1.5 HOURS Continuing Education

Early Intervention to Improve Sucking in Preterm Newborns

A Systematic Review of Quantitative Studies

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ABSTRACT

Background: Premature birth is associated with feeding difficulties due to inadequate coordination of sucking, swallowing, and breathing. Nonnutritive sucking (NNS) and oral stimulation interventions may be effective for oral feeding promotion, but the mechanisms of the intervention effects need further clarifications.

Purpose: We reviewed preterm infant intervention studies with quantitative outcomes of sucking performance to summarize the evidence of the effect of interventions on specific components of sucking.

Methods: PubMed, CINAHL, MEDLINE, EMBASE, and PSYCOLIST databases were searched for English language publications through August 2017. Studies were selected if they involved preterm infants, tested experimental interventions to improve sucking or oral feeding skills, and included outcome as an objective measure of sucking performance. Specific Medical Subject Headings (MeSH) terms were utilized.

Results: Nineteen studies were included in this review: 15 randomized, 1 quasi-randomized, and 3 crossover randomized controlled trials. Intervention types were grouped into 6 categories (i) NNS, (ii) NNS with auditory reinforcement, (iii) sensorimotor stimulation, (iv) oral support, (v) combined training, and (vi) nutritive sucking. Efficiency parameters were positively influenced by most types of interventions, though appear to be less affected by trainings based on NNS alone.

Implications for Practice: These findings may be useful in the clinical care of infants requiring support to achieve efficient sucking skills through NNS and oral stimulation interventions.

Implications for Research: Further studies including quantitative measures of sucking performance outcome measures are needed in order to best understand the needs and provide more tailored interventions to preterm infants.

Key Words: feeding, preterms/prematurity, sucking, training/intervention infant, efficiency, morphology, frequency, timing parameters

Sucking is one of the first coordinated muscular activities in infants, already observable in fetuses as young as 13 weeks.[1,2] Similar to other rhythmic actions (eg, locomotion), sucking is generally considered to be controlled by an innate neural network known as central pattern generator (CPG).[3] In human infants, there are 2 main types of sucking.[4] Nonnutritive sucking (NNS) is an ororhythmic behavior already occurring in utero. It is organized in bursts consisting of 6 to 12 suck cycles that occur at approximately 2 Hz, followed by pause periods.[5,6] Development of nutritive sucking (NS) begins later and finalizes at fluid intake. It comprises expression or the combination of suction and expression for fluid intake.[7,8] Suction is the negative intraoral pressure generated by lowering the tongue and jaw and closure of the nasopharynx to draw milk out, while expression is the stripping/compression of the nipple between the tongue and the hard palate to eject milk.[9,10]

To be effective, NS generally requires the infant to have mature and functional neural networks and coordinated swallowing and breathing.[11] For the successful development and function of NS, the organization of the suck, swallow, and respiration must occur at 2 levels. First, each of the 3 components must be well established for their synchronous function. Second, this cumulative mechanism function must be still effective with the introduction of the bolus to support transfer to the stomach.[12]

Because of the immaturity and significant medical needs of infants hospitalized in the neonatal intensive care units, these skills are not well established, especially in preterm infants, defined as neonate born prior

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to 37 weeks of gestation (GA), and can represent an important hurdle in their early development.[13] Chronic lung disease, infections, neurologic disorders, infections, and necrotizing enterocolitis are associated with feeding dysfunctions and neurodevelopmental outcomes in later childhood.[14] Infants in all categories of prematurity, including extremely preterm (<28 weeks of GA), very preterm (28 to <32 weeks of GA), moderate (32 to<34 weeks of GA), and late preterm (34 to < 37 weeks of GA), may require support for the attainment of coordinated sucking for functional and effective breastfeeding or bottle-feeding.[13-15,16]

Recent evidence suggests that GA age at birth and birth weight are the strongest predictors of the time for the transition from tube feeding to the first oral feeding and subsequent oral feeding independence. And while the achievement of oral feeding is typically one of the primary requirements for the discharge of a neonate, the initial neonatal intensive care unit discharge to home may take place while infant remains feeding through the feeding tube. This increases the risk of an increased rate of emergency department visits and rehospitalisation[17] and puts the feeding tube–dependent infants at an increased risk of significant neurodevelopmental challenges.[18]

Infants who were dependent on an orogastric tube upon discharge were recently reported to have significantly lower cognitive, communication, and motor scores on a standard developmental assessment at 2 years, independent of infant's brain injury and overall illness.[18] Therefore, the dependence on orogastric technology upon discharge presents long-term difficulties for the infant's neurodevelopment and the family overall.[17] Up to 40% of infants referred to feeding clinics in early months of life are reported to have been born preterm.[14] This is consistent with preterm birth often being accompanied by a number of medical and neurodevelopmental needs that have long-term developmental consequences, ranging from mild delays in general developmental that are overcome with supportive rehabilitative services to permanent disorders and disabilities.

Therefore, numerous studies have focused on intervention strategies to facilitate oral feeding of preterm infants while still hospitalized in the neonatal intensive care unit.[19] In particular, NNS via pacifier has been consistently proposed as an intervention to improve sucking in preterms and was found to decrease length of hospital stay and to facilitate the transition to full oral-/bottle-feeds.[20-22] Similarly, strategies based on sensorimotor inputs (such as cheek/chin support, oral, tactile, kinesthetic, auditory, and vestibular, and/or visual stimulation) were utilized in other studies showing beneficial effects on qualitative aspects of oral feeding performance in preterm infants.[23-27]

What This Study Adds

- Further studies on sucking interventions in preterm infants should include both direct and indirect quantitative and qualitative outcome parameters to maximize the evidence and increase the impact on clinical practice. Collecting data on the efficiency, morphology, and frequency parameters may be used to objectively determinate preterm infant's sucking skills.

