

# Preliminary evaluation of anorectal manometry in diagnosing Hirschsprung's disease in neonates

Yanlei Huang · Shan Zheng · Xianmin Xiao

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## Abstract

**Purpose** The aim of this paper was to assess the clinical value of anorectal manometry (ARMM) in the diagnosing of Hirschsprung's disease (HD) in neonates.

**Methods** From January 2003 to June 2005, 75 patients in whom HD was clinically suspected were analyzed. ARMM was performed using a desk, high rate gastrointestinal dynamic detection system and the results were compared with barium enema and rectal suction biopsy.

**Results** Based on rectal suction biopsies in 52 of 75 patients, the positive, false positive, negative, and false negative rates of ARMM in the diagnosis of HD in neonates were found to be 92.3, 1.9, 1.9, and 3.8%, respectively. Forty-three of 75 patients were diagnosed with HD by both ARMM and barium enema and the diagnoses were validated by pathologic results. The diagnosis of HD was excluded in 18 patients in whom HD was clinically suspected, but in whom the results of ARMM and barium enema were normal. Twelve patients who had ARMM results consistent with HD and a negative barium enema, had serial ARMM performed; a rectoanal inhibitory reflex (RAIR) was elicited in four patients, thereby excluding HD and the remaining eight patients were diagnosed with HD by review of barium enema and pathologic results. One of two patients with a positive barium enema for HD, but an ARMM showing the presence of RAIR was excluded by pathologic results and the other patient was lost to follow-up. The diagnostic accuracies of ARMM and barium enema for HD in neonates were 93.3

and 86.7%, respectively. There was no difference in rectal resting pressure and anal rhythmic wave frequency between neonates with HD and healthy neonates, but neonates with HD had higher anal sphincter pressures than healthy neonates ( $P = 0.0074$ ).

**Conclusions** ARMM is a simple, safe, and non-invasive method with high specificity for the diagnosis of HD in neonates.

**Keywords** Anorectal manometry · Hirschsprung's disease · Neonate

## Introduction

Hirschsprung's disease (HD) is a functional obstruction that arises from the distal colon where ganglion cells are lacking and contractions occur spastically. Up to two-thirds of patients with HD manifest symptoms during the neonatal period, but the diagnosis may be missed because the symptoms are usually not characteristic and the morphologic changes of the barium enema are not obvious. Thus, diagnosing HD in the neonate remains a clinical challenge.

Anorectal manometry (ARMM) offers a non-invasive method for diagnosing HD. This study has the advantage of being able to be done at the bedside or as an outpatient procedure and is associated with no complications. Its limitations include the need for the patient being in a normal physiologic and quiet state to avoid numerous artifacts. The technique relies on the absence of a relaxation reflex [i.e., rectoanal inhibitory reflex (RAIR)] after a distending bolus in the rectal lumen. Although RAIR has already been shown to be a high-specificity diagnostic target for HD, it is still rarely used in the neonate. Analysis of the basis for this may be attributed to the lack of

Y. Huang · S. Zheng (✉) · X. Xiao  
Department of Pediatric Surgery,  
Children's Hospital of Fudan University, 399 Wan Yuan Road,  
201102 Shanghai, People's Republic of China  
e-mail: szheng@shmu.edu.cn

maturity of the intermuscular plexus in the neonate and the high false negative rate. The aim of our study was to assess the clinical value of ARMM for diagnosing HD in the neonate.

## Materials and methods

### Clinical data

From January 2003 to June 2005, studies were performed in 75 full-term neonates (18 females and 57 males with a male-to-female ratio of approximately 3:1) in our hospital. The ages of the neonates ranged from 2 to 28 days (median  $13.6 \pm 2.8$  days). The infant birth weights ranged from 2.3 to 4.1 kg (median  $3.2 \pm 0.6$  kg). The clinical signs and symptoms suggestive of HD in these 75 neonates included abdominal distension (67 patients, 89.3%), delayed passage of meconium (60 patients, 80.0%), constipation (46 patients, 61.3%) and vomiting (26 patients, 34.7%).

