Comparison of Barium Enema and frozen section results in the diagnosis of Hirschsprung's Disease in a tertiary care hospital at Aceh, Indonesia

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ABSTRACT

Introduction: Hirschsprung's Disease (HD) also called congenital aganglionic megacolon is a disorder caused by undeveloped distal to proximal intestinal nerve ganglion cells. Diagnosis includes determining the aganglionic segment through barium enema radiology examination and histopathology of frozen section with permanent section as gold standard. Determining the diagnostic value of this modality is important for operative management decision.

Materials and Methods: The study was a retrospective, cross-sectional study with diagnostic test design. Patient data were obtained in the form of clinical symptoms, barium enema, and frozen section expertise were assessed for the suitability of the diagnostic value by referring to the permanent section as the gold standard.

Result: Thirty-four patient data were obtained. The sensitivity, specificity, and accuracy of barium enemas were 95%, 69.2%, and 82%, respectively. The values of sensitivity, specificity, and accuracy of frozen section were 95%, 92.8%, and 88%, respectively. The Cohen-Kappa statistic value was 0.62 (good agreement).

Conclusion: Accuracy of FS is better than barium enema in diagnosing HD. In health care center with limitation of histopathological facility, BE could be used as the alternative procedure as interrater comparisons showed good agreement. Therefore, either frozen section or barium enema can be carried out in common or in separate term.

KEY WORDS:
Barium Enema, Diagnostic Value, Frozen Section, Hirschsprung's Disease

INTRODUCTION

Hirschsprung's Disease (HD) or also called congenital aganglionic megacolon is an abnormality resulting from the malformation of nerve ganglion cells in the intestine starting from the internal sphincter of the anus extending to the more proximal part with various lengths.[1] This disorder is diagnosed in the neonatal period with symptoms of delayed meconium expenditure, abdominal distension, and bilious vomiting. Studies explained the failure of the neural crest cell (NCC) migration from the proximal to distal digestive tract, therefore, causing the myenteric plexus (Auerbach) and the submucosal plexus (Meissner) are not formed in the intestine.[2]

Demographic studies show that the incidence of HD throughout the world is estimated to be around 1: 5000 live births.[3] In Indonesia, prevalence data is still sparse. Kartono et al., reported 20-40 patients were referred to Cipto Mangunkusumo Hospital (RSCM), Jakarta each year.[4] Incidence data were obtained for 1 in 5000 births in 229 million among Indonesians population. There were many cases of HD in the province of Aceh each year. Based on patients records in dr. Zainoel Abidin General Hospital (RSUDZA) Aceh, Indonesia, more than 100 patients have been referred to this hospital since 2010 until 2013.[5] Establishment of HD diagnosis involves both of determining the presence of intestinal aganglionic segment, the extent of the segment, and increasing number of hypertrophic nerves. Barium enema (BE), anorectal manometry, and histopathology study are the modality of choice.[9] Suction and full-thickness biopsy can be prepared using frozen section (FS) with rapid intraoperative diagnostic decision, or as a permanent section (PS), which would take more than 48 hours before the result become available.[6] However, the diagnostic value of these modality were limited, particularly in our institution. Based on the description above, we are interested in assessing the comparison of the diagnostic value of barium enema with frozen section on the diagnosis of HD.

MATERIALS AND METHODS

This was a retrospective study with a diagnostic value design which was carried out by collecting data on patients who were suspected of having HD which included clinical symptom data from medical records, expertise on BE photos, and FS examinations. Then, the diagnosis was confirmed by using PS histopathology staining.

The patient data were taken from the Medical Record Division, Radiology Division and Anatomy-Pathology Laboratory of dr. Zainoel Abidin General Hospital Banda Aceh. Indonesia. The sample was taken by the total sampling

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method. The patients who had criteria1: (i) delayed meconium excretion since birth, abdominal distension, and bilious vomiting, (ii) had complete results of BE fluoroscopy, FS, and PS histopathology between July 2010 and July 2014, were included. Barium enema fluoroscopy were done by using Siemens Luminos Agile Max (Siemens Healthcare GmbH, Germany). The procedure was done under fluoroscopy in unprepared bowel using hand syringe and not-distended bulb Foley's catheter to ascertain transitional zone clearly visualised. Barium Enema was positive when the result showed three distinct zone (dilated, transitional, and contracted zone).[12] All of BE were interpreted by a radiologist. We found no complication due to barium use. Frozen section and PS histopathology specimens were cut by using Microm HM 550 (Thermo Fisher Scientific, Germany) and stained by Hematoxylin-Eosin. We did not use other staining method, such as histochemical with Acetylcholine Esterase due to unavailability of those methods. Frozen section and PS were positive when the result showed absence of ganglion cells in submucosal and/or myenteric plexus.[13]

