Kent Surrey and Sussex Neonatal Operational Delivery Network

Principles of Practice Gastro-Oesophageal Reflux Disease in Neonatal Infants

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Presented for approval to/on	KSS Clinical Governance Board July 2025
Last Reviewed	A new document
Review date *(Max 3 years)*	July 2028
Distribution	Neonatal Units in KSS
Implications of race, equality & other diversity duties for this document	

Aim of Recommendations

The aim of this document is to bring network units together to reduce unwanted variation, to the benefit of babies, their families and the healthcare professionals caring for them – particularly those who are rotational.

Background

Gastro-oesophageal reflux (GOR) is a commonly reported phenomenon encountered in the first weeks of life and is a normal physiological process which usually occurs following feeding[1]. However, GOR can cause distress and concern at an already challenging time.

Gastro-oesophageal reflux disease (GORD) is the reflux of gastric contents that causes troublesome symptoms and/or complications. It is particularly common among the preterm and low birthweight population. These babies are prone to frequent bouts of reflux and regurgitation, often up to 5 times per hour which in turn can lead to obstructive or central apnoea.

Most reflux events are caused by transient lower oesophageal sphincter relaxation triggered by postprandial gastric distention[2]. Frequent large-volume feedings, a short oesophagus with a low tone of the lower oesophagus and cardia paired with a more obtuse His angle as well as supine positioning predispose infants to regurgitation or vomiting induced by transient lower oesophageal sphincter relaxation.

Infants who develop Chronic Lung Disease are prone to GORD, which may in turn complicate enteral feeding and worsen an already compromised respiratory system by causing asymptomatic aspiration or by triggering bronchospasm.

Early recognition and management of symptoms for reflux must be explored and all treatment options considered. The importance of a feeding assessment and MDT approach to management is required.

To be able to provide appropriate reassurance to parents, all healthcare professionals must use clearly defined terminology. However, historically there has been great variation surrounding the definitions of GOR and GORD, with terms often used interchangeably (NICE, 2015)[1]. To effectively communicate with parents, the MDT must use the same terminology which is documented clearly in the infant's records.

What are the symptoms of reflux?

Generalised symptoms of reflux in babies can include:

- Bringing up milk or being sick during or shortly after feeding
- Coughing or hiccupping when feeding
- Being unsettled during feeding
- Swallowing, gulping or burping after feeding
- Crying and/or screaming and not settling
- Back-arching
- Drawing legs up
- Not gaining weight
- Discomfort when lying flat

If an infant displays any RED FLAG symptoms below[1] they require urgent medical review for investigation suggesting disorders other than GORD.

Gastrointestinal symptoms and signs	Possible diagnostic implications
Frequent, forceful (projectile) vomiting	May suggest hypertrophic pyloric stenosis in infants up to 2 months old
Bile-stained (green or yellow-green) vomit	May suggest intestinal obstruction
Haematemesis (blood in vomit) with the exception of swallowed blood, for example, ingested blood from a cracked nipple in some breast-fed infants	May suggest an important and potentially serious bleed from the oesophagus, stomach or upper gut
Onset of regurgitation and/or vomiting	Late onset suggests a cause other than reflux, for example a urinary tract infection (also see the NICE guideline on urinary tract infection in under 16s) Persistence suggests an alternative diagnosis
Blood in stool	May suggest a variety of conditions, including bacterial gastroenteritis, infant cows' milk protein allergy (also see the NICE guideline on food allergy in under 19s) or an acute surgical condition
Abdominal distension, tenderness or palpable mass	May suggest intestinal obstruction or another acute surgical condition
Chronic diarrhoea	May suggest cows' milk protein allergy (also see the NICE guideline on food allergy in under 19s)
Systemic symptoms and signs	**Possible diagnostic implications**
Appearing unwell Fever	May suggest infection (also see the NICE guideline on fever in under 5s)
Dysuria	May suggest urinary tract infection (also see the NICE guideline on urinary tract infection in under 16s)
Bulging fontanelle	May suggest raised intracranial pressure, for example, due to meningitis (also see the NICE guideline on bacterial meningitis and meningococcal disease)
Rapidly increasing head circumference (more than 1 cm per week)	May suggest raised intracranial pressure, for example, due to hydrocephalus or a brain tumour
Altered responsiveness, for example, lethargy or irritability	May suggest an illness such as meningitis (also see the NICE guideline on bacterial meningitis and meningococcal disease)
Infants and children with, or at high risk of, atopy	May suggest cows' milk protein allergy (also see the NICE guideline on food allergy in under 19s)

Management of Gastroesophageal reflux disease (GORD)

Given the physiological nature of GOR in preterm infants, it is important to carefully consider whether this is pathological GORD that would benefit from treatment.

