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de Lorijn, F.

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Chapter 4

Assessment of the rectoanal inhibitory reflex in preterm infants with delayed meconium passage

Fleur de Lorijn, Wieger P. Voskuil, Taher I. Omari,
Joke H. Kok, Jan A. Taminiau, Marc A. Benninga

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Abstract

Background

An inverse relation exists between gestational age and birth weight and the postnatal time of first bowel action. It is however unknown if the rectoanal inhibitory reflex (RAIR) is present in preterm infants with a delayed passage of meconium. We hypothesized that delayed passage of meconium could result from a delayed maturation of the RAIR.

Aim

To evaluate whether the RAIR is absent in very preterm infants 28-32 weeks postmenstrual age (PMA) with delayed meconium production.

Methods

Anorectal manometry was performed in 10 preterm infants (7 male) with delayed meconium production defined as having no meconium in the first 48 hours and a median PMA of 30 weeks (28-31 weeks) and a birth weight of 780 to 1930 g (median 1395 g) with a micromanometric assembly (od 2.0 mm). The assembly incorporated a 1.5-cm-long sleeve sensor for measurement of resting anal sphincter pressures and relaxation, and 4 side-holes recorded anal and rectal pressures. Rectal distension was performed with direct air insufflation to elicit the RAIR.

Results

The time from birth to passage of meconium ranged from 48 to 105 hours (median 82 hours). The mean anal sphincter pressure, rectal pressure, and anal sphincter oscillation frequency were 22.0 ± 5.0 mmHg, 6.9 ± 2.0 mmHg, and 9.8 ± 1.9 /min, respectively. A normal RAIR could be elicited all infants studied.

Conclusion

Anorectal manometry recordings in premature infants with a delayed passage of meconium (>48 hours) showed normal anorectal pressures and a normal RAIR, suggesting that delayed meconium passage is not related to the absence of a RAIR.

Introduction

Normal defecation depends on the complex interplay between colonic motility, rectal mechanical properties and sensation. When stool arrives in the rectum, filling of the rectum leads to stretch of the rectal wall with the subsequent triggering of the rectoanal inhibitory reflex (RAIR). This motor pattern leads to relaxation of the internal anal sphincter (IAS) allowing sensation to defecate and development of urge.

Ninety five percent of healthy term infants pass their first stool within 24 hours and 99% within 48 hours of birth and an inverse relation exists between gestational age and birth weight and the time of first bowel action¹⁻³. Approximately one third of preterm (≤ 32 weeks gestation) and low birth weight (< 2500 grams) infants have a delay in passage of the first stool^{1,3}. Delayed evacuation of meconium often leads to defecation problems or problems with enteral feeding. The exact reason for this delay is unclear, although it has been suggested that delayed maturation of the motor mechanisms of the gut could play a role³.

Anorectal manometry in the neonate offers a noninvasive diagnostic test for identifying the RAIR. Recently, sleeve manometry has been adapted and applied successfully to monitor the RAIR in healthy preterm and term infants, who had meconium production within 48 hours after birth^{4,5}.

The presence of the RAIR in preterm infants with a delayed passage of meconium has been not previously determined. We hypothesized that delayed passage of meconium could occur due to the absence of a normal RAIR and therefore we evaluated anorectal motility in premature neonates with delayed meconium production (> 48 hours) using anorectal manometry.

Methods

Subjects

Studies were performed in 10 preterm infants (3 female, 7 male) ranging in PMA from 28-32 weeks (median 30 weeks) (table 1). Infant birth weight ranged from 780 to 1930 g (median 1395 g), and weight at the time of study ranged from 770 to 1930 g (median 1320 g). We defined delayed meconium passage as having no meconium in the first 48 hours. A normal defecation pattern was defined as having ≥ 3 painless bowel movements per week without the use of laxatives¹³. The time from birth to passage of the first stool ranged from 48 to 105 hours (median 82 hours). After inclusion in the study anorectal manometry was performed 2-5 days after birth (median 4 days). Two infants (patients 6 and 7) had meconium production after receiving an enema because of abdominal distention, while the other 8 infants did not have meconium production at the time of measurement. During (patients 2,3,5 and 9) or immediately after (patients 1,4,8 and 10) the manometric measurement most children passed a large meconium plug. Transition to normal defecation was defined as the loss of dark pigmentation of stool and infants were able to defecate without the help of a thermometer or laxatives. Patients were not receiving prokinetic or oral/rectal laxative medication. None of the infants had anorectal malformations or neurological dysfunctions. Five infants were ventilated and 2 were receiving nasal continuous positive airway pressure at the time of

Table 1 Patient characteristics of the 10 premature infants with a delayed meconium passage (>48 hours).

