Published in final edited form as:

Neurogastroenterol Motil. 2016 April ; 28(4): 532–542. doi:10.1111/nmo.12748.

Effects of Pacifier and Taste on Swallowing, Esophageal Motility, Transit and Respiratory Rhythm in Human Neonates

Theresa R. Shubert, BA¹, Swetha Sitaram, MS¹, and Sudarshan R. Jadcherla, MD^{1,2}

¹

²

Abstract

Background—Pacifier use is widely prevalent globally despite hygienic concerns and uncertain mechanistic effects on swallowing or airway safety.

Aims—The effects of pacifier and taste interventions on pharyngo-esophageal motility, bolus transit and respiratory rhythms were investigated by determining the upper esophageal sphincter (UES), esophageal body, esophagogastric junction (EGJ) motor patterns as well as deglutition apnea, respiratory rhythm disturbances and esophageal bolus clearance.

Methods—Fifteen infants (6 males; median gestation 31 wks and birth weight 1.4 kg) underwent high resolution impedance manometry at 43 (41–44) weeks post-menstrual age. Manometric, respiratory, and impedance characteristics of spontaneous swallows, pacifier associated dry swallowing and taste (pacifier dipped in 3% sucrose) associated swallowing were analyzed. Linear mixed and generalized estimating equation models were used. Data are presented as mean $\pm$ SEM, %, or median (IQR).

Key Results—Pharyngo-esophageal motility, respiratory, and impedance characteristics of 209 swallows were analyzed (85 spontaneous swallows, 63 pacifier associated dry swallows, 61 taste associated swallows). Basal UES and EGJ pressures decreased upon pacifier ($P < 0.05$) and taste interventions ($P < 0.05$); however, esophageal motility, respiratory rhythm, and impedance transit characteristics were similar with both interventions.

Conclusions and Inferences—Oral stimulus with pacifier or taste interventions decreases UES and EGJ basal pressure, but has no effects on pharyngo-esophageal motility, airway

Correspondence and Reprint Requests: Sudarshan R. Jadcherla, MD, FRCPI, DCH, AGAF, Division of Neonatology, Innovative Feeding Disorders Research Program, Center for Perinatal Research, Nationwide Children's Hospital Research Institute, 700 Children's Drive, Columbus, OH 43205 Phone: (614) 355-6643; Fax: (614) 355-6675, sudarshan.jadcherla@nationwidechildrens.org.

AUTHOR CONTRIBUTION

TRS: Concept and design of project, acquisition, validation, analysis, and interpretation of data, and manuscript writing, editing, and approval of final version.

SS: Data and statistical analysis, data verification, reviewing and revising the manuscript, and approval of the final manuscript as submitted.

SRJ: Principal Investigator, concept and design, IRB process, performance of manometry studies, data analysis, validation, and interpretation, securing funding support, manuscript writing, editing, and approval of final version.

Funding and Disclosures:

LOCATION OF WORK: Nationwide Children's Hospital, Columbus, OH, USA

COMPETING INTERESTS:

The authors have no competing interests.

interactions, or esophageal bolus transit. A decrease in central parasympathetic-cholinergic excitatory drive is likely responsible for the basal effects.

Keywords

Esophageal Pressure Topography; Esophagogastric Junction; High resolution impedance manometry; Upper Esophageal Sphincter

As early as the Neolithic Period (10,000 BCE), some form of oral sucking apparatus has been used to console crying infants (1). Pacifiers have evolved through many material stages- from bone, coral, ivory or cloth- to most recently natural or synthetic rubber (1, 2). Alcohol, opium, food, and sucrose have also been used in conjunction with pacifiers to soothe the infant (3, 4) or provide analgesia (5). Pacifier use is widely prevalent, ranging from 63%-84% in infants and children up to 6 years old (6-8). At an estimated cost of about \$3-\$5 per pacifier, in conjunction with United States birth rate of roughly 4 million infants per year (9), and assuming an 80% prevalence rate, the pacifier industry generates an estimated \$9.6- \$16 million dollars annually from pacifier sales. This is a gross underestimation, as it assumes each infant only uses one pacifier.

The effectiveness of pacifier use is largely anecdotal; previous studies performed under different circumstances yielded conflicting conclusions (7, 8, 10, 11). For example, during a randomized controlled trial, Kramer et. al. observed an association between pacifier use and early weaning from breastfeeding. However, their data indicate pacifier use as a marker of breastfeeding difficulties, rather than a true cause of early weaning, as the aforementioned association was not observed when data was analyzed by randomized allocation (7). Additionally, in another randomized controlled trial, Jenik et. al. found that the recommendation to offer newborns a pacifier did not modify the prevalence or duration of breastfeeding when compared with not offering a pacifier (8, 11). Pacifier use has also been linked with a reduction in SIDS risk. In a case-control study of N= 260 SIDS deaths and N= 260 matched living controls, pacifier use was associated with a reduced SIDS risk for all evaluated categories using unconditional logistic regression to measure the association of pacifier use at last sleep with SIDS risk (10). However, the purported conditions of pacifier use as well as the therapeutic mechanisms remain unclear, anecdotal and largely controversial.

Modification of the pacifier with added stimulus has been explored. For example, patterned orocutaneous therapy using a pacifier has been associated with non-nutritive suck development and enhanced feeding performance (12), in addition to decreased length of hospitalization (13). Activation of music by infant sucking patterns has been associated with increased feeding rates and earlier achievement of full oral feeding in preterm infants (14, 15). The use of textured pacifiers has been shown to disrupt and reorganize suck central pattern generation (16). Adherence to an oral stimulation program, providing preterm infants with oro-facial stimulation using either a finger or pacifier (regardless of pacifier type), has been shown to accelerate the transition from tube to oral feeding (17, 18), despite uncertain mechanisms. Dipping pacifiers in milk or sucrose has also been a common practice in nurseries; however the effect of such modifications has not been systemically studied.

