric study was timed to coincide with the introduction of the first oral feeding attempt. All infants were 31-34 weeks corrected age (CA) (gestational age at birth + postnatal age) and were receiving full enteral feeds by nasogastric tube. The study protocol was approved by Research Ethics Committee of the Women’s & Children’s Hospital in Adelaide, Australia. Written informed consent was obtained from the parents.

Manometric technique

A custom designed silicone rubber manometric feeding assembly (OD 2.0mm) was used. The assembly incorporated eight recording sideholes spaced at 0.5cm intervals and a core lumen for gavage feeding. The catheter was perfused with degassed distilled water by a low compliance pneumohydraulic perfusion pump (Dentsleeve, Wayville, South Australia) at 0.04ml/min per channel. Pressures were registered for each perfused channel by
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external pressure transducers (Abbott Critical Care Systems, Chicago, IL, USA). Pressure signals were acquired at a sampling frequency of 25 Hz per channel using a computer based data acquisition system (Trace v1.2 manometry system, G Hebbard, The Royal Melbourne Hospital, Melbourne, Australia).

Manometric data were analyzed using Trace v1.2 software. Only swallows recorded during nutritive sucking bursts were included for analysis. Swallows observed singularly with UES pressure returning to baseline post swallow, were defined as ‘isolated’. Bursts of two or more consecutive swallows without UES pressure returning to baseline were defined as ‘consecutive’. In each recording, all isolated and consecutive swallows were identified and 10 of each were randomly selected, giving rise to 20 analyzed swallows per recording. The following nine manometric variables (a-i) were determined from the tracings (figure 1A and 8 for variables a-e and f-i respectively):

a. mean pharyngeal peak pressure representing the mean maximal strength (over all manometric channels) to which the pharyngeal constrictors contract during deglutition;
b. pharyngeal propagation velocity (a marker for the speed of pharyngeal peristalsis);
c. UES pressure at onset;
d. UES nadir pressure (lowest pressure reached in the UES during relaxation);
e. duration of UES relaxation (measured at nadir + 20% of UES relaxation onset-nadir difference) 11;

f. segmental pharyngeal peak pressure (peak pressure at a specific level in the pharynx);
g. UES relaxation response time (time needed by the UES to reach its most complete relaxation);
h. time between proximal (2.5 cm above the UES) pharyngeal peak amplitude and the UES nadir (as a marker for the coordination between pharyngeal contraction and UES function); and

i. time between distal (1.0 cm above the UES) pharyngeal peak amplitude and the UES nadir (as a marker for the effectiveness of bolus clearance mechanism). Pharyngeal parameters were calculated at five different pharyngeal levels (i.e., at 1, 1.5, 2, 2.5 and 3 cm above UES), resulting in a maximum of 100 (i.e., 20 x 5) measurements per recording All pressures were referenced to resting oropharyngeal (atmospheric) pressure as measured by the second to most proximal pharyngeal level.

Study protocol

All infants were studied in the Neonatal Intensive Care Unit of the Children’s Youth and Women’s Health Service, Women’s and Children’s Hospital North Adelaide, Australia. Infants were enrolled and studied longitudinally with repeat studies performed at weekly intervals up to a maximum of four recordings in any one infant. If the clinical necessity for tube feeding ceased to exist before the four week period was over, no further studies were performed.
After a 4 hour fast, infants were intubated transnasally with the manometric catheter approximately 30 minutes prior to feeding time. Using a real time on-screen spatio-temporal plot display, the catheter was positioned along the PE-segment such that five channels were located in the pharynx, two were straddling the UES and one was positioned in the proximal esophagus. The catheter was fixed in place by taping it to the infant’s face.

Infants were given a breast or bottle (expressed breast milk or formula) feed. They were held on the lap as routinely done and were allowed to suck and swallow at their own pace. Patterns of PE-motility were continuously recorded for the duration of the oral feed. If the full feed was not taken orally, the remaining feed was infused in the stomach through the central lumen of the manometric assembly. Once the feeding was finished, the manometric assembly was removed.

