Kent Surrey & Sussex Neonatal Operational Delivery Network

Prevention of Neonatal Necrotising Enterocolitis	
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Implications of race, equality & other diversity duties for this document	N/A

Content

1) Introduction:

Early recognition and aggressive treatment of Necrotising Enterocolitis (NEC) has improved clinical outcomes but the disorder still accounts for substantial long-term morbidity in survivors of neonatal intensive care, especially preterm, very low birth weight (VLBW) babies.

The multi-factorial aetiology of NEC (including ischaemia of the intestinal mucosa, associated inflammation and invasion of enteric gas-forming organisms) makes successful treatment a significant challenge. Prevention should therefore be the priority.

2) Incidence:

The percentage of NEC cases recorded across the UK is thought to be 6% (Badger data for < 32 weeks gestation, 2017, 2018 and 2019). Approximately 30 NEC cases (<32 weeks gestation) are recorded annually within the KSS Neonatal ODN. As the number of cases per unit is relatively small minor errors in data recording and case definition will impact significantly on data quality and reliability.

3) Aim:

The aim of this guideline is to reduce the incidence and severity of NEC across the KSS Neonatal ODN by implementing a prevention strategy.

Many preventative strategies for NEC have been researched but the evidence supporting these measures is variable. Since NEC occurs almost exclusively in preterm infants, prevention of preterm birth would have the greatest impact on NEC incidence. This guideline provides recommended, suggested and not routinely recommended prevention measures depending on the level of evidence available.

4) Recommended preventative measures:

Antenatal corticosteroids: Although primarily used to reduce respiratory distress syndrome there is also strong evidence for the reduction of NEC and other morbidities [1].

- All women at risk of preterm delivery should be given antenatal steroids, ideally within 7 days of delivery (Grade 1A).

Human milk feeding: The use of human milk lowers the risk of NEC compared with cow's milk protein based formula [2]. The benefits of fresh mother's milk include reduction of gastric acidity, enhanced gut motility and promotion of beneficial bacterial colonisation. Although donor milk has less protective benefits due to the process of pasteurisation and freezing there is still moderate quality evidence that it is associated with a lower risk of NEC [3,4]. The protective effect of human milk

seems to be dose dependent with a higher intake of human milk leading to higher protection against NEC [5].

- Preferentially use mother's fresh milk and if unavailable provide donor milk as a bridge (Grade 1A). Avoid the use of cow's protein formulas or fortifier until full maternal or donor milk feeds are safely established.

5) Suggested preventative measures:

Use a standardised feeding protocol: Systematic reviews of observational studies have shown that instituting a standardised feeding regimen lowers NEC rates in VLBW infants [5,6,7]. The underlying mechanism of this affect is unknown but likely to be associated with reduction in variability of feeding advancement amongst providers and with slowing of feeding when indicated. Each unit should have a standardised feeding regimen providing a consistent approach to trophic feeds, timing and rate of advancement and when to withhold and restart feeds [8]. Individualised feeding advancement is usually based on birth weight and / or gestational age:

- Administer drops of colostrum into an infant's mouth within the first day of life
- Commence trophic feeds (approximately 10 ml/kg/day) of maternal or donor milk as soon as possible. There is no advantage in purposely delaying trophic feeds (Grade 2B).
- Advance feeds cautiously according to an agreed protocol (Grade 2B). For instance the smallest babies may remain on trophic feeds until clinical criteria are favourable. A daily increment between 15 and 30 ml/kg/day of milk is commonly used. The feed volume is advanced when the infant is clinically stable and trophic feeds are tolerated. Regular clinical examination and assessment of gastric aspirates and passage of stools are necessary. There is no benefit from delaying advancement of enteral feeds.
- Use of total parenteral nutrition (TPN) with prolonged delay in enteral feeding for prevention of NEC is not recommended. Use TPN to support the cautious advancement of enteral feeding and to optimise nutrition.

Probiotics: There is inconsistent data around the routine use of probiotics to prevent NEC and they may not be as effective in ELBW infants [9,10]. Multi strain probiotics are likely to be better than single strain in lowering the rate of NEC [11,12]. However, there is still no established regimen of optimal strains, dosing and timing of administration. Adverse effects have been notified including bacteraemia from the probiotic strain or contamination of the probiotic product. However, other reviews of local data have recognised positive outcomes without safety problems [13].