The rationale for this study is to provide mechanistic data to quantify the ways in which pacifier intervention does or does not modify neonatal pharyngeal swallowing and esophageal motility, respiratory rhythms, or bolus transit characteristics. Our aims were to investigate the effect of 1) pacifier intervention and 2) taste on pharyngo-upper esophageal sphincter (UES), esophageal body, and esophagogastric junction (EGJ) motility; respiratory rhythm, and impedance characteristics. We hypothesized that pacifier intervention and/or taste intervention modifies pharyngo-esophageal motility, respiratory rhythms, and esophageal bolus transit characteristics associated with swallowing.

Materials and Methods

Subjects

Fifteen infants (6 males) born at 31 (28-34) wks gestation weighing 1.4 (1.0-2.3) kg were studied at 43 (41-44) wks postmenstrual age (PMA) weighing 3.6 (3.3-3.9) kg. Infants were studied at 43 (41-44) wks postmenstrual age (PMA). Infants with neurological injury (Grade 2 unilateral intraventricular hemorrhage or hypoxic ischemic encephalopathy), gastrointestinal surgery or genetic or congenital abnormalities were excluded.

Subjects were referred to and evaluated by the Neonatal and Infant Feeding Disorders Program at Nationwide Children's Hospital under the esophagus-airway interaction evaluation protocols. Studies and procedures were approved by the ethics committee at the Institutional Research Review Board (IRB) at Nationwide Children's Hospital Research Institute, Columbus, Ohio. The study protocol conforms to the guidelines of the local IRB policy and the health insurance portability and accountability acts (HIPAA). Informed consents and HIPAA authorization were obtained from parents prior to study.

Experimental methods and study protocol

High Resolution Impedance Manometry (HRIM) and Esophageal Pressure Topography (EPT) were used to investigate pharyngo-esophageal motility. Equipment included a single 6-FR solid state HRIM catheter with 25 pressure channel uni-directional sensors spaced 1 cm apart and 13 impedance electrodes spaced 2 cm apart (Unitip High Resolution Catheter, Unisensor USA, Portsmouth, NH). Dual band respiratory inductance plethysmography (RIP) (Respirace, Viasys, Conshocken, PA) was attached at the level of the thorax and abdomen to assess respiratory changes. A nasal air flow thermistor was used to assess air flow through the detection of thermal differences of inhaled and exhaled air. All modalities were used concurrently with HRIM/EPT. EKG and pulse-oximetry were used to ensure patient safety.

After calibration, the manometry catheter was passed nasally with the unsedated infant lying supine. Any indwelling feeding tubes were removed prior to catheter placement. The catheter was well secured, and not further manipulated throughout the course of the study. Infants were allowed to adapt to catheter placement for 15-20 minutes, and studied for an average of ~1.4 hours. Landmarks defining the UES and EGJ high pressure zones, transition zone, thoracic to abdominal pressure inversion point, and gastric region were manually positioned. Onset and offset of pacifier intervention or taste intervention was documented at study (Figure 1a&c). Spontaneous swallows in the absence of pacifier use were used as a

reference standard for primary peristalsis (Figure 1b). Comparisons were made between the characteristics of spontaneous swallow associated primary peristalsis in the absence of any oral stimulation, pacifier associated dry swallows (pacifier-swallows), and taste (pacifier dipped in 3% sucrose solution; taste-swallows) associated swallows.

A priori High Resolution Manometry and Esophageal Pressure Topography Definitions and Data Analysis

Manometry studies were analyzed using MMS software version 8.23 utilizing both QuickView and conventional settings (Medical Measurement Systems, Dover, NH). Automatic analysis was performed by algorithms embedded in MMS utilizing EPT, while manual analysis was performed using EPT, virtual channel settings, and conventional channel settings for esophageal motility and impedance characteristics. All respiratory measurements were taken at end expiration. Analysis was conducted to evaluate the response sensitivity to pacifier by defining the response latency to the occurrence of changes in pharyngeal waveforms, UES, esophageal peristalsis and EGJ.

Specifically, characteristics of the UES, esophageal body, and EGJ, were analyzed using modified (19-21) definitions of the Chicago Classification, which was developed for analysis of the adult population (22, 23), and previously published definitions in the neonates. Analysis included pacifier or taste associated swallowing, in addition to spontaneous swallows (generated in the absence of any oral stimulus, pacifier or otherwise) (Figure 2a). The following definitions were used: **a) UES Basal Tone (mmHg)**: average resting UES pressure, relative to atmospheric pressure, taken at end expiration calculated by automatic marker placement during esophageal and respiratory quiescence prior to deglutition onset (24, 25); **b) UES Relaxation Onset**: UES relaxation onset was determined using manual analysis with the virtual UES line plot, and defined as the decrease in UES pressure from resting pressure by 4 mmHg, concurrent with a swallow-associated pharyngeal peak; **c) UES Relaxation time (sec)**: calculation utilizing the virtual UES line plot, defined as duration between UES Relaxation Onset to the point where the UES pressure is restored to 4 mmHg below basal UES tone; **d) EGJ Basal Tone (mmHg)**: average resting EGJ pressure, relative to gastric pressure, taken at end expiration calculated by automatic marker placement during esophageal and respiratory quiescence prior to deglutition onset (26, 27); **e) Distal Contractile Integral (mmHg*s*cm)**: determined from automated analysis, based on markers centered at the proximal break in the 20 mmHg isocontour plot between the proximal and middle esophageal segments (which indicates the transition from skeletal to smooth muscle) to the upper border of EGJ associated with 20 mmHg isobar contraction (22-24, 28); **f) Contractile Deceleration Point (CDP)**: manual calculation, defined as the inflection point in the esophageal contraction along the 30 mmHg isobar signifying the transition from peristaltic propagation to late phase of esophageal emptying (22, 28); as this point is infrequently found in neonates, the point of esophageal contraction in the distal esophagus, just proximal to the upper border of the EGJ was used for this demarcation to calculate distal latency; **g) Total Deglutition Time (s)**: determined from manual calculation, the duration from onset of pharyngeal activity to esophageal propagation offset; **h) Distal Latency, (s)**: determined from automated analysis, defined as the duration between UES relaxation onset and CDP (24); **Completed Swallow**: is

determined by intact 20 mmHg isobaric contour associated with the swallow in the distal esophagus (29); **Contractile Vigor**: categorization of distal contractile integral into *failed* (100 mmHg*s*cm); *weak* (between 101 mmHg*s*cm and 450 mmHg*s*cm); *normal* (between 451 mmHg*s*cm and 4999 mmHg*s*cm); *hypercontractility* (5000 mmHg*s*cm) (23).

