Wydawnictwo UR 2022
ISSN 2544-1361 (online)
doi: 10.15584/ejcem.2022.2.8

http://www.ejcem.ur.edu.pl
European Journal of Clinical and Experimental Medicine
Eur J Clin Exp Med 2022; 20 (2): 194–201

ORIGINAL PAPER

Artur Szymczak [1,2], Anna Ogorzałek [2], Natalia Leksa [1], Anna Sęk-Mastej [1], Stanisław Orkisz [1]

The outcomes in children with Hirschsprung's disease treated with transanal endorectal pull-through method

[1] Institute of Medical Sciences, Medical College, University of Rzeszow, Rzeszow, Poland
[2] Department of Surgery, State Hospital 2 in Rzeszow, Rzeszów, Poland

ABSTRACT

Introduction and aim. The evaluation of functional results, complications and problems of children with Hirschsprung's disease treated with one-stage surgery (TEPT) or two-stage surgery (colostomy, TEPT) in Paediatric Surgery Clinic in Rzeszów.

Material and methods. Medical documentation of 41 children treated due to Hirschsprung's disease in years 2006-2018 in Rzeszów were retrospectively analysed. The results of the questionnaires conducted among the parents of operated children were surveyed.

Results. The average time of the radical surgery was 189 minutes. The mean length of the resected intestine in the classic form was 19 centimeters, in long-segment 35 centimeters. In the post-operative period, 15 patients had a blood transfusion. The mean time of the children's stay calculated from the date of surgery until the discharge equaled 13.4 days. Early post-operative complications: enterocolitis occurred in 6 patients (1 death in a septic shock mechanism), total dehiscence of anastomosis in 1 patient, abscess of perirectal space in 1 patient, anastomotic retraction in 1 patient and in 3 patients inaccurate intra-operative evaluation of the section (intra), buttock dermatitis appeared in all patients.

Late post-operative complications (a control trial of 38 patients): Soiling was confirmed in 9 patients, periodic constipation in one. The abnormal consistency of stool was signaled in 3 children. Two children were repetitively hospitalized due to enterocolitis. The frequency of defecation almost in all patients was reduced after a three, four-month period since the operation from 10-15 per day to the age norm. In one child, where the retraction of the anastomosis was diagnosed, the soiling and heightened frequency of defecation throughout the day persists. All of the parents of the older children view the outcome of the surgery as positive and the life quality of their children does not differ from their peers.

Conclusion. TEPT is a method which can be performed in newborns, infants, babies as well as in case of a long-segment aganglionosis. Barium enema is not reliable in evaluation of the length of the aganglionic section in the long-segment type of Hirschsprung's disease. The treatment of choice in the early post-operative enterocolitis should be colostomy.

Worse functional results were observed in children after two-stage treatment – especially, in cases where the colostomy was created due to the intestinal re-distention.

Keywords. aganglionosis, constipation, encopresis, soiling

Corresponding author: Artur Szymczak, e-mail: artszymczak@poczta.onet.pl

Received: 20.12.2021 / Revised: 20.03.2022 / Accepted: 6.04.2022 / Published: 30.06.2022

Szymczak A, Ogorzałek A, Leksa N, Sęk-Mastej A. Orkisz S. *The outcomes in children with Hirschsprung's disease treated with transanal endorectal pull-through method.* Eur J Clin Exp Med. 2022;20(2): 194–201. doi: 10.15584/ejcem.2022.2.8.

Introduction

Hirschsprung's disease is a congenital disorder caused by the lack of autonomic intramural ganglia of submucosal plexus (Meissner) and myenteric plexus (Auerbach) of the intestinal wall as a result of which the intestine lacking the proper innervation is in a state of constant spasm creating an obstruction in the passage of the food content. This state is accompanied by the constant and excessive pressure of the internal anal sphincter (achalasia). As a result of the excessive effort, the intestine above the obstruction imitatively becomes dilated.

