Digestive Diseases and Sciences, Vol. 37, No. 1 (January 1992), pp. 14–19

Maturation of Antroduodenal Motor Activity in Preterm and Term Infants

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Previous studies have shown that duodenal motility patterns differ in preterm and term infants, but antral motor activities were not compared. Using a validated, low-compliance, continuous-perfusion, neonatal manometric system, antral and duodenal motility was studied in 19 preterm and nine term infants. Antral motility consisted of isolated single contractions and clustered phasic contractions in term and preterm infants. There were no differences in the occurrence or amplitude of antral activity between the two groups of infants. Thus, there was no change of antral motor activity with advancing gestational age. As has been shown in other previous studies, however, intestinal motor characteristics were more immature in preterm than term infants; clustered phasic contractions occurred more frequently ($P < 0.02$) and were of shorter duration ($P < 0.02$) and lower amplitude ($P < 0.005$). Duodenal clusters were significantly less common, while their amplitudes were significantly increased with increasing gestational age. The proportion of antral clusters that were temporally associated with duodenal activity was significantly lower in preterm infants than in term infants ($P < 0.001$). Moreover, the degree of association of antral and duodenal activity increased significantly with gestational age ($r = 0.5$, $P = 0.006$). These data show that fasting antral motor activity per se *is comparable in preterm and term infants; they also suggest that the temporal association of antral and duodenal activity develops in association with progressive changes in duodenal motor activity in the preterm infant.*

KEY WORDS: neonatal gastrointestinal motility; preterm intestine.

Preterm and term infants recovering from respiratory illnesses frequently experience feeding difficulties with regurgitation and aspiration. These feeding problems may be due to immaturity of motor function, such as decreased lower esophageal sphincter basal pressure and delayed gastric emptying (1–4). Regurgitation and retention of gastric contents in infants also may be due to differences in antral motor activity, small intestinal motility, or to lack of motor coordination between antrum and duodenum.

Motor activity is responsible for the mixing of intraluminal contents and the aboral movement of nutrients. During fasting, motor activity cycles every 60–90 min through phase I (quiescence), phase II (irregular activity), and phase III (activity the migrates distally through the bowel). Phase III, or the migratory motor complex, contributes significantly to the aboral movement of nutrients (5). With feeding, the adult fasting cyclic activity is replaced by sustained motor activity. Although few studies have been performed in children, motor activity patterns also vary during fasting and feeding in young children.

Manuscript received November 28, 1990; revised manuscript received May 16, 1991; accepted May 16, 1991.
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This work was supported by grant number HD24558 from National Institutes of Health.
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Feeding disorders may occur in adults who exhibit motor activity abnormalities during fasting, feeding, or both, as the cyclic nature of fasting activity contributes significantly to the aboral movement of intraluminal contents. Although previous studies have described antral activity in newborns and infants (6, 7), no study has compared antral motility patterns in preterm and term infants. Previous studies of duodenum and small intestine show that small intestinal motility differs in preterm and term infants during fasting (8–10). Although term infants displayed complete interdigestive cycles, propagated activity was rarely recorded in preterm infants (8, 9). Clusters, or regular phasic nonpropagating activity, comprised approximately two thirds of the phase II activity seen in preterm and term infants (9). Clusters lengthened with increasing gestational age as the mature migrating motor complex (MMC) appeared (9). Preliminary studies also showed that antral and duodenal motility was poorly coordinated in the preterm infant (11). None of these previous studies evaluated or compared concurrently all three aspects of this motor activity in preterm and term infants.

The recent development of low-compliance, continuous-perfusion manometric techniques now permits prolonged studies of antral and duodenal motor activity in preterm and term infants (8, 9). The purpose of this study was to use these new techniques to compare antral and duodenal activity and its coordination in preterm and term infants.

MATERIALS AND METHODS

All 28 subjects who participated in this study were housed in the Newborn Intensive Care Unit (NICU) at Saint Marys Hospital in Rochester, Minnesota. The 19 preterm infants had been admitted for regulatory distress syndrome; the nine term infants had been treated for meconium aspiration or pulmonary hypertension. By NICU routine, all of these infants had received parenteral alimentation until their ventilator support had been withdrawn and their umbilical lines removed. Preterm infants ranged from 25 to 35 weeks of gestation (Table 1). All babies were studied within the first three weeks of life; none had received enteral nutrition prior to the study, and all received parenteral nutrition on the day of the study. This study was approved by the Mayo Institutional Review Board, and parents provided informed written consent for the infant to participate in this study.