A priori Respiratory Definitions and Data Analysis

Respiratory measurements were taken from the thoracic and abdominal waveforms, as well as the nasal airflow thermistor, and were analyzed relative to the onset of the pharyngeal waveform (Figure 2b). **Respiratory normalcy**: baseline respiration for each patient, as indicated by their overall pattern throughout the course of evaluation; **Respiratory rhythm disturbance**: an interruption in the regular sinusoidal breathing pattern lasting longer than 2 breaths as assessed from respiratory inductance plethysmography and nasal airflow thermistor, beginning either before, during, or directly after the pharyngeal waveform (during the duration of esophageal activity) associated with the swallow; Duration of respiratory rhythm disturbance (seconds): the period between the onset and end of the respiratory rhythm disturbance; **Deglutition Apnea**: the pause in respiration during the occurrence of a pharyngeal swallow (30, 31); **Deglutition apnea duration (seconds)**: the period between the onset and end of the deglutition apnea.

A priori Impedance Definitions and Data Analysis

Corresponding impedance channels demarcating the UES, distal esophageal segment just above the LES, and the LES were identified for each patient (Figure 2c) from which values were calculated. **Baseline impedance (Ω)**: average impedance taken over a duration of 5 seconds before the pharyngeal waveform using Vivosense software (Vivonoetics, San Diego, CA); **Nadir impedance (Ω)**: the minimum swallow associated impedance value measured in each corresponding impedance waveform locations; **Complete bolus clearance**: the presence of a 50% decrease in impedance from baseline, associated with a swallow (32-34); **Incomplete bolus clearance**: the presence of a decrease in impedance between 10% and 49% from baseline, associated with a swallow (32, 33); **Failed bolus clearance**: the presence of a decrease in impedance < 10% from baseline, associated with a swallow; **Bolus clearance time(seconds)**: the duration from the initial 50% drop in impedance, through the nadir, to recovery of 50%, relative to baseline (32, 33).

Statistical Analysis

Linear mixed models were used to compare the effects of pacifier versus taste on sphincter tone, bolus clearance, pharyngo-esophageal motility, respiration, and impedance. Generalized estimating equation models were used to compare deglutition apnea (%), respiratory change (%) and respiratory normalcy (%) between pacifier versus taste interventions. The Bonferroni Correction was used to account for multiple comparisons. Data were analyzed using SAS software (version 9.3, SAS Institute, Cary, NC). Data are presented as mean $\pm$ SEM, %, median (IQR), or as stated. A p-value of <0.05 was considered significant.

Results

Infants were studied at 43 (41-44) wks postmenstrual age (PMA), weighing 3.6 (3.3-3.9) kg. At evaluation, all infants had oral feeding skills with 7 (47%) infants oral feeding exclusively, 8 (53%) infants transitioning to independent oral feeding, 1 (7%) infant requiring nasal cannula, and the remaining 14 (93%) infants breathing room air. We analyzed 209 swallows (85 spontaneous, 63 pacifier-swallows, and 61 taste-swallows) from ~ 22 hours of cumulative data (~ 1.4 hours of data per patient). Per patient data analysis was 13 (8-17) swallows (spontaneous: 5 (3-9); pacifier- swallows: 2 (0-8); taste-swallows: 3 (0-5)).

Mechanosensitive Effect of Pacifier Intervention

Basal tone in both proximal and distal esophageal sphincters decreased ($P < 0.05$) following the onset of pacifier intervention (Table 1). However, esophageal motility characteristics, specifically, distal latency, distal contractile integral (DCI), total deglutition response time, and contractile vigor were all similar when compared between spontaneous swallowing and pacifier- swallowing (Table 2a&b); Mechanical Effect- Column 1 vs. 2).

Furthermore, respiratory characteristics, specifically presence of deglutition apnea (DA), duration of DA, change in respiratory rhythm, duration of respiratory rhythm change, and whether or not a swallow was associated with restoration of respiratory normalcy were also similar when compared between the groups (Table 3, Column 1 vs. 2).

Impedance characteristics in the regions of the UES, distal esophagus, and LES, specifically baseline impedance, nadir impedance, magnitude of swallow-associated impedance drop, and bolus clearance time were all similar when compared between the groups (Table 4, Column 1 vs. 2). The physical characteristics (air, mixed, or liquid) of the swallowed bolus for each segment of the esophagus for either type of swallow (spontaneous swallow, Figure 3a) or pacifier- swallow (Figure 3b) are shown. The distribution of the swallowed material is similar between the groups in all regions of the esophagus analyzed during pacifier intervention using impedance.

The distribution of complete, incomplete, and failed bolus transport based off of either impedance characteristics at the level of the EGJ (Figure 3d) or manometry (Figure 3e), is also characterized. This distribution is different during pacifier- swallows (vs. spontaneous swallows), for degree of completion at the level of the EGJ (Figure 3d).

Effect of Taste Intervention

Basal tone in both proximal and distal esophageal sphincters decreased ($P < 0.05$) following the onset of taste intervention (Table 1). Taste intervention was associated with a marginally increased number of swallows per minute compared with pacifier intervention alone (3.9 ± 0.5 swallows/min vs. 2.6 ± 0.5 swallows/min; $P = 0.08$; Figure 1a&c); furthermore, taste intervention resulted in decreased response latency to first pharyngeal swallow compared to pacifier intervention alone (4.7 ± 1.6 sec vs. 10.9 ± 1.2 sec; Figure 1a&c; $P = 0.03$). Moreover, during a respiratory rhythm disruption, when oral intervention was administered to help calm the infant, taste intervention rather than pacifier alone took ~3-fold less time

(although statistically similar, $P=0.1$) to restore respiratory normalcy (13.1 ± 1.4 sec vs. 36.0 ± 4.4 sec).

