Gastric Residual Evaluation in Preterm Neonates: A Useful Monitoring Technique or a Hindrance?

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It is routine practice in most neonatal intensive care units to measure the volume and color of gastric residuals (GRs) prior to enteral bolus feedings in preterm very low birth weight infants. However, there is paucity of evidence supporting the routine use of this technique. Moreover, owing to the lack of uniform standards in the management of GRs, wide variations exist as to what constitutes significant GR volume, the importance of GR color and frequency of GR evaluation, and the color or volume standards that dictate discarding or returning GRs. The presence of large GR volumes or green-colored residuals prior to feeding often prompts subsequent feedings to be withheld or reduced because of possible necrotizing enterocolitis resulting in delays in enteral feeding. Cessation or delays in enteral feeding may result in extrauterine growth restriction, a known risk factor for poor neurodevelopmental and growth outcomes in preterm very low birth weight infants. Although some neonatal intensive care units are abandoning the practice of routine GR evaluation, little evidence exists to support the discontinuation or continuation of this practice. This review summarizes the current state of GR evaluation and underlines the need for a scientific basis to either support or refute the routine evaluation of GRs.

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1. Introduction

Gastric residuals (GRs) are often evaluated in preterm infants who are being fed via an orogastric (OG) or nasogastric (NG) tube as a putative indicator of feeding intolerance (FI) or as an early symptom of necrotizing enterocolitis (NEC).\(^1\)\(^,\)\(^2\) Although GR measurement prior to feeding is routinely used to guide subsequent feeding advancement,\(^3\)\(^,\)\(^4\) little scientific evidence exists to justify this practice.\(^5\) Standards for the management of GRs are lacking, and reports in the literature indicate a wide variation in practice regarding the evaluation of feeding tube position, frequency of GR evaluation, standards that dictate the discarding or returning of GRs, and even what constitutes "significant" GR volume and/or quality.\(^2\)\(^,\)\(^6\) This lack of uniform standards\(^7\) often leads to a discontinuation or delays in the advancement of enteral feedings, which in turn may lead to an unnecessary prolongation of intravenous nutrition, increased risk of late onset sepsis, and extrauterine growth restriction.\(^8\) Because researchers now question the utility of routine GR evaluation,\(^9\) this study assessed this potentially unnecessary procedure and reviewed current literature regarding routine GR evaluations to underscore the need for additional research.

2. Gastric emptying: correlates and influence on GR

Evaluation of GRs is used in the neonatal intensive care to measure the volume of milk remaining in the stomach at a variable time after a feeding, and as an indicator of gastric emptying (GE).\(^10\) Compared to term infants, preterm infants have slower GE owing to intrinsic immaturities of the gastrointestinal (GI) tract,\(^11\) including suck-swallowing coordination, immature lower esophageal tone and function, low percentage of gastric electrical slow wave, and slower intestinal transit.\(^12\) Furthermore, intestinal motor patterns during fasting and feeding are immature in preterm infants. Motor patterns are characterized by short episodes of quiescence alternating with irregular contractions without clear migrating motor complexes.\(^13\) During fasting, the cluster amplitude and mean duration of the duodenal motor activity are lower in preterm than in term infants, whereas cluster frequency is higher in preterm infants.\(^14\) These physiologic characteristics are intrinsic factors responsible for delayed GE and increased GRs in preterm infants.

Many extrinsic factors such as hormonal input, drug administration, and nutritional management can also influence GE by accelerating GI development and increasing GE, whereas other factors can delay GE and lead to a larger GR volume. For example, antenatal steroid therapy stimulates fetal gastric secretion, thereby increasing neonatal gastric level after birth, which in turn strengthens antral contractions against the pylorus, and relaxes the pyloric sphincter, thereby stimulating GE.\(^15\) It also induces the release of intestinal mucosal enzymes and promotes gut development.\(^16\) However, formula milk has been shown to empty half as fast as expressed breast milk, which also has important implications for preterm infants with FI due to delayed GE.\(^17\)

