The Yorkshire and Humber Neonatal Operational Delivery Network

NHS

Yorkshire and Humber Neonatal ODN Clinical Guideline

Title: Probiotics

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This clinical guideline has been developed to ensure appropriate evidence- based standards of care throughout the Yorkshire and Humber Neonatal ODN. The appropriate use and interpretation of this guideline in providing clinical care remains the responsibility of the individual clinician. If there is any doubt discuss with a senior colleague.

Summary recommendations:

- All neonatal units in Yorkshire & Humber should have access to probiotics
- Start in all infants <32/40 or <1500g when tolerating 0.5ml/hour of feed (or equivalent e.g., 1ml 2hrly)
- Hold probiotics if feeds withheld e.g., during clinical sepsis or NEC
- Discontinue probiotics at or after 34 weeks' gestation once feeds tolerated for at least 2 weeks. May be continued at consultant discretion.

Contents

A. Introduction

1. Aim of Guideline

The aim of this guideline is to provide information on the use of probiotics for the prevention of necrotising enterocolitis in preterm infants.

B. Process

1. Background

Necrotising enterocolitis (NEC) is a potentially life-threatening condition that, in the UK, occurs in 1 in 20 preterm infants born at 32 weeks or below. Feeding with breast milk is protective, while increased use of antibiotics is associated with higher risk of NEC.

Probiotics has been used in neonatal units for some time, with the aim of reducing rates of NEC. However, development of a strong evidence base has been limited by studies with low power and lack of consistency between probiotic agents, treatment regimens and participant inclusion criteria, making direct comparison difficult. However, a 2020 Cochrane review by Sharif et al assessed 56 trials with over 10,000 infants who were <32 weeks or <1500g, comparing probiotics against placebo. They suggested use of probiotics was associated with a 46% reduction in risk of NEC (RR 0.54, 95% CI 0.45 – 0.65) with a number needed to treat of 33 (95% CI 25 to 50). Furthermore, probiotics were associated with an overall reduction in mortality (RR 0.76, 95% CI 0.65 to 0.89) with a number needed to treat of 50 (95% CI 50 to 100).[1]

Consideration of the best probiotic agent has more recently leaned towards multi-strain agents, as studies using specific single strains have struggled to consistently demonstrate statistical benefit. All three suggested probiotics in this guideline are multi-strain, one containing Bifidobacterium and Streptococcus species (ProPrems) and two containing Lactobacillus and Bifidobacterium species (Infloran and Labinic).

A 2013 prospective randomised control trial by Jacobs et al, assessing Bifidobacterium infantis, Bifidobacterium lactis and Streptococcus thermophilus demonstrated that risk of NEC was more than halved by use of the probiotic (RR 0.46 (95% CI 0.23 – 0.93).[2] In 2020, Morgan et al conducted a systematic review which showed Lactobacillus and Bifidobacterium combination was associated with a nearly 2/3 decrease in the odds of developing NEC (OR 0.35, 95% CI 0.20–0.59) and with a 44% reduction in odds of mortality (OR 0.56, 95% CI 0.39–0.80).[3]

Within the UK currently, Infloran and Labinic are the most frequently used probiotic products, while Proprems is a product which is likely to be more widely used in future.

Infloran: Capsule containing 1 billion colony forming units per 250mg capsule (Lactobacillus acidophilus and Bifidobacterium Bifidum).

Labinic: Liquid containing 1 billion colony forming units in 0.1ml (Lactobacillus Acidolphilus, Bifidobacterium Bifidum and Bifidobacterium Infantis).

Proprems: Sachet containing 1 billion colony forming units per 0.5g sachet (Bifidobacterium Infantis, Bifidobacterium Lactis, and Streptococcus Thermophilus).

2. Patient population

Use routinely for babies born less than 32 weeks gestation **or** below 1500 grams

Aim to start within 24 hours of tolerating 0.5ml/hour of feed (or equivalent e.g., 1ml 2hrly)

3. Prescribing of Probiotics

Suggested Probiotic dosing regimen:

Infloran:	250 mg (one capsule) OD
Labinic:	0.1 ml BD[4]
Proprems:	0.5 g (one full sachet) OD[5]

See Appendix 1 for administration and storage guidance.