Patient no.	Sex	PMA (weeks + days)	Birth weight (g)	First passage of meconium (hours)	Transition to normal defecation (days)	Ventilation
1	Girl	30+6	1400	84	10	CPAP
2	Boy	31+4	1540	48	240 *	No
3	Boy	30+5	1390	72	10	No
4	Girl	28+0	780	98	8	Yes
5	Boy	29+6	1240	74	9	Yes
6	Boy	29+6	1060	98	-	Yes
7	Girl	29+4	1010	86	60 **	CPAP
8	Boy	30+4	1455	105	11	Yes
9	Boy	31+4	1780	48	5	No
10	Boy	31+2	1930	80	10	Yes

PMA; Patient postmenstrual age, CPAP; nasal continuous positive airway pressure. *This patient had daily defecation with the help of a thermometer, ** This patient kept defecation problems. Rectal suction biopsy, contrast enema and manometry were performed and excluded Hirschsprung's disease.

measurement. The type of ventilation used did not influence intra-abdominal pressures in basic recordings. The research Ethics Committee of the Emma Children's Hospital approved the study protocol, and written informed consent was obtained before each study.

Manometric Technique

As described in earlier studies anorectal open water perfusion manometry was performed with a purpose-built silicone rubber micromanometric anorectal catheter (od 2.0 mm)^{4,5}. The design of the catheter was based on similar catheters used for measurement of anorectal motor function in children and adults but had a diameter smaller than a neonatal thermometer. The catheter incorporated a 1.5-cm-long sleeve sensor and an array of 3 side-holes spaced 0.5 cm apart for measurement of anal sphincter pressures and 1 side-hole located 0.5 cm proximal of the sleeve for measurement of basal pressure within the rectum. All side-holes were perfused with sterile degassed water at a rate of 0.04 mL/min. An air channel was present on the tip of the catheter for air insufflation to distend the rectum. Figure 1 shows a schematic drawing of the catheter positioned in the anorectum.

Pressures were measured by pressure transducers situated in each perfusion line and connected to PC Polygraph HR preamplifiers (Medtronic, Sweden). The measured signals from the preamplifier were converted to digital values by an analog-digital converter and information was transmitted via a fiber optic cable to a personal computer. Before each measurement a calibration of the polygraph was performed.

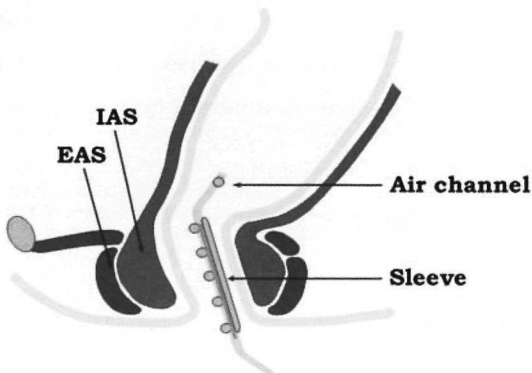


Figure 1 Schematic drawing of the anorectal manometry assembly *in situ*.

IAS: Internal anal sphincter, EAS: External anal sphincter

Protocol

Anorectal manometry was performed with the patient in the supine position. The catheter was positioned with the sleeve straddling the anal sphincter high-pressure zone and the air channel in the rectum. Bowel preparation or sedation was not necessary. With the catheter in position and after a 5-minute accommodation period, a baseline recording of anal sphincter pressure (ASP) and rectal pressure was made over a 2- to 3-minute period before an attempt was made to elicit the RAIR.

To elicit the RAIR, 1 to 3 mL of air was directly insufflated into the lumen of the rectum^{4,5}. Balloon distension was not used in this study because it was considered inappropriate for these young infants. The initiation of the reflex was characterized by an anal sphincter pressure drop of at least 5 mmHg over 2 to 5 seconds in association with cessation of rhythmic activity of the anal sphincter. The threshold air volume required to stimulate the RAIR was determined by increasing the volume of air injected in 1-mL increments in a stepwise fashion, to a maximum of 3 mL. Consecutive rectal distensions were performed at 1-minute intervals. When the threshold volume required to stimulate the reflex had been determined, 3 further distensions were then performed. Recording sessions lasted an average of 30 minutes.

Analysis of Manometric Records

Baseline values for anorectal motor patterns were obtained by analysis of the manometric recording that immediately preceded attempts to elicit the RAIR. Mean resting anal sphincter pressure, anal sphincter oscillation frequency, and rectal pressure were measured during a period of at least 60 seconds. Anal sphincter pressure was defined by the nadir of the pressure oscillation wave. The anal sphincter oscillation frequency (ASOF) was demonstrated by measuring changes in anal canal pressure in basal unstimulated conditions and was defined as the number of oscillations in a period of 60 seconds. Group mean data are expressed as mean \pm SEM.