The data analysis was performed using SPSS for Windows version 18.0 (IBM, New York). All the categorical data were expressed as frequencies and percentages. Diagnostic values, such as sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio, and accuracy were calculated using 2x2 cross-tabulation table and formula. The statistical significance was $p<0.05$. The Cohen-Kappa statistic were used to measure inter-rater agreement between BE and FS findings.[15]

RESULTS

Thirty-four samples of Hirschsprung's Disease (HD) patients who met the inclusion and exclusion criteria were collected. Baseline characteristics are explained in the following Table I.

In this research, the results of BE fluoroscopy were obtained preoperatively. There was no repetition in BE procedure and no 24-hour delayed imaging done in any patient due to avoid risk of perforation. We found no morbidity after the procedure. Frozen Section were obtained intraoperatively from full-thickness biopsy in patients at the time of definitive surgery. All of the patients underwent single-stage pull-through procedure as definitive surgery, including 14 patients which did not have HD as the PS results; however, the symptoms were consistent with HD. As aforementioned, due to staining unavailability, we did not examine the specimen any further, therefore any differential diagnosis such as hypoganglionosis and other intestinal neuronal dysplasias still could not be determined. Interpretations of results are grouped into HD and not HD. Then, the results confirmed by PS as the gold standard (Table II and III).

Comparative analysis of barium enemas with frozen section to assess agreement in diagnosing HD were done by using cross-tabulation table (Table IV) and Cohen-Kappa statistic. The test results used the Cohen-Kappa statistic to assess the agreement between the assessors (interrater) and the equation as follows[15]:

$$\kappa = \frac{observed\ agreement - chance\ agreement}{1 - chance\ agreement}$$

$$\kappa = \frac{Po - Pc}{1 - Pc}, \text{ with } Po = \frac{(a+d)}{N} \text{ and } Pc = \frac{\frac{(f1xg1)}{N} + \frac{(f2xg2)}{N}}{N}$$

DISCUSSION

The most common clinical symptoms in HD patients are abdominal distention of 30 subjects (88.23%), then there are six subjects (17.65%) experiencing delays in meconium expenditure (>24 hours), and 4 subjects (11.76%) suffering from greenish (bilious) vomiting. Haricharan et al., suggested that symptoms often experienced by HD subjects were abdominal distension (63-91%), delayed meconium expenditure (60-90%), greenish vomiting (19-37%), and food intolerance.[7] However, Izadi et al., found that the most common symptoms were chronic constipation (79%), abdominal distension (67.3%), and late release of meconium (17.3%) with fewer other symptoms proportion. This has to do with various factors, one of which is the age of the patient when diagnosed with HD.[8]

We found several complications such as intestinal obstruction (5.9%), perineal excoriation (26.5%), wound dehiscence (26.5%), stricture (17.6%), constipation (5.9), and enterocolitis (2.9%). Many studies divide complications into early and late stage. The study by Haricharan et al., found that early complications included anastomotic leak (1-10%), cuff abscess (5%), intestinal obstruction (7.5-10%), perineal excoriation, stoma complications, infection and wound dehiscence (4%). whereas the late complications include intestinal obstruction, constipation (37%), enterocolitis (5-42%), and stricture (0-35%).[7] Little et al., reported complication rates for enterocolitis (10.6%), constipation (7.9%), incontinence (7.1%), and stricture (5%).[10] Izadi et al., in their research suggest that the most early complication was anastomotic leak (10.2%) and further complications were incontinence (6.12%).[8] Complications are increasingly avoidable with the initial diagnosis of the disease. Thus, the quality of life of patients would be increased.[9]

This study obtained a diagnostic value of BE in the form of a sensitivity value of 95%, specificity of 69.2%, positive predictive value 79.2%, negative predictive value 90%, positive likelihood ratio 3.08, negative likelihood ratio 0.07, and accuracy of 82%. Martafani et al., obtained diagnostic value of BE on HD anatomical pathology results including sensitivity of 86%, specificity 30%, positive predictive value 77%, negative predictive value 43%, positive likelihood ratio 1.22, negative likelihood ratio 0.48, and accuracy of 73% (95% CI).[11] Different results were obtained by Muller et al., in which sensitivity of 72.1% and specificity of 90% in determining the radiographic transition zone (RTZ). This is because the determination of RTZ is influenced by various factors, such as patient preparation and use of contrast substances.[12]

This study obtained a FS diagnostic value in sensitivity of 95%, specificity of 92.8%, positive predictive value of 95%, negative predictive value 92.8%, positive likelihood ratio of 13.2, negative likelihood ratio of 0.05, and accuracy of 88%.

