JOHNS HOPKINS ALL CHILDREN'S HOSPITAL

Gastroesophageal Reflux Disease (GERD) Management in the NICU for Preterm Infants

Clinical Pathway

JOHNS HOPKINS
All Children's Hospital

Johns Hopkins All Children's Hospital

Gastroesophageal Reflux Disease (GERD) Management in the NICU for Preterm Infants Clinical Pathway

Table of Contents

1. Scope
2. Guideline Panel
3. Executive Summary
4. Published Data
5. Clinical Practice Guideline
6. Glossary
7. Appendix
8. References
9. Clinical Pathways Team Information

Updated: January 2022

Owners: Fauzia Shakeel, MD

Johns Hopkins All Children's Hospital

Gastroesophageal Reflux Disease (GERD) Management in the NICU for preterm Infants Clinical Pathway

SCOPE

This Clinical Practice Guideline (CPG) applies to:

All Children's Hospital, Inc., and

All Children's Health System, Inc.

- West Coast Neonatology, Inc.

Guideline Panel

Fauzia Shakeel, MD

Joana Machry, MD

Dipti Amin, MD

Carolyn Kelly, ARNP

Melanie Newkirk, MS, RD

Executive Summary

Gastroesophageal reflux (GER) is a functional self-limiting condition that occurs several times a day in healthy infants, lasting for <3 minutes, with few or no symptoms. About 70-85% of infants will have symptoms associated with GER in first 2 months of life and improves by 4 -18 months of age. It typically resolves in 95% of the infants by 1 year of age. It's a normal developmental phenomenon that resolves with maturation.

Pathologic GER occurs when reflux of acidic contents causes injury to the lower esophageal mucosa. In preterm infants most of the GER episodes are weakly or not acidic (70%) making esophageal injury unlikely. There are wide variations in management of signs, symptoms, and complications associated with gastroesophageal reflux disease (GERD) in the neonatal intensive care unit (NICU), with no evidence to support an empiric trial of anti-reflux medications.

The probable over diagnosis leads to unnecessary treatment, which may have unintended consequences. Premature infants have weakly acidic reflux rather than acidic reflux, and inappropriate use of acid suppressive medication has been linked to adverse clinical outcomes, like necrotizing enterocolitis and sepsis.

Standardization decreases variations in practice, and the risk for error, while improving patient outcomes. It promotes non-pharmacologic strategies, required evaluations, and as needed testing to determine appropriate use of anti-reflux medications. Lack of evidence of efficacy together with emerging evidence of significant harm (particularly with gastric acid blockade) strongly suggest limiting its use in preterm infants*. (AAP Committee on Fetus and Newborn, Pediatrics 2018 Recommendation)*

Published Data and Levels of Evidence

1. Definitions:
    a. GERD in premature infants:
        i. Recurrent emesis or reflux **and** poor weight gain, choking, gagging, coughing, significant irritability, frequent crying, discomfort, arching, feeding aversion or forceful vomiting of gastric contents

    b. Significant frequency of cardiorespiratory events (apnea or bradycardia with or without desaturations) associated with GER: [6-8]
        a. Apnea event:
            a. duration: ≥ 20 seconds or
            b. duration: ≥ 10 seconds with bradycardia or
            c. duration: ≥ 10 seconds with desaturations <90%
        b. Bradycardia: heart rate <80 bmp for >5 seconds for PMA <37 weeks and HR <70 bpm for > 5 seconds for PMA ≥37 weeks
        c. Desaturations: desaturations < 90% for >5 seconds

2. There is no clear association between GER and apnea of prematurity [2-5]
   Preterm infants have a hyperactive laryngeal response to chemoreceptor stimulation that precipitates apnea and bradycardia and studies suggest apnea is mostly provoked when larynx and not the pharynx is stimulated.

3. Additional risk factors to be considered: neurological impairment, gastrointestinal malformation, bronchopulmonary dysplasia (BPD).

4. If on formula thickening of feeds may reduce emesis, however it does not reduce reflux or cardiorespiratory events [9,10] (Moderate quality evidence and weak recommendation)

5. Consider other causes such as necrotizing enterocolitis (NEC), urinary tract infection (UTI), neurological abnormalities, metabolic disorders, cow's milk protein allergy).