**Figure 1. Manometric parameters for conventional and high resolution manometry.** (A) Definition of conventional manometry parameters used to describe PE motility: a. mean peak pharyngeal amplitude, representing the mean maximal strength (over all manometric channels) to which the pharyngeal constrictors contract during deglutition; b. pharyngeal propagation velocity (a marker for the speed of pharyngeal peristalsis); c. UES pressure at onset; d. UES nadir pressure (lowest pressure reached in the UES during relaxation), and e. duration of UES relaxation (measured at nadir + 20% of UES relaxation onset-nadir difference). (B) Definition of segmental manometry parameters used to describe PE motility: f. segmental pharyngeal peak pressure (peak pressure at a specific level in the pharynx), g. UES relaxation response time (time needed by the UES to reach its most complete relaxation), h. time between proximal (2.5 cm above the UES) pharyngeal peak amplitude and the UES nadir (as a marker for the coordination between pharyngeal contraction and UES function) and i. time between distal (1.0 cm above the UES) pharyngeal peak amplitude and the UES nadir (as a marker for the effectiveness of bolus clearance mechanism).
Statistical Analysis

A Mixed Model Analysis (MMA) was chosen to model the evolution of each of the swallowing parameters as a function of age. The mean of the 20 values of each swallowing parameter at each recording site was used as a response variable. The standard deviation score of these 20 values was calculated as an indicator of individual variability of the swallowing process, and was used as an additional response variable. Age was entered into the model as a categorical variable with three levels (31-32 weeks, 33-34 weeks, and 35-36 weeks post-conception).

All MMA’s used the Kenward-Roger degrees of freedom estimation method that is more robust against violations to assumptions of normality and more appropriate for small sample sizes. If necessary, log-transformations were applied to obtain normally distributed residuals.

<table>
<thead>
<tr>
<th>Subject number</th>
<th>Corrected age (gestational age + postnatal age) in weeks</th>
<th>Total number studies per subject</th>
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<td>x x x x</td>
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<tr>
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<td>x x x x</td>
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N = 18

N subjects 3 7 12 11 10 5 1 49
N swallows 60 140 240 220 200 100 20 980

Table 1: This table shows the distribution and frequency of the studies performed at different gestational ages. In total, 49 studies were performed and 980 swallows were analyzed. In each study (cross), 10 consecutive and 10 isolated swallows were identified and randomly selected during nutritive swallowing for further analysis.
To model the evolution of the conventional manometric parameters, a series of MMA's was calculated with subject as a random variable and with age category as a fixed variable. To model the evolution of the response variable of the novel segmental parameters, a series of MMA's was calculated with subject as a random effect and with age, pharyngeal level and age by pharyngeal level interaction as fixed effects. All post-hoc analyses were corrected for multiple comparisons using the Tukey procedure ($\alpha=0.05$). In a series of additional analyses swallow type (consecutive versus isolated) or feeding type (breastfeeding versus bottle feeding) was entered into the model as a between-subject variable. Descriptive data are given as mean ± standard deviation and are summarized in the ensuing graphics and tables.

RESULTS

Table 1 shows the distribution and frequency of all recordings based on gestational age of the infants. Data were collected over 49 recordings and 980 swallows were analyzed. Data are presented in the respective order of 31-32w, 33-34w and 35-36w CA. Table 2 summarizes the manometric data.

Subject characteristics

Eighteen (13 male) healthy preterm infants were studied with a mean gestational age at birth of 200±13.4 days (28±1.9 weeks), ranging from 184-213 days (26-33 weeks). Mean birth weight was 1213±297 grams (range: 850-1730 grams). At the first recording, infants were on average 32±0.9 (range: 31-34) corrected weeks old and had a mean weight of 1666±251 grams ranging from 1280-2170 grams. Infants were breastfed in 38/49 (77.6%) and bottle fed in 11/49 (22.4%) of the recordings. The manometric procedure was well tolerated by all subjects without clinically significant changes in cardio respiratory measures (heart rate, respiratory rate and oxygen saturation) or any notable side effects.

