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Hirschsprung's Disease: A Literature Review

Camyla Lemos Budib[1], *Jean Carlos Fontana*[1], *Hígor Guimarães Gomes*[1], *Rubens Moura Campos Zeron*[2], *Victor Campos de Albuquerque*[3], *Paulo Luiz Batista Nogueira*[4]

Abstract: The Hirschsprung's disease (HSCR) is a congenital malformation, which creates a defect in the ganglion cells migration to the distal intestine. This situation will cause a problem in the motor coordination generating a functional obstruction and retention of fecal content. The diagnosis of this disease is histological, and the treatment is the surgery.

Keywords: Hirschsprung's disease, congenital, obstruction.

Introduction

As a result of a change in the development of the Enteric Nervous System, (HSCR) is characterized by the absence of ganglion cells in the myenteric (Auerbach) and submucous (Meissner) plexuses, being classified according to the level of intestinal segment affected, from straight to whole large intestine (aganglionosis total), eventually including terminal portions of the ileum. It should be noted that the diagnosis, considering the delay of meconium passage in newborns, is basically clinical, which favors the achievement of adequate and early measures. It is known that about 90% of newborns who do not eliminate meconium in the first 24 hours of life are highly likely to have (HSCR)[1,2].

[1] Medical Student at Várzea Grande University Center – UNIVAG – MT, Brazil;
Contact: camylaabudib@hotmail.com
[2] Medical Student at Lusíada University Center – UNILUS – SP, Brazil;
[3] Medical Student at State University of Piauí – UESPI – PI, Brazil;
[4]Pediatric Surgeon and Professor at Várzea Grande University Center – UNIVAG – MT, Brazil;

Also, among the main signs and symptoms, in addition to the delay in the elimination of meconium, abdominal distension, refusal of food and enterocolitis are evident. In this respect, it is known that mortality is lower in children who do not present enterocolitis, so the early diagnosis of congenital Megacolon is essential. In addition, HSCR treatment is surgical and aims to remove the aganglionic intestinal segment. To avoid the evolution to bacterial enterocolitis it is necessary to maintain initial clinical measures, such as the performance of enemas and laxative measures to avoid bacterial translocation. Although the surgical procedure represents an improvement in the symptomatology of constipation, approximately 60% to 70% of the patients persist with difficulties to evacuate, even after surgery[3,4].

In addition, the importance of counseling the patient's family and the child about the need for treatment and adherence to it is explained: explaining the relevance of the interventions; the objectives of the therapy and the expected results. Being integral to the care provided to the child, since there is an emotional impact caused by the disease, the implementation of invasive procedures and the repercussion of the numerous medical consultations[5,6].

Thus, this article aims to perform a literature review on HSCR, evidencing the classification, history of the disease, epidemiological and genetic findings, as well as diagnosis and treatment, including the main surgical techniques.

Hirschsprung disease: Historical approach

For the historical understanding of the disease, prior research assigns to the Dutch anatomist, Frederik. Ruysch, the first description of the disease, since he reported the condition of chronic constipation in a girl of five years, who died for that reason. However, no sufficient evidence was found that would actually define Congenital Intestinal Aganglionosis in the patient. Subsequently, after several other physicians reported cases of children with severe colds and distentions of the colon, Dr. Harald Hirschsprung, pathologist, first described the condition of Aganglionosis Congenital Colic to the Society of Pediatrics in Berlin in 1886. Then, it became known as HSCR[9].

Hirschsprung's Disease, or Congenital Intestinal Aganglionosis, is also known as "Congenital Megacolon," however the terms are not synonymous. Megacolon is the result of a late diagnosis, becoming, then, a secondary manifestation.

