Gastric emptying in preterm infants

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Abstract

An ultrasonic technique was used to compare gastric emptying after a feed of expressed breast milk and formula milk in a blind, cross over study of preterm infants. Fourteen infants (median gestational age 33 weeks) were studied on 46 occasions. Each infant received a nasogastric feed of either expressed breast milk or formula milk, and the alternative at the next feed. Real time ultrasound images of the gastric antrum were obtained and measurements of antral cross sectional area (ACSA) were made before the feed and then sequentially after its completion until the ACSA returned to its prefeed value. The half emptying time (50% Δ ACSA) was calculated as the time taken for the ACSA to decrease to half the maximum increment. On average, expressed breast milk emptied twice as fast as formula milk: mean 50% Δ ACSA expressed breast milk 36 minutes; formula milk 72 minutes. The technique was reproducible and there was no significant difference between the emptying rates of feeds of the same type for an individual infant. These data show that breast milk has a major effect on gastric emptying, which may have important implications for preterm infants who have a feed intolerance due to delayed gastric emptying.

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Inadequate gastric emptying often prevents early enteral nutrition in preterm infants but its determinants are poorly understood. This is due in part to the lack of a method of measuring gastric emptying which is suitable for serial use in very small infants. Radioisotope studies are the 'gold standard' for estimating gastric emptying, but the technique is not suitable for widespread use in neonates. The test involves irradiation and access to a gamma camera. Most data in preterm infants have been obtained using either marker dilution and a single aspiration technique,¹ or a modified double sampling marker dilution technique.² Neither is entirely satisfactory. The former does not show the pattern of emptying for an individual feed. In the latter, the repeated withdrawal and reinsertion of milk from the stomach to ensure adequate mixing of the dye is unphysiological and may not be well tolerated by smaller infants. A non-invasive, non-isotopic method involving minimal disturbance to the infant and which does not interfere with the emptying process is therefore needed. Bolondi *et al* used an ultrasound technique to study gastric emptying of a meal of pasta in adults.³ A modified version of this

technique has been used successfully in preterm infants in our department⁴ and has been validated against radioisotope measurements in adults.⁵ The technique is based on serial measurements of the cross sectional area of the gastric antrum (ACSA) as it fills and empties during and after a feed.

Using this method we compared the emptying rates of maternal breast milk and a whey based formula milk (Cow and Gate Premium). In addition to other well recognised benefits, breast milk may have additional advantages with respect to more rapid gastric emptying than formula milk. In the only previous study,⁶ however, a potentially unphysiological marker dilution technique was used and the infants were not studied in a blind, cross over manner. Moreover, most patients studied only received a single milk type. As gastric emptying shows large interindividual variability this makes comparisons between milk type less informative. We have therefore used serial ultrasound measurements of the ACSA as a means of comparing, within individuals, the gastric emptying of expressed breast milk with a whey based formula, and of assessing the reproducibility of the technique.

Subjects and methods

SUBJECTS

The study was carried out on the regional neonatal intensive care unit at Birmingham Maternity Hospital. Infants were entered into the study if they fulfilled all the following criteria: preterm delivery (less than 37 weeks' gestation); absence of, or complete recovery from, respiratory illness; no evidence of gastrointestinal disease; no drug treatment; receiving full enteral feeds of whey predominant formula (whey 60%, casein 40%; Cow and Gate Premium) and/or expressed maternal breast milk via a nasogastric tube at a minimum of 150 ml/kg/day, with an interval of at least two hours between feeds. All infants were receiving some breast milk. Some were receiving formula milk as a supplement whereas others were receiving full breast milk feeds but had received formula milk previously. The latter group received a further formula feed for the purpose of the study only.

The first 14 consecutively available infants (nine boys, five girls) who fulfilled these criteria were recruited. The median (range) gestation of the group was 33 (30-35) weeks; birth weight 1650 (1130-2130) g, and post-natal age at the time of study 11 (4-26) days. Eight infants were appropriately grown for gestational age; six infants were growth retarded in that their birth weight was less than the tenth centile for gestation.

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One paired study was performed on each of the 14 infants and this was repeated in nine of 14 infants within a median (range) of 2 (1–6) days. During the paired study the infant received a bolus nasogastric feed of either expressed breast milk or formula milk and then the same volume of the alternative milk at the following feed. The examiner (AKE) was blind to milk type until analysis of the data was complete. The daily median (range) feed volume was 167 (150–235) ml/kg/day given at two, three, or four hourly intervals. The median (range) feed volume was 21 (13–29) ml/kg. Feeds were administered by nasogastric tube over a median (range) period of 6 (3–12) minutes.

Informed parental consent was obtained in each case and the protocol was approved by the local research ethical committee.

METHODS

Gastric antral transit was used as a proxy for gastric emptying. This was determined by measuring ultrasonically the changes in the cross sectional area of the gastric antrum which occur after a feed.⁴ Newell *et al*⁴ showed a highly significant correlation between intra-gastric milk volume and an increase in ACSA after the administration of 25, 50, 75, and 100% of a feed.