Pharyngeal motor function during nutritive swallowing

All infants exhibited a manometrically identifiable pharyngeal peristalsis that was initiated upon swallowing of a liquid bolus. Average pharyngeal peak amplitude across all segments did not increase with age ($p=0.11$, table 2), figure 1A parameter a). A detailed segmental analysis (figure 1B, parameter f), however, demonstrated that peak pharyngeal pressure at 1 cm above the UES was significantly lower than at 2 cm above the UES ($p=0.02$). In addition, pharyngeal peak amplitude at 31-32w CA was lower than in both older age groups ($p=0.03$).
Pharyngeal propagation velocity (figure 1A, parameter b) averaged 12±4, 14±12 and 20±18 cm/sec respectively at 31-32 weeks, 33-34 weeks and 35-36 weeks CA, but these differences were not statistically significant (p=0.22).

UES motor function during nutritive swallowing

Each subject exhibited a manometrically identifiable UES pressure zone that relaxed in response to a pharyngeal swallow. None of the parameters used conventionally, i.e. mean pressure at onset of the UES relaxation (figure 1A, parameter c), nadir UES pressure (figure 1A, parameter d) and the duration of the UES relaxation (figure 1A, parameter e) were significantly different between age groups (p=0.34, p=0.93 and p=0.46 respectively). The UES relaxation response time (figure 1B, parameter g), decreased significantly with age (p=0.02). Post-hoc testing showed that infants of 31-32 weeks needed a significantly longer time to reach full UES relaxation compared to infants of 35-36 weeks CA (figure 2) Interestingly, the individual variability also decreased significantly with increasing age (p=0.03). Post hoc testing showed that infants of 31-34 weeks clearly presented with more variability in the time needed than those of 35-36w of age.

<table>
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<tr>
<th>Swallow parameter</th>
<th>Mean values per age</th>
<th>Mean variability (STD DEV) per age</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>31-32w</td>
<td>33-34w</td>
</tr>
<tr>
<td></td>
<td>mean</td>
<td>SD</td>
</tr>
<tr>
<td>Peak pharyngeal amplitude (mean mmHg)</td>
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<tr>
<td>Propagation velocity pharynx (mmHg/sec)</td>
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<tr>
<td>UES pressure at onset (mmHg)</td>
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<td>7</td>
</tr>
<tr>
<td>UES nadir (mmHg)</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Duration UES relaxation (sec)</td>
<td>0.48</td>
<td>0.09</td>
</tr>
<tr>
<td>Time onset pharyngeal stripping wave and onset UES relaxation (sec, measured at 2.5cm)</td>
<td>0.06</td>
<td>0.02</td>
</tr>
<tr>
<td>Time UES nadir and peak pharyngeal amplitude (sec, measured at 2.5cm)</td>
<td>0.13</td>
<td>0.04</td>
</tr>
<tr>
<td>Time onset UES relaxation and UES nadir (sec)</td>
<td>0.48</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Table 2. Data (Mean and SD) and variability (mean and SD) of eight swallow parameters obtained from 18 healthy premature babies according to age. Data are presented in three age groups (31-32 w, 33-34 w and 35-36 w CA).
Coordination of pharyngeal and UES motor patterns during swallowing

Time between proximal pharyngeal peak amplitude and UES nadir as well as time between distal pharyngeal peak amplitude and UES nadir (figure 1B, parameter i & j) are presented in figure 3. In 31-32w old infants, the peak pharyngeal contraction occurs before the UES nadir. The more proximal the peak pharyngeal amplitude is measured, the shorter the time between the two events. From 33 weeks CA on, the pharyngeal peak tend to occur close to or after the UES maximal relaxation (nadir). Error bars depict 1 SD of the mean.

Figure 2. Averaged time differences and variability between the peak pharyngeal amplitude and the UES nadir according to age and different pharyngeal segments. In 31-32w old infants the peak pharyngeal contraction occurs before the UES nadir. The more proximal the peak pharyngeal amplitude is measured, the shorter the time between the two events. From 33 weeks CA on, the pharyngeal peak tend to occur close to or after the UES maximal relaxation (nadir). Error bars depict 1 SD of the mean.

