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Aspects of gastrointestinal motility in relation to the development of digestive function in neonates

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Abstract

Gastrointestinal motility is responsible for mixing and transport of digesta and elimination of undigested residues. The basis for the motility is the electrical activity of the gastrointestinal smooth muscle, which has a recurring pattern. In the small intestine of mature animals, this pattern is associated with periodic fluctuations of mesenteric blood flow, and gastric, pancreatic and biliary secretion, and with intestinal absorption. In general, feeding disrupts the cyclic pattern in the stomach and small intestine, replacing it with a continuous post-feeding pattern, and the duration of the post-feeding pattern is dependent on animal species, composition of the diet and feeding regime. The perinatal and weaning periods manifest drastic changes in digestive function and, thus, in gastrointestinal motility. Due to difficulties in performing studies in perinatal and neonatal animals, only few data on the development of gastrointestinal motility, and its synchronisation with other digestive functions, are available. Whereas some studies in the literature indicate that the development of gastrointestinal motility follows the maturation of the regulatory mechanisms, recent data also suggest that changes in gastrointestinal motility around birth and weaning reflect changes in nutrient supply. This paper deals with some aspects of gastrointestinal motility, primarily in the gastric antrum and small intestine, of neonatal animals. Certainly, changes in gastrointestinal motility in early life could be of paramount importance for proper digestive function and this research area requires further attention. © 2000 Elsevier Science B.V. All rights reserved.

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1. What is gastrointestinal motility?

Three basic parameters of intestinal motility can

be measured: transit of intraluminal contents, mechanical activity, i.e., contraction or pressure gradients, and myoelectrical activity. The myoelectrical activity is the basis for the mechanical activity, which in turn will influence the flow (mixing and propelling) of digesta. The myoelectrical activity consists of electrical control activity (ECA or slow

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wave) and electrical response activity (ERA or spike activity). ECA is an omnipresent oscillation of membrane potential that controls the excitability of the smooth muscles and largely controls the frequency of contraction, whereas ERA is under the influence of regulatory mechanisms and determines the contraction force (Sarna, 1989).

2. Gastrointestinal motility and digesta flow

In mature animals, the myoelectrical activity of the small intestine is characterised by intense electrical and contractile activity separated by quiescent periods, reflecting variation in the frequency of ERA. This pattern is known as the migrating myoelectric complex or MMC, and it migrates distally along the length of the small intestine (Code and Marlett, 1975).

In farm animals, there are three phases of the MMC; the quiescent phase (NSA or phase I), the irregular phase (ISA or phase II) and the activity front (RSA or phase III). There is very little muscle contraction or transit of gut contents during NSA. During the irregular phase, contractions mix the gut contents and propel them in an aboral direction (Girard and Sissons, 1992; Bueno and Fioramonti, 1994). The activity front or RSA is accompanied by intense muscular contraction that obliterates the lumen, preventing the back-flow of contents. As such, MMC serves as the “housekeeper” of the gut, promoting bacterial clearance and maintaining intestinal homeostasis (Code and Marlett, 1975).

The duration of each MMC component and the frequency of the cyclic occurrence of MMC is, as reported in the literature, considered to be species dependent (herbivores, carnivores, omnivores) (Bueno and Fioramonti, 1994). Furthermore, in most studies with single-stomached animals (dogs, pigs, rats) and humans, feeding disrupts the MMC, replacing it by a post-feeding pattern resembling phase II, whereas in ruminants this pattern is not disrupted (Wingate, 1981). However, for omnivores, such as the pig, the occurrence of a postprandial pattern is dependent on the feeding regime. Pigs fed once or twice daily exhibit a clear postprandial pattern, whereas ad libitum fed pigs (eating 10–14 meals per day) do not (Ruckebusch and Bueno, 1976).

