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Perioperative use of antibiotics in full-thickness rectal biopsies for Hirschsprung's disease

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Abstract

Background: There is no consensus on the use of perioperative antibiotic in full-thickness rectal biopsies (FTB) in children suspected for Hirschsprung disease. The primary objective of this study was to examine the effect of perioperative antibiotics on infectious and overall complications rate in FTB performed in children under the age of 1 year.

Methods: A retrospective chart review. Two time periods were compared—one with and one without the routine use of perioperative antibiotics. The treatment included cefuroxime 100 mg/kg and metronidazole 20 mg/kg administered intravenously at anesthesia induction followed by peroral administration of amoxicillin 50 mg/kg with Clavulanic acid 12.5 mg/kg three times a day t.i.d. for 3 days postoperative.

Results: In the group with perioperative antibiotics the infectious complications rate was 3.3% compared to 13.4% in the group without ($p = 0.03$) with fever as the most common. The overall complication rate was 11.3% and 15.2%, respectively ($p = 0.43$).

Conclusion: Perioperative antibiotics significantly reduced the rate of infectious complications, but not the rate of overall complication rate after a full thickness rectal biopsy in children under the age of 1 year.

Keywords: Children, Full-thickness rectal biopsy, Antibiotics, Complications, Fever

Background

The definitive diagnosis of Hirschsprung disease (HD) relies on the histological demonstration of the absence of ganglion cells in myenteric (Auerbach) and submucosal (Meissner) plexus from transanal rectal biopsies. The biopsies may be performed as full thickness biopsies (FTB) or as suction biopsies. By FTB the mucosa, submucosa and the muscular layers should be included with preservation of the outermost muscular fibers and the serosal layer, but this always carry the risk of perforation into the perirectal fatty tissue. An overall complication rate varying from 0 to 8.9% has been reported for FTB in larger studies [1–4].

The use of perioperative antibiotics has become a gold standard in gastrointestinal surgery [5]. The ERNICA guidelines on Hirschsprung´s disease do not include any recommendations on perioperative antibiotics at rectal biopsy [6]. There are no studies on the effect in FTB but it has been recommended in patients with congenital heart disease [2].

A newly published study has shown that the use of antibiotics within the first year of life increases the risk of bacteria carrying genes of resistance in the infant gut [7]. Therefore, the use of perioperative antibiotic must be weighed against the severity of complications, the number of patients needed to treat to avoid a complication and the risk of developing bacterial resistance [8].

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The primary objective of this study was to examine the effect of perioperative antibiotics on infectious and overall complications rate in FTB in children under the age of 1 year.

Material and methods

We performed a retrospective chart review of children below the age of 1 year who underwent FTB at Odense University Hospital (OUH), Denmark, which is a tertiary referral center for pediatric surgery in Western Denmark. Patients did not undergo any other diagnostic workup and no bowl preparation was performed prior to the FTB.

Routine administration of perioperative antibiotics was introduced in late 2015 for patients under the age of 1 year. Therefore, we included patients from two different time periods. One period without antibiotics from 1 January 2010 to 31 December 2014 and one with antibiotics from 1 July 2016 to 31 December 2019. There were no other differences in treatment or care between the two time periods.

At discharge, parents were informed to contact the department in case of fever defined as a temperature > 38.5 °C, visible rectal bleeding or pain that did not respond to paracetamol 12.5 mg/kg, t.i.d. The attending pediatricians at our institution is the primary responsible for the post-operative care after FTB and for contacts with parents after discharge.

Postoperative complication was defined as any contact to the department in relation to the biopsy either by phone or admittance within 30 days postoperative.

The following outcomes were registered: fever, bleeding, pain, vomiting, and readmission. In case of additional antibiotic treatment, the type and route of administration was registered.

Information on blood tests (white blood cell count, CRP concentration) and result of blood culture were retrieved for children readmitted with fever.

All complications were classified according to the Clavien-Dindo Classification (CD) [9] and the Comprehensive Complication Index (CCI) [10] was calculated for each child.

Surgical procedure

For the surgical procedure, a suture was placed in the posterior wall of rectum, approximately 2 cm above the dentate line. The rectal wall was raised by traction and a 3–5 mm FTB was cut out with scissors. Hemostasis was secured by bipolar electrocoagulation and the defect was sutured.