Several studies have demonstrated that early intervention strategies have beneficial effects on the oral feeding performance of preterm infants, and the majority of them used qualitative assessments as the primary outcome measures. A recent systematic review of NNS interventions and the effect on the physiologic stability of preterm infants showed significant decrease in the length of hospital stay and facilitation of the transition from gavage or partial oral feeds to full oral feeds, with limited information on the basic mechanisms underlying the observed improvements.[21] Similar results of improvements of some of the feeding/swallowing variables were reported in another review article exploring the effects of a wider range of interventions, namely, NNS and oral/perioral stimulation.[28] Yet, another Cochrane review reported benefits of NNS outweighing nonoral interventions and standard of care in regard to transition to oral feeding and duration of the initial hospitalization.[20]

A number of previous systematic reviews and meta-analyses have been published with valuable information about the types and outcomes of developmental interventions provided to preterm infants with oromotor or feeding difficulties, the use of pacifiers, and specific intervention protocols. In general, their conclusions show that interventions are promising for enhancing feeding performance in preterm newborns, although methodological heterogeneity and variations in results across studies hamper the application and the selection of the most appropriate intervention across preterm populations.

However, no review has focused on the quantitative categories of suck performance. This information may be useful in the implementation of early treatment and more individualized strategies of interventions. Therefore, the current review was designed to review preterm infant intervention studies with quantitative outcomes of sucking performance to summarize the evidence of the effect of interventions on specific components of sucking including efficiency, morphology, frequency, and timing parameters of preterm neonate feeding. These parameters are directly related to the infant nutrition capacity and therefore have a significant clinical relevance. Furthermore, to fill the gap in knowledge of the quantitative parameters of sucking maturation, this review included only randomized controlled trial designs of NS and NNS interventions with preterm infants with quantitative outcomes of sucking performance.

METHODS

Literature Search

Studies were identified by searching PubMed, CINAHL, MEDLINE, EMBASE, and PSYCOLIST databases. The searches were limited to peer-reviewed publications in English and included articles published through August 2017. References were exported into a bibliographic management database and duplicates were removed. The search strategy was performed using the following Medical Subject Headings (MeSH) terms: ("preterm infants" *or* "preterms" *or* "prematurity newborns") *and* ("sucking" *or* "suck" *or* "oral feeding skills") *and* ("intervention" *or* "training").

Study Selection

Criteria for inclusion in the study were established prior to the literature search. Inclusion was limited to randomized controlled trial designs. Studies were selected if they fulfilled the following criteria: (i) involved infants born preterm (gestational age at birth below 37 weeks), (ii) tested experimental interventions to improve sucking or oral feeding skills, and (iii) included quantitative outcome measure based on objective parameters of sucking performance.

Studies were excluded if they were protocols, not in English, did not include preterm infants, or were any study design other than randomized.

Validity Assessment

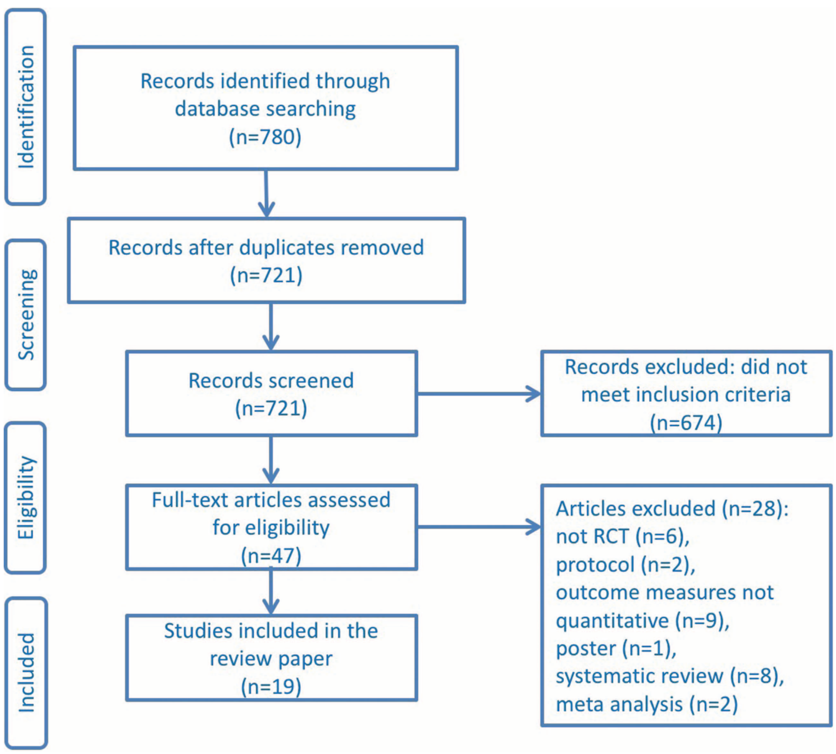
The methodological quality of the studies was assessed using the Cochrane Collaboration's tool[29] for assessing risk of bias and the following criteria were considered: sequence generation, allocation concealment, blinding of participants, personnel and outcome assessors, and completeness of outcome data. Each criterion was judged as "yes," "no," or "unclear." Two review authors separately assessed each study, and disagreement was resolved by discussion together with the senior author.