Regarding fetal development, it is known that enteric ganglion cells are derived from the neural crest and appear in the esophagus by the 5th week of gestation. These cells, also called neuroblasts, migrate to the rest of the developing intestine by about the 12th week in the craniocaudal direction. Subsequently, the distribution and migration of these cells to shallower and deeper layers of the gut wall occur, and a maturation sequence of the neuroblasts to ganglion cells occurs. Regarding the etiopathogenesis, the most accepted hypothesis is that HSCR results from the defect of migration of neuroblast to the primitive intestine. Therefore, there is the absence of these ganglion cells in variable extension, which constitutes a neurocristopathy by Bolande proposition. At the site of the absent ganglia, an abnormal collection of thickened nerve fibers is observed. In the aganglionic zone, the nerves that should end in the ganglia spread through the muscular layers. Although all cases are aganglionic, the intensity of intramuscular innervation varies in each case[10,11].

Rectus motricity and anal canal activity, more specifically the internal anal sphincter, are controlled by nervous structures with distinct characteristics that are the intrinsic nervous system, responsible for movement control and secretion, divided into two plexus, the myenteric or Auerbach plexus, and the submucosal or Meissner plexus, and the extrinsic nervous system, which may activate or inhibit the general functions of the gastrointestinal tract. At the level of the myenteric plexus of the rectum, there are different types of neurons that are related to smooth muscle cells. These excitatory neurons (cholinergic), inhibitory (adrenergic) neurons and excitatory neurons and non-adrenergic or non-cholinergic inhibitors, called purinergic, which mediate ATP and the vasoactive intestinal polypeptide. For the internal anal sphincter, the purinergic neurons are inhibitors. The persistent tonic activity of internal anal sphincter is due to the intrinsic (myogenic) activity, in addition to the activity of extrinsic innervation[7,9].

The aganglionic intestinal segment presents spastic causing a functional intestinal obstruction by the muscular contraction with retention of the fecal cake above this affected area with dilatation and, consequently, the megacolon. The disorder is characterized as organic chronic intestinal constipation and is caused by the absence of ganglion cells in the myenteric (Auerbach) and submucous (Meissner) plexuses, due to a change in the development of the Enteric Nervous System, resulting in poor motility and

inadequate intestinal function. The disease in question is a differential diagnosis in neonatal intestinal obstructions and is still common among cases of chronic constipation in infants and older children and should be included as a possibility in pediatric consultations[7].

Rating

HSCR can be classified according to the extent and location of the affected intestinal segment: short segment corresponding to the rectal ampulla and even portions of the sigmoid colon; a long or classic segment, which follows up to the splenic flexure or transverse colon and, finally, total aganglionosis, which may follow to the terminal ileum. It is observed that the extent of aganglionosis is defined at the moment the migration ceases, either because it has differentiated early or because it has not been able to survive, differentiate or proliferate in other places. If this interruption occurs until the 7th week of gestation, the total aganglionosis of the colon occurs. If it occurs until the 9th week of gestation, there is no innervation of the descending colon, sigmoid colon, and rectum. Also, if it happens until the 12th week, the absence of innervation is restricted to the sigmoid colon and/or to the rectum only. There are descriptions of abnormalities known as ultra-short, because of a defect in the distal end of the rectum which also causes symptoms of intestinal constipation[1,7,9,12].

Therefore, without intrinsic innervation, there is a greater expression of extrinsic innervation. The aganglionic zone has absence peristalsis and spastic, which compromises the free intestinal transit. Prior to this zone, an elongated, hypertrophied and enlarged ganglionic proximal segment of the colon is formed, that is, a region with morphological and functional disorders (diseased portion) justifies a secondary alteration in the anterior area of the colon (healthy portion). The rectum and internal anal sphincter are innervated by sacral parasympathetic centers (S1-S3). In the rectum, the fibers synapse with excitatory cholinergic intramural neurons (parasympathetic system) and with inhibitory purinergic neurons (sympathetic system). The parasympathetic excitatory pathway, which enhances a contraction present in the rectum, plays a role in the propulsive activity of this segment of the large intestine, allowing the propulsion of the fecal cake. Regarding internal anal sphincter, the role of the parasympathetic nervous

system is inhibitory, that is, it promotes relaxation of the sphincter muscle, according to tests performed on animals[1].