Another 30 term infants with non-gastrointestinal diseases, such as cleft lip, fracture, hemangioma, lymphangioma in the neck, and malformation in the urinary system, who were hospitalized in the same period served as the control group.

In this study all the examinations and operations were done with the consent of the parents and accorded with the norms of the ethical board in our country.

### ARMM

ARMM was performed using a desk, high rate gastrointestinal dynamic detection system (Polygram HR, Denmark). The catheter (outer diameter, 3.5 mm; inner diameter, 0.8 mm) contained four distal side holes (diameter, 0.5 mm) at 1 cm intervals and arrayed at 90 degree angles from one another. The most distal side hole was situated 1 cm from the tip of the catheter, where a balloon, 3 cm in length, was attached. All side holes were perfused with sterile degassed water at a rate of 0.5 ml/min. Bowel preparation with warm saline or defecation with cathartics was achieved 2 h before the study without sedation. The balloon was positioned 5 cm above the anal verge of the patient, who was in the supine position, and rapidly inflated to a volume of 5 ml, then increased by increments of 2 ml, but not exceeding 20 ml. The following parameters were assessed during ARMM: the anal resting pressure, the rectal resting pressure, the anal rhythmic wave frequency, and the presence or absence of RAIR. Based on the anal sphincter pressure, HD was suspected if the pressure was constant (negative reflex) or increasing (abnormal reflex), i.e., RAIR was absent.

### Barium enema

We observed the morphology of the rectum and colon after the catheter was inserted just inside the anus. Twenty-five percent barium sulfate was injected and a lateral abdominal radiograph was obtained 24 h later to determine whether the barium had been evacuated. HD was diagnosed if the barium enema showed the classic findings of the colon, including a spastic segment, a transition zone, a dilated segment, and retention of barium at 24 h. HD was suspected if the barium enema only showed retention of massive barium at 24 h.

### Rectal suction biopsy

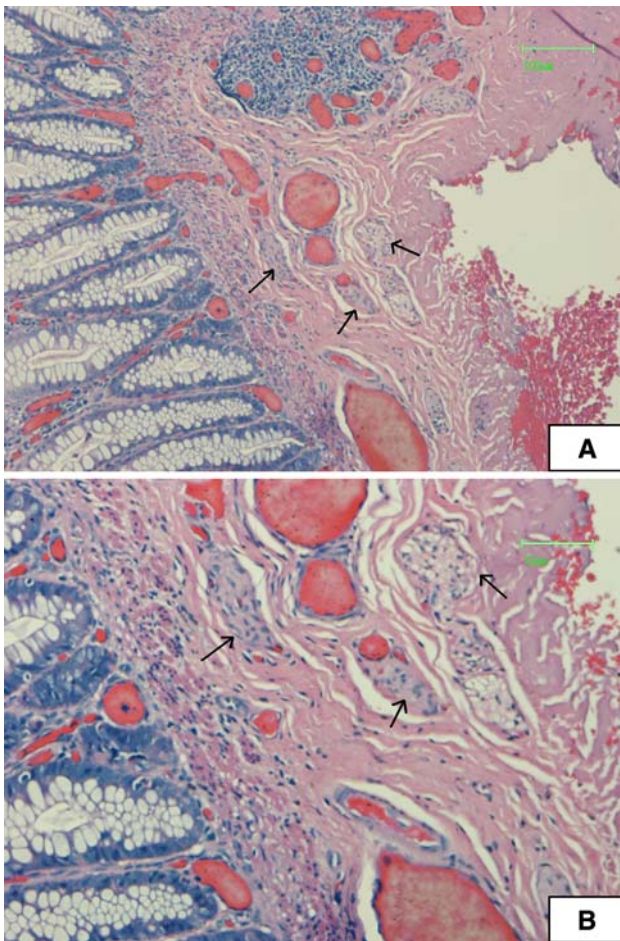
A rectal suction biopsy was performed in those patients in whom the results of ARMM or barium enema were consistent with HD. Because there is a length of hypoganglionosis above the dentate line, a more distal location, such as the myenteric plexus posterior at 1.5 cm or the mucosal rectum 2 cm above the dentate line was selected when performing a suction biopsy. Radical surgery could be done if HD was diagnosed by pathologic results.

