JOHNS HOPKINS ALL CHILDREN'S HOSPITAL

Oral Immune Therapy (OIT) with Mother's Own Milk (MOM) for Neonates Clinical Pathway

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(TITLE) Clinical Pathway

Rationale

Oral immune therapy (OIT), historically referred to as "oral care with colostrum/mother's own milk (MOM)" at JHACH, is a safe practice to promote immune function in premature neonates when initiated within 48 hours of birth. Current evidence supports this practice in the first seven days of life in neonates who are intubated and/or NPO.

Background / Published Data and Levels of Evidence

Colostrum is a fluid secreted by the mammary glands in the first postnatal days. It is rich in bioactive components that are protective to the newborn, especially those born prematurely. Colostrum and human milk contain cytokines, lactoferrin, immunoglobulins, and growth factors that modulate the immune system and stimulate gastrointestinal development.

There is interest in using colostrum for oral care in premature infants (termed oral immune therapy-OIT) as the oral cavity is an influential site of microbial colonization and the oral mucosa is an important juncture between microbiota, immune factors in colostrum, and the infant's immune system. It is hypothesized that administering colostrum directly onto the oral mucosa may stimulate the oropharyngeal-associated lymphoid tissue system, promote systemic absorption of protective factors through the buccal mucosa and act as a barrier, blocking microbial adhesions to the mucosa.[1]

Published Studies Related to the Use of Colostrum/MOM for OIT

A few studies have explored the potential impact of oral care with colostrum on immune properties. A study of 30 VLBW infants randomized to receive oral care with colostrum or sterile water from day of life (DOL) 2 to 7 found that salivary samples for IgA were significantly higher on DOL 7 with significant increases between DOL 2 to 7 but not from DOL 7 to 14[2] (LOE 2b) in the oral care group. A different study included 48 premature infants (<28 weeks gestation) and also compared oral care with colostrum to sterile water initiated by 48-96 hours of life and continued for a period of three days. Urine and saliva specimens were collected during the first 24 hours of life and at 8 and 15 days. They found that urinary levels of secretory immunoglobulin A and lactoferrin were significantly higher at one week in the colostrum group. Additionally, urine interleukin-1β level, salivary transforming growth factor-β1, and interleukin-8 were significantly lower at two weeks in colostrum group. This study also noted a significant reduction in the incidence of clinical sepsis in oral care with colostrum group (50% vs 92%, P = .003). (LOE2B) The authors suggested that oral care with colostrum might decrease clinical sepsis, inhibit secretion of pro-inflammatory cytokines, and increase levels of circulating immune-protective factors in extremely premature infants.[3]

A third study followed similar methodologies to investigate the benefits of OIT in very preterm infants. One-hundred VLBW infants were randomized to receive colostrum, n=48, (0.2 mL every 4 hours for 15 days) or control group, n=52) which received no colostrum. They looked at serum levels of IgA, IgM, IgG1, lactoferrin, and resistin at enrollment, DOL 3, 15 and 30. They found statistically significant increases of IgA and IgM at DOL 15 and 30 in the study group. Serum lactoferrin was higher in the study group at DOL 3, 15 and 30 however this only reached statistical significance at DOL 30. Resistin levels were significantly higher in the study group at DOL 15 but not at other time points. These authors also found that the colostrum group reached full enteral feedings sooner (7.2 +/-0.6 days) when compared to controls (9.1 +/-0.7 days), P=0.04. There was no difference between groups for NEC, sepsis, respiratory support, retinopathy of prematurity or brain ultrasound results within the study period, the first 30 days of life.[4] (LOE2B)

The impact of oral care with colostrum on clinical outcomes is of interest. In premature infants born < 32 weeks gestational age who received OIT for 3 days beginning at 48-96 hours, length of stay was significantly lower in the intervention group (n=48) 40 days vs controls (n=51) 56 days.[5] (LOE2B) In a retrospective study that compared preterm infant outcomes two years before and two years after the intervention of oral care with MOM as part of the ventilator associated pneumonia (VAP) prevention bundle, there was no difference for sepsis, ventilator days, or length of stay between groups. However the post-intervention group had an increased duration of receiving MOM (median 33 days vs median 15 days in pre-intervention group).In this study, neonates started with OIT in the first 48 hours of life and continued for a period of 5 days. [6] (LOE2B) At present there is no evidence that oral care with colostrum has direct effect on necrotizing entercolitis.[7]

Multiple studies in premature infants have found that oral care with colostrum is a feasible and safe practice when initiated in the first 48 hours of life.[3,8-10]. A small volume of 0.1 to 0.3 ml is gently painted over the tongue, around the gums and along the lips using a sterile swab at least every six hours and as frequently as every two to three hours. A study of 48 VLBW infants compared administration of colostrum via swab or syringe in the first 72 hours of life. They found that syringe administration led to significantly higher urine levels of IgA and lactoferrin at 72 hours of life compared to swab.[11] Infants who are ventilated and/or NPO can receive oral care and if on enteral feeds, this should be coordinated with feeding times. The majority of published studies have provided oral care for a duration of 2-5 days although one continued oral care for 15 days and another until neonates initiated oral feeding.

Gaps in the Scientific Literature

At present, there are no known studies that have investigated the use of donor human milk for oral care. In theory, donor human milk will not provide the same immune enhancing benefits as pasteurization significantly decreases lactoferrin and other immune enhancing factors in human milk. Additionally, there is little supporting the use of OIT longer than the first seven days of life and the ideal duration to provide OIT is not known. There are no known studies exploring the impact of OIT in neonates with conditions such as gastrointestinal surgery or congenital heart disease.