Results

Table 1 shows the patient characteristics. Seven out of the ten infants showed transition to normal defecation and a normal defecation frequency after 10 days (mean). Of the remaining infants, one died 1 week after birth due to severe sepsis and the other two continued to experience severe defecation problems. Hirschsprung's disease was suspected in one of these infants due to feeding problems and abdominal distension, however rectal suction biopsy showed normal ganglion cells, no abnormalities were found on contrast enema, excluding Hirschsprung's disease. Long term follow up of this infant showed normalization of her defecation pattern after 8 weeks. The remaining infant experienced the most severe defecation problems, which took a further 8 months to normalise. During this period, daily defecation was achieved with the help of a thermometer.

Anal sphincter tone and pressure oscillations were observed in all infants and, despite the delayed passage of meconium, a normal RAIR (figure 2) could be elicited in all infants even those with the most severe defecation problems. Measured parameters of anorectal motor function were similar to those previously reported in preterm infants with normal passage of meconium (table 2).

Figure 2 Anorectal pressure recordings showing elicitation of RAIR with air insufflation in premature infant 30 weeks' PMA with a delayed passage of meconium.

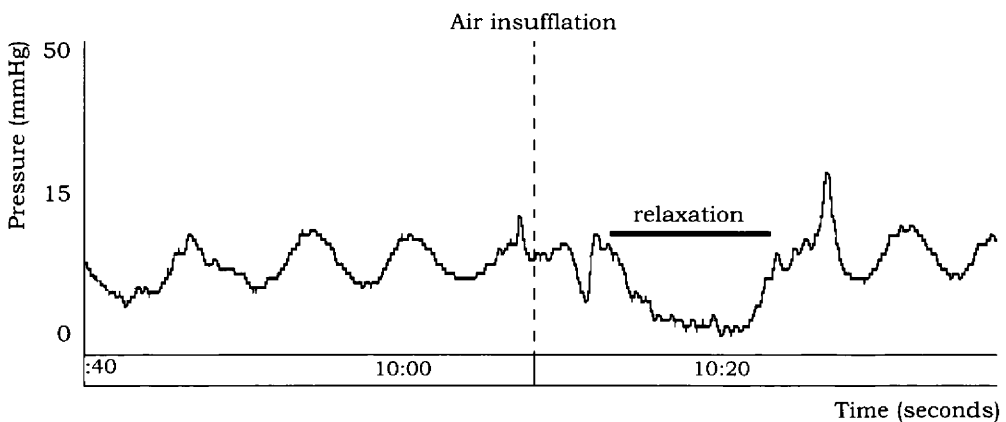


Table 2 Patient postmenstrual age (PMA) and parameters of anal sphincter function in 10 premature infants with a delayed meconium passage; comparison with previously published data from healthy premature infants.

Study	PMA	Parameters measured		Anorectal reflex		
		Anal sphincter pressure (mmHg)	Baseline rectal pressure (mmHg)	Anal sphincter oscillation frequency (No./min)	No. of infants with normal RAIR	Threshold distension volume (mL)
Current study (range)	28-31	22.0 ± 5.0 (16-29)	6.9 ± 2.0 (4-11)	9.8 ± 1.9 (7.5-11)	10 (100%)	2.4 ± 0.5 (2-3)
Benninga et al. ⁴ (range)	31-33	31.6 ± 13.0 (7-47)	9.0 ± 2.0 (1-22)	10.3 ± 1.4 (8-12)	11 (92%)	2.8 ± 1.3 (0.5-3.0)
De Lorijn et al. ⁵ (range)	27-30	24.5 ± 11.4 (5-46)	6.5 ± 4.8 (0-19)	11.1 ± 2.3 (9-17)	13 (81%)	3.4 ± 1.6 (1-5)

Results are expressed as the mean ± 1SD.

Discussion

Delayed passage of meconium is a common occurrence in pre- and dysmature infants in the absence of other clinical findings³. All infants in this study had a delayed passage of meconium (>48 hours) and seven out of ten infants developed a daily defecation pattern after their first passage of meconium. This study clearly shows that these infants exhibit a normal rectoanal inhibitory reflex. All other parameters of anorectal function measured were similar to those previously reported by our group in preterm infants of the same age who passed meconium within 48 hours^{4,5}. The development of colorectal motility is poorly understood in preterm infant. Using amniography, Mc Lain observed that progression of contrast material from the oral cavity to the colon took as long as 9h at 32 weeks of gestational age, but only half of that time by the time of term age⁶. Manometric investigations of small intestinal motility have shown that the migrating motor complex is immature at <34 weeks gestation⁷. Very little information is available regarding the prenatal development of colonic motility. In rhesus primates, the postprandial increase in colonic motility observed in the full term infant is similar to the human and adult response. In the preterm rhesus primate there is a lesser response to meals, suggesting that the colon response to meals matures late in gestation⁸. These studies suggest that preterm infants may have a delayed transit of luminal contents through the colon, however colonic motility has not been directly assessed in premature infants.