A stepwise approach is currently considered the best choice to manage gastroesophageal reflux (GOR) in preterm infants. Most preterm infants will not require anything more than simple positioning approaches. When considering when to escalate treatment beyond simple positioning or alteration of the feed regime it is important to consider carefully the risk-benefit ratio of any proposed treatment. In preterm infants with a high risk of NEC, we should not use any medication or thickener, at best pump feeding and in case of life-threatening events transpyloric feeding. Above a certain size and gestation, the recommendations can change as the risk of harm is low and the likelihood of effective treatment with medications is higher.

Positioning Measures and Modified Feeding

The Evidence

Some studies have suggested that acid reflux, measured by pH probe, is reduced when a baby is positioned in a prone or left lateral position compared with supine and right lateral positions. Moreover, although gastric emptying is slower in the left lateral position, the benefits to acid reflux were shown to outweigh this [3,4] Some studies also suggest that there may be marginal benefits to using 'head-of-bed' elevation to reduce acid reflux in adults but there is no data to determine the impact for the neonatal population [3,4.]

In the home environment or in the unmonitored baby supine position is strongly recommended due to the associated risks of SIDs in other positions. Positioning aids are also not recommended due to risks of suffocation [3,4]

Recommendations

- Support parents with skin-to-skin after a feed, to allow the food to settle – a reclined position in prone on parents' chest may reduce reflux.
- Trial elevating the head of the cot and monitor if this improves reflux symptoms. Before discharge home, cots should be flattened with the baby positioned in supine to the foot of the cot (with all nesting/positioning aids removed) in line with safe sleeping recommendations The Lullaby Trust - Safer sleep for babies, Support for families
- For some babies it is helpful for them to be fed in different positions. Support parents with feeding in a more upright position or in elevated side lying on the left (bottles) or cross cradle/rugby hold in left lateral or koala/upright hold (breastfeeding).
- Encourage modified responsive feeding with observing the baby's cues/stress signs and regular pacing/pauses to support coordination, breathing, regulation and winding.
- Avoid over-feeding, aiming for the nutritional requirements to be met at 150mls/kg/day and consider reducing volumes further to 135mls/kg/day or 120mls/kg/day maintaining adequate nutrient intake and growth
- Minimise activity and movement after feeds and time cares accordingly.
- Consider a left lateral position during tube feeds if parents not available to support with holding their baby or offering skin-to-skin.
- Where feasible support baby in either prone or left lateral positions post feeds for as long as possible. Encourage parents to hold their baby during tube feeds and after feeds.
- Non-nutritive sucking and tastes of milk during tube feeds can also support the digestive process and support the baby in developing skills for feeding.
- Encourage parents to access the Lullaby trust resources around safe sleep when preparing for home. Positioning aids to support elevation and sleeping in chairs/car seats are NOT recommended. The-Lullaby-Trust-Safer-Sleep-Advice-For-Premature-Babies.pdf

Extensively hydrolysed or amino acid formula in formula-fed infants or maternal dietary modification in breast fed infants

The role of food allergens as a cause of GORD remains controversial. An extensive literature search has found that whilst food proteins, in particular Cow's milk protein, can be a contributing factor to food-allergy (FA) associated GORD, it is difficult to distinguish between food allergy and non-food allergy-associated GORD[14]

The Evidence

- The joint ESPGHAN-North American Society for Paediatric Gastroenterology Hepatology and Nutrition guidelines on GORD from 2009 recognised the possible role of cow's milk allergy (CMA) and has further increased in prominence in the treatment pathway in the updated guidelines from 2018, with the consideration of a cow's milk elimination diet before the use of medication in infants [3,15]

- Both IgE-mediated, non-IgE-mediated or mixed IgE/non-IgE-mediated FA have been implied in the pathophysiology of GORD[16]. Whilst the relationship between FA and GORD is likely to be bidirectional, with GORD inducing changes in mucosal immunity that may in turn increase the risk of FA, the pathophysiology is still poorly understood[17]

- Stimulation of afferent nerve circuits via the brainstem during allergic reaction may cause dysregulation of sphincter tone and elicit GI symptoms[18]. A recent study by Omari et al, found that the elimination of cow's milk proteins (CMP) significantly improved GORD symptoms in infants with non-IgE-mediated CMA when compared with controls. That study also showed improved oesophageal peristaltic function and mucosal integrity, increased acid clearance and oesophageal mucosal impedance[19].

