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Suction rectal biopsy yields adequate tissue in children

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ABSTRACT

Background/purpose: Hirschsprung disease (HD) is diagnosed by rectal biopsy, with suction rectal biopsy (SRB), the preferred technique in neonates. Reported SRB adequacy has varied overall with concern for decreased diagnostic yield in older children. The study aim was to assess SRB adequacy by age in children with the current device used at our institution.

Methods: Following IRB approval, a retrospective cohort of children (1 to 18 years) evaluated by SRB for HD was identified through billing records. Data regarding demographics, procedure, results, and complications were collected and analyzed using SPSS.

Results: 56 children (median age 3.9 years) underwent SRB with an 80.4% overall success rate. Patients older than 5 years had 90.5% adequacy rate compared to 74.3% in those younger. Univariate analysis revealed weak association of inadequate specimens with younger age and males, and no association with insurance, race/ethnicity, weight–height or BMI percentile, sedation type, or procedure location. SRB under general anesthesia (GA) had 100% adequacy ($n = 6$). Patients with inadequate initial biopsy achieved diagnosis by SRB with increased sedation ($n = 5$) or full thickness biopsy under GA ($n = 5$).

Conclusion: With adequacy of 80.4% overall and 90.5% for patients greater than 5 years, SRB is effective in evaluating the older child for HD.

1. HD demographics and diagnosis

Occurring in 1 of 5000 live-born infants, Hirschsprung disease (HD) is a motility disorder resulting from the absence of ganglion cells in the Meissner and Auerbach plexuses of the gastrointestinal tract [1]. Full thickness rectal biopsy (FTB) under general anesthesia (GA) was the primary biopsy technique until 1965, when Dobbins and Bill [2] identified ganglion cells on suction rectal biopsy (SRB) and suggested the use of SRB to exclude HD. In 1969, Noblett [3] utilized a device that drew a portion of mucosa and submucosa into a side aperture via manometrically measured suction and excised the tissue using a cylindrical knife. Using this device, Noblett was [3] able to obtain adequate specimens from 116 biopsies in 45 children with no complications. Since that time, SRB has become the procedure of choice for evaluation of very young children with suspected HD. Despite the overall success of SRB, the complication rate (0–2.9%) [3–12] and specimen adequacy (73%–100%) [2,3,5–10,12–14] have varied significantly in the literature.

Currently, no evidence-based guideline exists for technique selection or sedation use to maximize the diagnostic yield of rectal biopsy in children greater than 1 year. In 2011, Hirsch et al. [15] performed a retrospective review of 668 biopsies performed during 167 endoscopies on 156 patients with the use of a flexible endoscope and jumbo biopsy forceps, usually under an inhalational anesthetic agent to reduce patient anxiety and ensure cooperation, and reported a success rate of rectal biopsy of 94% with no complications. This suggested that increased sedation may lead to improved biopsy adequacy in uncooperative patients.

1.1. Study aim

We hypothesized that rectal biopsy specimen adequacy is associated with younger age because of the narrower rectal wall thickness compared to older children, and improved with sedation due to enhanced patient cooperation. The aims of this study were to evaluate the SRB results of children aged 1 to 18 years, and to assess the impact of sedation on SRB adequacy in this population.

Abbreviations: HD, Hirschsprung disease; SRB, suction rectal biopsy; GA, general anesthesia; PO, oral; IV, intravenous; FTB, full thickness biopsy; BMI, body mass index; IQR, interquartile range.

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2. Materials and methods

2.1. Human subjects research protection and cohort identification

After Washington University Institutional Review Board approval (#201403128), a retrospective cohort of children between ages 1 and 18 years who underwent SRB to evaluate for HD at a single children's hospital was identified through billing records (CPT™ 45100). There were no exclusion criteria. The study period (4/2011 to 2/2015) coincided with the introduction of the *rbi2* SRB device (Aus systems Pty Ltd., Allenby Gardens, South Australia) at our institution.

2.2. Rectal biopsy technique and pathologic evaluation

The *rbi*2 SRBs were obtained approximately 2 to 4 cm proximal to the dentate line with negative suction achieved utilizing a syringe and pressure measured by the manometer provided with the device. Two to four specimens from the lateral and posterior rectum were collected at the time of each biopsy session, and specimens were placed in 10% buffered formalin. On analysis by an experienced pediatric pathologist, biopsies were regarded as inadequate due to 1) insufficient depth in which case there was inadequate submucosa for analysis or 2) the presence of squamous and/or transitional epithelium suggestive of a biopsy taken from the normally hypoganglionated anorectal transitional zone. All inadequate biopsies were later reviewed by a single pediatric pathologist with expertise in Hirschsprung disease (F.V.W.) and categorized as either inadequate owing to insufficient submucosa (submucosal thickness less than 25% of mucosal thickness) or to the presence of squamous and/or transitional epithelium.