Factors other than motility may also contribute to the delay in meconium passage. The meconium of premature infants differs in composition (glycoprotein, saccharides, calcium, copper, iron and phosphorus) making it thicker in consistency than the meconium of full term infants and therefore more difficult to expel⁹.

Two infants had persistent defecation problems following passage of the meconium plug, but both of these infants had normal anorectal motility on manometry. In the patient with suspected Hirschsprung's disease, the use of manometry alone could have excluded this condition, therefore reducing the need of the rectal suction biopsy. Both infants with the prolonged delay of defecation finally developed a normal defecation pattern at 8 weeks and 8 months of age respectively, but the causes of their ongoing problems remain unclear. Delayed maturation of interstitial cells of Cajal (ICC) has been reported in infants with severe meconium obstruction requiring ileostomy^{10,11}. It was not justified for us to perform full thickness anorectal

biopsies needed for investigation of ICC's in the anorectal region and the two patients studied that had persistent defecation problems did not require ileostomy as they responded to conservative therapy. Therefore we were unable to determine if maturation of ICC's played a role in either the acute or ongoing defecation problems experienced by the infants studied. ICC's are also essential for appropriate relaxation of the internal anal sphincter¹² and therefore as these mechanisms were normal it can be assumed that expression of ICC's in the anal sphincter was mature at the time of measurement in all infants.

In conclusion, as we found a normal RAIR in all infants and 7 out of 10 infants developed a daily defecation pattern after their first passage of meconium, we can suggest that at the time of measurement, anorectal motility was mature in these infants. This study shows that failure of relaxation of the internal anal sphincter does not contribute to delayed passage of meconium, but instead suggests that either the mechanisms of rectal propulsion were impaired, leading to failure of normal expulsion of the meconium plug, or that the meconium plug itself was too difficult to expel due to its consistency. In those infants who continued to experience difficulties with defecation following passage of the meconium plug, it was clear that mechanisms other than failure of the RAIR, perhaps delayed maturation of colonic motility was involved.

References

1. Weaver LT, Lucas A. Development of bowel habit in preterm infants. *Arch Dis Child* 1993;68:317-20.
2. Manning AP, Heaton KW, Harvey RF. Wheat fibre and irritable bowel syndrome. A controlled trial. *Lancet* 1977;2:417-8.
3. Verma A, Dhanireddy R. Time of first stool in extremely low birth weight (< or = 1000 grams) infants. *J Pediatr* 1993;122:626-9.
4. Benninga MA, Omari TI, Haslam RR et al. Characterization of anorectal pressure and the anorectal inhibitory reflex in healthy preterm and term infants. *J Pediatr* 2001;139:233-7.
5. de Lorijn F, Omari T, Kok J et al. Maturation of the rectoanal inhibitory reflex in very premature infants. *J Pediatr* 2003;143:630-3.
6. McLain CR. Amniography studies of the gastrointestinal motility of the human fetus. *Am J Obstet Gynecol* 1963;86:1079-87.
7. Dumont RC, Rudolph CD. Development of gastrointestinal motility in the infant and child. *Gastroent Clin North A* 1994;23:655-71.
8. Sarna SK. Physiology and pathophysiology of colonic motor activity. *Dig Dis Sci* 1991;36:998-1018.
9. Dimmitt RA, Moss RL. Meconium diseases in infants with very low birth weight. *Semin Pediatr Surg* 2000;9:79-83.
10. Kenny SE, Vanderwinden JM, Rintala RJ et al. Delayed maturation of the interstitial cells of Cajal: a new diagnosis for transient neonatal pseudoobstruction. *J Pediatr Surg* 1998;33:94-8.
11. Yoo SY, Jung SH, Eom M et al. Delayed maturation of interstitial cells of Cajal in meconium obstruction. *J Pediatr Surg* 2002;37:1758-61.
12. de Lorijn F, de Jonge W, Vanderwinden JM et al. Interstitial cells of cajal are involved in the rectoanal inhibitory. *J Pediatr Gastroenterol Nutr* 2003;364:A562.