Epidemiology

According to epidemiological findings, the overall incidence of HSCR is 1/4000 live births, and the disorder is approximately four times more common in males than in females. However, as the affected part increases, the male prevalence decreases, that is, in Aganglionose Total the ratio drops to 1.2: 1. Mortality caused by Congenital Intestinal Aganglionosis is the result, in most cases of enterocolitis, and corresponds to the global mortality of 25-30% among children who manifest the disease. It is estimated that among the ethnic groups - Caucasian, Black and Asian - occurs in 1.5: 2.1: 2.8 per 10,000 births, respectively[1,12,13].

Regarding the genetic studies, it is noted that the risk of the birth of twins with HSCR is too much and with little known reasons, being this occurrence of 4% against 0.02% in the general population. Research also demonstrates that the disease can occur as an isolated trait in 70% of those with Aganglionose Colic Intestinal, in 12% associated with chromosomal abnormalities and, finally, the other 18% or more may be a consequence of other congenital anomalies such as urogenital (8%), cardiac (4.5%) and Down's Syndrome (1.8%)[1,3,14-16].

Genetic Aspects

It can be said that HSCR is a disease of multigenic inheritance and with direct connection with the sex of the child. We found nine different genes from the human genome that are susceptible to the disease. According to research conducted, the gene of greatest influence is the RET gene (7-35%), which is located on the long arm of chromosome[10].

Also on the RET gene, studies were carried out to evaluate the possibility of a link between mutations in exon 10 of the RET gene to multiple endocrine neoplasia type 2A (NEM2A), taking into account the high epidemiological index of HSCR with this genetic syndrome. However, the findings were not sufficient to confirm this hypothesis. Other

genes commonly associated with this pathology are the EDNRB (7%) and END3 (less than 5%) genes[2,4,16].

Diagnosis

Congenital Megacolon presents its first signs and symptoms in the neonatal period being a common cause of intestinal obstruction in newborns. Abdominal distension is one of the most striking clinical manifestations of HSCR and occurs due to disproportionate growth of the colon of the large intestine (Megacolon), mainly of the descending and sigmoid colon caused by the difficulty of progression of the fecal cake in the spastic intestinal segment of the diseased colon. In neonates, the earliest manifestation is the delay in the elimination of meconium, caused by intestinal obstruction, which intensifies as solid foods are offered to the child[3,18-21].

In this phase bacterial translocation can occur, consequently, evolution to enterocolitis. In older children, the manifestations of intestinal constipation are more common, but the pictures of intestinal inflammations, also known as enterocolitis plus chronic constipation, contribute to the child's weight loss and short stature. As a result of the subocclusive or obstructive condition, and with the presence of abdominal distension, vomiting often occurs, initially biliary and progressing to fecal tumors depending on the level of lymph node involvement and the time of disease progression. It is also possible to notice respiratory distress in newborns, from abdominal distension, which can be expressed through cyanosis. Another characteristic sign of HSCR is the explosive elimination of feces when a rectal stimulus is performed on the patient, which is usually performed through a small caliber rectal catheter or suppository for children[24].

In addition, the most fearsome of HSCR complications is enterocolitis, formerly known as putrefactive diarrhea. It usually affects the newborns more, resulting in an elimination of putrid diarrhea, abdominal distension, and injury of the colon mucosa, which generates a serrated aspect at its edges, which will be referred to as "seal edges". Enterocolitis can progress to intestinal pneumatosis, perforation of the intestine and peritonitis. In addition, it can generate necrosis that will extend through the segments of the intestine, including the small intestine, and, consequently, may lead to death[18]. In summary, the most common symptom clusters are delayed meconium elimination, abdominal distension, vomiting and constipation[3,4].