RESULTS

Description of Studies

The PRISMA flow diagram of the review process is reported in Figure 1. The search, completed in September 2017, yielded 780 articles, and then 59 duplicates were removed. Two authors independently reviewed 721 articles on the basis of the titles

FIGURE 1



Records search and inclusion chart. Description: The flowchart outlines the process of the records search, screening, review, and inclusion. RCT indicates randomized controlled trial.

and abstracts, and selected 47 articles. Full texts of the selected articles were analyzed by 2 reviewers and the eligibility of the study inclusion was assessed independently; in case of mismatched opinion, consensus was reached after discussion. Twenty-eight of the 47 articles were excluded on the basis of failure to meet the inclusion criteria.

In particular, we excluded these studies because 6 were not randomized controlled trials, 2 were protocols, 9 did not include quantitative outcome measures, 1 was a poster, 8 were systematic reviews, and 2 were meta-analyses. The remaining 19 studies were included in this review: 15 randomized, 1 quasi-randomized, and 3 crossover randomized controlled trials.[5,7,30-46]

The methodological quality of the selected studies was evaluated as reported in Table 1. All studies had risk of bias in at least 1 of the 4 items.

Most of the studies involved low-risk preterm infants, and 2 studies included preterm infants with either specific respiratory pathology or with low birth weight.[5,41-43] Sample sizes ranged from 11 to 230 preterm infants. The types of interventions were grouped into 6 categories on the basis of their features: (i) NNS, (ii) NNS with auditory reinforcement, (iii) sensorimotor stimulation, (iv) oral support (OS), (v) combined training, and (vi) NS. Interventions occurred before, during, or after feeding (either by orogastric tube or bottle-feeding), or outside of the feeding times. Figure 2 summarizes the results of the review by category (efficiency, frequency, morphology, and duration).

Very preterm infants were included in 19/19, extremely preterm were included in 11/19, moderately preterm were included in 11/19, and late preterm were included in 2/19 included studies. Since all of the studies the majority of the included infants were born at the very preterm GA age category, we did not identify any patterns of the type of training and its effectiveness as it relates to the GA age at birth. Table 2 summarizes the population, intervention/s, and outcome measures of the included studies.

Outcome Parameters

In accordance with the specific aims of our review, we selected all outcome measures consisting of quantitative parameters. Based on their characteristics, sucking parameters were subdivided into 4 groups: (i) efficiency, (ii) frequency, (iii) morphology, and (iv) duration. They are described both in NS and the NNS.

Efficiency parameters were defined as those strictly related to the infant nutrition capacity, including milk volume measures and parameters referred to the coordination of sucking and swallowing. Frequency parameters were defined as those exploring the occurrence of a periodic event per unit time (burst, pause, suck, expression, and suction). Some of these parameters describe the whole sucking pattern (the alternation of sucking burst and pause) or the single suck cycle (alternation of expression and suction phases). Morphology parameters were defined as those describing the shape, size, and phase distribution of the sucking curves, including either suction/expression amplitude or pressure. Finally, duration parameters were defined as those exploring the time length of all events related to sucking (Table 3).

Effects of the Different Types of Intervention

Nonnutritive Sucking

Nonnutritive sucking alone was evaluated in 6 studies, generally consisting of a brief intervention before infant's feedings. Training modalities were heterogeneous and their total duration ranged from 5 days to 1 week, performed for 2, 5, or 15 minutes before feedings. Overall, NNS training studies showed inconsistent effects on quantitative outcome measures.

Four efficiency parameters were identified in 5 studies. The parameter reported to have been significantly affected by the training was the formula taken at first 5 minutes (1 study). The parameters unaffected by the training were overall transfer (4 studies) and proficiency (2 studies). One parameter, namely, rate of transfer, was affected in 1 study and unaffected in another 2. Three frequency parameters were explored in 2 studies. The parameter significantly affected by the training was frequency of pauses in NS (1 study). Two parameters, namely, frequency of bursts in NS and frequency of sucks per burst in NS, were affected in 1 study and unaffected in the other. Only 1 morphology parameter, suction

TABLE 1. Risk of Bias Assessed by the Cochrane Collaboration Tool[a]

Study (see Table 2 for Reference)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Adequate sequence generation?	X	X	✓	✓	U	X	U	U	✓	✓	✓	✓	X	✓	U	U	U	✓	✓
Allocation concealment?	U	✓	✓	✓	✓	U	U	U	U	U	U	✓	U	✓	U	X	U	U	✓
Blinding? All outcomes	✓	✓	U	X	X	X	U	✓	X	X	U	X	X	✓	X	X	✓	✓	✓
Incomplete outcome data addressed? All outcomes.	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X	✓	U	✓	X	X	X	U

[a]✓: low risk of bias; X: high risk of bias; U: uncertain risk of bias.