Similarly, other drugs can also impact GE by regulating GI function. Mydriatics, or drugs routinely used for retinopathy of prematurity screening in preterm infants, can cause delayed GE by inhibiting duodenal motor activity.\(^18\) Theophylline can delay GE by its action on cyclic adenosine monophosphate, calcium influx, or potassium-induced membrane depolarization.\(^19\) Gastroprotective agents such as domperidone significantly increase GE and may prove to be a useful agent for infants with FI.\(^20\) However, its safety still requires investigation because of a possible QT prolongation in infants >32 weeks in gestation.\(^21\) Another prokinetic agent, erythromycin, may also improve GE and feeding tolerance,\(^22\) but there is still insufficient evidence to recommend its routine use in preterm infants at risk of FI.\(^23\) As a result, it is currently recommended that erythromycin be used cautiously and selectively in preterm infants with moderately severe GI dysmotility.\(^24\) Lastly, another prokinetic, cisapride, is currently not used in the United States owing to reports of an associated long QT syndrome that predisposes infant to arrhythmias.\(^25\)

Studies suggest that certain supplements such as probiotics may increase GE, improve feeding tolerance, and promote gut maturation.\(^26\) Preterm newborns receiving Lactobacillus reuteri showed a significant decrease in regurgitation and mean daily crying time, and a larger number of stools compared with those given placebo. The GE rate was significantly increased and the fasting antral area was significantly reduced in both the newborns receiving L. reuteri and breast-fed newborns compared to placebo. There is currently no conclusive evidence to recommend routine probiotic supplementation in preterm infants.

The timing of initiation, type of enteral feeding, and mode of administration may also influence GE. Early enteral nutrition hastens the maturation of motor function, as demonstrated by enhanced duodenal motor activity,\(^28\) whereas the administration of minimal enteral feedings (feedings <24 mL/kg/day provided for intestinal maturation and protection rather than nutrition) has been shown to induce the appearance of mature migrating motor activity and promote GE.\(^29\)

Decreased osmolality combined with an increased feeding volume has also been shown to increase GE.\(^30\) Compared to formula, human milk has been shown to result in a more rapid GE in premature infants.\(^31\) However, it is unclear whether the use of human milk fortification influences GE. A study by Ever and Yu\(^32\) on the effect of human milk fortifier on GE in preterm infants reported that human milk fortifier may slow GE owing to an increased osmolality and a change in milk composition. However, Gathwala et al\(^33\) found no change in feeding tolerance when human milk was fortified.

The mode of enteral feeding administration may also influence GE. Compared to bolus feedings, feedings provided by continuous infusion enhance duodenal motor responses and hasten GE.\(^34\) However, a recent Cochrane review found insufficient evidence to support the use of continuous enteral versus bolus feedings.\(^35\)

Several diseases can also influence GE in preterm infants. Infants with severe hypoxemia often have significantly decreased GI blood flow and tissue oxygenation, which may lead to decreased GE and result increased gastric residual
volume (GRV).\textsuperscript{36} Other disease processes, including NEC, patent ductus arteriosis, severe hypotension, sepsis, and acute respiratory distress, can also decrease GE and increase the GRV.\textsuperscript{3} Whether the routine measurement of GRVs provides any efficacy in improving evaluation of FI under these circumstances remains unknown.

3. Clinical management of GRs

Uniform standards for what constitutes significant quantity and quality of the GR are lacking, and wide variations exist based on individual clinician preference or neonatal intensive care unit (NICU) protocol. This leads to one of the most controversial issues in GR management: the interpretation of what is clinically significant in terms of volume and qualitative characteristics.

Aspiration of GR has historically been used as an indicator of accurate gastric placement of OG and NG tubes. However, GR aspiration has been shown to be an unreliable indicator of proper OG/NG tube placement. Therefore, the use of other clinical indicators such as accurate measurement, aside from minimal insertion lengths, may be more appropriate indicators of proper OG/NG tube placement.\textsuperscript{37,38}