Simple radiography, opaque enema and histologic analysis of the rectum wall are the basis for the diagnosis of Hirschsprung's disease. Plain radiography should be the first examination performed if the disease is suspected, however, it will not be decisive for the diagnosis. From it, it will be possible to observe the diffuse abdominal distension simulating a mechanical intestinal obstruction. The opaque enema is used to diagnose both the short forms and the enlarged form of intestinal involvement, the total aganglionosis of the colon. This contrasted examination shows the diseased intestinal portion represented by a small caliber segment, followed by the transition area also known as the transition zone, represented by the shape of a cone. Adjacent to this area is a dilation, Megacolon, which already contains ganglion cells. In total colonic aganglionosis, the contrast image is the characteristic loss of the angles, hepatic and splenic angles of the colon, with an appearance that resembles a "question mark"[12,24].

Another method used for HSCR diagnosis is anorectal manometry, also known as "balloon method". Through it, it is possible to analyze the presence or absence of the recto-anal inhibitory reflex. HSCR patients do not have the relaxation reflex of the secondary anal sphincter when the balloon is inflated in the rectal ampulla during the procedure[2].

Histological examinations are considered the gold standard tests for the confirmation of the absence of ganglion cells in the intestinal wall, they are based on hematoxylin-eosin (H&E) biopsied digestive tissue staining and acetylcholinesterase activity (AChE) analysis. The diagnosis made by the interpretation of the biopsy stained by H&E is considered a diagnosis made by exclusion, since it is based on a histological negative, in the case the absence of ganglion cells. For the diagnosis to be performed safely, it is advisable that the biopsy is from the entire wall of the intestine, because in lower areas, the distribution of ganglion cells is irregular and varies according to the age of the patient, which can generate faulty results. In addition, another important factor for the safety of the diagnosis is the number of histological sections required, in this case, at least 20[24].

Another important histological examination is based on the use of acetylcholinesterase, where patients with HSCR show an increase in the activity of this enzyme. The diagnosis is summarized in the fact that in the absence of ganglion cells there is an increase in cholinergic fibers and, consequently, an increase in AChE activity. In this examination, a brown coloration is observed in the histological section, due to the

hydrolysis process of acetylcholine iodide performed by AChE, causing precipitation of copper ferrocyanide[24].

Surgical techniques and treatment

Once the diagnosis is confirmed, the only treatment for HSCR is the surgical one, which consists of the removal of the aganglionic segment. At the beginning of HSCR treatment, a staged treatment was started, which began with a temporary colostomy, and 6 to 12 months later, the colon was lowered. Today the indication of colostomy is restricted to cases of total aganglionosis of the colon or when there are signs of enterocolitis, due to the clinical conditions of the patient. During the last 50 years, the techniques have been improving, according to the variations of the concept of etiopathogenesis and the understanding of the pathophysiology of the disease.

There are several surgical techniques for Hirschsprung's disease, all with their peculiarities and with the principle of withdrawal from the aganglionic segment, are examples of these techniques: Swenson, Duhamel Soave and more recently the technique of De La Torre-Mondragon. Lowering by endoscopic video-assisted transanal endoscopic approach, laparoscopy, exclusive transanal lowering (De La Torre-Mondragon), transanal lowering with mini-laparotomy are also described[18,20,25].

The first successful treatment was in 1949, by Orvar Swenson, using the open rectosigmoidectomy technique. This technique is done through the abdominal approach, wherein the first time the resection of the colon aganglionic abdominal. In the second period, the aganglionic colon is everted and withdrawn through the anal canal where it is resected. The ganglionic colon is anastomosed near the pectin line using a remnant part of the anal canal. This procedure, however, is not widely used, since resection of the anterior segment of the rectum causes damage to the innervation of the sacral nerve plexuses and frequently operated patients present with significant changes in the bladder, such as urinary incontinence and, in boys, may cause impotence sexual[21].