Esophageal motility characteristics, specifically, distal latency, total deglutition duration, DCI, and contractile vigor were similar between the groups (Table 2a&b; Taste Effect-Column 2 vs. 3). Similarly, respiratory characteristics, specifically presence of deglutition apnea (DA), DA duration, respiratory change, duration of respiratory change, and whether or not a swallow was associated with restoration of respiratory normalcy were also similar between the groups (Table 3, Column 2 vs. 3). Impedance characteristics in the regions of the UES, distal esophagus, and EGJ, specifically baseline impedance, nadir impedance, magnitude of swallow-associated impedance drop, and bolus clearance time are also similar between the groups (Table 4, Column 2 vs. 3).

The physical characteristics of the swallowed bolus for the UES, distal esophagus, and EGJ are shown during pacifier (Figure 3b) and taste (Figure 3c) intervention. Specifically, the distribution of air, mixed (air and liquid), and liquid material is different ($P < 0.05$) in the UES vs. the lower esophageal segments (Figure 3c). The distribution of swallowed material is different in the distal esophageal segment during pacifier-swallowing (vs. taste; Figure 3b & 3c). The distribution of complete, incomplete, and failed bolus transport based off of either impedance at the level of the EGJ or manometry is also characterized (Figure 3d & 3e).

Comparing Manometry versus Impedance Bolus Transit Efficiency

Pooled analysis indicated that correlation of completeness between manometry and impedance was poor at the levels of the UES and EGJ (Figure 4a & 4b).

Discussion

Pacifiers are used as a means for providing mechanosensitive stimulus to the oro-facial and lingual sucking apparatus, activating the sensory-motor components of cranial nerves (CN) V, VII, IX, X and XII involved with safe feeding. In the current study, pacifier intervention significantly decreased UES and LES basal tone regardless of the addition of taste, suggesting a decrease in cholinergic excitatory output to both the UES and EGJ, mediated via CN X. The decrease in proximal and distal sphincteric basal tone may also be a calming manifestation of oral stimulation.

However, neither pacifier intervention, nor taste intervention provided via the pacifier dipped in sucrose had any impact on the magnitude of esophageal motility characteristics. Specifically; UES relaxation time, distal latency, total deglutition response duration, DCI, and contractile vigor were all similar with regard to mechanical stimulation or taste effects. Per the Chicago Classification 3.0, characterization of peristaltic breaks is non-specific, therefore, we analyzed contractile vigor by established metrics (23). The characterization of contractile vigor (failed: weak: normal: hypercontractile) was similar among the groups. Significantly, taste intervention resulted in primary peristalsis rhythm sequences occurring more rapidly ($P < 0.05$), as well as rapid restoration of respiratory normalcy.

Neither pacifier nor taste intervention modified swallow-associated respiratory characteristics. Specifically; presence of deglutition apnea, duration of deglutition apnea, presence of respiratory change, and duration of respiratory change were similar with regard to mechanical stimulation or taste effects. What restored respiratory rhythm normalcy was in fact completion of primary peristalsis, similar to that seen in infants with apparent life threatening events (35). The link between respiratory regulation and esophageal function has been established (35, 36). Taste intervention generated a swallow more quickly than did pacifier intervention alone, thus indicating either increased alertness or the importance of taste associated oral stimulation on vagus-mediated esophago-respiratory interactions, both of which participate establishing normal aerodigestive protective patterns. For example, the prevalence of SIDS is decreased in breast-fed infants (37), and it is likely that the nutritive or taste factors may be responsible for accentuating the stimulus in activating the neural networks for esophageal-respiratory regulatory interactions (30, 38). On the other hand, the relevance of pacifier intervention alone in modulating oropharyngeal or esophageal and respiratory interactions is not supported by the current study.

All swallow types (spontaneous, pacifier associated, taste associated) resulted in similar impedance characteristics at each esophageal locus (UES, DE, EGJ). Incidentally, the nadir impedance in the EGJ was decreased during pacifier associated swallowing (vs. spontaneous swallowing; $P < 0.05$). Although lowering of resting EGJ tone was noted, the number of transient lower esophageal sphincter relaxation events with either pacifier or taste intervention was negligible. Taste- swallowing had a different frequency of air, mixed (air and liquid), or liquid composition (vs. pacifier -swallowing) at the level of the distal esophagus. Specifically, air alone was not evident at this level for taste- swallows, which may be related to increased salivation. The physical composition of the swallowed bolus was liquid or mixed (air and liquid) (Figure 2a-c). This pattern is evident regardless of swallow type (i.e. spontaneous, pacifier -swallows, taste -swallows), supporting the fact that liquid stimulus is providing sensory input. Despite the fact that neonates have 2-3 completely propagated primary peristaltic events per minute (39), the proportion of aerophagia is minimal, indicating the presence of saliva in the majority of neonatal swallows. Air contributes to mixed bolus composition, which is the most commonly swallowed bolus. This is a likely cause of air in the stomach, which in excess, may be a factor in the causation of gastrointestinal distention, leading to burping, gastroesophageal reflux or colic.

The distribution of complete, incomplete, or failed bolus transit at the level of the EGJ was significantly different during intervention with a pacifier, regardless of taste, when compared with spontaneous swallows. The purpose of spontaneous swallowing is likely for swallowing saliva or protection of aerodigestive tract (40, 41), and this finding indicates that salivation may increase with pacifier intervention, regardless of taste. Salivation is regulated by the parasympathetic nervous system, specifically the chorda tympani branch of the facial nerve (CN VII) (42, 43). Supplementing EPT with impedance allows characterization of bolus composition.