- The type of feed (breast milk +/- fortifier, or formula) doesn't appear to affect GORD episodes [20,21]

- Studies have also been completed looking at MII-pH testing and pH-metry. MII-pH testing does not only measure episodes of acid reflux but also non-acid reflux. In one study using MII-pH testing, the authors looked at the intensity of symptoms and the acid GOR index in children diagnosed with primary GORD and GORD secondary to CMA/FA [confirmed by oral food challenge (OFC)]. The patients with GORD secondary to CMA had longer reflux episodes with a pH lower than 4.0 compared to those with primary GORD. However, in other studies, conflicting results were obtained with pH-metry showing a comparable degree of reflux indexes in those with/without FA-associated GORD. Nevertheless, the former studies showed that the postprandial decline in the oesophageal pH below 4.0 was especially noted for patients with CMA. They underwent 48 h MII-pH, with patients receiving amino acid formula (AAF) for the first 24 hrs and a cow's milk challenge in the subsequent 24 hrs. They found that although the total number of acid and weakly alkaline episodes did not differ, the number of weakly acidic episodes and episodes of gastric dysrhythmia increased during the CMP challenge compared to the period of AAF ingestion in patients with confirmed CMA. In the absence of alarm signs indicating complicated GORD, invasive diagnostic procedures are not recommended [14,22].

- "Maternal avoidance of cow's milk during breastfeeding may be required in some infants with non-IgE mediated cow's milk allergy; in around 5% of infants of FPIES); between 18 and 50% of infants with proctocolitis and the number of children with eosinophilic esophagitis (EoE) who react to milk via human milk is not clear. The need for maternal avoidance of cow's milk in children with IgE mediated cow's milk allergy, needs to be assessed on an individual basis by the Neonatal unit including a Neonatal/Paediatric Dietitian. If a maternal dietary restriction is required, a dietetic assessment is required to ensure the maternal diet is nutritionally sound and the necessary supplementation provided when required."[22]

Recommendations

- For infants unresponsive to currently recommended standard GOR treatment including positioning and modified feeding including and avoidance of overfeeding, FA needs to be considered,

particularly if the infant has other symptoms in addition to GORD (e.g. blood in the stools, diarrhoea, irritability, atopic dermatitis or a family history of allergy.

- There is consensus that an extensively hydrolysed formula is used for the first-line treatment in CMA-associated GORD, but the impact of growth and involvement in multi-organ systems may require the consideration of an Amino Acid for first-line treatment.

- The confirmation of FA-associated GORD is based on the elimination diet for a period of 2-4 weeks followed by reintroduction.

- Mothers who are breastfeeding/expressing breast milk should receive support to maintain breastfeeding and optimise their dietary adequacy on discussion with a Dietitian.

Intra-gastric Continuous or bolus feeds

There is some evidence to suggest that feeding volumes, feeding durations and feeding flow rates may influence GORD.

The Evidence

Delayed gastric emptying and transient lower oesophageal sphincter relaxation are key factors in GORD:

- Continuous feeding is generally thought to cause less gastric distension and offer less pressure to the lower oesophageal sphincter whilst permitting significantly faster gastric emptying when compared to bolus feeding. However, delayed gastric emptying does not appear to play a contributory role in GOR in preterm infants, as those demonstrating symptomatic GOR do not appear to have delayed gastric emptying when compared with other infants [23]

- Bolus feeding causes greater gastric distension because of the quick delivery of a larger feed volume, which subsequently weakens the lower oesophageal sphincter, and results in GORD.

- In a study conducted in 2012, the proportions of both acid and non-acid reflux episodes were different during the first, second and third post-prandial hours. Prolonged feeding duration was significantly associated with a decreased total non-acid GORD event. The authors also concluded that there was a significant positive correlation between feeding flow rate and feeding volume [21].