FIGURE 2

Study number (see table 3 for ref)	13	11	15	16	5	19	18	6	9	10	3	1	2	14	19	7	4	9	10	11	4	19	9	10	4	12	17	13	8
	NNS	NNS	NNS	NNS	NNS	NNS	NNS PAL	NNS PAL	EO	EO	IO	IO	IO	IO	PO IO	PO IO	PO IO	PO IO EO	PO IO EO	OS	OS	PO IO NNS	PO IO NNS	PO IO NNS	PO IO OS	PO IO NNS	PO IO NNS	NS	NS
EFFICIENCY																													
Mean Volume/Suck (first 5')																										●			
Expressions/Swallows										○									○					○					
Suck Stability										○									○					○					
Overall Transfer	●		●	●		●			○						●	○		○				●	○			●		○	○
Proficiency	●					●			○						●			○				○	○					○	
Rate of Transfer	●			●		○	○	○	○						○	○		○				○	○			●		○	○
Oral Volume Intake							○	○									○				○				○				
Volume Loss									○									○					○						
Formula taken (first 5')		○																		○						○			
FREQUENCY																													
num suction/s (NS)																○													○
num expression/s (NS)																○													○
NS num suck/burst		○		●							○									○									
num NS bursts		○		●																○									
num NS pauses		○																		○									
num NNS cycles/min												○	○	○															
Mean NNS cycles/burst												○																	
num sucks/min (first 5')																										●			
Expression Freq. (NNS)												○	○	○															
num NNS bursts/min												○	○	○															
num feeds/day								○									○				○				○		●		
MORPHOLOGY																													
Expression amplitude										○						○			○					○					
Suction amplitude					○					○						○			○					○					●
NNS Mean Pressure								○					●																
Mean max NNS Pressure											○						○				○				○				
DURATION																													
NS Pause Duration		●																		○									
NS First burst Duration			○	●																									
NS Burst Duration		○		●																○									●
Feeding Duration		○	●				○													○						●			○
Mean sucking activity (%)																	○				○				○				

Results of the review by category. EO indicates extraoral; IO, intraoral; MS, multisensory; NNS, nonnutritive sucking; NS, nutritive sucking; OS, oral support; Overall transfer, % volume taken/volume prescribed; PAL, pacifier-activated lullaby; PO, perioral; Proficiency, % volume taken within 5′/volume prescribed; Rate of transfer, volume taken per minute; Suck stability, mean time from expression to swallow; T, time; Volume loss, volume prescribed-volume taken; ●, parameter not significantly affected by training; O, parameter significantly affected by training.

amplitude, was explored (1 study) and was found to be affected by the training. Four duration parameters were explored in 3 studies. The parameters significantly affected by the training were pause duration (1 study). The only parameter unaffected by the training was pause duration in NS (1 study). Three parameters, namely, first burst duration in NS, burst duration in NS, and feeding duration, were affected in one study and unaffected in another.

NNS With Auditory Reinforcement

Nonnutritive sucking with auditory reinforcement was explored in 2 studies. They used a pacifier adapted so that a suck of predetermined strength activated an audio player with lullabies[36] or mother's voice.[37] Infants were trained for 15 to 20 min/d, in a range of 15 to 45 min before feedings, for 5 days.

Nonnutritive sucking with auditory reinforcement trainings showed significant effects on all quantitative outcome measures explored. In particular, they were found to be effective on rate of transfer and oral volume intake (efficiency parameters), number of feeds per day (frequency parameter), mean pressure in NNS (morphology parameter), and feeding duration (duration parameter).

Sensorimotor Stimulations

Sensorimotor stimulation programs were explored in 11 studies, some of which assessed more than 1 training type. Sensorimotor stimuli consisted of oral/intraoral (O/IO), perioral (PO), or extraoral inputs. The O/IO was generally based on gum and tongue stimulation that could be delivered by therapist's hands or via a pacifier. Barlow et al[5] applied an intraoral stimulus through a specific pacifier, a 'pulsating nipple' programmed to mimic the temporal features of a well-formed NNS burst. The treatment was administered for 3-minute epochs for 3 to 4 times per day for 10 days. Perioral stimulation programs, instead, were variable and composed of stroking and stimulating infants' cheeks and lips. In 3 studies,[7,35,38] the perioral stimulation was associated with an oral one. Treatment duration ranged between 10 and 14 days for 12 to 30 minutes per session. Finally, an extraoral