Table I: Baseline characteristics of patients (n=34)

Characteristics	Frequency	Percentage
Age		
• 0-6 month	19	55.8%
• 7-12 month	3	8.8%
• >12 month	12	35.3%
Sex		
• Male	26	76.4%
• Female	8	23.5%
Clinical symptoms		
• Delayed meconium	6	17.65%
• Greenish vomitus	4	11.76%
• Abdominal distention	30	88.23
• Enterocolitis	12	35,29%
• Constipation	28	82,35%
• Soiling	19	55,88%
Complications		
• Anastomosis leakage	0	0%
• Intestinal obstruction	2	5.9%
• Perineal excoriation	9	26.5%
• Wound dehiscence	6	26.5%
• Stricture	2	17.6%
• Constipation	9	5.9%
• Enterocolitis	1	2.9%
HD type		
• Rectosigmoid	33	97,05%
• Long Segment	1	2,94%
• Total Colon Segment	0	0%
Definitive procedure		
• Swenson procedure	0	0%
• Soave procedure	3	8,82%
• Duhamel procedure	0	0%
• TEPT	31	91,17%
Resected colon length		
• <10cm	0	0%
• 10-20cm	32	94,12%
• >20cm	2	5,88%

TEPT, Transanal Endorectal Pull-Through

Table II: Comparison of barium enema and permanent section (n=34)

Permanent section		HD	Not HD	Total
Barium	HD	19	5	24
enema	Not HD	1	9	10
	Total	20	14	34

Table III: Comparison of frozen section and permanent section (n=34)

Permanent section		HD	Not HD	Total
Frozen	HD	19	1	20
section	Not HD	1	13	14
	Total	20	14	34

Tabel IV: Contingency table for Kappa statistic

		Frozen Section		
		HD	Not HD	Total
Barium Enema	HD	19	5	24
	Not HD	1	9	10
	Total	20	14	34

The test results by using Kappa statistics to assess the agreement between assessors (interater) with the following equation:

$$\varkappa = \frac{observed\ agreement - chance\ agreement}{1 - chance\ agreement}$$

$$\varkappa = \frac{Po-Pc}{1-Pc}, \text{dengan } Po = \frac{(a+d)}{N} \text{ dan } Pc = \frac{\frac{(f1xg1)}{N} + \frac{(f2xg2)}{N}}{N}$$

$$\varkappa = \frac{0{,}82-0{,}54}{1-0{,}54} = 0{,}62$$

The results obtained were not much different from the study by Rouzrokh et al., In 201 infants and children obtained sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of FS was 85.8%, 90.2%, 93.9%, 78.3%, and 80.4%.6 Research by Shayan et al., in 304 intraoperative frozen section (IOFS) actions obtained 9 cases (3%) of different interpretations of IOFS and PS, including 2 false positives and 7 false negatives.[13] Maia et al., reported that from 93 IOFS actions there was 67% conformity with PS and 89% was generally in accordance with other examinations in HD patients.[14] It can be concluded that generally FS have a relatively high diagnostic value to assess positive or negative HD patients.

Due to technical issue during biopsy, specimen preparation, and pathologist experience, the ganglions have probability to be missed. The results of the analysis used the Cohen-Kappa statistic to compare interrater.[15] The results show $\kappa=0.62$ (95% CI, $p<0.005$) which means have a good agreement. Muller, et al., obtained a match between radiological examination and anatomical pathology in only 0.4 in the moderate category.[12] This study has limitations, namely the small number of patients because not all medical records have complete data on radiology and histopathological findings.

Further studies involving a larger number of patients and more complete data will increase the validity.

CONCLUSION

This study suggest that accuracy of FS is better than BE in diagnosing Hirschsprung's Disease. In health care center with limitation of histopathological facility, BE could be used as the alternative procedure as interrater comparisons showed good agreement. Therefore, either frozen section or barium enema can be carried out in common or in separate term.

ABBREVIATIONS

HD: Hirschsprung's disease; TEPT: Transanal endorectal pull-through; FS: Frozen section; PS: Permanent section.

CONFLICT OF INTEREST

None declared

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