- Findings from another study of 31 preterm infants suggested that continuous feeding may decrease the frequency and the oesophageal height of acid and non-acid GOR episodes in tube-fed preterm neonates compared to bolus feeding. There were significantly lower numbers of total, liquid, and mixed GOR episodes observed during continuous feeding compared to bolus feeds, however, the authors also noted that the overall incidence in the number of reflux episodes was low in their cohort which may have influenced results [24]

- However, a Cochrane review undertaken in 2014 and updated in 2019[9] did not find any randomised trials that directly evaluated the effects of continuous versus bolus tube feeding on GORD in preterm and low birthweight infants.

Recommendations

- Given the lack of evidence for the best delivery of feed concerning GORD management, consider a trial on continuous gastric feeding to increase the feeding duration and reduce the feeding flow rate. Practically, this could include slowing the delivery rate of each feed, using a feeding pump to administer the feed continuously over a longer period (e.g. over 1 hour and up to 20hours).

Gastric or Transpyloric (TP) feeds

The delivery of milk feeds directly to the small bowel (transpyloric feeding) rather than the stomach (gastric feeding) has the theoretical advantage of decreasing the potential for GOR and GORD, however there are also potential problems:

1) Transpyloric feeding tubes are difficult to position and require position confirmation with imaging.
2) There is a significant risk of tube migration back into the stomach.
3) There is a possible higher risk of necrotising enterocolitis in infants fed via the transpyloric route. Clinically, digestion in the stomach is by-passed and potentially pathogenic organisms (which would have been neutralised by stomach acid) may be transferred directly into the upper small bowel increasing the risk of NEC

The Evidence

Several observational studies [10,11] have suggested that transpyloric feeding may reduce the frequency or degree of GOR and GOR-related apnoea when compared to gastric feeds. However, these studies were designed to assess the effect of transpyloric versus gastric tube feeding on feeding tolerance, apnoeic episodes, growth and development and adverse consequences (CLD, death, GI disturbances and aspiration) and not the incidence of GORD. The authors assume that the apnoea event is caused by GOR in infants with clinical features of GOR without any other comorbidities, however the causal relationship between apnoea and GOR does remain controversial[25]

The mechanism is described as allowing the milk to bypass the stomach thereby reducing obstructive apnoea associated with milk refluxed to the proximal oesophagus and hypopharynx. However, it may be that transpyloric feeding simply decreases the gastric distension associate with poorer respiratory function in bolus fed preterm infant. The impact of transpyloric feeding on acid and non-acid reflux episodes hasn't been evaluated by RCT's [10,12.]

A Cochrane review in 2013 [13] consisting of nine randomised controlled trials of transpyloric versus gastric feeding in preterm infants concluded that there was no evidence for improved "feeding tolerance" or growth with TP feeds but found an increased risk for" GI disturbance" requiring cessation of feeds. The trials included in the review evaluated TP feeding as an initial feeding strategy versus gastric feeding for improved growth and feeding tolerance, whereas TP feeding has not been evaluated as a treatment method for reducing GORD episodes such as apnoea's and bradycardia occurring in very preterm infants suspected of having GORD.

Since uncertainty still exists as to whether GOR is an important cause of apnoea in preterm infants, further clinical trials are warranted to evaluate whether transpyloric feeding is an effective prevention or treatment option in preterm infants with clinical GORD.

Recommendations

- To only consider a trans-pyloric feeding trial if life-threatening events are clearly associated with feeding. Beware of the risks associated with the use of formula and fortified milk during this trial period.

GORD - Use of Feed Thickeners

Although studies have shown that feed thickeners are only moderately effective in treating GORD in healthy term infants[5], there is no currently available evidence to support the efficacy and safety of feed thickeners in the management of GORD in preterm populations[2].

The Evidence

Despite the lack of evidence to support a causative link between feed thickeners and NEC, there is sufficient clinical concern, both locally, nationally and internationally to recommend extreme caution in the use of feed thickening agents within the preterm population.

- Although no reported link between thickened feeds and undesirable gastrointestinal effects in infants has been found, there is a series of cases of NEC reported, with distinct epidemiologic features with a common cause of ingestion of feeds containing a xanthan gum-based [26,27,28]

- Thickeners may increase the energy density and osmolarity of feeds, leading to an increase in the frequency of relaxation of lower oesophageal sphincter and a delay in gastric emptying. Paradoxically, this has the potential to increase regurgitation episodes and worsen GOR [13.]

