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Anorectal manometry for the diagnosis of Hirschsprung Disease: new heights for the balloon or just hot air?

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In this issue of the *Journal of Pediatric Gastroenterology and Nutrition*, Meinds et al (1) report on the performance of a modified anorectal manometry (ARM) protocol for the diagnosis of Hirschsprung Disease (HSCR). In a prospective study of 105 patients suspected of having HSCR they showed that both the sensitivity and specificity of their modified ARM protocol were equivalent to rectal suction biopsy (RSB) with a 100% negative predictive value. They conclude that ARM is a viable screening tool for HSCR and could be used as a first diagnostic step to exclude HSCR across all age groups and ultimately reduce the need for rectal biopsies.

HSCR remains one of the most common identifiable enteric neuropathies with an incidence of 1 in 5000 births (2). The majority of HSCR patients present within the early neonatal period and virtually all are diagnosed by 3 months of life (3). An accurate diagnosis is essential given the enormity of the surgical intervention for HSCR. The mainstay of diagnosis has been the rectal biopsy by either rectal suction or full thickness biopsy with a frequent mantra that these diagnostic modalities are superior to ARM especially in the youngest children. A closer look at the literature, however, has long suggested that the difference between ARM and RSB has perhaps only ever been marginal. Indeed, in a systematic review of the literature published in this journal a decade or so earlier, de Lorijn et al looked across studies where infants underwent at least one of the following tests: Contrast Enema, ARM or RSB, followed by full-thickness biopsy and/or clinical follow-up as the reference standard (4). Although they found that RSB (14 studies, >900 patients) was the most accurate test, with the highest mean sensitivity (93%; 95% confidence interval [CI], 88%-95%) and mean specificity (98%; 95% CI, 95%-99%), the sensitivity and specificity of ARM (9 studies, 400 patients) were similar to those of RSB (91% vs 93%, P=0.73 and 94% vs 98%, P=0.08, respectively). In a subgroup analysis performed to

evaluate the value of ARM in infants younger than 6 months the mean values did drop with a sensitivity of ARM of 88% (95% CI, 66%Y96%) and specificity of 89% (95% CI, 57%Y 98%) and overall suggested that RSB was a slightly more accurate modality.

Jarvi et al looked at 81 patients all of whom were aged less than a year (median 2 months) of which thirty-three patients (41%) had HSCR (5). They found that a normal recto-anal inhibitory reflex (RAIR) on ARM excluded HSCR in all cases (100% negative predictive value) and no patient with HSCR exhibited a RAIR (100% sensitivity). The specificity and positive predictive value, however, of ARM for Hirschsprung disease were 83% and 80%, respectively, again inferior to RSB (both 100%) leading the authors to conclude that although in children under 1 year of age, HSCR is very unlikely in the presence of a RAIR, an ARM could not be recommended for use as a sole diagnostic tool. They suggested it be used where the histologic specimen from rectal biopsy is inadequate and/or condition such as functional constipation is the most likely diagnosis.

In summary these and other studies have suggested that although ARM is less invasive and carries a high sensitivity, its lower specificity and positive predictive value limit its clinical applicability and gives RSB superiority as the ‘gold standard’ tool for the diagnosis of HSCR.

Meinds et al essentially suggest that the diagnostic accuracy of ARM can be increased by technical improvements and with these the procedure can virtually exclude Hirschsprung disease and obviate the need for RSB. The technical ‘upgrades’ they suggest are relatively marginal consisting of inflating the rectal balloon serially until a RAIR was elicited as opposed to limiting

the distention volume to that considered maximal for the age of the patient. They report that none of the subjects reached a threshold of resistance to balloon insufflation or patient discomfort with the majority of patients needing at least 10mL to elicit an RAIR with a maximal balloon volume of 60mL, although it is not clear what these volumes were in the different age groups.

One could argue that the suggested optimisation of their protocol is not novel. Indeed, the recent ANMS-NASPGHAN consensus document on anorectal manometry suggests that the RAIR should be evaluated by inflating the rectal balloon in serial increments (5 mL increments in infants and newborns up to 20 mL and by 10 mL increments in older children), stating "The volume required to elicit the RAIR var- ies according to the size of the rectum and most centers recommend continuing to increase the volume to higher volumes (250–300 mL) in older children if complete relaxation is not obtained" (6).

The potential value and role of the ARM, as highlighted by this and other similar studies, potentially lies in the fact that the current 'gold standard,' rectal biopsies, are also subject to inherent limitations. Rectal biopsies carry a significant possibility of being inconclusive or indeed false positive tests given the requirement of expertise for both the acquisition of samples and their interpretation. An accurate diagnosis ideally requires either a more invasive open rectal biopsy or more than one suction biopsy taken at an appropriate level above the dentate line and including sufficient submucosa.(7) Up to a third of RSBs need to be repeated because their inadequacy (8-10). In addition, rectal biopsies in theory may miss so-called Ultrashort HD, with reported incidences of approximately 10% (11). Finally, although rare rectal biopsies carry an

actual risk of major complications, including perforation and bleeding (between 1.3% and 2.9%) (7, 12).

ARM has the advantages of being a less-invasive method carrying virtually no documented risk. Moreover, as for oesophageal manometry, in the last years the assessment of the anorectal function has experienced great technical development with the introduction of more advanced and miniaturized probes with novel pressure recording systems. High-resolution manometry may currently provide either 2-D or more sophisticated 3D representations of the anal canal both at rest and during physiologic events, such as RAIR and defecation maneuverers. These may well ameliorate the current 'shortfalls' even further and promote its definitive role in the diagnosis of HSCR.

However, ARM is by nature a highly technical evaluation and it will provides an accurate description of anorectal neuromuscular function, only if physical principles and equipment characteristics are respected. In general, ARM data are reliable only if the methodology used to acquire them is accurate. Moreover, all ARM operators go through a learning curve and perhaps in the same way as Meinds et al. each centre and operator should assess their own performance before committing to the accuracy of their ARMs or consideration be given to the test only being available in referrel centres with sufficient expertise and throughput.

The development of effective, accurate, accessible and less invasive tools for the diagnosis of enteric neuropathies are clearly needed. ARM clearly does have a place in the consideration of

HSCR but more data is required before it can fully replace the role of rectal biopsy. The ARM balloon has not burst and is arguably flying slightly higher.

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