Essentially these differences appear to relate to the flow of digesta to the duodenum. In ruminants, the flow of digesta to the duodenum is continuous, and the contractile activity of the MMC can handle the relatively small volumes. On the other hand, ingestion of large meals, e.g., in monogastrics and pre-ruminant calves, will cause sudden increases in the flow to the duodenum, and transport of digesta can only be achieved by increasing the contractile activity, thus disrupting the MMC pattern (Bueno and Ruckebusch, 1978; Girard and Sissons, 1992). Increasing the frequency of digesta deliverance to the duodenum, by ruminant function or increasing the meal frequency, reduces or eliminates the postprandial pattern (Bueno and Ruckebusch, 1978).

3. Gastrointestinal motility and other physiological functions of the gastrointestinal tract

Regulation of digesta flow through gastrointestinal motility is an important factor for digestion and absorption. Furthermore, in mature animals and humans, gastrointestinal motility is synchronised with exocrine biliary and pancreatic secretion, gastro-duodenal pH (Abello et al., 1988; Vantrappen et al., 1979), the level of some plasma hormones, i.e., pancreatic polypeptide, motilin and gastrin (Keane et al., 1980; Konturek et al., 1986; Rayner et al., 1987), and the mesenteric blood flow (Fioramonti and Bueno, 1984; Rasmussen et al., 1999). This apparent synchronisation is evidently of major importance for an optimal digestion and absorption process, and consequently a co-ordination between glucose and amino nitrogen absorption and MMC has also been observed (Rayner, 1991). This pulsatility and synchronisation between the various physiological functions of the gastrointestinal tract is postulated to represent gastrointestinal homeostasis (Zabielski and Naruse, 1999).

4. Maturation of gastrointestinal motility

A few studies in animals (Bueno and Ruckebusch, 1979) and more studies in human babies (e.g., Berseth, 1989, 1992; Berseth and Nordyke, 1993; Baker and Berseth, 1995; Chen et al., 1997; Liang et

al., 1998) have examined the gestational evolution of motility.

Dogs do not obtain a MMC until 15 days postnatally, whereas sheep and humans have a MMC pattern already before birth (at 95–99% of term) (Bueno and Ruckebusch, 1979; Milla, 1996), which reflects the relative development of the central nervous system (CNS), enteric nervous system (ENS) and pacemaker activity of the smooth muscle (Ruckebusch, 1986; Liu et al., 1998). For example, in neonatal mice, smooth muscle pacemaker activities that initiate repetitive action potentials were not fully developed until 2 days after birth (Liu et al., 1998). Therefore, development of basic neonatal motility is considered a programmed event, related to the gestational and postnatal age of the animal by some authors (Ruckebusch, 1986; Milla, 1996).

Interestingly, however, studies in preterm babies have shown that early enteral feedings can promote gut maturation and increase the postnatal fasting levels of certain gastrointestinal tract hormones, such as gastrin and gastric inhibitory peptide (Berseth, 1989, 1992; Berseth and Nordyke, 1993). Furthermore, these studies have demonstrated that artificial milk formulas promote maturation to a greater extent than oral administration of water, suggesting that components of the diet cause maturation (Berseth and Nordyke, 1993).

However, although some species display a triphasic pattern already before or just after birth, this does not necessarily reflect full maturation, i.e., patterns identical to those obtained in older/mature animals. Developmental changes may still occur after birth in terms of the response to feed and coordination with other digestive functions. Previous studies in neonatal piglets have shown that the MMC cycles of 7- to 14-day-old piglets were much shorter (50 min) than those of adult pigs (80 min) (Burrows et al., 1986). The cycles were also much more irregular and variable in length (4–156 min), and the authors suggested that this variation was due to immaturity of the enteric nervous system or the extrinsic modulating systems.