2.3. Sedation

The decision to provide sedation during the SRB was determined by the operating physician. For our study, sedation was recorded when administered, and patients were characterized as receiving no sedation, light-deep sedation (PO or IV midazolam, IV ketamine, inhaled nitrous oxide) or GA.

2.4. Data management and analysis

Using REDCAP for data management [16], we recorded the following variables: gender, race, ethnicity, insurance type, age, weight, height, date of biopsy, performing physician, sedation received, dose, and biopsy results. Weight for length (for children <2 years) [17] and body mass index (BMI) (for 2–18 years old) percentile for age and gender [18] were determined. Study outcomes included adequacy of specimen and procedural complications, such as bleeding, blood transfusion and readmission. Descriptive statistics and univariate analysis (chi-square, Fisher's exact, and Mann–Whitney U test) were performed using SPSS Statistics (v.22, IBM, Armonk, NY).

3. Results

3.1. Demographics and outcomes

56 patients were identified in the cohort who underwent SRB during the study period. Cohort demographics, procedural details and outcomes are summarized in Table 1. The median age was 3.9 years with interquartile range (IQR) of 3.83, and weight/length or BMI percentile was 59.2% with IQR of 52.1%. 21 patients underwent SRB without sedation and 35 patients received sedation. In 11 patients (19.6%) an inadequate specimen was obtained with 9 of the 11 occurring in patients aged 1 to 5 years ($n = 35$). Children older than 5 years ($n = 21$) had adequate specimens in all but 2 patients, a 90.5% success rate of SRB versus a 74.3% success rate in children 1–5 years. For patients with an inadequate biopsy on initial attempt, sufficient specimens were ultimately obtained either with a second SRB utilizing increased sedation ($n = 5$) or with FTB under GA ($n = 5$). One patient with an initial inadequate biopsy was lost to follow-up.

Table 1
Cohort demographics, procedural details and outcomes summary.

Variable	*n* (%)
Age category	
1–5 years	35 (62.5)
>5 years	21 (37.5)
Gender	
Female	32 (57.1)
Race/ethnicity	
Caucasian	49 (87.5)
African-American	3 (5.4)
Hispanic	2 (3.6)
Other	2 (3.6)
Sedation category	
None	21 (37.5)
Light-Deep	29 (51.8)
General	6 (10.7)
Provider	
Gastroenterologist	53 (94.6)
Surgeon	3 (5.4)
SRB sample adequacy	
Adequate	45 (80.4)

On review of all inadequate specimens, nine biopsies were deemed inadequate because of the presence of squamous and/or transitional epithelium and two biopsies were inadequate because of insufficient submucosa. There was 100% concordance between original and reviewed diagnoses.

The incidence of HD was 3.6%, and the complication rate was 1.8% (one child readmitted for bleeding without need for transfusion). There were no intestinal perforations or other complications.

3.2. Risk factors for inadequate SRB specimen

Although not statistically significant, univariate analysis showed weak associations between inadequate specimens and age <5 years ($P = 0.14$) and (Fig. 1) male gender ($P = 0.12$) (Table 2). No significant difference in specimen adequacy in sedated versus nonsedated groups was found. Insurance, race/ethnicity, weight–height or BMI percentile, sedation type (categorized as none, light (oral or IV midazolam), deep (inhaled nitric oxide or IV ketamine) or GA), and procedure location were not associated with biopsy adequacy. All patients who underwent SRB under GA had adequate specimen ($n = 6$).

4. Discussion

Current literature suggests varying biopsy adequacies using SRB devices from 73% to 100% [2,3,5–10,12–14] with controversy regarding SRB effectiveness in the older child. In infants, suction rectal biopsy is documented as having sensitivity of 93% and specificity of 98% for HD [14]. In 1986, Kurer et al. [19] confirmed that SRB was as accurate as FTB for the diagnosis of HD in patients aged from a few weeks to 17 years. Yet, a 1998 retrospective study by Alizai et al. [5] regarding SRB using the Noblett device found inadequate samples in 13% of patients and, despite failing to reach statistical significance, suggested that suction biopsies were less likely to be adequate in children over 6 months of age compared to those younger (82.5% vs. 90.9%). In 2007, Croffie et al. [9] similarly found that SRB was adequate for diagnosis in 73% of patients 1 to 3 years of age, and only 50% of patients older than 3 years in a prospective study of children undergoing SRB. Finally, in 2012 Hayes et al. [12] found that, while not significant, patients younger than 3 years were more likely to have adequate SRB specimens than those older than 3 years (81% vs. 70%). The proposed reasons for these results are multifactorial. First, older children may have increased rectal thickness caused by chronic constipation, which may interfere with