The manometric/feeding tube used for these studies had a 3.7-mm outer diameter, four proximal manometric ports spaced 2.5 cm apart, and a distal feeding port. The manometric ports were continuously perfused by a low-compliance, continuous-perfusion system. This system, which has been described and validated previously (8), provides an infusion rate of 0.01 cc/min/port and has a response rate of 57 mm Hg/sec at 10 psi. On the day enteral feedings were to be initiated, the nursing staff placed the tube while the infant was still fasting. The infant was placed supine with the right side down. The tube was perfused by the manometric infusion system, and pressure changes characteristic of fasting antrum and intestine were used to identify when the distal ports passed from the antrum to the duodenum. The tube was positioned so that at least one manometric port remained in the antrum and one or more were located in the duodenum. The position of the manometric/feeding tube was confirmed by the presence of fasting phase II motor activity occurring at a frequency of 3–5/min in the antrum and 9–11/min in the intestine. Previous studies using this manometric system have validated the occurrence of these activity frequencies in ports positioned under fluoroscopy (8, 9). The average time for tube placement was 20 min, with a range of 10–120 min. All attempted tube placements were successful. Manometric tracings were obtained for 3–6 hr during fasting.

TABLE 1. CHARACTERISTICS OF STUDY PARTICIPANTS*

Characteristic	*Preterm* (N = *19*)	*Term* (N = *9*)
Birth weight (g)	1285 ± 96	3219 ± 283
Gestational age at birth (weeks)	29.7 ± 2.8	37.6 ± 2.4
Postnatal age at study (days)	7.5 ± 7.0	10.6 ± 5.7
Gestational age at study (weeks)	30.0 ± 0.6	40.1 ± 0.9

*Values are means ± SEM.

Data Analysis. Motor activity was analyzed in 30-min segments for 3–6 hr independently by three observers who agreed to the presence of activity when interobserver discrepancy existed. An antral pressure wave was defined as any positive deflection occurring in an antral lead with amplitude exceeding 5 mm Hg and duration exceeding 8 sec. An antral cluster was defined as a series of four or more antral pressure waves with a frequency of 3–5/min. A coordinated cluster was defined as any antral cluster temporally associated with phasic activity occurring in the duodenum within 1 min of the completion of the antral cluster. The time window of 1 min between antral and duodenal clusters was calculated to coincide with the antral and duodenal migration velocities previously reported in neonates (2.4–2.6 cm/min) and adults (5.0–6.0 cm/min) (7). Activity occurring simultaneously in antrum and duodenum was not considered to be coordinated. When an antral cluster was temporally associated with an intestinal cluster, the duration of the cluster was calculated by averaging the duration in minutes of the cluster in each antral and duodenal lead. The antroduodenal velocity was calculated from the time of appearance of the onset of the most proximal antral cluster to the appearance of the onset of the most distal duodenal cluster in cm/min. The percent of antral clusters associated with duodenal clusters was calculated for each infant as: (number of coordinated clusters ÷ total number of antral clusters) × 100.

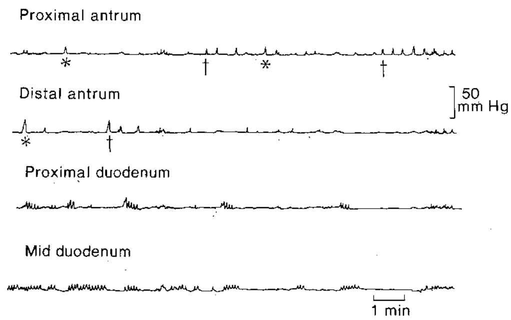

Fig 1. Antroduodenal motor activity in a preterm infant. The upper line represents activity from the most proximal port and the lowest line the most distal port. In this figure the top two pressure tracings are from antrum and the bottom two from duodenum. Note the occurrence of isolated antral pressure waves (designated by *) and clusters of phasic activity (designated by †) in the two antral leads. Also shown are clusters of phasic activity in the duodenal leads.