TABLE 2. Included Studies

	Author	Population/GA	Age at Assessment/ Outcome	Type of Training	Outcome Measures	Design
1	Barlow et al (2008)[5]	31 Very Preterm infants 2 groups: treatment (20) GA (29.11 ± 2.32) or Control (11) (29.24 ± 3.10) birth GA	Treatment: Pre (34.84 ± 2.10) Post (38.10 ± 2.27) PMA Control: Pre (34.67 ± 2.65) Post (38.24 ± 1.48) PMA	T: patterned oral somatosensory stimulation during gavage feeds with device: 3 min. Epochs 3-4 times daily for 10 d. C: Soothie pacifiers during gavage feeds	(1) Total oral compression, (2) non-NNS compression per minute, (3) burst cycle per minute, (4) NNS bursts per minute, (5) mean cycle per burst, (6) NNS cycles % total, (7) daily % oral feed	RCT
2	Barlow et al (2014)[41]	160 preterms 23-37 births GA 3 groups: 39 HI 49 respiratory distress syndrome (RDS), 74 chronic lung disease (CLD)	HI: mean 222.1 d RDS: mean 214.5 d CLD: mean 188.1 d	Ntrainer pneumatically pulsed pacifier stimulation during gavage feeds, or control sham with Soothie pacifier, 3 times daily for 10 d	(1) Total oral compressions: sum of all pressure events per minute, (2) NNS cycles: suck compression cycles with cycle periods 1200 ms and occurring within the NNS burst structure per minute, (3) number of NNS bursts: nipple compression cycles. NNS performance: (4) mean number NNS cycles/burst, and (5) NNS pressure amplitude (cmH2O)	RCT
3	Barlow et al (2017)[45]	180 extremely preterms: 24-29 births GA 2 groups: treatment or sham control	3 times weekly for 4 wk, from 30 wk PMA	Ntrainer pulsed orocutaneous simultaneous or sham with tube feedings 3 times daily for 4 wk	(1) Salivary gene expression profiles, (2) number of NNS bursts, (3) NNS cycle events, (4) total oral compressions, and (5) NNS compression pressure	RCT
4	Boiron et al (2007)[38]	43 preterms 29-34 births GA 4 groups: Stimulation + support: n = 14 Stimulation, n = 11 Support, n = 10 Control, n = 13	Stimulation + Support: 33.3 PMA Stimulation: 33.4 PMA Support: 33.3 PMA Control: 33.1 PMA	Oral stimulation: 12 min once daily, 30 min before gavage, for the last 14 consecutive days of the period of gavage. Oral support twice daily for a maximum of 10 min, with at least 1 bottle session between during the transition period until autonomous feeding	(1) Maximum pressure for each suck burst (mm Hg), (2) burst duration for each sucking burst, (3) number of bottle feeds taken daily, and (4) quantity of milk ingested per day	RCT
5	Bernbaum et al (1983)[34]	30 preterms (birth weight <1500 g) 2 groups: Treatment and control: mean 31.5 ± 1.3 and 31.5 ± 1.6 birth GA	Weekly assessment 34-38 wk PMA	Treatment: oral stimulation: pacifier during all gavage feeds Controls: gavage feedings without oral stimulation	(1) Expression frequency of NNS, (2) NNS bursts per minute, (3) Number of NNS cycles per minute, and (4) NNS mean pressure Sucking patterns classified as organized or sporadic	RCT

(*continues*)

TABLE 2. Included Studies (*Continued*)

	Author	Population/GA	Age at Assessment/ Outcome	Type of Training	Outcome Measures	Design
6	Chorna et al (2014)[37]	94 preterms 34-36 wk GA 2 groups: PAL or control	24 h after the training period	PAL group: 5 daily 15-min sessions Control: routine NNS sucking	(1) Oral feeding rate, (2) volume of oral intake measured during 24 h after the last intervention, (3) number of oral feedings daily, and (4) suck pressure measured only in the intervention group	RCT
7	Fucile et al (2005)[7]	32 preterms 26-29 wk birth GA 2 groups: experimental or sham	Experimental 36.1 ± 1.8 PMA Control: 36.9 ± 1.8 PMA	Experimental: nonnutritive oral stimulation or sham control. Both started prior to oral feeds, once daily for 10 d, 15-30 min before a tube feeding	(1) Overall intake (volume taken/volume prescribed, %), (2) rate of milk transfer (mL/min), (3) sucking frequency, (4) amplitudes of suction, and (5) expression (mm Hg)	RCT
8	Fucile et al (2009)[44]	30 preterms 26-29 wk birth GA 2 groups: CFVFB (controlled flow vacuum-free bottle system) and SB (standard bottle)	Suck assessment when 1-2 and 6-8 oral feedings per day. Mean PMA of CFVFB 34.2 ± 0.8, SB group: 34.3 ± 1. Postassessment CFVFB: 36.8 ± 2 PMA, SB: 36.3 ± 1.5 PMA	The CFVFB: nipple-bottle system that delivered milk to the nipple chamber from an open reservoir that was adjusted such that the milk level was maintained continually at the level if the infant's mouth.	(1) Overall transfer (percent volume of milk taken over the prescribed volume), (2) rate of milk transfer (volume transferred per unit time mL/min), (3) frequency of suction (#S/s), (4) expression (#E/s), (5) suction amplitude (mm Hg), and (6) sucking burst duration	RCT
9	Fucile et al (2011)[39]	75 preterms, mean birth GA 29 ± 0.3 wk 4 groups: Oral (O), tactile/kinesthetic (T/K), combined O + T/K, and control	Suck assessment performed serially, started at mean 33.2-34.2 PMA	O: twice daily stroking of the cheeks, lips, gums, and tongue for 12 min, NNS for 3 min. T/K: twice-daily stroking of the head, neck, back, arms, and legs for 10 min and passive range of motion to the limbs for 5 min. Combined: 15 min of O or T/K each once a day, in random order. Control: placing her hands in the incubator without touching infant for 15 min twice daily	(1) Proficiency (volume of milk taken during the first 5 min as a percentage of the total), (2) volume transfer (volume consumed as a percentage of the prescribed volume), (3) rate of transfer (volume of milk consumed relative to the duration of the oral feed session [mL/min]), and (4) volume loss	RCT

(*continues*)

TABLE 2. Included Studies (*Continued*)