A second surgical technique emerged in 1960 with Duhamel, which involves lowering the colon through the retro-rectal space, maintaining the anterior part of the rectum and the entire perirectal tissue, avoiding the injury of the nerve plexuses near the bladder and prostate in men. Therefore, the objective of this study is to use the sensory properties of the denervated rectum by adding the motor activity that is absent by the juxtaposition of the healthy colon in a lateral-lateral anastomosis, thus assembling a tube

in which the first half is formed by the rectum and the second half through the colon. As early as 1964, Franco Soave contributed with another surgical technique in which only the distal aganglionic mucosa is dissected and resected while a muscular tube through which the lymph node descends, thus avoiding lesions in the pelvic structures[18,21,22].

However, for the Swenson or even Duhamel technique, a peritoneal cavity is required, laparotomically and in some cases, by laparoscopy to manage the abdominal cavity. In addition to being performed in two times, the need for a temporary bowel bypass is likely. Thus, after the teachings disclosed by De La Torre-Mondragon, surgery can be performed in only one time and without the need for a colostomy and a laparoscopy. The technique consists of the submucosal detachment of the rectal wall approaching the peritoneal cavity inside the rectum. Thus, the diseased aganglionic zone can be resected and the anastomosis of the normal colon segment can be made with the anal canal. The De La Torre-Mondragon technique significantly changed HSCR treatment, being less invasive and with better recovery[21].

Treatment of Total Colonic Aganglionosis requires special care. Since there is an involvement of every colon, including part of the terminal ileum, this type of aganglionosis must first be treated with an ileostomy and after 2 years the ileoanal lowering is advised because in this phase the child already presents an adaptation to the fecal content modification (25). This procedure has the possibility of being carried out with or without a bag, to increase water absorption.

The most used techniques with purse are those of Kimura and Martin-Duhamel. The first one uses a bag measuring approximately 15cm of aganglionic right colon: in this, the ileum is anastomosed laterally with the right aganglionic colon, its first stage being an ileostomy and after two months an ileocolostomy with a lateral-lateral anastomosis is performed ileostomy and the ascending colon aganglionic. Finally, after five to fifteen months Swenson is lowered. The second technique, Martin-Duhamel, advocates a bag of the left aganglionic colon, maintains the whole rectum until its junction with the sigmoid, is based on the improbability of development of fecaloma, even with the long rectal stump, since there is no colon present for the absorption of water[25].

After the operation, most children start bowel movement and feedback can be done within 72 hours. However, through a long treatment and the size of the surgery, the family receives food and training guidelines to encourage the child to evacuate. In addition, the child receives psychological and physiotherapeutic guidance from the multi-

professional team of postoperative care. It is important to emphasize to parents that there is often an initial alteration in the postoperative intestinal functioning, taking a few days to regularize it[26].

Conclusion

HSCR is a congenital intestinal malformation in which there is a great diagnostic possibility when the release of meconium does not occur in the first 24 hours. As it is a genetic disease, several factors can favor the non-migration of the neuroblasts to the primitive intestine, since the twin pregnancy is 200 times more likely to occur in relation to normal pregnancy.

We emphasize the importance of early diagnosis, thus requiring contrast radiological tests to identify the affected area and then confirmation of the condition through an intestinal biopsy. Untreated cases can progress to death, with enterocolitis being the most serious condition. Currently, the treatments and complementary tests are better elucidated, given the greater number of published works with the subject and understanding about the pathology. Finally, because it is a disease that refers to invasive treatment techniques, the need for family support and involvement in order to provide better postoperative results and consequently the patient's quality of life is noted.

