Probiotics for the prevention of necrotising enterocolitis (NEC) in premature infants

Background:
Necrotising enterocolitis of at least Bell’s stage 2 and above occurs in 4-5% of premature infants and is associated with a mortality of 25%. The aetiology of NEC remains unclear. However, colonisation with pathogenic organisms, increased gut permeability and excessive inflammatory response due to immature expression of innate inflammatory response genes are implicated. Probiotics are live microbial supplements that colonise the gut and have been shown to reduce mortality and the incidence of severe NEC by 30%. The probable mechanism of action is by preventing colonisation of the gut by pathogens, (competitive exclusion) improving maturity of gut mucosal barrier and by modulating immune system.

Choice of product:
Infloran® is the most studied and widely available probiotic product. It contains *B. bifidum* and *L. acidophilus* (both $10^9$ colony-forming units, Infloran®). Quality control data for Infloran is available from UHW Microbiology department and also the company.

Regulatory considerations:
Infloran is not licensed as a medicine but is categorised as a food product similar to breast milk fortifier (HMF). The MHRA have no objection to the import of this product for use in a hospital setting. However, for safety and quality control reasons probiotics will be subject to the same strict regulation controls as any other drug in the hospital.

Eligible population:
Infloran is offered to all those at highest risk of NEC. Hence, all neonates <32 weeks gestation and/or <1500g will be given Infloran.

Information to parents:
Use of probiotics is to be considered part of routine practice in the unit and as such specific consent is not needed. However, it is good practice to discuss probiotics with parents at the time of admission. Parents will be provided a written information leaflet which will be included in the admission pack.

Prescribing probiotics:
Infloran should be prescribed on the drug prescription chart. The dose is **125mg twice daily** and is mixed with water and then administered as a bolus via the NGT. Continue until 34 weeks corrected gestation or until discharge, whichever is sooner. Infloran is safe to give even if feed volumes are as low as 0.5ml 2 hourly (assuming feeds are tolerated). Do not use if on continuous feeds. Consider stopping Infloran if the baby is very unwell, septic or has signs of evolving NEC. Only give Infloran to babies tolerating milk. If feeds are stopped for whatever reason, this is also an indication for stopping Infloran.

Preparation and administration of probiotics:
Infloran is to be administered after checking by two nursery nurses. Infloran comes as a capsule containing 250mg of probiotic granules – the capsule can easily be split and approximate half the contents given. It is not necessary to give exactly half the capsule – a rough approximation is satisfactory. **Give as a bolus of 0.5ml (do not add to continuous feeds)**

Preparation of probiotics should be carried out in designated areas and disposal of any excess product should be carried out in to designated sharp bins and should not be tipped in to sinks.
Clinical audit standards and Governance:

In theory there is a small risk of infection to the patient from the organisms in the probiotics. It is also known that the risk of gut translocation of bacteria increases when babies are unwell. However, this possibility is considered unlikely as there were no infections secondary to probiotic organisms detected in over 2000 babies studied for probiotic research. Moreover, the current antibiotic regime is appropriate to treat any potential infections derived from probiotics. Any seriously unwell baby that has received probiotics should be discussed with the neonatal consultant and further microbiology advice sought if there are specific concerns regarding sepsis.

Key outcomes (incidence of NEC, sepsis etc.) will be routinely recorded for infants that receive probiotics. These audit figures will be presented yearly.

There is currently much discussion at regional, national and international levels to establish an international register for preterm infants treated with probiotics. This would be similar to the TOBY cooling registry use for logging infants treated with therapeutic hypothermia.

Key Practise points:

1. Give Infloran to any baby born <32 weeks or <1500 g.
2. Speak to parents, offer them written information (parent information sheet – see appendix) and document in the medical case notes that this has been done.
3. Aim to start Infloran as soon as enteral feeds are commenced (this will usually be on day 1-3 of life). If EBM is unavailable on day 1, probiotics may still be administered at the consultant discretion (provided the patient is considered eligible to receive feeds).
4. Prescribe Infloran 125 mg twice daily (half a capsule twice daily) on the NICU Drug Prescription Chart.
5. Mix the contents of half a capsule (125 mg) with 0.5ml of sterile water. It is safe to provide this volume even in babies tolerating minimal volumes of 0.5 ml 2hourly.
6. Continue probiotics until 34 weeks corrected age provided full enteral feeds have been established for a 2-week period. Earlier or later discontinuation of probiotics is at consultant discretion.
7. Consider withholding in any baby who is seriously unwell, septicaemic, and/or has suspected NEC.
8. Discuss with consultant before starting or restarting in a baby who has had previous likely episodes of NEC.
9. Ensure that for each baby treated, ‘Infloran’ is selected in “Badger” for the baby’s daily data entry for “Drugs given” (search for and select ‘Infloran’ from drugs menu).

References:


R Bendapudi, V Patel, S Cherian May 2013 to be re-evaluated by May 2016