### Statistical analysis

Results are expressed as the mean  $\pm$  SD or percent. Statistical analysis utilized either unpaired *t*-tests or  $\chi^2$  test, with a *P* value  $< 0.05$  being considered significant.

## Results

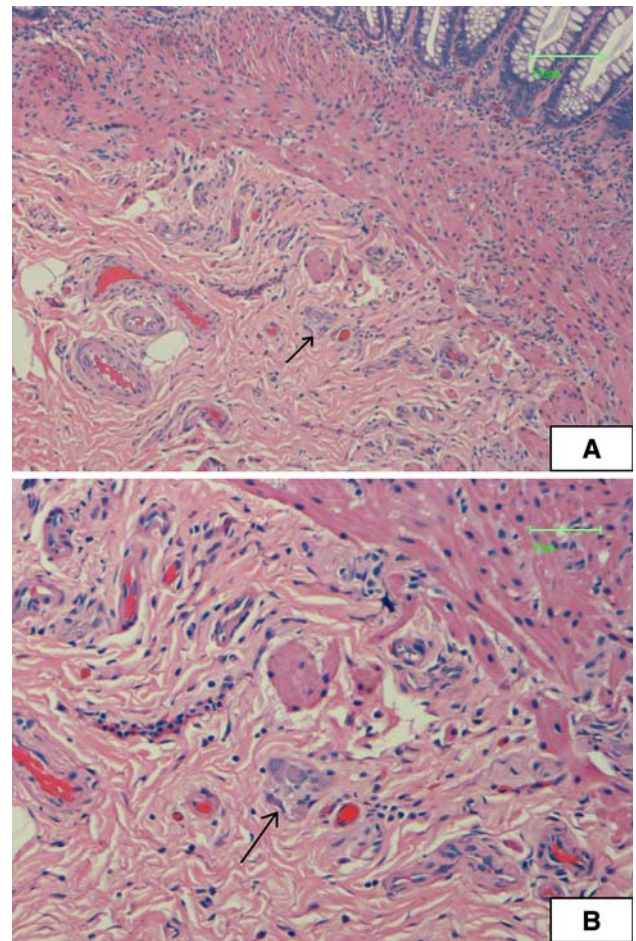
All the patients in this study had done ARMM and barium enema. The first ARMM was performed on all the neonates, aged between 4 and 28 days, with an average of 13.8 days. The ages of the patients at the time of their first barium enemas ranged from 4 to 32 days, averaging 17.3 days. Only 52 out of 75 patients in this study, aged between 20 days and 2.5 months, who were clinically suspected to have HD had rectal suction biopsies performed, and the rest who declined to have biopsies done had been followed up clinically for 2 years. Forty-eight of 52 patients were diagnosed with HD by both ARMM and the pathologic results, proving the absence of the ganglion cells throughout the submucosa of the rectum (Fig. 1a, b). One of 52 patients whose ARMM results showed HD was excluded because the pathologic results showed the presence of ganglion cells in the submucosa of the rectum (Fig. 2a, b). Another patient of 52 patients was excluded because both the ARMM and pathologic results were normal and the other two patients were diagnosed with HD by the pathologic results, even though the results of the



**Fig. 1 a, b** There were hypertrophic nerve trunks (*arrow*) and aganglionosis in the submucosa of the rectum (hematoxylin–eosin stain  $\times 100$ ,  $\times 200$ , respectively)

ARMM were normal. Comparing the results of ARMM and histological pathology in 52 patients undergoing rectal suction biopsies, this study showed that the positive, false positive, negative, and false-negative rates of ARMM for the diagnosis of HD in neonates were 92.3, 1.9, 1.9, and 3.8%, respectively (Table 1).