It is unclear whether it is possible to manage enteral feedings in premature infants without routine GR measurements. This widespread practice has become a standard in NICU care largely based on tradition, without scientific basis, and may be associated with some potentially significant complications. Theoretically, the negative pressure created by aspiration of GRs in combination with the close contact of the tip of the NG/OG tube with the gastric mucosa has the potential to damage the gastric mucosa. This is especially a concern when the procedure is repeated 8–12 times a day depending on the infant’s feeding regimen. Confusion as to what constitutes problematic gastric aspirations may also relate to the amount subsequently fed to the patient. A recent prospective before-and-after study by Poulard et al\textsuperscript{39} evaluated the impact of not measuring GR in mechanically ventilated, critically ill adult patients fed continuous feedings. In this study, not measuring GR was associated with increased daily volume of feeding and less FI, without increasing emesis or ventilator-associated pneumonia. Similar studies have not been done in preterm infants.

Decisions regarding when to discard GR are not based on scientific evidence but are generally made according to the nurse’s experience, unit tradition, and the physician’s advice. In a small study of NICU nurses, only 4% consistently replaced GR after aspiration.\textsuperscript{40} The GRs included nutrients, gastric acid, and enzymes that may assist in promoting intestinal motility and maturation. If discarded, these may negatively influence GE and the maturation of the GI system.\textsuperscript{41,42} Juvé-Udina et al\textsuperscript{42} in a randomized trial of GR management in critically ill adult patients, suggested the reintroduction of a limited amount of GR as advantageous and a decrease in amount of GRV without increased risk. Criticisms of the study design may have thwarted changes in clinical practice, but this study still gives evidence regarding the management of GR in the adult population.\textsuperscript{41}

4. Relationship between GR and FI

Very low birth weight (VLBW) infants frequently experience what is clinically described as FI because of immature intestinal immaturity and decreased intestinal motility. Although the definition of FI varies in this population, the term has been based historically on the presence of increased volume or bilious GR, abdominal distention, and emesis. However, controversy exists regarding the usefulness of GR as an indicator of FI. One of the most contentious issues is the volume of GR that is indicative of FI, because a wide variation in the acceptable volume is reported. For some authors, FI is defined as a GRV of >2 mL in infants weighing <750 g or >3 mL in infants weighing 751–1000 g.\textsuperscript{3,4,6} Others have defined the GRV indicating FI to be a GRV ≥2 mL/kg, >50% of the previous feeding volume.\textsuperscript{43}

Furthermore, the necessary frequency of GRV measurement also varies in the literature. Although it is most often performed 8–12 times daily, it also depends on the number of feedings provided every day and unit tradition,\textsuperscript{44} and may also vary according to study design.\textsuperscript{45} Variations in both the definition of significant GRV and the frequency of evaluation can directly affect the study findings and clinical practice.

No consensus exists regarding the use of GR as an indicator of whether to administer subsequent enteral feedings. Mihatsch et al\textsuperscript{4} defined significant GRV as >2–3 mL depending on birth weight. They also found that green GRs were not indicative of FI and suggested that their presence should not delay the advancement of feeding volumes in the absence of other clinical signs and symptoms. Shulman et al\textsuperscript{4} concluded that GR is an unreliable indicator to predict the attainment of full gavage feedings. Although clinical decisions are often made according to the volume of aspirated gastric contents, this practice is not a reliable measurement of GRV. Accurate measurement of GR volume is dependent on body position,\textsuperscript{46} position of the OG/NG port in the gastric antrum, and size of the OG/NG tube.\textsuperscript{47} It has also been reported that the volume of GR may be underestimated on average by 25%.\textsuperscript{46} This variability has been shown to increase as GR volume decreases, which may be particularly important in VLBW infants whose gastric contents are smaller than those of an older child or adult.\textsuperscript{46}

Because of specific criteria or characteristics for abnormal GR volume, enteral feedings may be inappropriately discontinued or delayed, resulting in the prolongation of parenteral nutrition and delays in the attainment of full enteral feedings. The volume of feedings provided to this population and the time necessary to attain full enteral feedings are inversely related to the number of GR with higher volumes.\textsuperscript{4} The importance of adequate enteral nutrition, including achievement of full enteral feedings during the first few weeks following delivery in VLBW infants, is well known.\textsuperscript{48} A delay in attainment of full enteral feedings is associated with adverse neurodevelopmental outcomes in premature infants, thereby emphasizing the critical need for strategies to optimize enteral nutrition in this population.\textsuperscript{49} When the volume of enteral feedings is insufficient to promote normal growth and development, the period of total parenteral nutrition (TPN) required is
extended. Administration of TPN to VLBW infants is associated with increased incidence of parenteral nutrition associated with liver disease (PNALD). The longer the infant receives TPN, the greater the incidence and severity of the PNALD. Moreover, a percutaneous central venous line is often required for the delivery of TPN, leading to an increased risk of late-onset sepsis and the possibility of more serious CVL-related complications.