5. Temporal co-ordination of secretion and motility in neonates

Since the enteric nervous system and secretory and

regulatory mechanisms are known not to be fully developed, e.g., in mice (Saffrey and Burnstock, 1994; Liddle, 1997), it is important to study whether the periodicity or synchronisation between motility and other digestive functions takes place in neonatal animals. Lack of co-ordination could cause digestive malfunction and gastrointestinal disturbances. To study such a temporal co-ordination, a sophisticated and rather complex animal model is necessary and, therefore, few results are available. Like in mature animals, Zabielski et al. (1993) found in neonatal milk-fed calves, that the interdigestive exocrine pancreatic outflow of juice, protein and bicarbonate display periodic fluctuations which are co-ordinated with the duodenal MMC. The nadir of secretion occurred in the quiescent phase (NSA) and increased during ISA with a maximum secretion just prior to the onset of RSA in a manner similar to, for example, older pigs (Abello et al., 1988; Zabielski et al., 1993). They also found that feeding the calves with milk replacer twice daily suspended the regular MMC cycles (lasting an average of 32 min), replacing them with high-amplitude activity for 30–70 min (Zabielski et al., 1993).

Recently, we have noted a similar co-ordination in unweaned suckling piglets although some irregularity was seen both in the occurrence of MMC cycles and in the fluctuations of pancreatic juice secretion (Fig. 1, Lærke et al., unpublished observations).

6. Influence of diet

Meal structure and composition (energy, fat, dietary fibre, solid/liquid, etc.) affects gastric emptying and the intestinal motility pattern (Ruckebusch, 1981; Bueno and Fioramonti, 1994). In sheep, rabbits, dogs, pigs and humans, it has been shown that the duration of the gastroduodenal postprandial pattern is significantly longer after a solid than a liquid meal (Grivel and Ruckebusch, 1972; Code and Marlett, 1975; Rayner and Wenham, 1986; von Schönfeld et al., 1997). Protein, as in milk or as peptides, is less effective than glucose or sucrose and lipids at inducing a postprandial pattern (De Wever et al., 1978; Schang et al., 1978). In neonatal calves, the abomasal emptying and the duration of the duodenal postprandial pattern increases with the

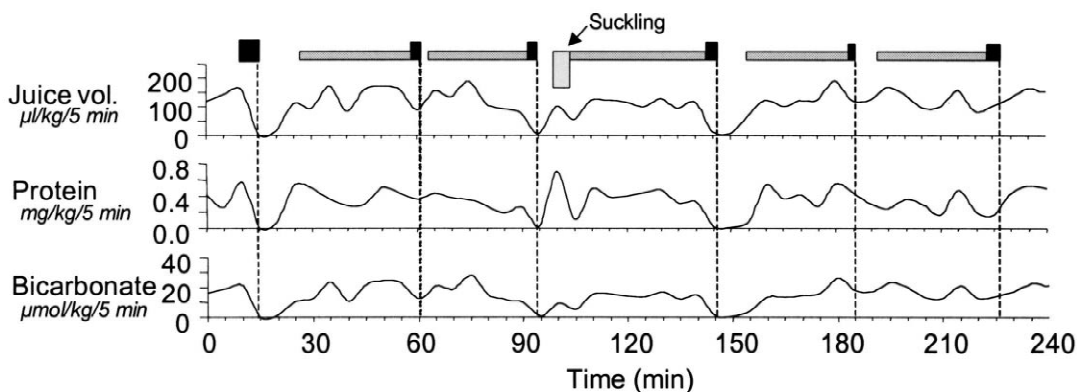


Fig. 1. Example of output of pancreatic juice, protein and hydrogencarbonate collected in 5-min intervals together with continuous recording of duodenal myoelectric activity for 4 h in one 20-day-old piglet before and after suckling. Black boxes represent RSA, grey boxes represent ISA, no box represents NSA.

amount of milk consumed (Sissons, 1983; Girard and Sissons, 1992) and is also affected by the source of dietary protein (Hara et al., 1992; Zabielski et al., 1998). In neonatal piglets, sow's milk decreases the contractile activity of the gastric antrum when compared with the interdigestive state (Lesniewska et al., 2000b). This leads to the role of bioactive components of maternal milk. It has been shown that opioid peptides (casomorphins), as well as glycomacropeptides released from milk casein during digestion, can slow gastrointestinal motility (Stan et al., 1983; Daniel et al., 1990). In suckling rats, epidermal growth factor (EGF) in milk delayed gastric emptying as well as intestinal transit time (Shinohara et al., 1996). Moreover, milk contains gastrointestinal hormones such as gastrin, cholecystokinin and somatostatin (Zabielski, 1998) which are all known as regulatory factors of gastrointestinal motility (Vergara et al., 1996; Shulkes, 1994). This suggests that maternal milk as a source of bioactive regulatory components is an important factor for the characteristics of intestinal motility in neonates.