The antibiotic regime consisted of intravenous administration of cefuroxime 100 mg/kg and metronidazole 20 mg/kg administered perioperative followed by oral administration of a mixture of amoxicillin 50 mg/kg and clavulanic acid 12.5 mg/kg, t.i.d. for 3 days.

Inclusion and exclusion criteria

A search was conducted in the local pathology database to identify patients eligible for inclusion: "T68*" ("rectal mucosa") and "TX9600" ("rectum"), combined with M21000 ("aganglionosis") or M01000 ("normal tissue") or M09011/M09010 ("material not suitable for a conclusive diagnosis."

Exclusion criteria were children older than 1 year of age at the time of biopsy, biopsy taken as part of another surgical intervention, administration of antibiotics within 2 days prior to the day of biopsy and any deviation from the standard perioperative antibiotic treatment during the intervention period.

Statistical analysis

Study data were managed using REDCap (Research Electronic Data Capture) [11] hosted by OPEN (Open Patient data Explorative Network)

Continuous data are presented as mean and standard deviation or medians and ranges. Categorical data are presented as counts and proportions. Student's test was to compare the differences in temperature. Mann-Whitney *U* test were used to compare the differences in CRP, white blood cell count and CCI. Fisher's exact test was used to compare the differences in the frequencies of complications. Pearsons's chi-squared test was used when calculating differences in sex and age. Statistical calculations were performed using Stata software (StataCorp., 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp. LLC). *P* values below 0.05 were considered statistically significant.

Results

A total of 112 patients fulfilled the inclusion criteria in the first period without perioperative antibiotics and 115 patients in the second period with perioperative antibiotics.

Complications were registered in 13 children (11.3%) with perioperative antibiotics and 17 children (15.2%) in the period without ($p = 0.43$) (Table 1). The CCI was 1.31 $\pm$ 4.40 in the group with perioperative antibiotics and 2.75 $\pm$ 7.44 in the group without, $p = 0.09$.

Fever was the most common complication and registered in 5 children (3.3%) with perioperative antibiotics and in 15 children (13.4%) without ($p = 0.03$). The majority (90%) of patients who developed fever after FTB across the two groups presented themselves within 48 h.

Patients who did not receive perioperative antibiotic had a significant higher rate of postoperative fever

Table 1 Descriptive data and incidence of complications within 30 days after full-thickness rectal biopsies

	FTB without antibiotics (01.01.2010–31.12.2014)	FTB with antibiotics (01.01.2016–31.12.2019)	*P* value
Patients included (*n*)	112	115	
Age in month (median and range)	4 (0–12)	3 (0–12)	0.21
Gender (*n*)			
Male	63 (56.25%)	63 (54.78%)	0.82
Female	49 (43.75%)	52 (45.22%)	
Complications (*n*)	17 (15.18%)	13 (11.30%)	0.43
Fever	15 (13.39%)	5 (3.3%)	0.03
Pain	0	1 (0.87%)	1
Bleeding	2 (1.76%)	6 (5.22%)	0.22
Vomiting	0	1 (0.87%)	1
CCI (mean ± SD)			
All patients	2.75 ± 7.44	1.31 ± 4.40	0.318
Readmissions	10 (8.18 %)	5 (4.35%)	0.21

FTB full-thickness rectal biopsy

rated as a ≥CD-II which was treated with intravenous antibiotics (9% vs 1%, $p = 0.006$).

The absolute risk reduction (ARR) of fever with antibiotics was 10.1% and the number needed to treat (NNT) was 10 (Table 2).

Among patients readmitted with fever there were no significant differences in temperature, white blood cell count or CRP concentration at first assessment, between the two groups (Table 3). All blood cultures in both groups were negative.

Discussion

This study found that the use of perioperative antibiotics significantly reduced the rate of infectious complications, but not the rate of overall complications.

The frequency of complications with a ≥ CD-II was significantly higher in the group without perioperative antibiotic. When complications were weighted based on their severity and reported as CCI, no significant differences were found. CCI has shown to be more sensitive to describe the severity of complications compared to CD alone [12, 13].

Severe complications after rectal biopsies are rare. In this study the overall complication rate for CD-IIIb was 2%. Treatment included drainage of a rectal abscess, electrocoagulation of biopsy site, and treatment of an anal fistula with a Seton suture. All patients recovered with no sequelae.