The oral phase of swallowing has been well characterized (44-46), as have the effects of oral stimulation and non-nutritive sucking on continuing development of oral skills (12, 13, 16,

17, 46-49). The current study suggests that the presence of oral stimulation with either pacifier intervention, or taste intervention may not significantly or acutely modify pharyngo-esophageal motility, respiration, or impedance characteristics of swallowing. Further studies are needed to assess the timing and effects of multimodal stimulus as well as longitudinal changes in outcomes.

There are some methodological limitations with this project. The sample size of N= 15 infants can be limiting when considering the effects of heterogeneity and confounders. Future studies are needed to assess these elements. Additionally, all subjects were former preterm infants. While pharyngo-esophageal motility does mature with increasing age, former preterm infants studied at term equivalent PMA have esophageal motility skills approaching those of infants born at term gestation (50, 51). Therefore, the results are directly applicable to former preterm born infants when they reach term PMA, however, it is also appropriate to extrapolate the results as applicable as well to infants born at term gestation (50, 51). As has been demonstrated for manometry analysis algorithms using Chicago Classification in adults, when dealing with a pediatric or neonatal population, modifications are necessary to account for changing parameters with patient age and size (19-21); however, the precise application of these adjustments is unknown for neonates. Our finding that the majority of the swallows analyzed fell into the 'weak' category for contractile vigor, despite the majority characterization of completeness of peristaltic wave, may indicate that modification indeed may be necessary in neonates for such categories.

Published adult data regarding impedance utilize the decrease of 50% of baseline impedance to indicate bolus entry into specific regions of the esophagus (33, 34). However, in neonates, while bolus entry on impedance was evident, the proportion of swallows reaching the 50% decrease from baseline was not well correlated with manometric peristalsis. Therefore, we categorized those events that have reached between 10% and 49% of baseline as incomplete bolus clearance, and < 10% of baseline as failed clearance. Despite this adjustment, bolus clearance did not correlate well with completed peristaltic waveforms. Further studies are needed to evaluate the effects of a measured bolus on esophageal motility, respiratory rhythms, and bolus transit characteristics.

In conclusion, although pacifier use is widely prevalent, the mechanistic effects of pacifier use on swallowing and airway safety are limited. The implications of our data are that the presumed beneficial effects of pacifier use alone on respiratory rhythms are also weak and cannot be supported by this data, as no pharyngo-esophageal, respiratory rhythm, or bolus transit mechanisms unique to pacifier use were identified. Taste indeed provided the opportunity for additional acute sensory stimulation linking neural networks involved with feeding and swallowing. Therefore, early oromotor feeding opportunities will be beneficial and may optimize aerodigestive sensory-motor interactions.

Acknowledgements

FUNDING: Supported in part by grant funding from NIH-2R01-DK 068158 (Jadcherla)

References

1. Castilho SD, Rocha MA. Pacifier habit: history and multidisciplinary view. *J Pediatr (Rio J)*. 2009; 85(6):480–9. [PubMed: 20016867]
2. Adair S. Pacifier use in children: a review of recent literature. *Pediatr Dent*. 2003; 25(5):449–58. [PubMed: 14649608]
3. Barr RG, Pantel MS, Young SN, Wright JH, Hendricks LA, Gravel R. The response of crying newborns to sucrose: is it a “sweetness” effect? *Physiol Behav*. 1999; 66(3):409–17. [PubMed: 10357429]
4. Barceloux, DG. Medical Toxicology of Drug Abuse. John Wiley & Sons, Inc.; 2012. Heroin and the Opium Poppy Plant (*Papaver somniferum* L.); p. 546-78.
5. Stevens B, Yamada J, Lee GY, Ohlsson A. Sucrose for analgesia in newborn infants undergoing painful procedures. *Cochrane Db Syst Rev*. 2013; (1)
6. Degan VV, Puppini-Rontani RM. Prevalence of pacifier-sucking habits and successful methods to eliminate them—a preliminary study. *J Dent Child (Chic)*. 2004; 71(2):148–51. [PubMed: 15587099]
7. Kramer MS, Barr RG, Dagenais S, Yang H, Jones P, Ciofani L, et al. Pacifier use, early weaning, and cry/fuss behavior - A randomized controlled. *J Am Med Assoc*. 2001; 286(3):322–6.
8. Jenik AG, Vain N. The pacifier debate. *Early Hum Dev*. 2009; 85(10 Suppl):S89–91. [PubMed: 19762175]
9. Hamilton BE, Martin JA, Ventura SJ. Births: preliminary data for 2012. National vital statistics reports : from the Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System. 2013; 62(3):1–20.
10. Moon RY, Tanabe KO, Yang DC, Young HA, Hauck FR. Pacifier Use and Sids: Evidence for a Consistently Reduced Risk. *Matern Child Hlth J*. 2012; 16(3):609–14.
11. Jenik AG, Vain NE, Gorestein AN, Jacobi NE, Grp PBT. Does the Recommendation to Use a Pacifier Influence the Prevalence of Breastfeeding? *J Pediatr-Us*. 2009; 155(3):350–4.
12. Barlow SM, Finan DS, Lee J, Chu S. Synthetic orocutaneous stimulation entrains preterm infants with feeding difficulties to suck. *J Perinatol*. 2008; 28(8):541–8. [PubMed: 18548084]
13. Barlow SM, Lee J, Wang J, Oder A, Hall S, Knox K, et al. Frequency-modulated orocutaneous stimulation promotes non-nutritive suck development in preterm infants with respiratory distress syndrome or chronic lung disease. *J Perinatol*. 2014; 34(2):136–42. [PubMed: 24310444]
14. Chorna OD, Slaughter JC, Wang L, Stark AR, Maitre NL. A pacifier-activated music player with mother's voice improves oral feeding in preterm infants. *Pediatrics*. 2014; 133(3):462–8. [PubMed: 24534413]
15. Standley JM. The effect of music-reinforced nonnutritive sucking on feeding rate of premature infants. *J Pediatr Nurs*. 2003; 18(3):169–73. [PubMed: 12796858]
16. Oder AL, Stalling DL, Barlow SM. Short-Term Effects of Pacifier Texture on NNS in Neurotypical Infants. *Int J Pediatr*. 2013; 2013:168459. [PubMed: 23737804]
17. Fucile S, Gisel E, Lau C. Oral stimulation accelerates the transition from tube to oral feeding in preterm infants. *J Pediatr*. 2002; 141(2):230–6. [PubMed: 12183719]
18. Fucile S, Gisel EG, Lau C. Effect of an oral stimulation program on sucking skill maturation of preterm infants. *Dev Med Child Neurol*. 2005; 47(3):158–62. [PubMed: 15739719]
19. Singendonk MM, Kritas S, Cock C, Ferris L, McCall L, Rommel N, et al. Applying the Chicago Classification criteria of esophageal motility to a pediatric cohort: effects of patient age and size. *Neurogastroenterol Motil*. 2014; 26(9):1333–41. [PubMed: 25053225]
20. Goldani HA, Staiano A, Borrelli O, Thapar N, Lindley KJ. Pediatric esophageal high-resolution manometry: utility of a standardized protocol and size-adjusted pressure topography parameters. *Am J Gastroenterol*. 2010; 105(2):460–7. [PubMed: 19953088]
21. Gupta A, Jadcherla SR. The relationship between somatic growth and in vivo esophageal segmental and sphincteric growth in human neonates. *J Pediatr Gastroenterol Nutr*. 2006; 43(1): 35–41. [PubMed: 16819375]