- Proceed according to the KSS Neonatal ODN guideline for probiotics. Note that the European Society of Paediatric Gastroenterology Hepatology and

Nutrition and the Food and Drug Administration in the U.S.A. have not approved probiotics for routine use in the prevention of NEC.

Avoid prolonged antibiotic use: Observational evidence suggests that prolonged use of empiric antibiotic therapy may increase the risk for NEC [14,15].

- ELBW infants with sterile blood cultures and low inflammatory markers should have antibiotics stopped in a timely fashion (Grade 2B).

Avoid medications that reduce gastric acidity: Gastric acidity has a role in regulating pathogenic microbes that might colonise the gut. Observational data suggests that H2 blockers are associated with an increased risk of sepsis and NEC [16].

- H2 blockers and proton pump inhibitors should be avoided in VLBW infants (Grade 2B).

Avoidance of severe anaemia: There is observational data that has associated the onset of NEC to be within 48 hours of a packed cell transfusion. Severe anaemia may cause intestinal injury due to hypoxia or immunologic mechanisms and a transfusion may further trigger NEC due to changes in viscosity, inflammation and gut perfusion [17].

- Low risk measures to avoid anaemia such as delayed cord clamping and limiting blood tests.

There is no firm evidence on the association between feeding, transfusion and NEC [18].

- A conservative approach is to withhold feeds during transfusion (Grade 2B).

Other suggested preventative measures:

- Avoid low oxygen saturation targets (85 to 89%)
- Avoid hyperosmolar feeds, electrolyte supplements and medications
- Avoid polycythaemia
- Remove umbilical catheters as soon as clinically possible or without delay if there are signs of thrombosis or reduced lower limb perfusion.

The American Academy of Pediatrics, advises that formulas for normal infants should have an osmolality no greater than 400 mOsm/L (approximately 450 mOsm/kg). The osmolality of breast milk is approximately 300 mOsm/kg but may increase to levels above 400 mOsm/kg by addition of human milk fortifiers, nutritional supplements and medications. There is no consistent evidence that feed osmolality of 300–500 mOsm/kg poses a safety risk to newborn infants [19].

6) Not routinely recommended preventative measures:

Immunoglobulins: Immunoglobulin therapy should not be used on the basis of current evidence.

Nutritional supplements: There is currently no evidence for the use of Lactoferrin, Human milk oligosaccharides arginine or glutamine in the prevention of NEC

Erythropoietin: has shown a protective effect against NEC but only in experimental models.

Prophylactic antibiotics: The control of infection is essential in the management of epidemic NEC but the use of prophylactic antibiotic treatment (such as Kanomycin) to prevent NEC is not recommended.

7) Auditable standards:

i. Compliance with suggested preventative measures
ii. Incidence of NEC (Bell stage 2 and above) across the KSS Neonatal ODN.

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Scope of Guideline:

Applies to all Neonatal Units covered by SEC Neonatal ODN.

Kent, Surrey and Sussex	
Medway Hospital NHSFT	Medway Maritime Hospital, Gillingham
East Kent Hospitals University NHSFT	William Harvey Hospital, Ashford Queen Elizabeth the Queen Mother, Margate
Ashford and St Peter's NHSFT	St Peter's Hospital, Chertsey
Brighton and Sussex University Hospitals NHST	Royal Sussex County Hospital, Brighton Princess Royal Hospital, Haywards Heath
Frimley Health NHSFT	Frimley Park Hospital
Surrey and Sussex Healthcare NHST	East Surrey Hospital, Redhill
Maidstone and Tunbridge Wells NHST	Tunbridge Wells Hospital, Pembury
Dartford and Gravesham NHST	Darent Valley Hospital, Dartford
Western Sussex Hospitals NHSFT	Worthing Hospital, Worthing
East Sussex Healthcare NHST	Conquest Hospital, Hastings
Royal Surrey NHSFT	Royal Surrey County Hospital, Guildford