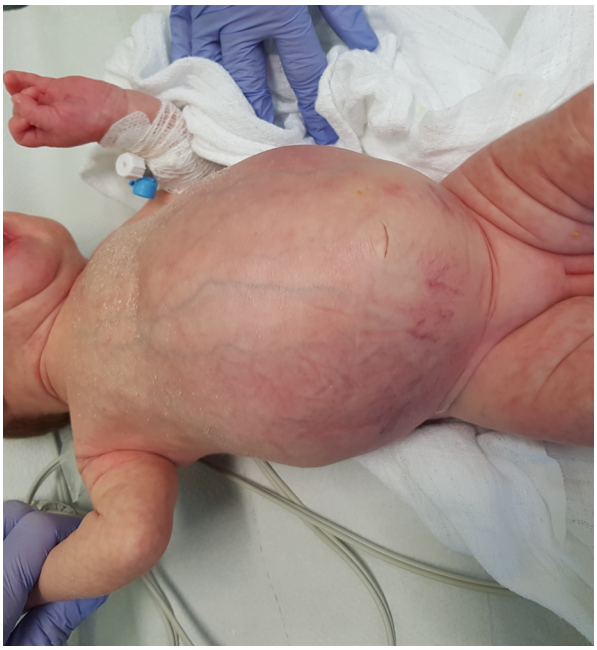

Fig. 1. Abdominal distension – a typical symptom of Hirschsprung's disease

In 1888 Harald Hirschsprung was the first to present the description of the disease symptoms, observed in two unrelated boys who died from chronic constipation. As a cause of the disease, he mistakenly diagnosed congenital megacolon.[1] Hirschsprung's disease has a multi-factor genetic background, caused by the mutation of genes: RET, ECE1, EDNRB, GDNF, SOX10, PHOX2B, KIAA1279. The most common of them is the mutation inactivating RET proto-oncogene, responsible approximately for 50% of family and 15% of occasional cases of the disorder's prevalence. The signal transduction gene-dependant becomes dysfunctional which leads to faulty migration of neural crest cells along the digestive tract wall toward the caudal. Dysfunctions appear between sixth and twelfth week of gestational age, while the time of activity of migration inhibitory factor determines the length of the aganglionic section.[2-5] According to EUROCAT data, the incidence of Hirschsprung's disease is 1,3 in 10 000 live births. More often it concerns the males (4:1). It can appear in the isolated form (70%) or in a syndromic one. It may be associated with Down syndrome or Shah-Waanderburg syndrome.[6,7] According to data published by Anderson et al., who analyzed the population of 9 million children born in California in 1995-2013, it can be clearly concluded that the scope of incidence of Hirschsprung's disease amounted to 2.2 cases in 10 000 live births with the majority of Afro-Americans and Mongoloid race.[8-10]

The classification of the disease type is based on the length of the aganglionic section. In 75% the aganglionosis relates to rectosigmoid segment – the classic type of the disorder, in 15% the aganglionic intestine reaches the left transverse colon flexure, while in 6% the disease concerns the entire large intestine. In rare cases, the aganglionosis might involve the whole intestine up to the duodenum. The clinical symptoms of the disease appear most often upon birth in a form of neonatal intestinal obstruction. The main ailment is constipation. The pathognomonic symptom is the delayed passage of meconium (>24 h after birth). Additionally, abdominal distention appears (Fig. 1) as well as vomiting with bile content. In some cases, the disease may clinically demonstrate itself in a later stage of life, even in adulthood.[11]

The most dangerous complication, which may appear in children with Hirschsprung's disease, is enterocolitis that may have a violent course and can result in a short time in death in a septic shock mechanism. The diagnostics of the disease is based on taking medical history, clinical examination and running diagnostic tests. In the clinical examination, apart from the abovementioned symptoms of obstruction, the symptom of a sudden defecation and gas release after inserting the catheter into rectum appeared. Barium enema, especially in cases of delayed diagnostics in patients with a re-distention of a correctly innervated intestine, may reveal a transitional zone of the intestine (cone syndrome) as well as the length of the aganglionic intestine (Fig. 2)

The supplementary examination in diagnosis and classification of innervation dysfunction of a digestive tract is manomentry of a lower part of a digestive tract. However, the relaxation of the internal sphincter (rectoanal reflex RAR) excludes aganglionosis. The examination determining the diagnosis in Hirschsprung's disease is the result of histopathology of a sample of a posterior rectal wall, which should be taken depending on the child's age from 0,5 to 1,5 centimeters above the dentate line (physiologically aganglionic zone). The lack of ganglia cells and the presence of overgrown nerve trunks producing excessive levels of acetyl cholinesterase confirms the diagnosis. The increased activity of this enzyme is diagnosed by histochemical method. In recent years, the immunohistochemical test of calretinin was introduced as a tool for diagnosis of Hirschsprung's disease. The combination of acetyl cholinesterase histo-

chemical test with the immunohistochemical test of calretinin encourages growth in sensitivity and specificity, as well as enhances precision of diagnostics of aganglionosis.[12-15]