Of those readmitted with fever, there were no significant differences in temperature, white blood cell count, and CRP concentration between the two groups. All blood cultures performed in both groups were negative. This indicates that early postoperative fever is most likely a response to surgery and not an infectious complication [14].

Due to the relatively small number of patients included we did not perform an analysis of the risk factors for complications in relation to the different pathology coding.

There are several limitations to this study, including those inherent to any single-center retrospective chart study, e.g., missing variables, difficulty in establishing cause and effect and variance in the quality of information recorded by medical professionals. Nonetheless, this study is to our knowledge the first to examine the overall

Table 2 Complications for children who had a full-thickness rectal biopsy performed with and without perioperative antibiotics along with type of treatment

Without antibiotics *n* = 112	Symptoms	CD-I	CD-II	CD-IIIb	Treatment
	Fever	5	7	3	CD-II: Intravenous antibiotics CD-IIIb: Anal examination in GA Seton suture (*n* = 1), abscess drainage (*n* = 1)
	Bleeding	2			
	Overall	7	7	3	
With antibiotics *n* = 115	Symptoms	CD-I	CD-II	CD-IIIb	Treatment
	Fever	4	1		CD-II: Intravenous antibiotics
	Pain	1			
	Bleeding	5		1	CD-IIIb: Anal examination in GA hemostasis with cautery
	Vomiting	1			
	Overall	11	1	1	

CD Clavien-Dindo classification, *GA* general anesthesia

Table 3 Analyses of various characteristics for children with a fever of 38.5 °C or higher

	FTB without antibiotics *N* = 15	FTB with antibiotics *N* = 5	*P* value
Blood culture (*n*)			
None taken	5	2	
Negative	10	3	
Positive	0	0	
Temperature at first assessment			
Median and range	39.0 (38.5–40.0)	39.0 (38.5–40.3)	0.594
White blood cell count ($\times 10^9$/l) assessment			
Median and range	*n* = 14 14.5 (7.5–36.0)	*n* = 3 12.2 (8.4–25.5)	0.556
CRP at first assessment (mg/l)			
Median and range	*n* = 13 31.8 (1.2–260.0)	*n* = 4 25 (0.5–50)	0.254

FTB full-thickness rectal biopsy

rate of complications to FTB with and without perioperative antibiotics.

We are fully aware that the gold standard for perioperative antibiotic in gastrointestinal surgery is a single dose covering both anaerobe and gram-negative bacteria administered within 1 h prior to surgery. Perioperative antibiotics should generally be discontinued within 24 h if there is no sign of infections [15, 16]. The regimen used in the present study with an extended postoperative regime for 3 days was chosen to obtain maximal effect. Whether the postoperative administration had an additive effect is unknown.

These findings may indicate that perioperative antibiotics is not needed when performing full thickness rectal biopsies in children under 1 year of age. To answer this question, the research group have a large-scaled randomized controlled study in the pipeline which hopefully will include multiple centers.

Conclusion

Perioperative antibiotics significantly reduced the rate of infectious complications, but not the rate of overall complication rate after a full thickness rectal biopsy in children under the age of 1 year.

Abbreviations

CCI: Comprehensive Complication Index; CD: Clavien-Dindo Classification; FTB: Full-thickness biopsies; HD: Hirschsprung disease; OPEN: Open Patient data Explorative Network; OUH: Odense University Hospital; REDCap: Research Electronic Data Capture.

Supplementary Information

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Additional file 1.

Additional file 2.

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Authors' contributions

N.S Schiellerup conceived and designed the study, collected and analyzed the data, and drafted the manuscript. S. Möller analyzed the data and approved the final version of the manuscript. A. Linneman and P. Ehlers provided critical revisions and approved the final version of the manuscript. N. Bjørn, N. Qvist, and M.B. Ellebæk conceived and designed the study, provided critical revisions, and approved the final version of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

Data will be uploaded as an appendix

Declarations

Ethics approval and consent to participate

The introduction of the antibiotic regimen was based on an institutional decision without the necessity of any approvals from local ethical committee. All parents were informed preoperatively by the procedure, possible complications, and peri-and postoperative treatment. Local and regional authorities approved the journal access and data retrieval. Danish Patient Safety Authority Approval nr 3-3013-2822/1
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Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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