22. Bredenoord AJ, Fox M, Kahrilas PJ, Pandolfino JE, Schwizer W, Smout AJ, et al. Chicago classification criteria of esophageal motility disorders defined in high resolution esophageal pressure topography. *Neurogastroenterol Motil.* 2012; 24(Suppl 1):57–65. [PubMed: 22248109]
23. Kahrilas PJ, Bredenoord AJ, Fox M, Gyawali CP, Roman S, Smout AJ, et al. The Chicago Classification of esophageal motility disorders, v3.0. *Neurogastroenterol Motil.* 2015; 27(2):160–74. [PubMed: 25469569]
24. Jadcherla SR, Duong HQ, Hoffmann RG, Shaker R. Esophageal body and upper esophageal sphincter motor responses to esophageal provocation during maturation in preterm newborns. *J Pediatr.* 2003; 143(1):31–8. [PubMed: 12915821]
25. Jadcherla SR, Duong HQ, Hofmann C, Hoffmann R, Shaker R. Characteristics of upper oesophageal sphincter and oesophageal body during maturation in healthy human neonates compared with adults. *Neurogastroenterol Motil.* 2005; 17(5):663–70. [PubMed: 16185304]
26. Pena EM, Parks VN, Peng J, Fernandez SA, Di Lorenzo C, Shaker R, et al. Lower esophageal sphincter relaxation reflex kinetics: effects of peristaltic reflexes and maturation in human premature neonates. *Am J Physiol Gastrointest Liver Physiol.* 2010; 299(6):G1386–95. [PubMed: 20864655]
27. Mittal RK, Liu J. Flow across the gastro-esophageal junction: lessons from the sleeve sensor on the nature of anti-reflux barrier. *Neurogastroenterol Motil.* 2005; 17(2):187–90. [PubMed: 15787938]
28. Staiano A, Boccia G, Miele E, Clouse RE. Segmental characteristics of oesophageal peristalsis in paediatric patients. *Neurogastroenterol Motil.* 2008; 20(1):19–26. [PubMed: 18031473]
29. Bulsiewicz WJ, Kahrilas PJ, Kwiatek MA, Ghosh SK, Meek A, Pandolfino JE. Esophageal pressure topography criteria indicative of incomplete bolus clearance: a study using high-resolution impedance manometry. *Am J Gastroenterol.* 2009; 104(11):2721–8. [PubMed: 19690527]
30. Jadcherla SR, Gupta A, Wang M, Coley BD, Fernandez S, Shaker R. Definition and implications of novel pharyngo-glottal reflex in human infants using concurrent manometry ultrasonography. *Am J Gastroenterol.* 2009; 104(10):2572–82. [PubMed: 19603008]
31. Shaker R, Li Q, Ren J, Townsend WF, Dodds WJ, Martin BJ, et al. Coordination of deglutition and phases of respiration: effect of aging, tachypnea, bolus volume, and chronic obstructive pulmonary disease. *Am J Physiol.* 1992; 263(5 Pt 1):G750–5. [PubMed: 1443150]
32. Omari T, Tack J, Rommel N. Impedance as an adjunct to manometric testing to investigate symptoms of dysphagia: What it has failed to do and what it may tell us in the future. *United Eur Gastroent.* 2014; 2(5):355–66.
33. Cho YK, Choi MG, Park JM, Oh JH, Paik CN, Lee JW, et al. Evaluation of esophageal function in patients with esophageal motor abnormalities using multichannel intraluminal impedance esophageal manometry. *World J Gastroenterol.* 2006; 12(39):6349–54.
34. Sifrim D, Castell D, Dent J, Kahrilas PJ. Gastro-oesophageal reflux monitoring: review and consensus report on detection and definitions of acid, non-acid, and gas reflux. *Gut.* 2004; 53(7):1024–31. [PubMed: 15194656]
35. Hasenstab KA, Jadcherla SR. Respiratory Events in Infants Presenting with Apparent Life Threatening Events: Is There an Explanation from Esophageal Motility? *J Pediatr.* 2014; 165(2):250–55. [PubMed: 24681180]
36. Dodds WJ, Stewart ET, Hodges D, Zboralske FF. Movement of the feline esophagus associated with respiration and peristalsis. An evaluation using tantalum markers. *J Clin Invest.* 1973; 52(1):1–13. [PubMed: 4682383]
37. Vennemann MM, Bajanowski T, Brinkmann B, Jorch G, Yucesan K, Sauerland C, et al. Does Breastfeeding Reduce the Risk of Sudden Infant Death Syndrome? *Pediatrics.* 2009; 123(3):e406–e10. [PubMed: 19254976]
38. Jadcherla SR, Gupta A, Coley BD, Fernandez S, Shaker R. Esophago-glottal closure reflex in human infants: a novel reflex elicited with concurrent manometry and ultrasonography. *Am J Gastroenterol.* 2007; 102(10):2286–93. [PubMed: 17617206]
39. Jadcherla SR, Peng J, Moore R, Saavedra J, Shepherd E, Fernandez S, et al. Impact of Personalized Feeding Program in 100 NICU Infants: Pathophysiology-based Approach for Better Outcomes. *J Pediatr Gastroenterol Nutr.* 2012; 54(1):62–70. [PubMed: 21694638]