References

1. Gugelmin ES, Torres LFB. The accuracy of acetylcholinesterase reaction in rectal suction biopsy in the diagnosis of Hirschsprungs disease. *J Bras Patol e Med Lab* [Internet]. SBPC, SBP, SBC; 2005 Dec [cited 2014 Dec 12];41(6):431–6. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1676-24442005000600010&lng=pt&nrm=iso&tlng=en

2. Morais MB de, Sdepanian VL, Tahan S, Goshima S, Soares ACF, Motta MEFA, et al. A manometria anorretal (método do balão) no diagnóstico diferencial da doença de Hirschsprung. *Rev Assoc Med Bras* [Internet]. Associação Médica Brasileira; 2005 Dec [cited 2014 Dec 11];51(6):313–7. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0104-42302005000600013&lng=pt&nrm=iso&tlng=ptEducação Médica - F.M.U.F.M.G

3. Villar MAM, Jung M de P, Cardoso LC de A, Cardoso MHC de A, Llerena Junior JC. Doença de Hirschsprung: experiência com uma série de 55 casos. *Rev Bras Saúde Matern Infant* [Internet]. Instituto Materno Infantil de Pernambuco; 2009 Sep [cited 2014 Dec 12];9(3):285–91. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1519-38292009000300007&lng=pt&nrm=iso&tlng=pt

4. Bigélli RRHM, Fernandes MMIM, Galvão LC, Sawamura R. Estudo retrospectivo de 53 crianças com doença de hirschsprung: achados clínicos e laboratoriais. *FRMP- Med* [Internet]. 2002 [cited 2014 Dec 14]; 35: 78–84. Available from: http://revista.fmrp.usp.br/2002/vol35n1/estudo_retrospectivo_criancas.pdf

5. Gilbert MJ, Mello DF de, Lima RAG de. Experiências de mães de filhos com doença de hirschsprung: subsídios para o cuidado de enfermagem. *Esc Anna Nery* [Internet]. UFRJ; 2009 Dec [cited 2015 Jan 20];13(4):793–801. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1414-81452009000400015&lng=en&nrm=iso&tlng=pt

6. Marques GMN, Martins JL, Nobre VDRP. Comparison between perfusion and balloon techniques for performing anorectal manometry in children with intestinal constipation. *Acta Cir Bras* [Internet]. Acta Cirúrgica Brasileira/SOBRADPEC; 2008 Oct [cited 2014 Dec 12];23(5):405–11. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0102-86502008000500003&lng=pt&nrm=iso&tlng=en

7. Tuo G, Pini Prato A, Derchi M, Mosconi M, Mattioli G, Marasini M. Hirschsprung's Disease and Associated Congenital Heart Defects: A Prospective Observational Study from a Single Institution. *Front Pediatr* [Internet]. 2014 Jan [cited 2014 Dec 15]; 2: 99. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4166232&tool=pmcentrez&rendertype=abstract

8. Morais MB de, Maffei HVL, Melo M do CB de, Guimarães EV, Torres MRF, Steiner SA, et al. Constipação intestinal [Internet]. *Educação Médica - F.M.U.F.M.G.* 2014 [cited 2014 Dec 15]. p. 147–S156. Available from: http://www.saudedireta.com.br/docsupload/1396186529constipation_criancas.pdf

9. Chen SH. *Hirschsprung Disease* [Internet]. - A Sages Wiki Article. [cited 2014 Dec 16]. Available from: http://www.sages.org/wiki/hirschsprung-disease/

10. Smith B. Pre- and postnatal development of the ganglion cells of the rectum and its surgical implications. *J Pediatr Surg* [Internet]. 1968 Jun [cited 2015 Jan 20];3(3):386–91. Available from: http://www.ncbi.nlm.nih.gov/pubmed/5671309

11. Bolander R. The neurocristopathies A unifying concept of disease arising in neural crest maldevelopment. *Hum Pathol* [Internet]. 1974 Jul [cited 2015 Jan 20];5(4):409–29. Available from: http://www.sciencedirect.com/science/article/pii/S0046817774800213

12. *Obstrução intestinal neonatal: diagnóstico e tratamento* [Internet]. Projeto diretrizes. 2005 [cited 2014 Dec 15]. Available from: http://projetodiretrizes.org.br/4_volume/25-Obsintes.pdf