From Table 2, we can see that 43 of 75 patients were shown to have HD by both ARMM and barium enema, as validated by pathologic results, and subsequently had a transanal Soave one-stage endorectal pull-through procedure performed. Eighteen patients with clinically suspected HD whose ARMM and barium enema results were normal were excluded from having HD on 2-year follow-up since they had no symptoms, such as abdominal distension and constipation. Twelve patients in whom the ARMM results were suggestive of HD, but with negative barium enema results, had serial ARMM performed after birth ranging from 1 to 7 months; four patients whose RAIR was elicited were excluded from having HD and the other eight patients whose results of ARMM still showed HD were diagnosed



**Fig. 2 a, b** There were ganglion cells (*arrow*) in the submucosa of the rectum (hematoxylin–eosin stain  $\times 100$ ,  $\times 200$ , respectively)

**Table 1** Comparison of the results of ARMM and histological pathology in 52 patients undergoing rectal suction biopsies

ARMM	Pathologic diagnosis		Sum
	Positive number (%)	Negative number (%)	
Positive number (%)	48 (92.3)	1 (1.9)	49
Negative number (%)	2 (3.8)	1 (1.9)	3
Sum	50	2	52

as HD after review of the barium enema and pathologic results and underwent surgery. The diagnosis of HD was excluded in one of two patients, in whom a barium enema was consistent with HD, but in whom an ARMM showed the presence of RAIR, based on the pathologic results; the other patient was lost to follow-up. This study showed that the diagnostic accuracies of ARMM and barium enema for HD in neonates were 93.3% (70 of 75, 43 add 18, add 8 of 12, add 1 of 2 amounts to 70) and 86.7% (65 of 75, 43 add 18, add 4 of 12 amounts to 65), respectively, and the



**Table 2** Comparison of results of ARMM and barium enema in 75 patients

ARMM	Barium enema		Sum
	Positive number	Negative number	
Positive number	43	12	55
Negative number	2	18	20
Sum	45	30	75

consistency between the two examinations was 81.3% (61 of 75).

In addition, this study showed that there was no statistical difference in rectal resting pressure ( $12.1 \pm 1.8$  vs.  $11.8 \pm 2.3$  mm Hg) and anal rhythmic wave frequencies ( $10.5 \pm 0.5$  vs.  $11.2 \pm 0.6$  No./min) between neonates with HD and healthy neonates, but neonates with HD had higher anal sphincter pressures than healthy neonates ( $35.2 \pm 10.4$  vs.  $29.4 \pm 9.2$  mm Hg;  $P = 0.0074$ ; Table 3).

## Discussion

HD is a common alimentary tract anomaly, whose incidence ranges from 1 in 4,400 to 7,000 live births, and males predominate by a 4:1 ratio [1–4]. It is very difficult to diagnose HD in neonates owing to the absence of classic clinical symptoms and the obvious morphologic changes of barium enemas in this period, which easily lead to missed diagnoses in the early stages. The absence of RAIR is accepted as a high-specificity and non-invasive method for diagnosis of HD and its diagnostic positive rate is up to 90% [5]. The accuracy of diagnosing HD in neonates using ARMM in this study was 93.3%, which is higher than the 71.43% in domestic reports [6]. The high accuracy in this study may have resulted from repeatedly performing RAIR (average 3–5 times) and selecting term neonates as cases. According to past statements, the intermuscular plexus in neonates may not be mature after birth, so that RAIR cannot be elicited. De Lorijn reported that RAIR might be elicited, even in premature neonates, and the incidence was higher at 26 weeks [7] and 30 weeks [8] of gestational age (81.0 and 95.5%, respectively). Further, all term neonates can elicit RAIR, which

indicates that ARMM at term is a feasible and effective method.