40. Jadcherla SR, Parks VN, Peng J, Dzodzomenyo S, Fernandez S, Shaker R, et al. Esophageal sensation in premature human neonates: temporal relationships and implications of aerodigestive reflexes and electrocortical arousals. *Am J Physiol Gastrointest Liver Physiol*. 2012; 302(1):G134–44. [PubMed: 21852361]
41. Jadcherla SR, Chan CY, Fernandez S, Splaingard M. Maturation of upstream and downstream esophageal reflexes in human premature neonates: the role of sleep and awake states. *Am J Physiol Gastrointest Liver Physiol*. 2013; 305(9):G649–58. [PubMed: 24008357]
42. Proctor GB, Carpenter GH. Salivary secretion: mechanism and neural regulation. *Monogr Oral Sci*. 2014; 24:14–29. Epub. [PubMed: 24862591]
43. Proctor GB, Carpenter GH. Regulation of salivary gland function by autonomic nerves. *Auton Neurosci*. 2007; 133(1):3–18. [PubMed: 17157080]
44. Barlow SM. Oral and respiratory control for preterm feeding. *Curr Opin Otolaryngol Head Neck Surg*. 2009; 17(3):179–86. [PubMed: 19369871]
45. Barlow SM, Estep M. Central pattern generation and the motor infrastructure for suck, respiration, and speech. *J Commun Disord*. 2006; 39(5):366–80. [PubMed: 16876186]
46. Lau C, Smith EO. Interventions to improve the oral feeding performance of preterm infants. *Acta Paediatr*. 2012; 101(7):e269–74. [PubMed: 22404221]
47. Zimmerman E, Barlow SM. Pacifier Stiffness Alters the Dynamics of the Suck Central Pattern Generator. *J Neonatal Nurs*. 2008; 14(3):79–86. [PubMed: 19492006]
48. Lau C, Kusnierczyk I. Quantitative evaluation of infant's nonnutritive and nutritive sucking. *Dysphagia*. 2001; 16:58–67. [PubMed: 11213247]
49. Bache M, Pizon E, Jacobs J, Vaillant M, Lecomte A. Effects of pre-feeding oral stimulation on oral feeding in preterm infants: a randomized clinical trial. *Early Hum Dev*. 2014; 90(3):125–9. [PubMed: 24461572]
50. Jadcherla SR, Wang M, Vijayapal AS, Leuthner SR. Impact of prematurity and co-morbidities on feeding milestones in neonates: a retrospective study. *J Perinatol*. 2010; 30(3):201–8. [PubMed: 19812589]
51. Jadcherla SR, Shubert TR, Malkar MB, Sitaram S, Moore RK, Wei L, et al. Gestational and postnatal modulation of esophageal sphincter reflexes in human premature neonates. *Pediatr Res*. 2015; 78(5):540–6. [PubMed: 26270576]

Key Messages

- Oral stimulation with a pacifier (with or without taste) likely decreases central parasympathetic-cholinergic excitatory drive as indicated by significantly decreased upper esophageal sphincter (UES) and esophagogastric junction (EGJ) basal pressure; pharyngo-esophageal motility, airway interactions, or esophageal bolus transit characteristics were not significantly modified by pacifier intervention (with or without taste).
- Our aims were to investigate the effect of pacifier and taste intervention on pharyngo-upper esophageal sphincter, esophageal body, and esophagogastric junction motility, respiratory, and impedance characteristics.
- Neonates (N=15) underwent pacifier or taste (pacifier dipped in 3% sucrose solution) intervention during High Resolution Impedance Manometry/ Esophageal Pressure Topography concurrent with Respiratory Inductance Plethysmography and nasal thermistor.
- Basal UES and EGJ pressures were decreased upon both pacifier and taste interventions; esophageal motility, respiratory rhythm, and impedance transit characteristics were similar with either intervention.

Figure 1. Manometric Representation of Swallow Occurrence

Note the identification of pacifier and taste intervention onset and offset, in addition to the occurrence of spontaneous swallowing, in the absence of any intervention. The time period between interventions and spontaneous swallowing is subject to variability. Also to note, increased response latency to the first pharyngeal swallow with (a) pacifier intervention vs. (c) taste intervention.

Figure 2. Schematic of Analysis Parameters used for Pharyngo-Esophageal Motility, Respiratory, and Impedance Characteristics

A) Labelled parameters used for analysis of pharyngo-esophageal motility characteristic.

Note the inset indicating a more detailed view of the upper esophageal sphincter. B)

Labelled parameters used for analysis of respiratory characteristics. C) Labelled parameters

used for analysis of impedance characteristics.

Figure 3. Physical Bolus Characteristics and Characterization of Peristaltic Completeness

A) * $P < 0.01$ vs. distribution in the distal esophagus; Distribution of mixed and liquid swallowed material in the UES, distal esophagus, and EGJ during spontaneous swallowing. B) Distribution of air, mixed, and liquid swallowed material in the UES, distal esophagus, and EGJ for pacifier- swallows. C) * $P < 0.01$ vs. distribution in the distal esophagus and EGJ; † $P < 0.002$ vs. distribution in the distal esophagus for pacifier- swallows; Distribution of air, mixed, and liquid swallowed material in the UES, distal esophagus, and EGJ during taste- swallows. D) * $P < 0.05$ vs. distribution for either pacifier associated dry swallows or taste associated swallows. Distribution of complete, incomplete, and failed bolus transport at the level of the EGJ using impedance characterization during spontaneous swallows, pacifier- swallows, and taste- swallows. Note the distribution of complete: incomplete: failed is different for spontaneous swallows vs. pacifier- swallows and vs. taste- swallows. E) Distribution of complete, incomplete, and failed swallows using manometry characterization.