5. Relationship between GR and NEC

NEC, a devastating disease owing to its high morbidity and mortality, predominantly occurs in VLBW infants. Symptoms include abdominal distension, abdominal wall discoloration, and bloody stools. Radiologic findings include pneumatisos intestinalis, portal venous gas, and pneumoperitoneum. Although some studies suggest that increased GRV may be an early indicator of NEC, this relationship has not been clearly substantiated. Cobb et al reported significantly greater maximum GR in infants 6 days before the diagnosis of NEC (4.5 mL per feed or 40% of a feed) compared to infants without NEC (2 mL per feed or 14% of a feed). However, the clinical significance of these findings is uncertain. Similarly, Bertino et al reported statistically greater maximum GR from birth to the onset of NEC. The volume of GR that is considered a significant early indicator of NEC is also unclear. There is a lack of consensus concerning the GRV threshold indicative of NEC. Cobb et al suggested that a GVR of >3.5 mL in VLBW infants may be associated with higher risk of NEC, whereas Bertino et al reported the mean maximum GR in VLBW infants without NEC to be 4 mL, which exceeds the 3.5 mL reported in a previous study even though the cutoff value for GRV was not evaluated in the study. Mihatsch et al, in a randomized, multicenter study of 99 extremely low birth weight (ELBW) infants, found that the mean GRV 24 hours prior to diagnosis of NEC was only 1.2 mL in the five infants diagnosed with NEC. They concluded that increased GRVs were not predictive of NEC. Similarly, the timing of increases in GRV based on the percentage of the previous feeding volume has been used to predict NEC. However, this arbitrariness in defining the duration of maximum GR obviates its reliability to predict NEC in VLBW infants.

The color of GRs has also been evaluated as an indicator of NEC. Bertino et al reported a correlation between bloody residuals and NEC, but that correlation did not extend to bilious colored residuals. Similarly, Mihatsch et al found that green-colored GRs <2 mL/kg were not associated with an increased incidence of NEC in ELBW infants in the absence of other abnormal clinical manifestations. They suggested that accepting the GRVs >5 mL/kg might be considered safe in ELBW infants. Nevertheless, in clinical practice, enteral feedings are frequently discontinued because of yellowish or slightly green GR potentially resulting in unnecessary delays in the attainment of full enteral feedings. Caution is warranted in the presence of bilious emesis or GRs owing to the association with volvulus, intestinal obstruction, and ileus. It is currently unclear whether routinely checking GRs is a useful or perhaps even a detrimental practice. Randomized studies are currently underway to evaluate this. Figure 1 shows a feeding algorithm for preterm infants that appears to be

![Figure 1](image_url)
reasonable given current practice standards and available evidence. However, future studies may show routine evaluation of GRs to be unnecessary and that there may even be benefits to not routinely checking. Nonetheless, implementation of a standardized feeding regimen or nutritional guidelines has been associated with a decrease in the incidence of NEC.\textsuperscript{58} Indeed, variations in clinical practice, especially enteral feeding practices, have been suggested as an iatrogenic component in the pathogenesis of NEC.\textsuperscript{58,59}

6. Summary

The routine practice of checking GR prior to enteral bolus feeding in VLBW infants is not evidence-based and may be harmful. Whether this practice should be discontinued or should only be used to evaluate infants showing other clinical signs of FI is an important question that needs to be addressed by well-designed, randomized controlled trials.

Conflicts of interest

J. Neu declares that he is a consultant for Infant Microbial Therapeutics, and he is on the Scientific Advisory Board of Medela. The other authors have no conflicts of interest to declare.

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