This study showed that ARMM is superior to barium enema in diagnostic accuracy (93.3 vs. 86.7%), which may be attributed to non-obvious passive distention of the colon in the neonatal period, and the lack of difference between the dilated segment and the narrowed segment in the neonate. Rectal washouts were not performed before barium enema in the patients in this study, which may have avoided obliterating a dilated segment after defecating. Several technical points are relevant when performing barium enema for suspected HD. In our opinion, a urinary catheter is recommended for this examination since the red rubber tube may cause dilation of the narrow segment, leading to no discernible differences in diameter between dilated and narrowed segments. In addition, pressure and velocity should be controlled, avoiding excessive injection of the barium solution. The initial contrast is infused slowly in a controlled mode and a follow-up lateral abdominal radiograph is obtained after 24 h to confirm barium evacuation. Therefore, the diagnostic accuracy of a barium enema for neonates in this study was higher than in domestic reports (86.7 vs. 45.23%) [6].

Anatomically, the resting anal canal pressure consists of the internal anal sphincter (80–85%) and the external anal sphincter (15%). Changes in the highest resting anal canal pressure indicate changes in the structure and functions of the internal anal sphincter. The resting rectal pressure contains intra-rectal pressure, intra-abdominal pressure, contraction and elasticity in rectum. The resting rectal pressure is lower in normal condition, and may be higher when being not at rest. Table 3 showed that there was no marked difference in rectal resting pressures and anal rhythmic wave frequencies between neonates with HD and healthy neonates. Although patients with HD had higher anal sphincter pressures, all these data were within normal ranges (10–73.6 mm Hg) [9]. According to the literature, the anorectal pressure of premature infants is roughly the same as that of term infants [7, 8], but whether the anorectal pressure of neonates with HD is similar to that of healthy neonates is an issue for further research.

Suction rectal biopsy is the current gold standard in the diagnosis of HD and barium enema is thought to be useful in evaluating the level of aganglionosis and deciding on the

**Table 3** Comparison of results of ARMM between patients with HD and healthy neonates

	Rectal resting pressure (mm Hg)	Anal sphincter pressure (mm Hg)	Anal wave frequency (no./min)
Patients ( $n = 43$ )	$12.1 \pm 1.8$	$35.2 \pm 10.4^*$	$10.5 \pm 0.5$
Controls ( $n = 30$ )	$11.8 \pm 2.3$	$29.4 \pm 9.2$	$11.2 \pm 0.6$

\*  $P < 0.05$

surgical approach [10, 11]. So, in association with rectal suction biopsy and barium enema in evaluating patients for HD, there is broad agreement that ARMM is unnecessary to diagnose HD [11]. But in our experience, the diagnostic accuracy of suction rectal biopsy is attributed to the judgment of the pathologist and the difference in the quality of the suction rectal biopsy instruments leading to adequate specimens with sufficient amounts of submucosa or inadequate specimens with insufficient amounts of submucosa. In addition, use of a barium enema in the first month of life, however, may be particularly difficult in diagnosing HD because of the failure to show a transition zone. Furthermore, a barium enema should be mostly avoided if the newborn has clinical enterocolitis because of the risk for perforation. Especially for those patients with ultrashort or short HD, rectal suction biopsy and barium enema are not the right choices in the neonatal period, because of a normal length of hypoganglionosis above the dentate line and the failure to show an obvious narrow, transition, and dilated zone. And that, in our study ARMM seems to be a simple, safe, and non-invasive method with high-specificity for the diagnosis of HD in neonates, especially for ultrashort or short HD. But care must be taken that ARMM does not replace rectal suction biopsy as the definitive test to rule out HD, only as another study complement except for barium enema. Thus, ARMM is recommended for neonates with suspected HD.

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