Real time ultrasonic images of the same longitudinal section of the gastric antrum were obtained with the infant in the right lateral position using the vertebral bodies and the aorta, at the level of the superior mesenteric artery, as constant anatomical landmarks. The Hewlett Packard ultrasound imaging system (model 77020A) with a 5 MHz sector scanning probe (model 21210A0) held perpendicular to the anterior abdominal wall, just below the xiphisternum, produced satisfactory images during all studies. The ACSA was measured using a steerable cursor and integral software within the machine.

The stomach was aspirated before a feed to remove residual air or milk. The ACSA was measured before the feed, as soon as the feed was completed, and sequentially at about 10 minute intervals until it returned to its prefeed value. We defined 50% Δ ACSA as the time taken for the ACSA to decrease by half of the maximum change seen during gastric filling.

Figure 1 Half emptying times (50% Δ ACSA) for expressed breast milk (EBM) and formula feed.

Figure 2 Gastric emptying of expressed breast milk (EBM) and formula feed within individual infants: (A) first paired studies and (B) repeated paired studies ($p < 0.0001$).

Paired studies were analysed using Student's paired *t* test.

Results

COMPARISON OF BREAST MILK AND FORMULA MILK

The technique was well tolerated. No infant vomited or appeared distressed during the studies. One set of paired studies was performed in all 14 patients. In nine of 14 infants the paired studies were repeated, making a total of 23, one of the pair being breast milk and the other formula milk. The mean half-emptying times (50% Δ ACSA) for breast milk were significantly lower than those for formula milk, with means of 36 and 72 minutes respectively (fig 1). There was considerable variation for each milk and a degree of overlap between the two. This reflects the natural physiological variability of gastric emptying and the differing volumes and feed intervals within the study group.

When the differences between 50% Δ ACSA for expressed breast milk and formula milk are compared within an individual infant (fig 2), it can be seen that expressed breast milk emptied faster from the stomach than formula milk during every paired study and that this difference is highly significant ($p < 0.0001$). Figure 3 shows the mean change in ACSA in all 23 studies for each milk type against time.

Figure 3 Mean (SEM) percentage change in ACSA after a bolus feed of expressed breast milk (EBM) or formula feed.

Figure 4 Gastric emptying of same feed type within individual infants (not significant). EBM=expressed breast milk.

Emptying of breast milk was characterised by a more rapid initial emptying phase.

REPRODUCIBILITY

In the nine infants in whom two paired studies were performed we compared 50% Δ ACSA for a feed of the same type within an individual infant. The data are represented in fig 4 and show that although there is some variation within the two groups, in most 50% Δ ACSA is about the same, within an individual, for the same milk type. There was no significant difference within an individual infant; $p=0.4$ for expressed breast milk and $p=0.9$ for formula milk.

Discussion

We compared the effect of maternal breast milk and a commonly used formula milk on gastric emptying in preterm infants, using a method which is particularly well suited to this group. We have confirmed Cavell's findings⁶ and shown that breast milk empties from the stomach much more quickly than formula milk.

A number of previous studies have investigated gastric emptying in preterm infants. The data have often been conflicting, possibly a reflection of the different methods of analysis and feed type used. The most commonly used methods involved a marker dilution technique of either the single aspiration type¹ or the double sampling method of George.² Using these methods it has been shown that an increased calorific density⁷ and carbohydrate composition of feeds,⁸ the presence of hyaline membrane disease,⁹ and congenital heart disease¹⁰ can slow gastric emptying. The effects of fat content,^{8,11} phototherapy,^{12,13} and the posture of the infant^{9,14} are less clear. Feed osmolality^{15,16} and the temperature of feeds^{12,17} do not appear to have an effect. Cavell suggested that, in general, breast milk empties faster than formula milk.⁶ His studies did not investigate the differences in emptying times for the two milks within individual infants, however. As most gastric emptying data suggest a great deal of interindividual variation, a cross over study such as ours is more appropriate.

The differences between breast milk and formula milk are marked and it is difficult to account for them by differences in crude macronutrient content. What mediates these differences? Widström *et al* have shown that human milk contains peptides such as gastrin and somatostatin,¹⁸ but the effects of these on infant gut motility have yet to be elucidated. Lucas *et al* have shown differences in gut peptide profiles in plasma after a breast milk or formula milk feed.¹⁹ This effect may be a contributing factor to the differences in emptying rates we have shown.

The observation that breast milk empties so much faster may have important implications in preterm infants who appear to be intolerant of formula feeds. The significance of slower gastric emptying in infants who appear to tolerate feeds has yet to be established. It is known that asymptomatic gastro-oesophageal reflux is a common finding in preterm infants²⁰ and that the aspiration of milk is not uncommon on neonatal units.²¹ Delayed gastric emptying has been shown to be a cause of gastro-oesophageal reflux in older children,²² but the relation between slower gastric emptying and gastro-oesophageal reflux in preterm infants is not known.

In summary, breast milk empties faster from the stomachs of preterm infants than formula milk. Although we do not understand how these differences are mediated it is clear that they are present despite attempts to humanise cows' milk formula. The effect may reside in the presence of prokinetic agents in breast milk. There are obvious advantages in the use of human milk in neonates in whom delayed gastric emptying is preventing the successful use of enteral feeding.

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