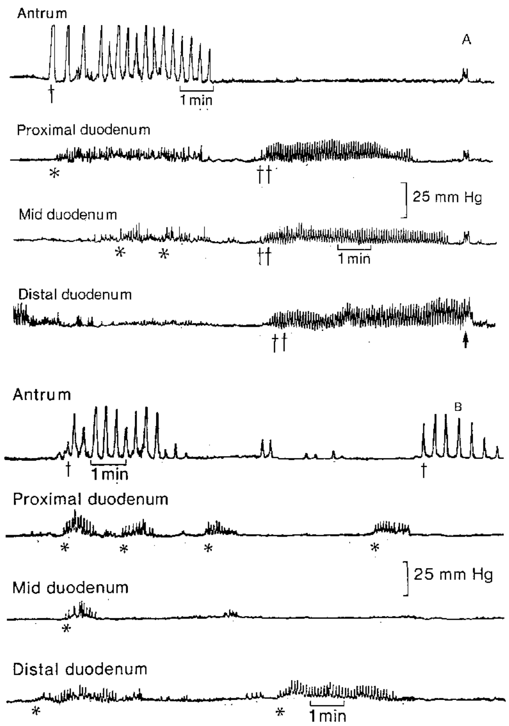

Fig 2. (A) Antroduodenal motor activity in a term infant, with the same orientation as Figure 1. In this figure the uppermost tracing is from antrum and the lower three from duodenum. Phasic activity is present in the antrum (designated by †) and it is temporally coordinated with migratory phasic activity in all three duodenal sites (designated by ††). Three other duodenal clusters (designated by *) fail to migrate. Arrow indicates the presence of movement artifact. (B) Antroduodenal motor activity in a preterm infant. Two antral clusters (designated by †) are present; phasic activity occurs only in the first and third middle duodenal sites (designated by *), while the second duodenal site contains little activity. None of the duodenal phasic clustered activity migrates and occurs asynchronously with respect to the two antral clusters.

The numbers of antral pressure waves and antral clusters per hour were noted. Also noted were cluster duration and amplitude, the occurrence of temporal association with duodenal clusters as the percentage of all antral clusters, and the antral motility index. Motility index was calculated as the $\log_e$ (sum of amplitudes $\times$ number of waves + 1) (13). Antral motor characteristics were compared between the preterm and term infants by unpaired t testing. Antral and duodenal cluster characteristics also were evaluated as a function of gestational age by regression analysis. The baby's gestational age at the time of the study was used for these analyses.

RESULTS

Antral Activity. Antral motility consisted of high-amplitude pressure waves. Approximately one third of antral pressure waves occurred as isolated events with no temporal association to other isolated events in more distal leads (Figure 1). Two thirds of antral activity was comprised of clusters of antral pressure waves occurring with a frequency of approximately three waves per minute (Figure 2A). In preterm infants, antral clusters occurred four times per hour with an average duration of 4.2 min per cluster (Table 2). In term infants, antral clusters occurred 3.5 times per hour with an average duration of 4.3 min (Table 2). There was no difference in the average amplitude of antral clusters in the nine term and 19 preterm infants. The motility index was similar in the two groups. The number of antral pressure waves, antral cluster occurrence, and antral cluster duration were similar in the two groups of infants. Antral cluster occurrence and amplitude were not a function of gestational age (Figure 3A,B).

Duodenal Activity. We confirmed that there were significant differences in characteristics of cluster motor activity in preterm and term infants (8, 9). Preterm infants had more clusters than term infants (Table 3; $P < 0.02$). The average cluster duration and amplitude were significantly greater in term than preterm infants (Table 3; $P < 0.02$ and 0.005, respectively). Cluster occurrence decreased significantly with gestational age (Figure 3C). Moreover, mean cluster amplitude increased significantly with gestational age (Figure 3D). Mean cluster duration did not vary with gestational age (r=0.38; P=0.07).

Antroduodenal Coordination. Of 28 infants, 24 had two or more ports positioned in the duodenum to assess the presence of antroduodenal coordina-

TABLE 2. CHARACTERISTICS OF ANTRAL MOTOR ACTIVITY IN PRETERM AND TERM INFANTS*

Characteristic	*Preterm*	*Term*
Antral pressure waves per hour	82.3 ± 8.0 (41.0–149.7)	80.8 ± 8.9 (38.0–111.3)
Antral clusters		
Frequency of phasic waves (peaks/min)	3.2 ± 0.1 (2.9–3.6)	3.4 ± 0.1 (2.9–42.)
Amplitude (mm Hg)	26.4 ± 2.9 (12.9–50.2)	34.6 ± 5.2 (15.6–64.3)
(N)	4.1 ± 0.3 (2.0–6.0)	3.4 ± 0.3 (2.8–4.7)
Mean cluster duration (min)	4.8 ± 0.8 (1.8–5.7)	4.5 ± 0.6 (1.6–6.4)
Motility index	11.9 ± 0.2 (10.4–13.1)	12.1 ± 0.3 (10.8–13.5)

*Values are means ± SEM; values in parentheses are ranges.