6. Consider cow's milk protein allergy as both conditions may co-exist in 42-58% of cases with similar symptoms. (Moderate quality evidence and strong recommendation)

7. Metabolic Bone disease of prematurity defined as Alkaline Phosphatase ≥ 800 iu/L and phosphorous ≤ 4 mg/dL. [13]

Clinical Practice Guideline

a. Symptomatic patients at any age < 37 weeks PMA

Provide supportive measures/ Non pharmacological measures at any time during course of suspected GERD: (High quality evidence and strong recommendation)
Including:

i. Left lateral decubitus post prandial, prone [14,15]

ii. Mother's own milk, if available versus formula

iii. Lengthening of gavage feeds (pump over 2 hours)

iv. Consider trans pyloric feeds (Low quality evidence and strong recommendation)

v. Reasonable time of 2 weeks and then consider alternative therapy

b. Patient > 37 weeks PMA and NO Metabolic Bone Disease:

vi. Consider trial of extensively hydrolyzed protein formula (Nutramigen®/Alimentum®) for 1-2 weeks [9] (Moderate quality evidence & strong recommendation)

vii. If suspected milk protein allergy recommend mother to start dairy free diet

viii. Consider pharmacologic therapy

ix. Prior to starting pharmacologic therapy, order pH probe with multi-channel impedance testing [11] (High quality evidence and strong recommendation)

x. PH probe monitoring include total number of reflux episodes and reflux index (RI), which is percentage of total recording time with an esophageal PH<4. In studies, an RI >7 % is considered abnormal, an RI of <3 % considered normal, and RI between 3-7% are indeterminate.[1] If acid reflux positive on pH probe with impedance may use proton pump inhibitor.[12] (Low quality evidence in infants and weak recommendation). In RCT double blinded placebo-controlled trials, both omeprazole and lansoprazole were ineffective in reducing GER signs in infants.

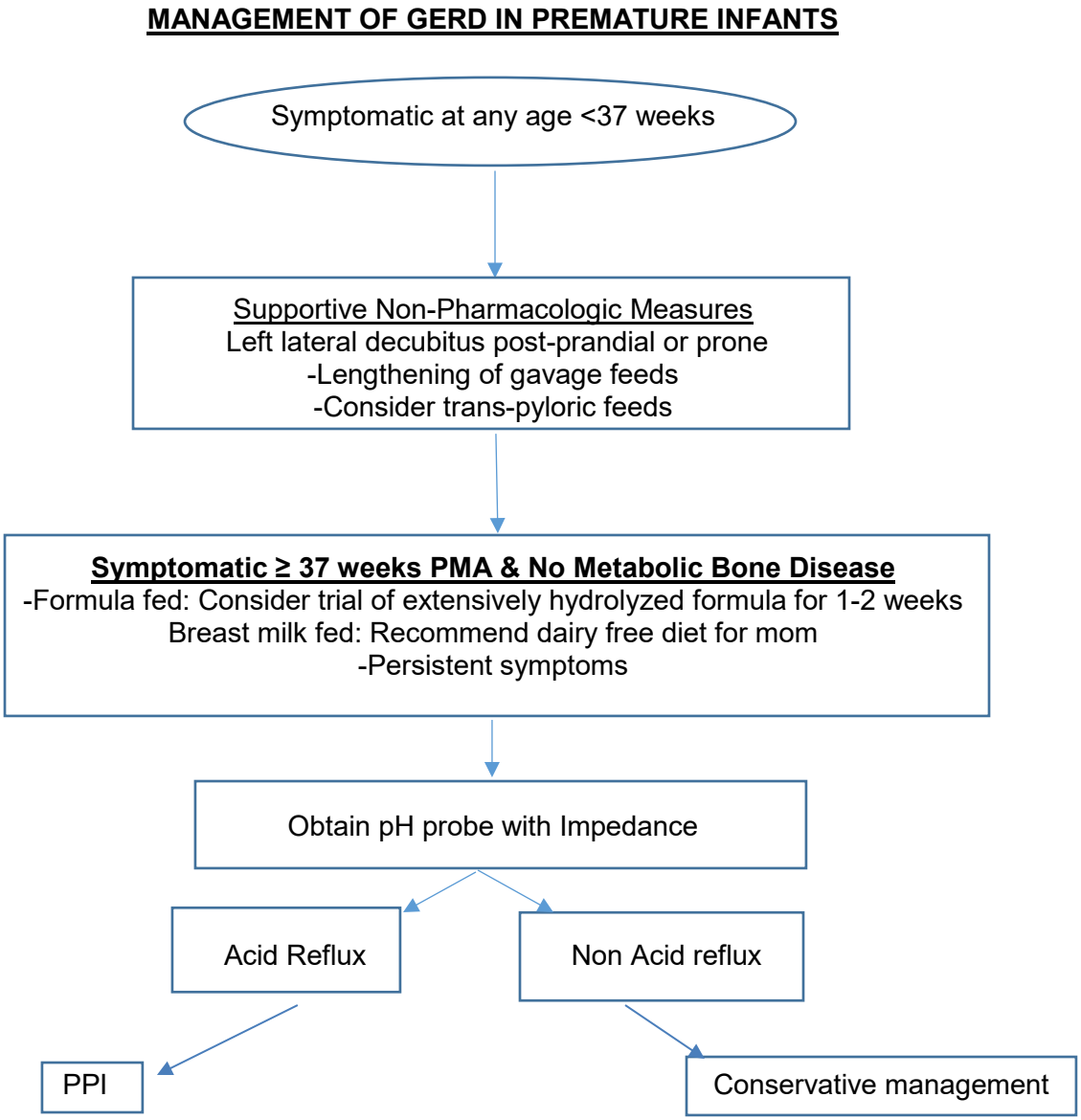
xi. Studies have shown that GER signs were rarely associated with documented reflux events on PH probe and impedance testing and preterm infants' behaviors commonly ascribed to reflux are, in reality not associated with GER and treatment should NOT be based solely on clinical signs.

