

Dear pediatric surgeons from the Pediatric Colorectal and Pelvic Learning Consortium!

I am always very surprised to read your articles. In 2014, you publish 4 articles every month. It seems that you do not think about the scientific nature, and therefore the value of your proposals. I use as an example the article by Kwon et al was on Antegrade Colonic Enema [1]. The article summarizes statistical data from different centers, based on which the authors conclude that: - "There is variation in practice of ACE channel placement. At specialty pediatric colorectal centers, age at time of placement and type of channel placement varied across institutions. Further work is needed to better characterize diagnosis- and age-focused patient centered outcomes to clarify recommendations for our patients who benefit from these procedures". Firstly, this is not a scientific work, but a combination of statistical data from different centers that did not lead to new knowledge. Secondly, it carries false information, since complications are not indicated among the statistics. Thirdly, idiopathic constipation in children at the age of 7-9 years cannot be considered a refractory especially if the treatment did not correspond to the pathophysiology of the disease.

1. What is the difference between an antegrade enema and a retrograde one?

A). From a physiological point of view, there is no difference from which side water enters the rectum. The volume of water causes an increase in pressure to the threshold level of defecation, when the feces have not yet had time to become formed, and therefore are easily passed through a poorly functioning anal canal. An enema allows to get rid of constipation and fecal incontinence during long-term use. But this is a symptomatic, not pathogenetic treatment of the disease.

B). Doctor Pena Bischoff wrote on Facebook: - "What is the difference between retrograde and antegrade enema? We always tell patients and families that the only difference is how the solution enters the body. One is not more effective than the other. For self-administration antegrade enemas are a little easier in the majority of cases." An antegrade enema was first proposed for patients after removal of a rectal tumor, to make it easier for patients to take care of themselves. However, children aged 5-11 years of age are cared for by their parents, so at this age there is no advantage to either enema option. For example, Matsuno et al concluded "that retrograde colonic enema was not inferior to Malone antegrade continence enema on the fecal continence [2].

C). In children after ACE, stomal incontinence and stenosis are the most common issues reported, and a surgical revision rate of 17% [3]. Most articles are devoted to ACEs in children with spina bifida and other neurogenic colorectal dysfunction. Despite the high complication rate, there is justification for the use of ACE because these children are difficult to care for otherwise. In adults with functional constipation, use of ACE resulted in a disappointed overall success rate of 37%. Nine (30%) patients developed a postoperative complication [4].

D). Unfortunately, this is not a mistake, but a systematic approach in which there is no idea of the pathophysiology of functional megacolon. In the article Knaus et al. post ACE, 35 (90%) were clean with daily flushes and 6 (15%) eventually successfully transitioned to laxatives only [5]. The authors concluded "that ACE are successful treatment options for patients with severe constipation and fecal incontinence... Larger studies are needed to identify predictive factors of poor outcomes". Without evidence, one cannot say that ACE are successful treatment options. Firstly, 10% were not clean. Secondly, only 15% transitioned to laxatives. The rest

continued treatment with ACE and there was no mention of complications. Looking for predictive factors of poor outcomes is a strange goal. Why was this article written if and this goal was not achieved?

2). On the pathophysiology of functional megacolon (FM)

The cause of chronic constipation in children without congenital megacolon (Hirschsprung's disease), secondary megacolon (ARM) and acquired stenosis is the discrepancy between the width of the rectum, in which the feces are formed, and the throughput of the anal canal. Wide feces cannot pass through the anal canal, if the diameter during its opening is less than the diameter of the feces. Thus, the key factor is the megarectum, which is always accompanied by megacolon [6]. In this case, the anal canal changes, which is sometimes defined as achalasia of the anal canal [7]. Из-за этого the pelvic floor muscles are damaged, which is called descending perineal syndrome. Stretching of the puborectalis leads to encopresis, and stretching and weakness of the levator plates does not open the anal canal during an attempt to defecate, which sharply increases the resistance to the movement of feces [8].

3). Treatment of functional megacolon

It should be borne in mind that laxatives and enemas are to a very small extent a treatment for the disease (FM), since they do not affect the damaged anal canal.

A). Bischoff et al believed that by prescribing Senna dose of 67mg (range: 5-175mg), which is tens of times higher than the dose allowed by the pharmacopoeia, they achieved successful management of idiopathic constipation. The most common side effect experienced by patients was cramping (n=47). This group of patients required a significantly higher amount of senna as compared with those that did not complain of cramping (96 mg compared to 62 mg). Out of the 215 patients who underwent the laxative protocol, 41 (19%), who refused enemas due to unbearable pain ultimately underwent colonic resection [9]. It is known that Senna causes an increase in the tone of the intestinal muscles, which in therapeutic doses with intermittent administration improves rectal emptying. But large doses cause spasm of the intestine and anal canal, which prevents the evacuation of feces from the rectum. This unfounded cruel experiment has no justification [10]. Firstly, because there is no point in refusing a cleansing enema. Secondly, as Duhamel showed, "Recto-sigmoidectomy does not improve these children" [7]. Thus, the definition of FM as refractory to treatment based on the use of large doses of Senna is erroneous.