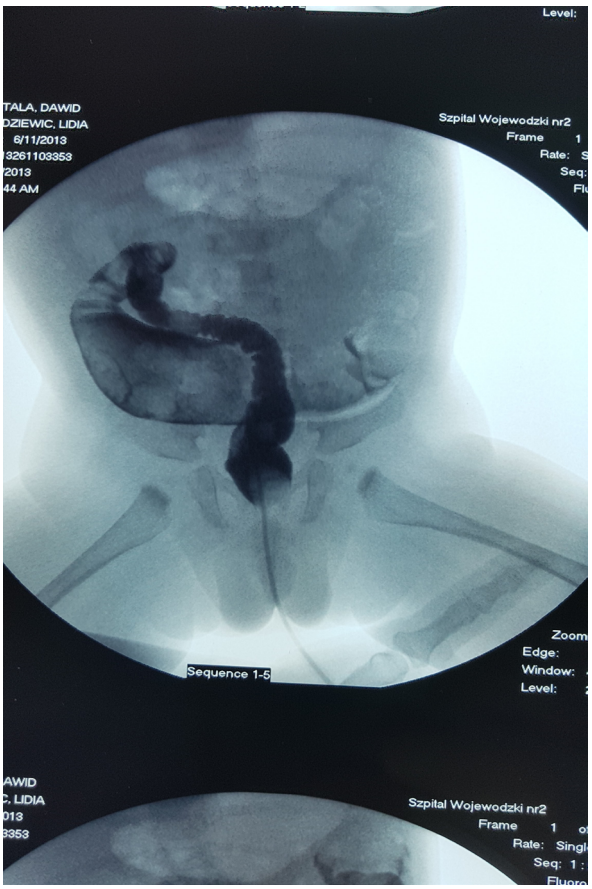

Fig. 2. Barium enema – narrow aganglionic intestine with a syndrome of cone in a transitional zone

The treatment of Hirschsprung's disease is surgical and requires the removal of aganglionic intestine and anastomosis of properly innervated intestine with the rectum just above the external anal sphincter. Depending on the clinical state of the patient, the length of the aganglionic section, the time for diagnosis and as a consequence the diameter of the re-dilated properly innervated intestine section, the treatment might be performed in a one-stage procedure or two and three-stage one.[16]

The standard surgical techniques performed in various modifications with abdominal or abdominal-perineum incision include Rehbein, Duhamel, Swenson and Soave methods.[17-20] In 1998 de La Torre and Ortega modified intra-abdominal Soave technique and presented the outcomes of children's treatment be means of new method, which they called transanal resection of the aganglionic section (TEPT). This technique involves circular incision of the rectum mucosa about 1 centimeter above the dentate line and then dissecting the rectum mucosa from its' muscular cuff up to pelvic diaphragm. In the next stage, the muscle cuff should be circularly incised in order to open the peritoneal cavity and to be able to further dissect the aganglionic intestine supplying it's mesentery up to its' macroscopic dilatation (transitional zone). In a subsequent stage, the sample of the intestinal wall is taken to the intra-operative histopathology biopsy in order to confirm its' normal innervation (Fig. 3). After confirmation of the presence of normal ganglion cells in the intestine, the anastomosis is done between the intestine and the rectal wall about 1 centimeter above the dentate line. De La Torre method in uncomplicated cases comes down to one-stage, successful treatment of children with Hirschsprung's disease and was very quickly accepted by the majority of paediatric surgery centres dealing with this defect.[21]

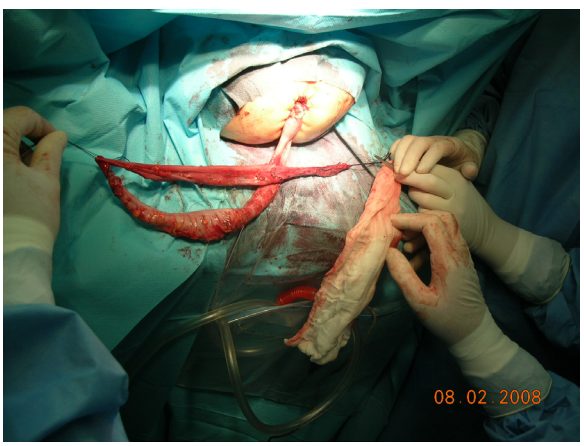

Fig. 3. Transrectal resection of the aganglionic section (TEPT)

Aim

The aim of the study was to compare functional results, complications and problems of children at various ages with Hirschsprung's disease treated surgically with one-stage (TEPT) or two-stage procedure (colostomy, TEPT) along with the validity of performing barium enema in order to assess the length of the aganglionic intestine.

Material and methods

The study was approved by the local bioethics committee (25/02/2019). In 2006-2018 in Paediatric Surgery Clinic in Rzeszów, 41 children with Hirschsprung's disease were treated. This group comprised of 35 boys and 6 girls (Fig. 4).

The classic type of the disease was observed in 36 children, the long-segment type in 4 and 1 had total intestinal aganglionosis (Fig. 5). In 5 cases the Down syndrome was recognized. In 26 children the correct diagnosis was made in the neonatal period, while in 13 in infancy. At the latest, diagnoses were made in children aged 1.5 and 3.5 years. In all patients, the clinical symptoms presented themselves in the neonatal period.