Coordination of pharyngeal and UES motor patterns during swallowing

Time between proximal pharyngeal peak amplitude and UES nadir as well as time between distal pharyngeal peak amplitude and UES nadir (figure 1B, parameter i & j) are presented in figure 3. In 31-32 week old infants, the proximal pharyngeal peak amplitude at 2.5 cm above the UES occurs before the UES nadir (mean: -0.05 sec). However, in 33-34 and 35-36 week old infants the pharyngeal peak amplitude occurs after nadir pressure (0.08 sec and 0.06 sec respectively (figure 3). Statistical analysis of the timing between peak pharyngeal amplitude and UES nadir showed no effect of age (p=0.07), an effect of pharyngeal level (p<0.0001) and a significant age by pharyngeal level interaction (p=0.018) as well as an effect of age on the variability (p=0.0008). Post hoc testing showed that the time difference between proximal pharyngeal contraction peak and UES relaxation nadir was significantly shorter in infants of 31-32w compared to infants of 33-34w and 35-36w of gestation (figure 3). The latter two age groups did not differ from each other, but 35-36w old infants present with less variability in duration than the 33-34w infants (p=0.0014). Hence, in the youngest age group UES relaxation was less complete at the time of maximum proximal pharyngeal contraction.
With respect to the distal peak amplitudes (measured at 1 cm above the UES) similar age differences were seen with post hoc testing showing that the time difference in infants of 31-32 w CA was significantly shorter compared to infants of 33-34 weeks of CA (p=0.03, figure 3). The critical difference however is that the peak contraction in the distal pharynx occurs after the UES nadir has been reached.

**Figure 3. With nadir values matched in time, time differences from the onset of the UES relaxation to the UES nadir according to age are presented.** The shape of the relaxation part of line plot is simulated whereas the amplitude and timing of UES relaxation onset and nadir are real. (A) This figure summarizes the timing between peak pharyngeal amplitude in the proximal pharynx (at 2.5 cm above the UES) and UES relaxation onset relative to UES nadir (B) This figure summarizes the timing between peak pharyngeal amplitude in the distal pharynx (at 1 cm above the UES) and UES relaxation onset relative to UES nadir.

With respect to the distal peak amplitudes (measured at 1 cm above the UES) similar age differences were seen with post hoc testing showing that the time difference in infants of 31-32 w CA was significantly shorter compared to infants of 33-34 weeks of CA (p=0.03, figure 3). The critical difference however is that the peak contraction in the distal pharynx occurs after the UES nadir has been reached.
Influence of type of feed and type of swallow

No age effect of breast or bottle feeding on the swallow physiology was observed (all interactions (p>0.1). Similarly the type of swallow (consecutive or isolated) selected for analysis did not influence the studied swallow parameters.

DISCUSSION

This prospective cohort study investigated for the first time the motor mechanisms regulating pharyngeal and UES function during nutritive swallowing in premature infants. We demonstrated subtle, but important, changes in pharyngeal peak pressures and in the timing of UES relaxation with pharyngeal peak pressures possibly related to maturity and the development of oral feeding competency.

Two predominant biomechanical characteristics of the pharyngeal swallow clearly developed with age in the premature infants studied.

Firstly, we observed a reduced pharyngeal peak pressure localized at 1 cm above the UES high pressure zone (figure 1B, parameter f). This region of reduced pressure was only apparent at 31-32 weeks and disappeared with increasing age and therefore may be due to immaturity of neural or myogenic mechanisms regulating contractile strength or, alternatively, may be secondary to anatomical changes which reduce the degree of luminal occlusion at the site. This finding is remarkable as adequate pharyngeal peristalsis initiated by the pharyngeal constrictors is known to be essential for bolus flow through the PE segment during deglutition. Decreased peak amplitude in this region most-proximal to the UES and adjacent laryngeal opening, may reduce the effectiveness of pharyngeal contraction for clearing pharyngeal residues. This may lead to increased risk of post-swallow residue and subsequent aspiration and possibly limits feeding capacity.