	Author	Population/GA	Age at Assessment/ Outcome	Type of Training	Outcome Measures	Design
10	Fucile et al (2012)[40]	75 preterms, mean birth GA 29 ± 0.3 wk 4 groups: Oral (O), tactile/kinesthetic (T/K), combined O + T/K, and control	When infants taking 1-2, 3-5, and 6-8 oral feedings per day	O: twice-daily stroking of the cheeks, lips, gums, and tongue for 12 min, NNS for 3 min T/K twice-daily stroking of the head, neck, back, arms, and legs for 10 min and passive range of motion to the limbs for 5 min Combined: 15 min of O or T/K each once a day, in random order. Control: placing hands in the incubator without touching infant for 15 min twice daily	(1) Suction amplitude, (2) expression amplitudes (mm Hg), (3) suck-swallow ratio, (4) stability of suck-swallow interval	RCT
11	Hill et al (2005)[31]	156 preterms: 29.98 ± 2.78 to 30.33 ± 2.54 wk birth GA 3 groups: Oral support (OS), NNS, control	Before intervention, immediately after, and at 1-wk follow-up. The Postnatal Baseline at 23.4 ±16.86 d with NNS, at 26.35 ± 16.86 d in the OS and at 23.81 ± 15.25 d in the controls	7-d intervention of oral support or NNS	(1) Formula taken during the first 5' (2) total length of feeding time and nutritive sucking patterns (registered by a stretch-sensitive gauge WMSG) (3) NS number of suck/burst, (4) number of NS bursts, and (5) number of NS pauses	Quasi-RCT
12	Hwang et al (2010)[42]	19 preterms, mean birth GA 28.1 ± 2.6 wk	Ranged 32.3-40.3 wk PMA (mean: 5.8 ± 1.8)	Transition to full oral feeding, participants served as own controls. A 5-min oral stimulation applied before feedings. Oral stimulation: 3 min of manual peri- and intraoral stimulation, 2 min of sucking on a pacifier	(1) Sum feeding duration in minutes, (2) % of prescribed volume ingested (mL/min), (3) sucking frequency, and (4) mean volume ingested per suck (mL per suck). Level of alertness coded from videotaped observations based on a modification of the Neonatal Behavioral Assessment Scale	Crossover RCT
13	Lau and Smith (2012)[30]	70 very low birth-weight preterm infants 24-33 wk birth GA 3 groups: swallowing, sucking, control	Feeding monitored when infant reached 1-2, 3-5, and 6-8 oral feedings per day	Swallowing group: placing a milk bolus (0.05-0.2 mL) on the tongue where the bolus rests before entering the pharynx 15 min/d, 5 d weekly Sucking group: active sucking on a pacifier 15 min/d, 5 d weekly Control group: standard care	(1) Days from start to independent oral feeding, (2) total volume prescribed, (3) volume taken at 5 min, (4) volume taken during entire feed (mL), and (5) duration of oral feeding (min) Parameters indicative of performance: (a) overall transfer (% volume taken per volume prescribed), (b) proficiency (PRO, % volume taken at 5 min per volume prescribed), and (c) rate of transfer (RT, mL/min) over the entire feeding	RCT

(*continues*)

TABLE 2. Included Studies (*Continued*)

	Author	Population/GA	Age at Assessment/ Outcome	Type of Training	Outcome Measures	Design
14	Medoff-Cooper et al (2015)[46]	230 prematures 29-34 wk birth GA 2 groups: ATVV (auditory, tactile, visual, and vestibular) or control	Mean PMA: 9.29 d/33.89 wk at baseline assessment	ATVV: 10 min of auditory (female voice), tactile (moderate touch stroking or massage), and visual (eye to eye) stimulation, followed by 5 min of vestibular stimulation (horizontal rocking) Controls: standard feeding and nursing care	(1) Number of sucks, (2) number of sucks per burst, (3) sucking maturity index, and (4) suck pressure	RCT
15	Pickler et al (1996)[32]	13 preterms, 28-34 wk birth GA Prefeeding NNS or no prefeeding NNS	1-38 d PMA (mean: 17.5 ± 11)	Prefeeding NNS: offered the infant a pacifier for 2 min Control: no prefeeding NNS	Feeding performance: (1) the initiating of nutritive sucking, (2) duration of first nutritive suck burst, (3) duration of the bottle-feeding, (4) the percentage of prescribed formula consumed, (5) behavioral organization (heart rate and oxygen saturation), and (6) behavioral state (level of arousal and wakefulness on the Anderson Behavior State Scale)	Crossover RCT
16	Pickler and Reyna (2004)[33]	10 preterm infants, 28-31 wk birth GA	33-40 wk PMA (mean: 36 ± 2.2) at observation	NNS condition was offered for 2 min before bottle-feeding. At another feeding, no NNS was offered. The 2 feedings occurred within 24 h of each other	Characteristics of NS (1) number of suck/bursts, (2) sucks/burst, (3) suck/burst length, feeding efficiency, (4) percentage of prescribed formula consumed, (5) formula consumed per minute of feeding, (6) number of breath bursts, (7) breaths/burst, and (8) breath burst length	Crossover RCT
17	Rocha et al (2007)[43]	98 very low birth-weight preterm infants, 26-32 wk birth GA 2 groups: treatment or sham control	Baseline (when reached a full enteral diet (100 kcal/kg/d), postintervention	Treatment: sensory-motor-oral stimulation + NNS Control: gavage tube diet + sham procedure Sessions were15 min daily for 10 d	(1) Number of feeds per day	RCT
18	Standley (2003)[36]	32 prematures (poor feeders) mean birth GA 31.7 wk 2 groups: Pacifier Activated Lullaby (PAL) or control	Assessment: at a mean 30.8-d PMA	PAL: 15- to 20-min trial between 4 pm and 5 pm, 30-60 min before feed trial Control: standard of care	(1) Nutritional amount ingested, (2) length of feeding time, and (3) feeding rate	RCT