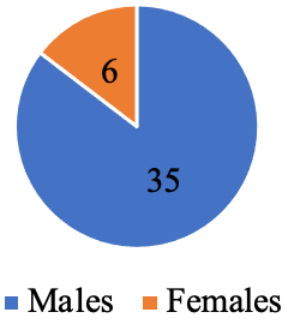

Fig. 4. Children operated on Hirschsprung's disease, division according to sex

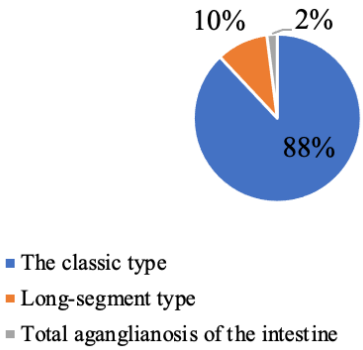

Fig. 5. The length of aganglionic section

The one-stage surgery – TEPT was performed in 25 children (this group included 4 children, in which TEPT was supported with minilaparotomy in order to mobilize the aganglionic section of the intestine. 15 patients received a two-stage treatment – in the first stage the colostomy was created, in the second one TEPT was performed with a simultaneous loop colostomy and anastomosis of a normal intestine with the wall of anal canal just above the external anal sphincter. One child received a three-stage treatment. In the first stage, the colostomy was created, in the second TEPT was performed and after healing of anastomosis and its' dilatation, the child had the continuity of the digestive tract restored (Fig. 6).

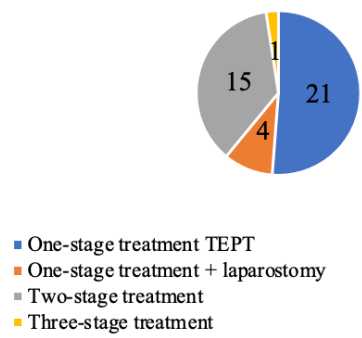

Fig. 6. Children operated on Hirschsprung's disease according to the number of stages of surgical treatment

Colostomy was performed in children due to three reasons. In case of a late diagnosis – in order to decompress and constrict the re-dilated intestine in seven children, associated congenital anomalies (Down syndrome and heart disorders) in two children, and in six children due to the lack of possibility to decompress the intestine in the preoperative period.

Results

Radical surgery was performed in 40.6 week of a child's life on average (the earliest in third week, and at the latest in the age of 4 years and two moths). The average time of the surgery was 188,8 minutes (in the range from 100 minutes to 450 minutes). The median length of the intestine resected in classic type equaled 19 centimeters. In patients with a long-segment disease – 35 centimeters.

None of the patients required a blood transfusion throughout the surgery. In the post-operative period, 15 patients received blood.

All the children were administered wide spectrum antibiotics after the surgery. The average time of children's hospitalization until the date of discharge was 13.4 days (range 7 to 30 days).

In the early post-operative period, in six (14.6%) children symptoms of toxic enterocolitis appeared. In three of them colostomy was created, which was closed on average after 5 months. The other children with toxic enterocolitis received conservative treatment. One child died due to the septic shock (2.4%), in two after the initial improvement of the general condition, later, after the discharge, the symptoms of seasonal, passing obstruction of digestive tract appeared, accompanied by symptoms of enterocolitis – currently, these children have the ileostomy created.

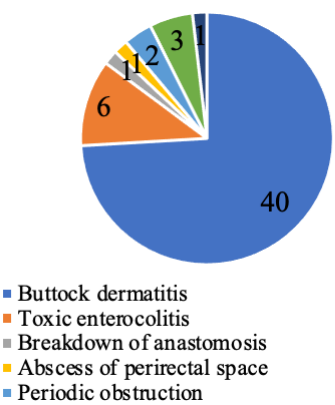

Fig. 7. Early post-operative complications

In one case, on the third day after the surgery, total dehiscence of anastomosis occurred. The child had colostomy created and colorectal re-anastomosis. In one patient, abscess of perirectal space was diagnosed – the

patient had colostomy created, which was closed after 4 moths. In two cases, in the early post-operative period, a passing obstruction of a digestive tract appeared. Both patients received conservative treatment with satisfactory results.

Buttock dermatitis in the anus area appeared in all operated patients (Fig. 7)

In 3 cases, wrong intra-operative evaluation was made, as a result of which in theses patients a radical resection was not made. One patient underwent another TEPT 6 months after the first surgery, in the second case, colostomy was created and afterwards the child underwent a surgery of Duhamel method in another centre. In another patient with the wrong intra-operative diagnosis, the ileostomy was created – the child is in the process of diagnostics in another centre. Two children with the ileostomy created are being diagnosed and treated. In another 38 children, the study was carried out in a form of a survey.

