

Safety of Biopsy Techniques for Hirschsprung Disease

Hirschsprung Disease (HD) is due to aganglionosis of the colon that presents in the distal colon and then proximally. HD typically presents in the first few days of life, and early diagnosis is imperative to provide corrective surgery and to prevent complications such as enterocolitis. Several colonic biopsy techniques exist which help determine the presence of HD, and the authors of this study performed a meta-analysis using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA) for patients younger than 18 years of age with potential HD. All included studies had to include at least 5 patients or at least 5 rectal biopsy specimens. Biopsy types included suction, open surgical, endoscopic, or punch biopsy. Various staining techniques to diagnose HD included hematoxylin and eosin staining, acetylcholinesterase staining, and calretinin staining.

Although an initial analysis by text and abstract screening produced 469 articles, only 159 articles met inclusion criteria after full-text review. A total of 300 patients in the meta-analysis underwent endoscopic biopsy while 3369 patients underwent open biopsy, 1507 underwent punch biopsy, and 20,775 patients underwent suction biopsy. The mean age of patients ranged from 27.84 months (suction biopsy group) to 50.40 months old (punch biopsy group). Interestingly, although no significant difference was present between the conclusive rate result of the various biopsy techniques, the heterogeneity between meta-analysis of biopsy types (using the I^2 statistic) was significant ($P < 0.001$). Funnel plot analysis for suction biopsy and open biopsy suggested a possible publication bias.

There was no difference in age (defined as less than 36 months of age and greater than 36 months of age) for conclusive results for patients undergoing suction rectal biopsy, and not enough evidence was available to determine effectiveness of results using the other rectal biopsy techniques. No difference was seen between the various staining techniques in determining conclusive results for HD; however, there was significant study heterogeneity between staining types ($P < 0.001$). Various staining techniques were not significantly

different for patients undergoing open surgical biopsy for HD although significant heterogeneity existed between the study groups ($P < 0.001$) while no significant heterogeneity existed for patients undergoing suction rectal biopsy. Finally, the pooled complication rate for the various biopsy techniques was 2% with a significant rate of complications noted for patients receiving punch biopsy versus those receiving suction biopsy.

This study demonstrates that all biopsy techniques for the diagnosis of HD likely are equal in their capacity to generate conclusive results. The authors state that the safety of suction rectal biopsy (including the potential lack of need of sedation) makes it a first-line method for diagnosing HD in children.

Comes G, Ortolan E, Moreira M, de Oliveira Junior W, Angelini M, El Dib R, Lourencao P. Rectal biopsy technique for the diagnosis of Hirschsprung disease in children: a systematic review and meta-analysis. *Journal of Pediatric Gastroenterologists and Nutrition* 2021; 72: 494-500.

Food to Improve the Microbiome May Help Children with Malnutrition

Prior research has demonstrated that children from low- and middle-income countries have a specific microbiome taxa that change in the setting of malnutrition, and such changes may contribute to malnutrition. This study from Bangladesh recruited children between 12 and 18 months of age with moderate acute malnutrition. Such children were randomized to consume either a newly developed microbiota-directed complementary food (MDCF) or a standard ready-to-use supplementary food (RUSF) for three months. The MDCF used in this study was MDCF-2 which is a new formulation that previously has been shown to change the microbiome to beneficial taxa. Anthropometric data was measured every 15 days, and fecal samples were obtained one month after the intervention. Besides anthropometric data, all patients underwent plasma proteomic profiling and gut microbiota determination.

A total of 123 subjects were enrolled (61 received MDCF-2 and 62 received RUSF). No

difference was present regarding anthropometrics and social demographics between the two treatment groups. Both weight-for-length z scores and weight-for-age z scores significantly improved in the MDCF-2 group compared to the RUSF group. Plasma protein analysis showed that 714 proteins significantly increased or decreased in patients receiving MDCF-2 versus 82 proteins which significantly increased or decreased in patients receiving RUSF. Specific proteins that increased significantly in the MDCF-2 group included intermediate layer protein 2 (which improves articular cartilage formation), thrombospondin-4 (which helps develop bone and skeletal muscle), and SFRP4 (which is an osteoclast inhibitor). Fecal analysis demonstrated that 23 bacterial taxa (identified by amplicon sequence variants) were significantly associated with weight-for-length z scores (21 positively associated; 2 negatively associated). Interestingly, 5 of these taxa promoting growth had been identified previously in gnotobiotic mouse studies. Finally, these specific 21 bacterial taxa associated with increased weight-for-length z scores were significantly increased in children receiving MDCF-2 compared to children

receiving RUSF and had a positive correlation with 70 plasma proteins associated with improving weight-for-length z scores.

This study demonstrates that changing the fecal microbiome via dietary manipulation may reverse the effects of malnutrition. This finding is intriguing as such effects also could occur in the setting of various types of intestinal inflammation. It is interesting to note that the significant improvements in malnutrition in children receiving MDCF-2 occurred despite this formulation having less caloric density compared to RUSF.

Chen R, Mostafa I, Hibberd M, Das S, Mahfuz M, Naila N, Islam M, Huq S, Alam A, Zaman M, Raman A, Webber D, Zhou C, Sundaresan V, Ahsan K, Meier M, Barratt M, Ahmed T, Gordon J. A microbiota-directed food intervention for undernourished children. *N Engl J Med* 2021; 384: 1517-1528.

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Answers to this month's crossword puzzle:

1	A	C	H	A	L	A	S	I	A	6	K	R	O	G	H			
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16	A	C	C	R	E	T	I	O	N		18	C	O	C	C	I		
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36	D	E	E	P			37	L	A	X	A	T	I	V	E			