- Concerns have also been raised about nutritional consequences, such as impaired adsorption of nutrients from feed that has been thickened with indigestible complex carbohydrate thickeners [29]

Recommendations

- The use of feed thickeners is **not considered for preterm infants** with a birth weight less than 1.5kg. Extreme caution is recommended when considering the use of feed thickening agents for all preterm infants born < 37weeks.

Medication Management

The published evidence for the pharmacological management of reflux in neonates demonstrates a lack of efficacy. Reflux symptoms may not improve with pharmacological treatment.

General recommendations:

- Do not offer acid-suppressing drugs to treat overt regurgitation in infants occurring as an isolated symptom
- If red flag symptoms are not present but the infant is showing signs of distress, only consider pharmacological intervention after non-pharmacological interventions have been introduced and given a trial period (recommended 2 weeks)
- Pharmacological treatment should be prescribed for a defined trial period, with regular efficacy reviews. Treatment should be discontinued if there is no benefit at the end of the trial period.
- If there is felt to be a need for medication use beyond Gaviscon Infant® and Omeprazole, consider a discussion or referral to paediatric gastroenterology for specialist advice

1. Gaviscon Infant® (Alginate)[30,32,33,34,36]

Efficacy: There is insufficient literature published on the effect of alginate-only formulations on infant reflux to comment on efficacy. One observational study (43 infants) concluded that alginate significantly decreases the number and extent of both acid and non-acid reflux episodes and associated symptoms in infants.

Mechanism of action: Physical action – reacts with acidic gastric contents to form a viscous gel to stabilise stomach activity.

Risks/cautions:

- DO NOT USE WITH FEED THICKENER – risk of intestinal obstruction
- Contraindicated if suspected intestinal obstruction
- May cause constipation
- Use with caution in renal impairment – may contribute to hypernatremia

Recommendations:

- If non-pharmacological interventions have been unsuccessful, consider a 2-week trial of Gaviscon Infant® in infants at least **>33 weeks CGA and >1.5kg only**
- Ensure Gaviscon Infant® is not given alongside feed thickener
- Review regularly for signs of improvement.
- If there is no evidence of benefit after a 2-week trial, stop treatment.

- Do not prescribe for long-term use

2. Omeprazole[30,32,35,36]

If a Proton Pump Inhibitor (PPI) is indicated, Omeprazole is the PPI of choice in infants.

Efficacy: The evidence for efficacy in infants with GORD is very uncertain. Trial data for vs placebo has shown no clear benefit on symptoms from either omeprazole or esomeprazole. Trials vs Ranitidine concluded that Omeprazole may or may not provide symptomatic benefits equivalent to ranitidine.

Mechanism of Action: Irreversible binding to the H^+/K^+ ATPase pump in gastric cells, which reduces gastric acid production. Therapeutic effect of Omeprazole is extended beyond the half-life of the drug because the binding is irreversible – therapeutic effect will last until there has been synthesis of new H^+/K^+ ATPase pumps (approximately 24 hours).

Absorption: Absorbed in the small intestine. Complete absorption of an enteral dose takes 3-6 hours, however peak plasma levels are achieved 1-2 hours after the dose. Bioavailability of 40% after a single dose, which increases to 60% on repeated dosing. Note that administration with feeds will decrease absorption by approximately 20%.

Metabolism: Metabolised via CYP2C19. There is reduced metabolism and clearance until 6 months old while this metabolic pathway develops. There is an increased risk of accumulation in infants <3 months old who are receiving doses >1.4mg/kg/day. Metabolism is also impaired in hepatic dysfunction and in 2-6% of the population with genetic polymorphism leading to decreased expression of CYP2C19.

Elimination: Omeprazole has a short half-life (but an extended therapeutic effect) and is eliminated 80% in urine, mainly as metabolites.