Soiling was stated in 9 patients, periodical constipation in 1. After one-stage TEPT, soiling is present in 4 patients, who were operated in the third week of life (1 patient), in the seventh week (2 patients) and in tenth week (1 patient). In a group of 16 children receiving a two-stage treatment, soiling was reported in 5 of them (among them, 4 with created colostomy due to the late diagnosis and intestine re-dilatation). Incorrect, loose, sticky texture of stool was reported in 3 children. Two children were hospitalized several times due to enterocolitis (Fig. 8)

In two children (one child with a long-segment Hirschsprung's disease and the other one with a post-operative enterocolitis) anastomotic stricture was diagnosed, requiring multiple dilatations in general anesthesia. Improper development was not stated in any case. Frequency of defecation in almost all patients had decreased after three, four-month period since the surgery from 10-15 per day to the age norm. In one child, who was diagnosed with anastomosis retraction, soiling and increased frequency of defecation persist throughout the day.

All of the parents of the older children view the outcome of the surgery as positive and the life quality of their children does not differ from their peers (Tab. 1).

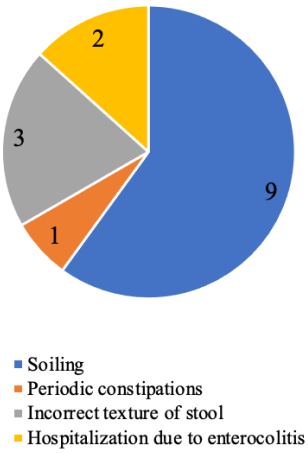

Fig. 8. Late postoperative complications

Discussion

The successful surgical treatment of Hirschsprung's disease aims to resect aganglionic intestine and anastomose of the normally innervated intestine with the rectum wall just above the external anal sphincter. In the second half of 20th century, the methods of Swenson and Bill, Soave, Rehbein and Duhamel gained the recognition and popularity. Treatment of children was performed in stages. In a first stage, the colostomy was created, in the second one, the radical surgery was done. In the third one, the ostomy was closed, restoring the gastric tract continuity. In complication-free course of treatment, the patient underwent laparotomy three times with all possible negative consequences resulting thereof. In recent years, the goal of surgical practice was to perform the radical surgery without ostomy. We presented the outcomes of surgical treatment with TEPT method in our patients with Hirschsprung's disease in years 2006 and 2018. In our material, the majority of patients were boys and the classic type of the disease prevailed – which is consistent with literature. In the first period after the implementation of this method, we operated on children who turned 3 months. Currently, the newborns are operated with TEPT method. The oldest child on the day of surgery was 4 years old. Every patient had barium enema in order to determine the length of the aganglionic section. However, in none of the long-segment cases nor in the total aganglionosis, barium enema was consistent

Table 1. Long-term outcomes of treatment on the basis of surveys conducted among parents

	Improvement of functioning	Soiling	Periodic constipations	Hospitalization due to enterocolitis	Stricture of anastomosis
One-stage treatment n=23 (60%)	23 (100%)	4 (17%)	0	1 (4%)	1 (4.3%)
Two-stage treatment n=14 (37%)	14 (100%)	5 (35%)	1 (7%)	1 (7%)	1 (4.3%)
Three-stage treatment n=1 (3%)	38 (38%)	0	0	0	0
Total n=38 (100%)		9 (23%)		2 (5%)	2 (5%)

with the intra-operative image of agnaglionosis. Moreover, barium enema performed in the neonatal period was not always reliable due to the lack of re-dilatation of normally innervated intestine.[22,23]

In most paediatric surgery centres, the diagnosis of Hirschsprung's disease is made on the basis of the result of histopathological examination obtained by means of suction biopsy, which advantages include little invasiveness of the procedure and lack of complications.[24]

In our centre, the patients are qualified for surgery according to the result of pathomorphological examination of the section taken surgically from the posterior rectal wall. The section of at least 0.8×0.5 cm is taken from above the physiologically aganglionic zone. It is always a full histopathology examination, not intra. It offers a possibility of a reliable pathomorphological evaluation of the whole section and substantially reduces the risk of wrong diagnosis. Furthermore, it shortens the time of the surgery in cases where the decision on the radical surgery is made immediately after obtaining the intra results.[24]

The disadvantage of such management is the waiting time for the results of histopathology test and the scaring in the collection site that during the radical surgery may hinder the dissection of mucosa from the muscle cuff. No complications were observed in any case of the surgical collection of the section.