xii. Histamine -2 Receptor blockers: Like ranitidine and famotidine efficacy in preterm infants has not been studied and has been linked to an increased incidence of necrotizing enterocolitis and higher incidence of late onset infections and death [19, 20]. (High quality evidence and strong recommendation)

xiii. If non-acidic reflux on pH probe with impedance, continue supportive and conservative management.

xiv. Prokinetic Agents: are promotility agents and include metoclopramide and erythromycin which seems to improve gastric emptying, reduce regurgitation and enhance lower esophageal tone but neither of these drugs have shown to reduce GER symptoms in preterm infants [17,18]. Because of lack of data about efficacy and all having potential for significant adverse effects and concerning safety profile, these drugs should NOT be used in preterm infants. (High quality evidence and strong recommendation)

Appendix:


MANAGEMENT OF GERD IN PREMATURE INFANTS
Symptomatic at any age <37 weeks
Supportive Non-Pharmacologic Measures
Left lateral decubitus post-prandial or prone
-Lengthening of gavage feeds
-Consider trans-pyloric feeds
Symptomatic ≥ 37 weeks PMA & No Metabolic Bone Disease
-Formula fed: Consider trial of extensively hydrolyzed formula for 1-2 weeks
Breast milk fed: Recommend dairy free diet for mom
-Persistent symptoms
Obtain pH probe with Impedance
Acid Reflux
Non Acid reflux
PPI
Conservative management

Glossary

GERD management in neonates

pH probe and Impedance testing

References

1. Vandenplas Y, Rudolph CD, Di Lorenzo C, et al. Pediatric gastroesophageal reflux clinical practice guidelines: Joint recommendations of the north american society for pediatric gastroenterology, hepatology, and nutrition (NASPGHAN) and the european society for pediatric gastroenterology, hepatology, and nutrition (ESPGHAN). *J Pediatr Gastroenterol Nutr*. 2009;49(4):498-547.

2. Di Fiore J, Arko M, Herynk B, Martin R, Hibbs AM. Characterization of cardiorespiratory events following gastroesophageal reflux in preterm infants. *J Perinatol*. 2010;30(10):683-687.

3. Corvaglia L, Zama D, Gualdi S, Ferlini M, Aceti A, Faldella G. Gastro-oesophageal reflux increases the number of apneas in very preterm infants. *Arch Dis Child Fetal Neonatal Ed*. 2009;94(3):F188-92.

4. Slocum C, Arko M, Di Fiore J, Martin RJ, Hibbs AM. Apnea, bradycardia and desaturation in preterm infants before and after feeding. *J Perinatol*. 2009;29(3):209-212.

5. Poets CF, Brockmann PE. Myth: Gastroesophageal reflux is a pathological entity in the preterm infant. *Semin Fetal Neonatal Med*. 2011;16(5):259-263.

6. Butler TJ, Firestone KS, Grow JL, Kantak AD. Standardizing documentation and the clinical approach to apnea of prematurity reduces length of stay, improves staff satisfaction, and decreases hospital cost. *Jt Comm J Qual Patient Saf*. 2014;40(6):263-269.

7. Finer NN, Higgins R, Kattwinkel J, Martin RJ. Summary proceedings from the apnea-of-prematurity group. *Pediatrics*. 2006;117(3 Pt 2):S47-51.