(*continues*)

TABLE 2. Included Studies (*Continued*)

	Author	Population/GA	Age at Assessment/Outcome	Type of Training	Outcome Measures	Design
19	Zhang et al (2014)[35]	120 preterm infants 29-34 wk birth GA 4 groups: NNS, oral stimulation, NNS + OS, control	Assessment: at baseline, after 3 d, after 6 d, at full oral feed	NNS: sucking on pacifiers for 5 min 7-8× daily Oral stimulation (OS): stroking the cheeks, lips, gums, and tongues 12 min Combined: NNS + OS Control	(1) Transition time (d), (2) milk transfer (mL/min), (3) proficiency (intake first 5 min per volume ordered), (4) volume transfer (volume transferred during entire feeding/volume prescribed), (5) weight, and (6) length of stay	RCT

Abbreviations: CFVFB, controlled- flow vacuum-free bottle system; GA, gestation age; HI, healthy preterms; NNS, nonnutritive sucking, NS, nutritive sucking; OS, oral stimulation; PMA, postmenstrual age; RCT, randomized controlled trial; SB, standard bottle; WMSG, Whitney mercury strain gauge (WMSG)

stimulation program implemented by Fucile and colleagues[44] included sensorimotor tactile input to the infants' head, neck, trunk, and limbs, even in combination with IO/PO stimuli. The treatment duration was 12 minutes, twice daily, for 10 days.

Studies in this group showed significant effects of sensorimotor training on the majority of quantitative outcome measures explored.

Seven efficiency parameters were explored in 5 studies and were all found to be significantly affected by the training, except for the overall transfer and proficiency that were unaffected in 1 study.[35] Seven frequency parameters were explored in 5 studies and were all found to be significantly affected by the training. Four morphology parameters were explored in 4 studies and were all found to be significantly affected by the various sensorimotor trainings with the exception of mean NNS pressure, which was unaffected in 1 study.[41] A single duration parameter, mean sucking activity, was explored in one study[38] and was found to be improved by the training.

Oral Support

Oral support was assessed in 2 studies and consisted of cheeks and chin support during feeding sessions. Studies used different treatment duration and time distribution.

The efficiency parameters explored, formula taken at first 5 minutes in one and oral volume intake in the other, were significantly affected by the training. Frequency (4 parameters), morphology (1 parameter), and duration (4 parameters) were explored in both studies and were always found to be significantly affected by the training.

Combined Training

Seven studies combined sensorimotor stimulation with either NNS (5 studies) or OS (1 study) or with other stimuli (1 study).

Nine efficiency parameters were explored in 5 studies and were all found to be significantly affected by the training. The exceptions were overall transfer, unaffected in 2 studies, and mean volume per suck and rate of transfer, unaffected in 1 study. Three frequency parameters were explored in 4 studies. Frequency of sucks per burst was affected in 1 study.[46] Frequency of sucks per minute was unaffected (1 study) and frequency of feeds per day was unaffected in one and unaffected in the other study. Three morphology parameters were explored in 3 studies and were all found to be significantly affected by the different types of trainings. Two duration parameters were explored in 2 studies. Mean sucking activity was affected (1 study) and feeding duration was unaffected (1 study).

Nutritive Sucking

Two studies applied an NS intervention.[30,44-46] The swallowing program consisted of placing a milk

TABLE 3. Assessment Parameters Classification

Parameters Classification	Definition for the Purpose of This Review
Efficiency	Infant nutrition capacity: milk volume and sucking and swallowing coordination
Frequency	Periodic event per unit of time: burst, pause, suck, expression, and suction
	Describe the entire progression of the sucking pattern (eg, sucking burst and pause) or a single suck cycle (eg, expression and suction)
Morphology	Shape, size, and phase distribution of sucking curves
	Includes either suction/expression amplitude or pressure
Duration	Length of time of all events related to sucking

bolus on the tongue to facilitate swallow mechanisms for 15 minutes for 5 days. The intervention proposed by Fucile et al[44] was based on a particular device, a controlled flow vacuum-free bottle system, capable to maintain milk continually at the level of the infant's mouth. The experimental group received feeding session with this device for 20 minutes.

Both of the studies demonstrated a good effect on efficiency outcome parameters, in particular, in overall transfer and rate of transfer. The swallow program also demonstrated an effect on proficiency outcomes. Fucile and colleagues[44] also reported significant differences between experimental and control groups in frequency outcomes (suction frequency and expression frequency) and in feeding duration. However, no differences were found in suction amplitude and NS burst duration.

DISCUSSION AND CONCLUSIONS

The main aim of this systematic review was to determine the effects of early intervention on quantitative parameters of sucking in preterm infants as reported by randomized controlled designs studies. In general, the results demonstrate that most types of interventions aimed at improving sucking in preterm infants yield significant effects on quantitative parameters of sucking, with the exception of trainings based exclusively on NNS. The studies using NNS-only training report inconsistent results. Of the 12 different outcome parameters explored in those studies, 3 were positively affected by training, 3 were not affected by training, and the remaining 6 showed inconsistent results among studies.