Until the surgery date the children's digestive tract was decompressed by means of enemas and dilators to anal canal in order to relax the sphincter. Once the effective release of the stool retention was impossible, the patient was qualified for the laparotomy, during which mapping of the intestine was performed and double barrel colostomy was created divided onto the normally innervated intestine. In 21 cases a one-stage TEPT was performed, in another 4 TEPT with minilaparotomy in order to mobilize the intestine. In many centres, in order to mobilize the intestine, the laparoscopic technique is currently used.[24,25]

Out of our 41 patients, 16 received a two-stage treatment. In the first stage, the colostomy was created (delayed diagnosis with re-dilatation of the intestine, children with Down syndrome, in case of ineffective conservative treatment). In the second stage, TEPT was performed taking the normally innervated proximal "barrel" of the fistula down transrectally and anastomosing it with the rectal wall. In these cases the intra-operative histopathology examination was not performed, as a result of which the shortening of surgery time was achieved and avoidance of incorrect diagnosis of intra. A three-stage treatment was performed in 1 patient: colostomy, TEPT, colostomy closure.

In all patients, in the early post-operative period we diagnosed perianal inflammatory lesions of buttock. It is a frequent complication described especially in newborns operated before the third month of life. [24,26,27] In one case, these changes were intensified with skin erosion and fever.

In 3 patients, the intra-operative sections were wrongly evaluated. In one case TEPT was performed again with a satisfactory outcome, in the other, the colostomy was created. Later, this patient underwent Duhamel method surgery in another centre. Another child is in the process of diagnostics. The ileostomy has been created. Other authors emphasize that the correct intra-operative evaluation of the section depends mainly on the experience of professional pathomorphologist, their availability and the quality of a material sample sectioned by the surgeon.[24,28]

The patients with long-segment form of Hirschsprung's disease and a child with a total aganglionosis were operated with TEPT method with laparotomy in order to mobilize the intestine. None of the patients had previously created colostomy. Two patients underwent surgery in the 3rd week of life, another ones in second and third months, and the patient with total aganglionosis in the seventh month of life. All the patients with long-segment type prior to the surgery had barium enema performed, which in none of the cases implied the possibility of long-segment presence. Moreover, the clinical symptoms were not intensified compared with the children with a classic type of the disease.

In 6 patients in the early post-operative period, the symptoms of enterocolitis appeared. 3 of them were treated conservatively. One child died, in two the symptoms of gastrointestinal obstruction occurred later. At present, these children have ileostomy created and require further treatment. In 3 cases of enterocolitis, the colostomy was created (which was closed after 5 months on average). Currently, these children do not make any complaints concerning the digestive tract.

In the group of 41 children operated on for Hirschsprung's disease, 1 died (2.4%) on the 14th day after the operation due to the septic shock secondary to sepsis caused by toxic enterocolitis. In the studies by Elhalaby as well as Anderson, who presented the outcomes obtained in large group of children with aganglionosis, mortality in Hirschsprung's disease in the first year of life equaled approximately 2%.[8,26] Also, in the studies presented by Granstomm and Wester, toxic enterocolitis develops in about 5-42% of children with Hirschsprung's disease and is the most common cause of death.[8,26,29]

Out of 40 patients, 38 completed the treatment. Two have ileostomy created and are under supervision of a referential paediatric surgery centre. Out of 38 patients invited to participate in the control trial, 32 appeared in person. In the remaining 6, medical history was taken over the phone in a form of questionnaire. In the whole group, only one patient has periodic constipation. Also 1 child was hospitalized twice due to the

enterocolitis. Soiling is present in 9 children: in 4 out of 23 treated one-stage and in 5 out of 16 treated two, three-stage, where four of them had a colostomy created due to the late diagnosis of Hirschsprung's disease and re-dilatation of intestine (these were the children who underwent surgery after the 6 month of life and older).

Only in two patients the stricture of anastomosis was diagnosed, which required dilatation in general anaesthesia. On the 7th day after the operation, an everyday dilatation of the anastomosis by means of dilators begins, which lasts after the discharge and is continued by parents for the period of about 6 months. Such manner of conduct prevents leaving permanent scar in the site of anastomosis. Parents of all children observed a gradual decrease in frequency of defecation in the period of 3-4 weeks to few months after the operation. In their subjective opinion, there is no difference in the quality of life between peers or siblings of the treated child. Similar functional results of children treated with TEPT method were presented by Sood et al.[35] The most common late functional problems are encopresis (soiling), enterocolitis and constipation. According to some authors, better results are seen in patients operated on after 3rd month of life with a classic form of the disease. According to others, the patients' age does not greatly influence the results. The most crucial factor is the length of the aganglionic intestine.[16,26,30-33]

According to Hung et al., the risk factors for the development of post-operative enterocolitis is low birth weight, lowered level of IgA, long aganglionic segment and the surgery performed before the 2nd month of life.[34] Nonetheless, all the authors emphasize the gradual improvement of intestinal function along with a reduction in late complications with age.[33-39]

Conclusion

TEPT is the most effective surgical method, which can be applied both in classic type and long-segment one in children with Hirschsprung's disease at various age. Barium enema is not always reliable in evaluation of the length of the aganglionic intestine.