Clinical Management

A. Initiate OIT with colostrum as soon as possible and within 48 hours of birth.
B. OIT using colostrum or MOM should be provided for the first seven days of life for infants meeting one or more of the following criteria:
    a. Intubated
    b. NPO
    c. Receiving only enteral feedings
C. After seven days of life, OIT with MOM may continue until 30 days of age for infants meeting one or more of the following criteria:
    a. Remain intubated
    b. Remain NPO
    c. Are still receiving only trophic enteral feedings
D. OIT should be provided with hands on care, or at least every 6 hours.
E. OIT is not provided with fortified milk or donor milk.
F. OIT is not nutritive and is not to be interpreted as taste stimulation or documented as an oral feeding.
G. Colostrum/MOM will be dispensed by the Milk Depot in 0.2 increments in 1 ml syringes upon provider order.
    a. When enteral feedings reach >40 ml/kg/day the 0.2 ml of milk used for oral care should be taken from infant's syringe after scanning and prior to initiating enteral feeding.
H. The bedside nurse should instruct and supervise the parents/caregivers. Parents should be encouraged to provide oral care.
I. Mothers are urged to bring freshly pumped colostrum to the bedside and provide oral care under supervision. They may also express their colostrum/milk directly at the bedside to administer to the infant.
J. Mothers are encouraged to provide colostrum for their hospitalized neonates whether they plan to breastfeed or not.
K. In the absence of MOM, sterile water can be used to provide oral care but will not provide the equivalent benefit.
L. Discontinue OIT:
    a. When the infant reaches 40 ml/kg of enteral feedings
    b. After 30 days of age in those who remain intubated and/or NPO or on trophic enteral nutrition.

Procedure for Providing OIT

Steps for performing oral care with colostrum or MOM at the bedside:

1. Obtain oral care syringe from designated refrigerator or obtain fresh milk from parent. Do not warm.

2. Perform hand hygiene.

3. Double check the patient identification band, using two patient identifiers and JHACH Breast milk scanning system.

4. Suction excess secretions from the mouth and oropharynx with oral suction device only if needed.

5. Use syringe designated for oral care in neonates with approximately 0.2 ml of colostrum/MOM.

6. Gently drop the colostrum/MOM inside the mouth, including the tongue, gums, and buccal area using a syringe.

7. Milk will be delivered directly by the syringe. Drops of milk into the buccal area will assure that colostrum/MOM is optimally delivered to the infant and not absorbed by the swab.

8. Continually monitor the infant and pace according to the infant's cues and physiological response.

9. Perform hand hygiene.

10. Instruct and supervise parents when they are performing oral care with colostrum or MOM.

11. Mother's freshly expressed colostrum/milk does not need to be scanned if it has remained in mother's possession until administered as oral care.

12. Document oral care in the patient medical record.

Summary

OIT, also known as oral care, should be initiated in the first 48 hours of life to promote immune system function. Based on current published studies, OIT should continue for the first seven days of life. OIT is often grouped together with mouth care and taste stimulation which are separate entities. It may be prudent to continue OIT for up to 30 days of age in neonates who remain intubated and are either NPO or on minimal enteral nutrition although this is not a consistent practice in the published literature.

Oral Immune Therapy (OIT) with Mother's Own Milk (MOM) for Neonates Algorithm / Pathway

N/A

Glossary

A. Colostrum: Human mammary gland secretion containing living immune cells and factors (cytokines, lactoferrin, oligosaccharides) as well as antibodies that confer passive immunity to the neonate. Thick and yellow in color, it is secreted in the first days after giving birth.

B. Cytokines: Proteins that are essential for immune function and provide protection against infection in early life. These are often deficient in neonates.

C. Lactoferrin: Iron-binding protein with robust antimicrobial, anti-inflammatory, and immunomodulatory properties.

D. Oligosaccharides: Carbohydrates found in human milk that decrease risk of infection by acting as prebiotics to healthy gut flora and inhibit the adhesion of pathogens to the epithelial lining of the gastrointestinal tract.

E. Oral Care: Process of gently cleaning the oral cavity with colostrum, breast milk or sterile water which reduces the bacterial content of the mouth thus decreasing risk of infections.

F. Oral Immune Therapy (OIT): Process of providing colostrum to the buccal mucosa to promote immune function.

G. MOM: Mother's Own Milk

H. NPO: (Nil per os) Defined as no nutrition provided via the gastrointestinal tract.

I. Taste Stimulation: Non-nutritive provision of a small volume of breast milk or formula to stimulate taste receptor cells of the tongue in preparation for oral feeding.

J. LOE – level of evidence (based on Centre for Evidence-based Medicine, United Kingdom, 2015)[39]
   - 1a - Systematic review (with homogeneity) of randomized controlled trials (RCT)
   - 1b - Individual RCT with narrow confidence interval (CI)
   - 2a - Systematic review (with homogeneity) of cohort studies
   - 2b - Individual cohort studies and low-quality RCTs
   - 3a - Systematic review (with homogeneity) of case-control studies
   - 3b - Individual case-control studies
   - 4 - Case series, poor-quality cohort and poor-quality case-control studies
   - 5 - Expert opinion without explicit critical appraisal

   If a minus sign is suffixed (e.g., 1a− or 1b−), it denotes either a single study with wide CI or a systematic review with troublesome heterogeneity.

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Outcome Measures

NICU adherence to the proper use of OIT

Clinical Pathway Team

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