Risks:
- Hypomagnesaemia with duration of treatment >3 months
- Increased fracture risk with prolonged use
- Increased infection risk
- C. difficile diarrhoea
- Necrotising Enterocolitis (NEC)
- Micronutrient deficiencies
- Very low risk of subacute cutaneous lupus erythematosus

Recommendations:
- If Gaviscon Infant® is unsuccessful or not appropriate, consider a 4-week trial of a PPI in infants at least **>33 weeks CGA and >1.5kg only** if:
    - Non-pharmacological interventions have been unsuccessful AND
    - There is overt regurgitation AND at least 1 of:
        - Unexplained feeding difficulties
        - Distressed behaviours
        - Faltering growth
- Review regularly for signs of improvement.
- If there is no evidence of benefit after a 4-week trial, stop treatment
- Be mindful of the risks associated with long-term PPI use (see above).

3. Domperidone [31,32,37,38]

The use of domperidone in managing infant reflux is no longer common practice in infants and small children, following the withdrawal of its license for reflux treatment and its use in individuals under 12 years

old or weighing less than 35 kg. Published studies have failed to demonstrate a significant improvement in reflux symptoms with domperidone, especially in term newborns and infants.

However, preterm babies have multiple immaturities such as lack of coordination between sucking and swallowing, gastric emptying delay, and small intestinal and colonic dysmotility. These immaturities are often manifested by regurgitation, vomiting, increases in gastric residual volume, abdominal distention and delays in passing stool. Some of these symptoms and signs can be difficult to distinguish from reflux.

Prokinetics like domperidone are drugs that have successfully been used in cases of gut motility problems in all age groups, including preterm newborns. Data indicate that domperidone may be a useful and safe agent for the treatment of symptomatic gastroesophageal reflux and significantly reduces gastric emptying in preterm babies. This may account for its effect in cases of disturbances related to gut motility.

The concerns reported about prolonged QT interval have mainly been reported in the elderly population, especially when on higher doses or multiple medications or when other CYP3A4 inhibitors were taken concomitantly. No serious complications in preterm newborns without congenital heart diseases have been reported so far at all.

Hence, a trial of domperidone could be considered in preterm babies if:

- All other treatment options have failed.
- The potential benefits outweigh the risks, e.g. profound desaturations, apnoea's and bradycardias due to suspected GERD
- All contraindications have been carefully assessed and excluded; particularly hyperkalaemia, concomitant use of omeprazole, CYP3A4 inhibitors or a family history of cardiac diseases.

If domperidone is to be initiated:

- The decision must be made by a consultant.
- A trial period of two weeks with regular reviews can be conducted to assess for any signs of benefit. If no improvement is observed after a maximum of two weeks, treatment should be discontinued.
- The dose should be gradually increased within the dosing range to establish effectiveness during the trial period.

Note: There is no clear guidance for newborns regarding performing an ECG before or during domperidone treatment, but consideration of an ECG or ECG monitoring in any doubt is reasonable.

KEY POINTS

1. Define GOR or GORD and ensure effective communication to parents and team

2. Preterm babies have multiple immaturities such as lack of coordination between sucking and swallowing, gastric emptying delay, and small intestinal and colonic dysmotility. These immaturities are often manifested by regurgitation, vomiting, increases in gastric residual volume, abdominal distention and delays in passing stool. Some of these symptoms and signs can be difficult to distinguish from GERD.