The most serious post-operative complication is toxic enterocolitis, which should be treated by early colostomy creation. Worse functional results were observed in children operated on after 6th month of life, after a two-stage treatment with the colostomy created due to the late diagnosis and re-dilatation of the intestine.

Declarations

Funding

This research received no external funding.

Author contributions

Conceptualization, A.S. and A.O.; Methodology, A.S.; Software, A.S.; Validation, A.S., A.O. and N.L.; Formal Analysis, A.S.; Investigation, A.S.; Resources, A.S.; Data Curation, A.S.; Writing – Original Draft Preparation, A.S.; Writing – Review & Editing, A.S.; Visualization, A.S.; Supervision, S.O.; Project Administration, A.S.; Funding Acquisition, A.S.M.

Conflicts of interest

The authors declare no conflict of interest.

Data availability

Data supporting the results of this study shall, upon appropriate request, be available from the corresponding author.

Ethics approval

The study was approved by the local bioethics committee.

References

1. Hirschsprung H. Stuhlträgheit Neugeborener in Folge von Dilatation und Hypertrophie des Colons. *Jahrbuch für Kinderheilkunde und physische Erziehung*. 1888;27:1-7.
2. Tang SC, Li, Lai FP, et al. Identification of Genes Associated With Hirschsprung's Disease, Based on Whole--Genome Sequence Analysis, and Potantial Effects on Enteric Nervous System Development. *Gastroenterology.* 2018;155(6):1908-1922.
3. Wei W, Weijue X, Jiangbin L, et al. Whole Exome Sequencing Identifies a Novel Pathogenic RET Variant in Hirschsprung's Disease. *Front Genet.* 2018;9:752.
4. Tilghman J, Ling A, Turner T, et al. Molecular Genetic Anatomy and Risk Profile of Hirschsprung's Disease. *N Engl J Med.* 2019;180:1421-1432.
5. Jurkowicz B, Abu-Bonsrah D, Zhang D, Hutson J, Newgreen D. Transserosal migration of enteric neural stem cells: Developing an avian colon mode. *J Pediatr Surg.*2018;53(12):2435-2439.
6. EUROCAT central Registry:Eurocat Statistical Monitoring Report - 2012-2016.
7. Shahid M, Mahmood A. A Case of Waardenburg-Shah Syndrome Type 4 Presenting with Bilateral Homochromatic Blue Irises from Pakistan. *Cureus.* 2018;10(8):3143.
8. Anderson J, Vanove M, Saadai P, Stark R, Stephenson J, Hirose S. Epidemiology of Hirschsprung's disease in California from 1995 to 2013. *Pediatr Surg Int*. 2018;34(12):1299-1303.
9. Taghavi H, Goddard L, Evans SM, et al. Ethnic variations in the childhood prevalence of Hirschsprung's disease in New Zealand. *ANZ J Surg.* 2018;89(10):1246-1249.
10. Gunadi, Karina SM, Dwihantoro A. Outcomes in patient with Hirschsprung's disease following definitive surgery. *BMC Res Notes.* 2018;11:644.
11. Zelga M, Zelga P, Dziki A, Piaseczna-Piotrowska A. Choroba Hirschsprunga u dzieci i dorosłych – kompendium wiedzy dla chirurga ogólnego. *Nowa Med.* 2017;24(2):59-72.