8. Abu Jawdeh EG, Martin RJ. Neonatal apnea and gastroesophageal reflux (GER): Is there a problem? *Early Hum Dev*. 2013;89 Suppl 1:S14-6.

9. Corvaglia L, Mariani E, Aceti A, Galletti S, Faldella G. Extensively hydrolyzed protein formula reduces acid gastro-esophageal reflux in symptomatic preterm infants. *Early Hum Dev*. 2013;89(7):453-455.

10. Lasekan JB, Linke HK, Oliver JS, et al. Milk protein-based infant formula containing rice starch and low lactose reduces common regurgitation in healthy term infants: A randomized, blinded, and prospective trial. *J Am Coll Nutr*. 2014;33(2):136-146.

11. Shin MS, Shim JO, Moon JS, et al. Impedance-pH monitoring and conventional pH monitoring are complementary methods to detect association between gastroesophageal reflux and apnea-related symptoms in preterm infants and neonates. *J Matern Fetal Neonatal Med*. 2012;25(11):2406-2410.

12. Tighe M, Afzal NA, Bevan A, Hayen A, Munro A, Beattie RM. Pharmacological treatment of children with gastro-oesophageal reflux. *Cochrane Database Syst Rev*. 2014;11:CD008550.

13. Moreira A, Jacob R et.al. Metabolic bone disease of prematurity. Neo Reviews 2015; 16(11): e 631-641

14. Martin R, Juliann D, et.al. Gastroesophageal reflux in preterm Infants: Is positioning the answer? *J Peds.* 2007; 585-591

15. Corvaglia L, Rotatori R, et al. The effect of body positioning on gastroesophageal Reflux in premature infants: Evaluation by combined impedance and pH monitoring. *J Peds*.2007; 151: 59

16. Eric C. Eichenwald and COMMITTEE ON FETUS AND NEWBORN. Pediatrics July 2018, 142 (1) e20181061; DOI: https://doi.org/10.1542/peds.2018-1061

17. Hibbs AM, Lorch SA. Metoclopramide for treatment of gastroesophageal reflux disease in infants: a systematic review. Pediatrics2006;118(2): 746-752

18. Corvaglia L, Monari C, et al. Pharmacological therapy of gastroesophageal reflux in preterm infants. Gastroenterol Res pract.2013;2013:714564

19. Guillet R, Stoll B, et al. National Institute of Child Health and Human Development Neonatal Research Network. Association of H2-blocker therapy and higher incidence of necrotizing enterocolitis in very low birth weight infants. Pediatrics 2006 Feb;117(2): e137-42

20. Terrin G, Passariello A et al: Ranitidine is associated with infections, necrotizing enterocolitis and fatal outcome in newborns. Pediatrics.2012;129(1).

21. Orenstein SR, Hassall E.et al: Multicenter, double-blind. Randomized placebo-controlled trial assessing the efficacy and safety of proton pump inhibitor lansoprazole in infants with symptoms of gastroesophageal reflux disease. J Pediatrics,2009.154(4)514-520

Clinical Pathway Team

Gastroesophageal Reflux Disease (GERD) Management in the NICU for preterm Infants Clinical Pathway

Johns Hopkins All Children's Hospital

Owner(s): Fauzia Shakeel, MD

Also Reviewed by:

Infectious Diseases:
Hospitalists:
Intensive Care:
Emergency Center:
Resident Physicians:
Nursing:
Pharmacists:
Johns Hopkins Children's Center Team:
Others:

Clinical Pathway Management Team: Joseph Perno, MD; Courtney Titus, PA-C

Date Approved by JHACH Clinical Practice Council:

Date Available on Webpage: 2_24_2022

Last Revised: January 2022

Last Formatted: February 2022

Disclaimer

Clinical Pathways are intended to assist physicians, physician assistants, nurse practitioners and other health care providers in clinical decision-making by describing a range of generally acceptable approaches for the diagnosis, management, or prevention of specific diseases or conditions. The ultimate judgment regarding care of a particular patient must be made by the physician in light of the individual circumstances presented by the patient.

The information and guidelines are provided "AS IS" without warranty, express or implied, and Johns Hopkins All Children's Hospital, Inc. hereby excludes all implied warranties of merchantability and fitness for a particular use or purpose with respect to the information. Johns Hopkins All Children's Hospital, Inc. shall not be liable for direct, indirect, special, incidental or consequential damages related to the user's decision to use the information contained herein.