7. Gastrointestinal motility around weaning

Weaning may be defined as a process by which mammals cease suckling and begin to ingest solid feed (Counsilman and Lim, 1985). This is one of the

most sensitive periods in the young animal's life. Drastic changes occur in the digestive system, and some of these may be related to changes in nutrient supply whereas other changes may depend more on the age or developmental stage of the animal.

In neonatal calves, the duration of MMC cycles and phases of MMC increase with age of the animal (Zabielski et al., 1994). Furthermore, in calves before weaning, feeding with milk 2–3 times per day induced a postprandial pattern whereas, after weaning (when the calves begin to ruminate), ingestion of solid feed when the calves began to ruminate did not affect MMC (Ruckebusch and Bueno, 1973; Zabielski et al., 1997).

Studies from our group suggest that the length of the MMC cycle in the duodenum of piglets increases with age, but weaning induces a momentary drop in duration (Lesniewska et al., 2000a). Furthermore, the proportion of NSA to ISA decreases after weaning, which might reflect the change from liquid feed during nursing to solid feed after weaning (Rayner and Wenham, 1986; Lesniewska et al., 1998; Lesniewska et al., 2000a). Alternatively, a reduction in feeding frequency with a concomitant increase in meal volume may induce changes in gastrointestinal motility around weaning. Szabo and Fewell (1990) have previously shown that a commercial milk formula fed three times daily causes postprandial disruption of the MMC for 147 min, similar to the

disruption seen with solid feed. This favours the hypothesis that the meal volume and/or frequency of feeding are major determinants for postprandial gastrointestinal motility. Recent observations from our group indicate that both the interdigestive and postprandial antral and duodenal motilities are affected by weaning (Lesniewska et al., 2000b). The frequency of the response potentials of the electrical response activity in the antrum and duodenum is increased by ingestion of solid feed after weaning, presumably due to distension and/or chemical composition of the diet. In contrast, in the unweaned piglet, suckling, compared with the interdigestive state, decreased the response potentials in the antrum, but had no significant effect in the duodenum (Lesniewska et al., 2000a,b). As previously mentioned, our interpretation of these observations is that components of the sow's milk inhibited the antral activity. However, as changes also occurred with age, this component was difficult to separate from the effect of milk versus solid feed on gastrointestinal development around weaning.

8. Development – a programmed event or adaptation?

The irregularity in motility and its co-ordination with pancreatic secretion, as observed in suckling pigs, again leads to a central question about the development of gastrointestinal motility in neonates. Is the development of motility an inherently programmed event, or do changes in motility pattern simply reflect changes in the form and composition of nutrient supply?

If the maturation of gut motility was only a programmed event following the maturation of the regulatory mechanisms, it would not be possible to modify the onset of the developmental process, as seen in preterm infants. On the other hand, the changes in gut motility around weaning is unlikely to be solely an effect of adaptation, since this would imply that the changes in motility pattern would be reversible processes. However, to our knowledge, no studies have ever dealt with this issue. Presumably, the maturation process in neonates is a combined action of inherent developmental factors triggered by dietary manipulation in neonates.

9. Conclusion

The motility pattern is developed to varying degrees in different species at birth, but the maturation process presumably continues after birth. The development seems to be strongly dependent on the composition and amount of the meal fed. Considering that the secretory and regulatory mechanisms of the GIT in neonates are not fully developed, even with a well-developed physiological response of motility, digestive disturbances may occur.

Future studies should investigate the influence of the meal quality and structure on gastrointestinal tract motility in relation to gastrointestinal tract secretion, absorption and health.

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