12. Nabi Z, Shava U, Sekharan A, Nageshwar Reddy D. Diagnosis of Hirschsprung's disease in children: Preliminary evaluation of a novel endoscopic technique for rectal biopsy. *JGH Open*. 2018;2(6):322-326.
13. Zheng Z, Zhang F, Jin Z, et al. Transanal endorectal stepwise gradient muscular cuff cutting pull-through method: Technique refinements and comparison with laparoscopy-assisted procedures. *Exp Ther Med*. 2018;16(3):2144-2151.
14. Jeong H, Jung H, Hwang I, et al. Diagnostic Accuracy of Combined Acetylocholineterase Histochemistry and Calretin Immunohistochemistry of Rectal Biopsy Specimens in Hirschsprung's Disease. *Int J Surg Pathol*. 2018;26(6):507-513l.
15. Rakhshani N, Araste M, Imanzade F, et al. Hirschsprung's Disease Diagnosis: Calretin Marker Role in Determing the Presence or Absence of ganglion Cells. *Iran J Pathol.* 2016;11(4):409-415.
16. Sosnowska P, Błaszczyński M, Moryciński S, Porzucek W, Mańkowski P. Are there any factors influencing the course of multistage treatment in Hirschsprung's disease?. *Przegląd Gastroenetrolgiczny*. 2016;11(2):131-135.
17. Błaszczyński M, Sosnowska P, Analiza technik operacyjnych choroby Hirschsprunga w leczeniu jednoetapowym na przestrzeni lat 2000-2011. *Borgis – Nowa Pediatria.* 2012;3:47-50.
18. Duhamel B. A new operation for the treatment of Hirschsprung's disease. *Arch Dis Child,* 1960;35:38-39.
19. Soave F. A new operation for the treatment of Hirschsprung's disease. *Surgery*. 1964;56:1007-1014.
20. Swenson O, Rheinlander HF, Diamond I. Hirschsprung's disease: a new concept of the etiology. *N Engl J Med*. 1949;241:551-556.
21. de La Torre-Mondragon L, Ortega-Salgado JA. Transanal endorectal pull – through for Hirschsprung's disease. *J Ped Surg.* 1998;33:1283-1286.
22. Jester I, Holland-Cunz S, Loff S, Hosie S, Reinhagen K. Transanal pull -through procedure for Hirschsprung's disease: a 5 year experience. *Eur J Pediatr Surg*. 2009;19(2):68-71.
23. Elhalaby A, Hashish A, Elbarbary M, Soliman H, Wishahy M. Transanal one – stage endorectal pull – through for Hirschsprung's disease: a multicenter study. *J Pediatr Surg*. 2004;29(3):345-351.
24. Sreedher G, Garrison A, Novak R, Keisling M, Ganpathy S. Congenital intestinal hypoganglionosis: A radiologic mimic of Hirschsprung's disease. *Radiol Case Rep*. 2019:14(2):171-174.
25. Marginean CO, Melit LE, Gozar H, Horvath E, Marginean CD. Atypical inset of total colonic Hirschsprung's disease in a small female infant. *Medicine (Baltimore)*. 2018;97(38):12315.
26. de La Torre L, Langer J. Transanal endorectal pull – through for Hirschsprung's disease: technique, nontroversies, pearls, pitfall, and an organized approach to the management of postoperative obstructive symptoms. *Seminars in Pediatric Surgery*. 2010;19:96-106.
27. van de Ven T, Sloots C, Wijnen M, et al. Transanal endorectal pull – through for classic segment Hirschsprung's disease: with or without laparoscopic mobilization of the rectosigmoid? *J Pediatr Surg*. 2013;48(9):1914-1918.
28. Adiguzel U, Agengin K, Kiristioglu I, Dogruyol H. Transanal endorectal pull – through for Hirschsprung's disease: experience with 50 patients. *Ir J Med Sci*. 2017;186(2):433-437.
29. Gupta D, Khanna K, Sharma S. Experience with the Redo Pull – Through for Hirschsprung's Disease. *I Indian Assoc Pediatr* Surg. 2019;24(1):45-51.
30. Granstromm A, Wester T. Mortality in Swedish patients with Hirschsprung's disease. *Pediatric Surg Int*. 2017;33(11):1177-1181.
31. Zhu T, Sun X, Wei M, et al. Optimal time for single--stage pull – through colectomy in infants with short--segment Hirschsprung's disease. *Int J Colorectal Dis*. 2019;34(2):255-259.
32. Chung P, Wong K, Tam P, et al. Are all patients with short segnment Hirschsprung's disease equal? A retrospective multicenter study. *Pediatr Surg Int*. 2018;34(1):47-53.
33. Hadidi A. Transanal endorectal pull – through for Hirschsprung's disease: experience with 68 patients. *J Pediatr Surg*. 2003;38(9):1337-1340.
34. Neuvonen M, Kyrklund K, Rintala R, Pakarinen M. Bowel Function and Quality of Life After Transanal Endorectal Pull – Through for Hirschsprung's Disease: Controlled Outcomes up to Adulthood. *Ann Surg*. 2017;265(3):622-629.
35. Huang W, Li X, Zhang J, Zhang S. Prevalence, Risk Factors, and Prognosis of Postoperative Complications after Surgery for Hirschsprung's Disease. *J Gastrointest Surg.* 2018;22(2):335-342.
36. Sood S, Lim R, Collins L, et al. The long – term quality of life outcomes in adolescents with Hirschsprung's disease. *J Pediatr Surg*. 2018;53(12):2430-2434.
37. Dahal G, Wang J, Guo L. Long-term outcome of children after single-stage transanal endorectal pull – through for Hirschsprung's disease. *World J Pediatr*. 2011;7(1):65-69.
38. Stensrud KJ, Emblem R, Bjornland K. Functional outcome after operation for Hirschsprung's disease-transanal vs transabdominal approach. *J Pediatr Surg.* 2010;45(8):1640-1644.
39. Bragagnini R, Gonzalez Ruiz Y, Siles Hinojosa A, et al. Functional outcomes in postsurgery for Hirschsprung's disease. *Cir Pediatr.* 2017;30(4):191-196.
40. Aslan M, Karaman A, Erdogan D, Cavusoglu Y, Cakmak O. Our experience with transanal pull-through in Hirschsprung's disease. *Eur J Pediatr Surg*. 2007;17(5):335-339.