Secondly, we observed changes in the UES relaxation time and in the UES relaxation relative to pharyngeal contraction. Bolus flow through the PE segment during deglutition is highly dependent on appropriate UES relaxation and opening. Our analysis shows that UES physiology in terms of UES pressure at onset of the UES relaxation (figure 1A, parameter c), nadir UES pressure (figure 1A, parameter d) and duration of the UES relaxation (figure 1A, parameter e) remains similar from 31 weeks CA onwards. This suggests that UES characteristics are stable from an early age except for the UES relaxation response time, the only UES characteristic that did change with increasing age. In infants of 31-32 weeks, the UES took longer to fully relax compared to older infants. Also, the variability of UES relaxation response time, used as a parameter of maturation, decreased with increased age indicating the development of a more consistent motor mechanism. It is likely that the ability of the UES to rapidly and fully relax is crucial for the preterm infant to be able to
sustain consecutive nutritive swallows and limits bolus retention in the hypopharynx and thus risk for aspiration.

The coordination between pharyngeal contraction and UES relaxation is most important for effective bolus flow during deglutition. We measured the timing of occurrence of peak pharyngeal amplitude and the UES nadir both in the proximal and distal pharynx. Our results show that in infants of 31-32w, the maximal contraction of the proximal pharyngeal wall (responsible for bolus transport) occurs before maximal UES relaxation and that the time from UES relaxation onset to complete UES relaxation was prolonged compared to older age groups. In infants from 33 weeks onwards, the peak contraction occurs after the nadir has been reached. Although infants of 33-34w and 35-36w of age do not statistically differ from each other, the 35-36w old infants present with less variability in time difference than the 33-34w infants. This implies that the 35-36w infants are more consistent in their timing of PE coordination, which may indicate that swallowing coordination is most effective at this age.

Comparable to the observations in the proximal pharynx, is the fact that distal pharyngeal contractions (important for adequate pharyngeal clearance) do not occur optimally. Whilst they do occur after UES nadir was reached, consistent with a normal swallow, the time from nadir to contraction peak is minimal (0.08sec) in 31-32w infants and half that (0.19sec) of older infants.

Our findings imply that bolus transport and clearance in the youngest infants is highly inefficient and potentially increases the resistance to bolus flow across the UES during each swallow. This may be due to immaturity of neural mechanisms regulating timing of pharyngeal contraction with UES relaxation or alternatively may be related to the compliance of the UES itself. The differences in timing are subtle but may nevertheless greatly influence swallowing bursts, increasing the potential for fatigue during multiple consecutive swallows and therefore interruption of the normal suck, swallow and breathe pattern necessary for effective nutritive swallowing.

By using a HRM approach and segmental analysis, we were able to discern subtle differences in the timing of pressure events critical for normal passage and clearance of a swallowed bolus. We also demonstrate that perfusion manometry has utility for identifying these timing differences. Pharyngeal HRM may therefore be a valuable diagnostic tool to assess the swallow capacity of infants. While pharyngeal and UES motor function has been characterized previously for non nutritive swallowing in infants, none of these previous studies have described the developmental changes in swallowing physiology.

In order to evaluate PE motility in infants, we suggest performing a segmental manometric analysis. Such segmental analysis has previously been carried out in the pediatric esophagus. The strength of the segmental analysis performed in the PE segment is its ability to objectively measure deglutition and to differentiate pathology and
developmental change. This will allow the clinician to select the most appropriate feeding strategy for these high risk infants.

Our study has potential weaknesses. Due to ethical considerations and technological limitations, we could not simultaneously assess bolus flow with medical imaging or intraluminal impedance. We are well aware of the limitations of perfusion manometry such as the underestimation of peak pharyngeal contraction compared to solid state manometry.\(^{22,23}\) However the same equipment was used to track changes over time and we describe differences in timing that are not subject to the effects of hydraulic dampening.

In conclusion, we have reported for the first time developmental changes in infant pharyngeal and UES physiology during orally administered boluses. The immaturity of timing of pharyngeal and UES pressure patterns in infants less than 34 weeks correlates with the observation that infants of that age are only beginning to develop the ability to feed. Whilst there has been an emphasis on the ability of the preterm infant to suck as the primary cause of poor oral feeding, our data re-focuses attention onto pharyngoesophageal segment. The methodologies and findings described may provide a means to differentiate between poor feeding due to physiological immaturity of the pharynx and poor feeding due to other pathology.

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REFERENCES