B). At the age of 7-9 years, FM, in principle, cannot be a refractory to treatment disease. The use of laxatives and enemas is useful, but not sufficient for treatment for rectoanal achalasia. In stage 3 megacolon, treatment can be long-term with the sequential use of different methods: 1) Anal dilation described in the article by Clayden and Lawson leads to improvement in approximately 36% of cases [6]. Botox injections into the rectum can be repeated and have been proven to be effective [11]. The long-term follow-up study shows that «the vast majority of internal anal sphincter achalasia patients have normal bowel control following internal sphincter myectomy» [12]. In (62.5%) patients at the time of follow-up had regular bowel motions without the use of laxatives. In 25% patients had regular bowel motions but remained on small doses of laxatives. The 8.3% patients who suffered from constipation and soiling required twice weekly enemas to remain clean [12].

Conclusion Conservative treatment with laxatives and enemas is an effective fight against constipation and fecal incontinence. As shown above, ACE has no advantage over retrograde enema, because any enema at this age in patients with FM is performed by the parents. However, a retrograde enema has a huge advantage, since it is not associated with leakage and stenosis of the fistula and does not require surgical treatment to eliminate complications.

Based on the above irrefutable evidence, I am obliged to ask the members of the Pediatric Colorectal and Pelvic Learning Consortium. How can ACE be recommended for children with functional megacolon without mentioning complications, without comparing it with the results of a retrograde enema, without indicating the degree of rectal dilatation, without using a whole range of safe and effective treatment methods?

Dear pediatric surgeons from the Pediatric Colorectal and Pelvic Learning Consortium, I am writing to you with the hope that you will pay attention to the studies that provide different approaches to the treatment of children with functional megacolon. You have a responsibility to choose better methods for the benefit of your patients.

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My website: <http://www.anorectalmalformations.com>

References

1. Kwon EG, Kreiss J, Nicassio L, Austin K, Avansino JR, Badillo A, Calkins CM, Crady RC, Dickie B, Durham MM, Frischer J, Fuller MK, Speck KE, Reeder RW, Rentea R, Rollins MD, Saadai P, Wood RJ, van Leeuwen KD, Smith CA, Rice-Townsend SE. Variation in Practice Surrounding Antegrade Colonic Enema Channel Placement. *J Pediatr Surg*. 2024 Apr 19:S0022-3468(24)00260-4. doi: 10.1016/j.jpedsurg.2024.04.009. Epub ahead of print. PMID: 38760309.
2. Matsuno D, Yamazaki Y, Shiroyanagi Y, et al. The role of the retrograde colonic enema in children with spina bifida: is it inferior to the antegrade continence enema? *Pediatr Surg Int*. 2010 May;26(5):529-33. doi: 10.1007/s00383-010-2585-6.
3. Chan YY, Gonzalez R, Kurzrock EA. Malone antegrade continence enema: Is cecal imbrication essential? *J Pediatr Urol*. 2018 Dec;14(6):546.e1-546.e5. doi: 10.1016/j.jpuro.2018.05.019.
4. Sturkenboom R, van der Wilt AA, van Kuijk SMJ, et al. Long-term outcomes of a Malone antegrade continence enema (MACE) for the treatment of fecal incontinence or constipation in adults. *Int J Colorectal Dis*. 2018 Oct;33(10):1341-1348. doi: 10.1007/s00384-018-3088-5. Epub 2018 Jun 22.

5. Knaus ME, Lu PL, Lu A, Maloof ER, Ma J, Benedict J, Wood RJ, Halaweish I. Antegrade continence enemas in children with functional constipation and dyssynergic defecation: Go or no go? *J Pediatr Surg*. 2022 Aug;57(8):1672-1675. doi: 10.1016/j.jpedsurg.2022.04.007. Epub 2022 Apr 23. PMID: 35534277.
6. Clayden GS, Lawson JO. Investigation and management of long-standing chronic constipation in childhood. *Arch Dis Child*. 1976 Dec;51(12):918-23. doi: 10.1136/ad.51.12.918.
7. Duhamel B. Physio-pathology of the internal anal sphincter. *Arch Dis Child*. 1969 Jun;44(235):377-81. doi: 10.1136/ad.44.235.377.
8. Levin MD. Functional megacolon in children.
https://www.anorectalmalformations.com/_files/ugd/4d1c1d_a41e68ac8aab479d9bb38ef9e5c77ced.pdf
9. Bischoff A, Brisighelli G, Dickie B, Frischer J, Levitt MA, Peña A. Idiopathic constipation: A challenging but manageable problem. *J Pediatr Surg*. 2018 Sep;53(9):1742-1747. doi: 10.1016/j.jpedsurg.2017.09.022.
10. Levin MD. Letter to the Editor. *J Pediatr Surg*. 2018 Aug;53(8):1634-1635. doi: 10.1016/j.jpedsurg.2018.03.007. Epub 2018 Mar 20. PMID: 29661574.
11. Kajbafzadeh AM, Sharifi-Rad L, Nabavizadeh B, Ladi-Seyedian SS, Alijani M, Farahmand F, Motamed F, Alimadadi H, Fallahi A, Fallahi GH. Intrarectal Electromotive Botulinum Toxin Type A Administration in Children With Intractable Constipation: A Randomized Clinical Trial. *Am J Gastroenterol*. 2020 Dec;115(12):2060-2067. doi: 10.14309/ajg.0000000000000940. PMID: 33009066.
12. Doodnath R, Puri P. Long-term outcome of internal sphincter myectomy in patients with internal anal sphincter achalasia. *Pediatr Surg Int*. 2009 Oct;25(10):869-71. doi: 10.1007/s00383-009-2436-5. PMID: 19680665.