TABLE 3. CHARACTERISTICS OF DUODENAL CLUSTER MOTOR ACTIVITY IN PRETERM AND TERM INFANTS*

Characteristic	*Preterm (N = 16)*	*Term (N = 6)*
(*N*/hr/lead)	13.7 ± 0.8 (5.7–18.6)	9.1 ± 1.7† (5.8–14.2)
Mean cluster duration (min)	1.4 ± 0.1 (0.6–2.6)	2.0 ± 0.1† (1.4–2.4)
Amplitude (mm Hg)	14.1 ± 1.1 (7.7–22.8)	24.7 ± 2.7‡ (19.7–31.7)

*Values are means ± SEM; values in parentheses are ranges.
†$P < 0.02$.
‡$P < 0.005$.

tion. Of term infants, all but one had at least one episode of antral cluster activity temporally associated with duodenal activity (Figure 2A). Ten of the 17 preterm infants had no temporal association of antral and duodenal activity (Figure 2B); seven preterm infants had at least one episode of antroduodenal coordination. While infants as young as 25 weeks gestation had one episode of antroduodenal coordination, the percentage of coordination was significantly lower in preterm infants than term infants (Table 4; $P < 0.01$). The mean duration of a coordinated event and antroduodenal migration velocity was not significantly different between preterm and term infants (Table 4). The percentage of antroduodenal coordination increased significantly with gestational age (Figure 3E).

DISCUSSION

Antroduodenal motility has been studied in a limited number of preterm infants (6, 7). These previous studies did not compare motor activity in preterm infants to term infants, nor did they assess the effect of gestational age on motor activity characteristics. In the current study, the antral activity was similar in preterm and term infants. Although a limited number of term infants were studied, and differences between preterm and term infants may not have been detected, antral cluster duration and occurrence for both groups of infants were similar

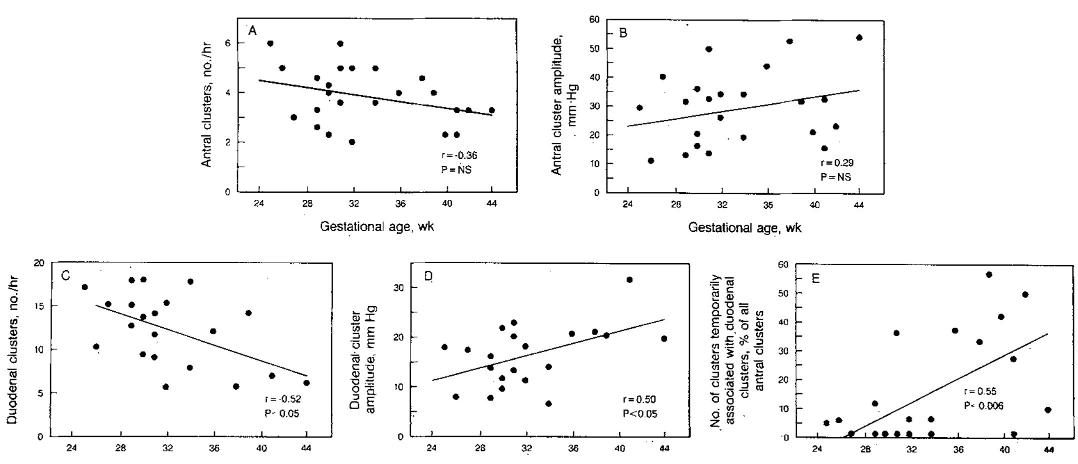

Fig 3. Characteristics of antral and duodenal motor activity as a function of gestational age. (A) Antral cluster occurrence, expressed as number of clusters per hour of recording, was not related to gestational age. (B) Antral cluster amplitude, expressed as mm Hg, was not related to gestational age. (C) Duodenal cluster occurrence, expressed as number of clusters per hour of recording, was significantly inversely related to gestational age. (D) Duodenal cluster amplitude, in mm Hg, was significantly related to gestational age. (E) The incidence of temporal association of antral and duodenal clusters for each individual subject was expressed as a percentage of all antral clusters in that individual. The percentage of occurrence of temporally associated antral and duodenal clusters was significantly related to gestational age.