13. Neville HL. *Pediatric Hirschsprung Disease* [Internet]. 2014 [cited 2014 Dec 16]. Available from: http://emedicine.medscape.com/article/929733-overview

14. Romeo G, Ronchetto P, Luo Y, Barone V, Seri M, Ceccherini I, et al. Point mutations affecting the tyrosine kinase domain of the RET proto-oncogene in Hirschsprung's disease. *Nature* [Internet]. 1994 Jan 27 [cited 2015 Jan 20];367(6461):377–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/8114938

15. Martucciello G, Favre A, Takahashi M, Jasonni V. Immunohistochemical localization of RET protein in Hirschsprung's disease. *J Pediatr Surg* [Internet]. 1995 Mar [cited 2015 Jan 20];30(3):433–6. Available from: http://www.sciencedirect.com/science/article/pii/0022346895900497

16. Kim J-H, Cheong HS, Sul JH, Seo J-M, Kim D-Y, Oh J-T, et al. A genome-wide association study identifies potential susceptibility loci for Hirschsprung disease. Cherny S, editor. PLoS One [Internet]. *Public Library of Science*; 2014 Jan [cited 2014 Dec 15];9(10):e110292. Available from: http://dx.plos.org/10.1371/journal.pone.0110292

17. Santos JM dos S. Megacolón - Parte I: Doença de hirschsprung. *Rev Bras Coloproct* [Internet]. 2002 [cited 2014 Dec 14];3:196–209. Available from: http://www.sbcp.org.br/revista/nbr223/P196_209.htm

18. Medeiros LC da S, Morais MB de, Tahan S, Fukushima É, Motta MEFA, Fagundes-Neto U. Características clínicas de pacientes pediátricos com constipação crônica de acordo com o grupo etário. *Arq Gastroenterol* [Internet]. IBEPEGE, CBCD e SBMD, FBG, SBH, SOBED; 2007 Dec [cited 2014 Dec 15];44(4):340–4. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-28032007000400011&lng=en&nrm=iso&tlng=pt

19. Tannuri U, Tannuri ACA. Megacolo congênito no recém-nascido: qual o melhor tratamento? *Rev Assoc Med Bras* [Internet]. Associação Médica Brasileira; 2007 Apr [cited 2014 Dec 14];53(2):100–1. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0104-42302007000200008&lng=en&nrm=iso&tlng=pt

20. Castro Guevara JE. Nuevas perspectivas para el tratamiento de la enfermedad de Hirschsprung en Camagüey. *Rev Arch Médico Camagüey* [Internet]. 1996, Editorial Ciencias Médicas Camagüey; [cited 2015 Jan 20];17(1):6–9. Available from: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1025-02552013000100003&lng=es&nrm=iso&tlng=es

21. Santos JCM. Megalocón – Pate I da doença. *Rev. Brasileira de Coloproctologia*, 2002 Avaliable from:http://www.inst-medicina.com.br/programas/mega_colon_parte1.php

22. Maksoud JG. *Moléstia de Hirschsprung*. IN: Maksoud JG. Cirurgia Pediátrica. Volume 2, 2nd ed. Rio de Janeiro, Revinter Ltda. 2003 pág. 806-825.

23. Souza JCK, *Malformações do Sistema Neuroentérico*. IN: Souza JCK, Cirurgia Pediátrica – Teórica e Prática. São Paulo: Rocca, 2007.pag. 421-443.

24. Aguilar-Nascimento JE, Bicudo-Salomão A, Caporossi C, Silva RM, Cardoso EA, Santos TP et al . Abordagem multimodal em cirurgia colorretal sem preparo mecânico de cólon. *Rev. Col. Bras. Cir.* 2009 July; 36(3): 204-209. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-69912009000300005&lng=en. http://dx.doi.org/10.1590/S0100-69912009000300005.

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