Figure 4. Comparing Completeness of Bolus Transit: Manometry vs. Impedance

Note the difference in distribution of complete:incomplete:failed bolus propagation upon comparison of impedance vs. manometry methods.

Table 1

Effect of Pacifier Intervention on Sphincter Tone

Resting Pressure, mmHg	Intervention Type	Pre Intervention	During Intervention	Post Intervention	P-Value
Mean Upper Esophageal Sphincter	Pacifier	29.6 ± 4.0 *	26.4 ± 3.6 *	20.0 ± 4.0	0.03
	Taste	30.6 ± 3.1 *	22.2 ± 2.7 †	16.6 ± 3.1	0.0002
Mean Esophagogastric Junction	Pacifier	41.8 ± 3.6 *	34.3 ± 3.2 †	32.4 ± 3.6	0.03
	Taste	40.0 ± 4.9 *	34.5 ± 4.0	25.7 ± 4.9	0.04

data presented as mean ± SE; comparisons between pacifier and taste intervention pressures were not significant.

* P< 0.05 vs. post intervention

† P< 0.05 vs. pre intervention

Table 2a

Effect of Pacifier and Taste Intervention on Pharyngo-esophageal Motility

Characteristic	Mechanical Effect		Taste Effect
	Spontaneous Swallows	Pacifier Associated Dry Swallows	Taste Associated Swallows
UES Relaxation Time, s	0.5 ± 0.08	0.4 ± 0.1	0.6 ± 0.1
Distal Latency, s	5.3 ± 0.3	5.1 ± 0.3	5.3 ± 0.3
Total Deglutition Duration, s	8.2 ± 0.3	7.6 ± 0.3	7.3 ± 0.4
Distal Contractile Integral, mmHg*cm*s	392.9 ± 64.6	366.5 ± 67.4	369.9 ± 69.3

Data Presented as mean ± SEM; comparisons between spontaneous swallows vs. pacifier associated dry swallows and between pacifier associated dry swallows and taste associated swallows were similar ($P > 0.05$).

Table 2b

Categorization of Contractile Vigor

	Mechanical Effect		Taste Effect
	Spontaneous Swallows	Pacifier Associated Dry Swallows	Taste Associated Swallows
Failed, n	14	19	27
Weak, n	44	30	25
Normal, n	27	4	4
Hypercontractile, n	0	0	0

Data Presented as mean $\pm$ SEM; comparisons between spontaneous swallows vs. pacifier associated dry swallows and between pacifier associated dry swallows and taste associated swallows were similar ($P > 0.05$).

Table 3

Effect of Pacifier and Taste Intervention on Respiratory Characteristics

Characteristic	Mechanical Effect		Taste Effect
	Spontaneous Swallows	Pacifier Associated Dry Swallows	Taste Associated Swallows
Deglutition Apnea, yes, n (%)	60 (94)	44 (98)	54 (95)
Deglutition Apnea Duration, s	1.1 ± 0.2	1.4 ± 0.2	1.7 ± 0.2
Respiratory Change, yes, n (%)	28 (44)	14 (30)	31 (48)
Duration of Respiratory Change, s	15.8 ± 5.3	12.2 ± 6.1	18.1 ± 5.7
Swallow Restores Respiratory Normalcy, yes, n (%)	19 (68)	13 (53)	8 (42)

Data presented as mean ± SEM or n (%); comparisons between spontaneous swallows vs. pacifier associated dry swallows and between pacifier associated dry swallows and taste associated swallows were similar ($P > 0.05$).

Table 4

Effect of Pacifier and Taste Intervention on Bolus Clearance Characteristics

Characteristic	Mechanical Effect		Taste Effect
	Spontaneous Swallow	Pacifier Associated Dry Swallows	Taste Associated Swallows
UES ^a Baseline, Ω	1046.0 $\pm$ 97.8	1034.0 $\pm$ 100.4	945.2 $\pm$ 100.6
Nadir UES, Ω	670.3 $\pm$ 62.7	594.2 $\pm$ 66.2	618.1 $\pm$ 66.3
% UES decrease	33.1 $\pm$ 3.3	41.2 $\pm$ 3.8	34.2 $\pm$ 3.8
UES BCT ^b , s	0.8 $\pm$ 0.2	0.4 $\pm$ 0.2	0.2 $\pm$ 0.2
DE ^c Baseline, Ω	800.9 $\pm$ 82.1	728.1 $\pm$ 87.5	752.2 $\pm$ 87.7
Nadir DE, Ω	537.0 $\pm$ 65.3	453.5 $\pm$ 69.3	498.8 $\pm$ 68.9
% DE decrease	34.6 $\pm$ 3.8	36.5 $\pm$ 4.1	38.0 $\pm$ 4.1
DE BCT, s	1.0 $\pm$ 0.6	0.7 $\pm$ 0.5	1.8 $\pm$ 0.4
EGJ ^d Baseline, Ω	479.3 $\pm$ 80.7	407.5 $\pm$ 86.5	420.0 $\pm$ 85.3
Nadir EGJ, Ω	295.0 $\pm$ 48.6	222.5 $\pm$ 50.5 [*]	255.4 $\pm$ 50.5
% EGJ decrease	42.2 $\pm$ 6.1	43.8 $\pm$ 6.5	43.8 $\pm$ 6.5
EGJ BCT, s	2.3 $\pm$ 0.7	1.8 $\pm$ 0.7	3.0 $\pm$ 0.8

Data presented as mean $\pm$ SEM or %^aUpper Esophageal Sphincter^bBolus Clearance Time^cDistal Esophagus^dEsophagogastric Junction.

^{*} P = 0.05 vs. spontaneous swallow; all other comparisons between spontaneous swallows vs. pacifier associated dry swallows and between pacifier associated dry swallows and taste associated swallows were similar (P > 0.05).