It is of interest that the types of parameters most frequently found to be unaffected by the NNS-only training were the efficiency parameters, which are considered to be most directly related to the infant nutrition capacity and therefore may have the highest clinical relevance. Our findings might appear in conflict with other reviews, which found significant reduction of premature infants' length of hospital stay and improved bottle-feeding performance and transition from tube to bottle as potential positive clinical outcomes of NNS training.[21-28] However, these outcome measures are not comparable with the objective sucking parameters explored in our review, as most of them represent general clinical variables. Moreover, clinical quantitative variables, such as weight gain, energy intake, oxygen saturation, or intestinal transit time, were not found to be affected by the training.

One of the proposed reasons for the limited effect of NNS-only trainings on sucking parameters is habituation to the teat.[47] In this view, the positive effect of NNS on sucking in the trained infant gradually fades out and a novel stimulus is necessary to revitalize the sucking behavior. This interpretation aligns with many studies in which NNS was coupled with sensorimotor reinforcement (ie, sensorimotor stimulation, OS) and showed significant effects of training on sucking parameters. In those studies, the reinforcement provided by the sensory stimulation, which was human-mediated in the great majority of the cases, is likely to be responsible for the persistence of the positive effects on sucking patterns. This is also confirmed by the results obtained with interventions based on NNS with auditory reinforcement. Music or mother's voice was used as a contingent reward to promote NNS during the intervention sessions.

Following NNS, which was the most common intervention in our review (13/19 studies), sensorimotor stimulation was the second most common intervention, applied in 11 out of 19 studies. Most sensorimotor stimulation programs showed to positively affect sucking performance. This applied to all 4 domains explored and, in particular, to morphology and frequency. This finding is consistent with another recent review of oral motor interventions with preterm-born infants that highlighted quantitative parameters of oral feeding success.[48] The sensorimotor stimulation seemed to be effective irrespective of the stimulated region, that is, intra-, peri-, or extraoral. This might suggest that benefits could be related to a broader effect of the intervention on the infant's state regulation rather than a direct effect on the coordination of sucking. Also, a critical role is played by the adult-infant relationship, as the sensorimotor stimulation involved a human caregiver. It

Summary of Recommendations for Clinical Practice and Research	
What we know:	• A variety of interventions are effective in enhancing quantitative aspects of sucking. Efficiency parameters are the most frequently explored, as they are directly related to the infant nutrition capacity and therefore have the highest clinical relevance. • Efficiency parameters are positively influenced by most types of interventions, although less affected by NNS training only.
What needs to be studied:	• Further characterization of the most useful treatments to improve sucking skills, in terms of treatment features, duration, intensity, and type of administration. • Tailored approaches based on individual sucking pattern and infant clinical comorbidities.
What can we do today:	• Include quantitative parameters including efficiency, morphology, and frequency into clinical sucking assessments. • Take efficiency, morphology, and frequency parameters of sucking into consideration when making decisions about the most appropriate intervention for the patient.

is noteworthy, however, that the training was also effective in the 3 studies adopting a mechanical device to provide the intraoral stimulation.[5,41,45]

Two of the 11 studies using sensorimotor stimulation, either alone or in combination, showed predominantly nonsignificant results. Hwang et al[42] found no effects of combined training (PO/IO + NNS) in efficiency, frequency, and time but reported an increase of formula intake in the first 5 minutes of a feeding as a result of the training intervention. This apparently conflicting finding may be due to the small sample size ($n = 16$) and heterogeneous infant clinical characteristics. Nonsignificant results were also reported by Rocha and colleagues[43] although their study explored only 1 quantitative parameter (the number of feeds per day), and the quality of the study was low.[43]

Both studies[31-38] assessing the effects of OS showed improvements in all areas of sucking performance, both when the training was used in isolation and when it was combined with oral stimulation. Oral support seems to provide the necessary stability for the jaw and to assist the infants in maintaining a more organized sucking pattern. Also, NS studies generally report positive effects on sucking performance, although the small number of studies and the different types of interventions do not allow for definitive conclusions.

Several limitations need to be considered in the interpretation of the results of this review, principally related to the heterogeneity of the reviewed studies. For example, sample size ranged from 10 to 160 preterm infants and subject characteristics were not homogeneous, particularly in terms of gestational age at birth, birth weight, and respiratory support. Quantitative outcome measures were also very heterogeneous and were assessed differently, preventing the possibility to perform a meta-analysis. Lastly, this review does not include information about the practices of breastfeeding versus bottle-feeding methods, as this was outside of the scope of this work. Most institutions caring for hospitalized infants provide or have information about the community source of supportive and rehabilitative services, including lactation specialists, speech-language pathologists, occupational therapists, and other professionals. These services assist mothers and primary caregivers in informed decision making and provide information and support to ensure successful feeding methods for their infants.

In conclusion, the evidence indicates that a variety of interventions, based on different principles and methodologies, are effective in enhancing quantitative aspects of sucking. Efficiency parameters are the most frequently explored, as they are directly related to the infant nutrition capacity and therefore present the highest clinical relevance. They are positively influenced by most types of intervention, though are less affected by NNS training only. Frequency, morphology, and efficiency parameters outline some of the mechanisms of functional sucking but are infrequently investigated. Future studies may benefit from the concurrent exploration of the different types of outcome measures. This could serve as a support for a better tailored therapeutic approach consisting of the selection of more personalized interventions based on a pretraining profiling of the specific sucking components that are compromised or weakened.

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