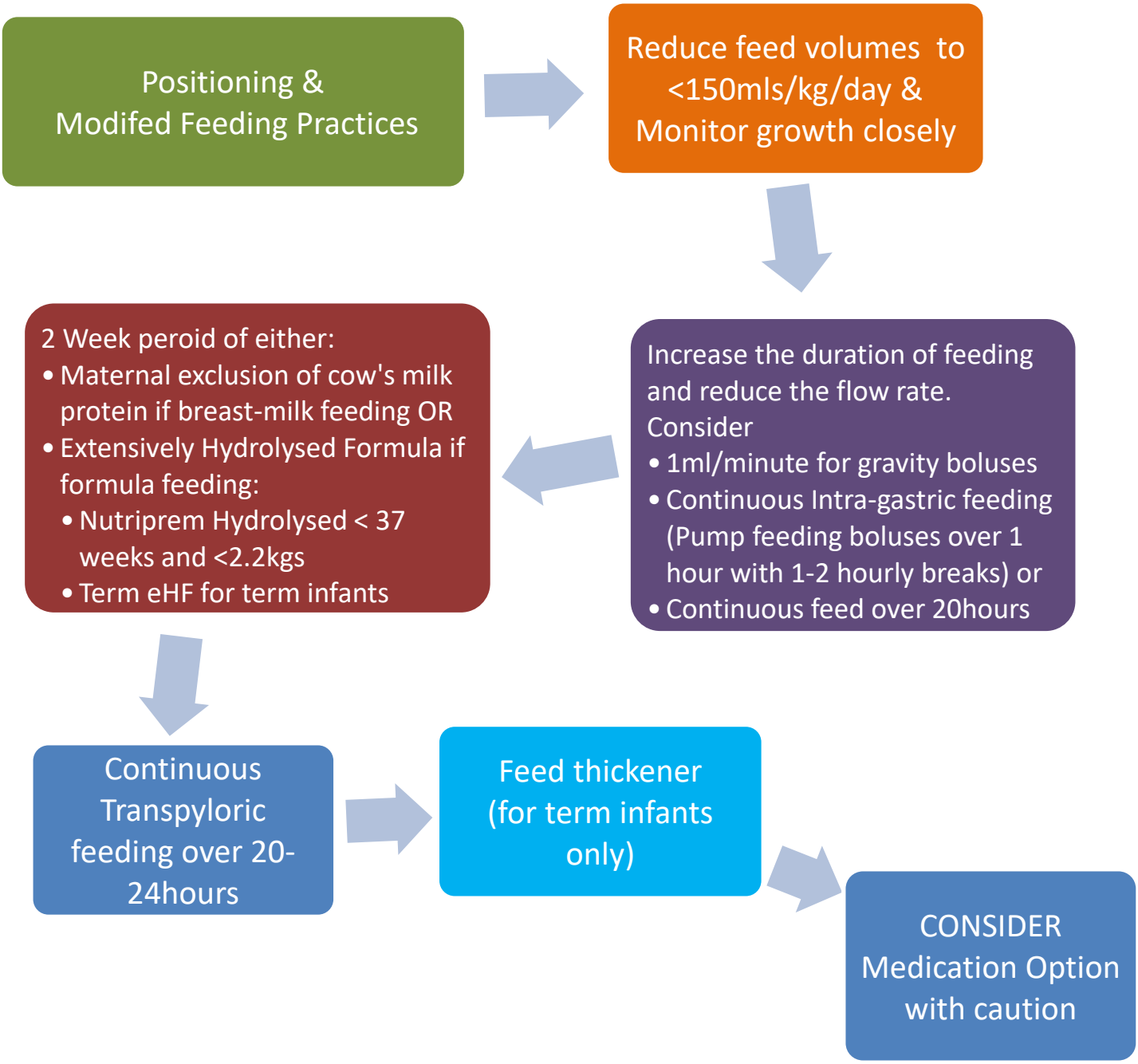
3. Review non-medication treatment options are optimised prior to initiating any medication

4. Prokinetics like domperidone are drugs that have often been used in cases of gut motility problems and in the treatment of GERD in adults, children and neonates.

5. Consider the evidence for your rationale of treatment options.

6. Work collaboratively with your MDT to ensure the most appropriate treatment for each individual infant

SUMMARY ALGORITHM



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Appendices

Appendix 1: Contributors from KSS Neonatal Nutrition Group

Name	Position	Neonatal Unit
Dr Ramon Fernandez	Consultant	UHSussex
Dr Vennila Ponnusamy	Consultant	St Peters Hospital
Dr Vimal Vasu	Consultant	William Harvey Hospital
Dr Toria Klutse	Consultant	East Surrey NHS Trust
Christian Chadwick	Pharmacist	UHSussex
Catherine Casewell	Dietitian	St Peters Hospital
Sukvinder Kaur	Dietitian	Dartford and Gravesham NHS Trust
Chantelle Hearfield	Dietitian	Surrey and Sussex
Carole Davidson	Dietitian	UHSussex
Sarah Sabey	Dietitian	East Surrey NHS Trust
Ruth Cousins	Advanced Neonatal Nurse Practitioner	Maidstone and Tunbridge Wells
Kate Jones	SLT	UHSussex

Scope of Guideline Framework

The guideline applies to all Neonatal Units covered by Kent Surrey and Sussex Neonatal ODN. This includes the following hospitals:

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,

Version Control:

Version	Date	Details	Author(s)	Comments
Review date:				