TABLE 4. CHARACTERISTICS OF ANTRODUODENAL COORDINATED CLUSTERS (CC) IN PRETERM AND TERM INFANTS*

Characteristic	*Preterm* (N = *17*)	*Term* (N = *7*)
Number of infants with coordinated clusters	7	6
Percent coordination [(*N*CC/total AC) × 100]	5.0 ± 3.0 (0–37)	31.0 ± 8.0† (0–57)
Duration (min/lead)	6.1 ± 1.5 (2.8–7.4)	6.2 ± 1.1 (3.7–10.8)
Antroduodenal migration velocity (cm/min)	2.0 ± 0.9 (0.5–6.8)	1.6 ± 0.1 (0.9–2.0)

*Values are means ± SEM; values in parentheses are ranges.
†$P < 0.01$.

to those reported for adults (7, 12). Amplitude of antral contractions was approximately one half to one third that seen in healthy adults. Although antral cluster amplitude appeared to be lower in preterm infants than term infants, this difference was not statistically significant. In addition to the similarities in antral motor activity during fasting in preterm and term infants reported here, we also have noted that preterm and term infants display similar antral motor activity in response to feeding (14). Collectively, these data suggest that some aspects of neonatal antral motor activity are similar to those seen in adults while other aspects are not. Antral activity is present as early as 25 weeks of gestation, but increasing antral amplitude may occur postnatally as increased muscle mass in both antrum and duodenum or increased force of muscular contraction occurs with growth. Alternatively, muscle contraction may not be as forceful in response to factors that regulate motor activity. In rabbits, antral smooth muscle contractility is less in new born rabbits compared to adults (15), for example, and there are postnatal changes in antral response to bethanechol, substance P, and bombesin (16).

Duodenal motor activity differed in preterm and term infants. Cluster amplitude and mean duration were less in preterm than term infants, and cluster frequency was higher in preterm infants. Conversely, quiescence increases in prominence with age (17). These differences in duodenal motor activity have been shown in previous studies (3, 4, 10, 18).

An important finding was that the temporal association of antral and duodenal clusters was a rare event in preterm infants. Although a single episode of temporal association was present in approximately one third of the preterm infants, the overall percentage of antral activity associated with duodenal activity was fivefold lower in preterm infants than in term infants. We speculate that these temporally associated events represent coordination of antral and duodenal activity. When these temporally associated events occurred in preterm infants, the duration and migration velocity of these events were similar to those of term infants. However, migration velocity of neonatal antroduodenal activity was approximately half that seen in adults (7). Only one-third of antral activity was temporally associated with duodenal activity in term infants. In healthy adults, approximately two thirds of antral activity is coordinated with duodenal activity (12), suggesting that further changes in antroduodenal coordination occur during infancy. Moreover, the gestational changes in the temporal association of antral and duodenal clusters mirrored those of duodenal motor activity changes rather than those of antral motor activity.

The clinical implication of the "immaturity" of antroduodenal coordination in neonates is not clear from this preliminary study. In adults studied during fasting, 75% of episodes of antroduodenal coordination are associated with transient acidification of duodenal contents (12). Conversely, antroduodenal reflux during fasting is associated with the absence of coordinated activity in antrum and duodenum (24). Coordinated antroduodenal activity is associated with normal gastric emptying (19, 21, 22), whereas gastric emptying is abnormal when antroduodenal motility is not coordinated (19, 22–24). Although this study did not provide dynamic evaluation of gastric emptying with feeding, gastric emptying can be impaired when fasting activity is abnormal (23). However, gastric emptying of liquids is also a function of fundal motor activity; thus, we cannot be certain that the current findings of antroduodenal incoordination would delay gastric emptying of milk in the preterm infant.

The current study shows that maturation of fasting motor activity of the stomach and duodenum is incongruent; duodenal motor activity differs in preterm and term infants, while antral activity is similar. This incongruency suggests that motor activity of stomach and small intestine is controlled by different neurologic and hormonal modulators or that the appearance of these modulating systems occurs at different times. The presence of antroduodenal coordination appears to be associated with changes in duodenal motor activity and not antral activity. Hence, the use of manometrics to assess the readiness of the preterm intestine for feeding should be focused on maturation of intestinal motor activity and the modulating mechanisms that control its maturation.

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