Probiotics are not licensed as a medication in the UK but are considered a food supplement. However, this may vary between NHS Trusts and some may still classify probiotics as a medication. The MHRA have no objection to the import of this product for use in a hospital setting.

Parental consent is not required prior to prescribing, but it is good practice to keep parents informed regarding the use of probiotics, for example through use of a parent information leaflet.

4. When to stop Probiotics:

Hold Probiotics if feeds are withheld, such as during clinical sepsis or NEC.

Discontinue probiotics at or after 34 weeks' gestation once feeds have been tolerated for at least 2 weeks.

If feed tolerance is poor, probiotic course may be extended at consultant discretion.

C. Audit criteria

- Prescription and administration in line with this guidance
- NEC rates in local units/NNAP data for NEC

D. References

1. Sharif S et al. (2020) Probiotics to prevent necrotising enterocolitis in very preterm or very low birth weight infants. Cochrane Database Syst Rev. 2020 Oct 15;10:CD005496. doi: 10.1002/14651858.CD005496.pub5
2. Jacobs SE et al & ProPrems Study Group. (2013) Probiotic effects on late-onset sepsis in very preterm infants: a randomized controlled trial. Pediatrics. 2013 Dec;132(6):1055-62. doi: 10.1542/peds.2013-1339. Epub 2013 Nov 18. PMID: 24249817.
3. Morgan RL et al & McMaster Probiotic, Prebiotic, and Synbiotic Work Group (2020). Probiotics Reduce Mortality and Morbidity in Preterm, Low-Birth-Weight Infants: A Systematic Review and Network Meta-analysis of Randomized Trials. Gastroenterology, 159(2), 467–480
4. Labinic Product Information. Available from: https://www.biofloratech.com/documents/Labinic%20Product%20Information%20Sheet.pdf
5. Proprems Product Information. Available from: https://proprems.eu/docs/productspecification.pdf, https://proprems.eu/how-to-use/

E. Sources

- Bradford Royal Infirmary. Probiotics Getting the right gut flora from the start Neonatal Guideline. S Oddie, S Wallis. April 2019
- Hull and East Yorkshire NHS Trust. Use of Oral Probiotics (Labinic) for Preterm Infants.
- Jessop Wing Probiotic Guideline. P Bustani.
- Ashford and St Peter's Hospital. Probiotic Guideline. P Reynolds. March 2018
- South West Neonatal Network Guideline. The Use of Probiotics in Preterm Babies. R Annable. March 2017
- Norfolk and Norwich University Trust Guideline for the use of probiotics in high-risk preterm infants to prevent necrotising enterocolitis. P Clarke. December 2019
- University Hospital of Leicester NHS Trust. Probiotic Administration in preterm infants. D Panjwani et al. Sept 2018

F. Working group

Members of working group: J Buckley (Neonatal dietician), Dr Morven Dockery, Dr C Forster, Dr S Oddie, Dr C Smith, Dr H Yates, Dr H Talbot.

G. Appendix 1 – Storage and Administration of Probiotics

Infloran

- Storage – In a fridge, between 2 – 8 degrees.
- Administration
    1. Clean preparation area
    2. Open one capsule (250mg) into a sterile galipot
    3. Add 1ml of EBM or sterile water and stir until dissolved
    4. Aspirate back into syringe and administer as a nasogastric bolus
    5. Dispose of waste as you would with infectious waste

Labinic[4]

- Storage – Store at 8 – 25 degrees. Dispose once bottle opened for 30 days.
- Administration
    1. Clean preparation area
    2. Gently shake bottle then wait 30 seconds for contents to settle
    3. Using a sterile oral syringe, draw up 0.1ml of Labinic solution
    4. Administer via nasogastric tube with milk feed, or directly into the mouth
    5. Dispose of waste as you would with infectious waste

Proprems[5]

- Storage – Store below 25 degrees. Shelf life of 2 years post-manufacturing when kept at room temperature.
- Administration
    1. Clean preparation area
    2. Shake Proprems sachet (0.5g), then open and pour entire contents into a sterile galipot
    3. Add 1-3ml of sterile water from a syringe and stir until dissolved
    4. Aspirate back into syringe and administer as a nasogastric bolus
    5. Dispose of waste as you would with infectious waste