Can high doses of Senna be used to treat children with chronic constipation?

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The seventh issue of the Journal of Pediatric Surgery (2026) published an article by Alzate-Ricaurte et al., "Longitudinal changes in senna-based laxative dosing in pediatric constipation: A single-center retrospective study." It presents data on the treatment of chronic constipation in 75 patients from July 2016 to July 2023 at the International Center for Colorectal and Urogenital Care, Children's Hospital Colorado [1]. Idiopathic constipation was the most common diagnosis, seen in 49 patients (65.3%). The remaining patients had anorectal malformations, distributed in perineal fistula (21.3%) and vestibular fistula (8.0%), bulbar fistula (2.7%), rectal atresia (1.3%), and rectal stenosis (1.3%). Objective of this study was to evaluate whether prolonged senna use in pediatric patients is associated with the development of drug tolerance. In this context, the term "tolerance" refers to a condition in which, with prolonged use of high doses of senna, the colon stops responding as before, requiring an increase in dosage to overcome tolerance [2].

The follow-up time was years 3.29 (2.14–4.55) years. Patients were 8 years (5–12 years) old at the start of Senna treatment and 12 years (9–16 years) at the final stage. The total daily dose of Senna increased significantly between the first visit and the last control examination, rising from a mean value of 45 mg (30–75) to 60 mg (37.5–90; $p < 0.001$). An increase of 33%. However, in 42 (56%) patients the dose increased, and in 33 (44%) the dose decreased. From this it follows that in those patients whose Senna dose was increased, it significantly exceeded 33% of the initial dose. Secondly, the ratio of dose to patient weight is incorrect for two reasons. It should have been calculated only for those whose dose was increased. In addition, the very principle of correlating with weight is incorrect, since Senna preparations are almost not absorbed, quickly pass through the small intestine and are concentrated only in the colon. Third, in the graph in Figure 1B, four patients received a dose greater than 100 grams (Figure 1), raising doubts about the veracity of the data. For some reason, the authors did not explain why they reduced the maximum dose of 180 grams of Senna, which Peña and Bischoff administered from June 2005 to October 2012 [3].

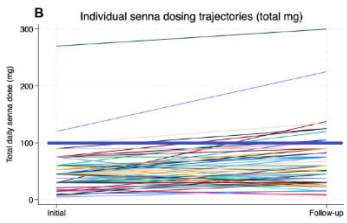

Figure 1. Graph of individual Senna dosing trajectories (total mg). I drew a horizontal line (blue) at 100 mg. Four trajectories end above this line to the right.

This analysis shows that the authors' assertion that the Senna dose increased proportionally to the patients' weight by the end of the study is incorrect. First, it increased only 56% of the patients. Second, determining the amount of Senna per kilogram of body weight is inaccurate, as Senna is not absorbed in the intestine. Therefore, the amount of Senna increased at the end of the study, meaning the absence of tolerance has not been proven.

An article on the treatment of patients must provide evidence that the treatment is scientifically sound, safe, and more effective than other methods. It must include treatment outcomes for all patients, including long-term results. This article only includes cases where Senna doses were recorded over several years. However, in a previous article on the treatment of idiopathic constipation, "out of the 215 patients who underwent the laxative protocol, 41 (19%) ultimately underwent colonic resection" [3]. The authors unjustifiably excluded from the analysis a group of patients who had undergone surgery, as well as those who refused surgery and stopped visiting the department. Why did the authors not provide long-term results for patients treated between 2005 and 2012?

Non-compliance with scientific methodology at the International Center for Colorectal and Urogenital Care, Children's Hospital Colorado, Aurora, CO, USA, has long been known.

For example, Levitt and Peña published an article on transanal rectosigmoid resection for severe intractable idiopathic constipation, in which, as in Hirschsprung disease, the dilated rectosigmoid segment was removed along with the proximal two-thirds of the internal anal sphincter (IAS). The authors recommended this surgery because "of 14 patients with more than 3 months of follow-up, the preoperative laxative dose was 68 mg of senna/d (range, 52-95 mg), which decreased to 8.6 mg postoperatively ($P < .001$)" [4]. This surgery was not scientifically justified, since IAS is known to provide 50% fecal continence. Secondly, short-term results after a new surgery should not be published. Unsurprisingly, Gasior et al.'s article claimed that transanal resection failed to sufficiently reduce the need for laxatives but resulted in a high rate of fecal incontinence due to significant anal canal distension and loss of the rectal reservoir [5]. There is no doubt that fecal incontinence was caused by resection of 2/3 of the IAS.

I propose comparing the results of surgical procedures for functional constipation with the experience of the Belarusian Center for Pediatric Surgery in Minsk, where I worked and still

maintain contact. The center's scientific director, Professor V.I. Averin, confirmed to me that, as before, there have been no cases of surgery in children with functional constipation. Treatment includes anal distension under general anesthesia, enemas, and laxatives only in the recommended dosages [6, 7].

Literature data on complications after taking Senna preparations.

Cassia senna is one of the herbal medicines known to have adverse effects [8]. Therefore, its dosage and duration of use in children are limited. Ulbricht et al. [9] suggested:

- **2-6 years: 4.3–17.2 mg sennosides per day**
- **6-12 years: 8.6–34.4 mg ----------**
- **>12 years: 17.2–68.8 mg ----------**

The authors note that treatment is generally recommended for no more than 1 week without medical supervision, as senna is a stimulant laxative [9].

Tabbers et al., recommend the following doses [10]:

- **2-6 years: 2.5–5 mg/day**
- **6-12 years: 7.5–10 mg/day**
- **>12 years: 15–20 mg/day**

The following are cited as reasons limiting the dosage and duration of continuous treatment with Senna:

• **melanosis coli** - a dark pigmentation of the colonic mucosa that occurs with prolonged use of Senna. It is currently believed to be associated with epithelial cell apoptosis and lipofuscin accumulation in mucosal macrophages. The change is usually reversible after discontinuation of the drug.

• **the effect of senna on the enteric nervous system** -experimental studies on animals have reported: degenerative changes in intestinal wall neurons; decreased density of nerve plexuses; changes in motility after prolonged exposure. However, study results are contradictory.

• **the risk of "cathartic colon"** - colonic dilation, loss of haustration, decreased motility in patients who have abused stimulant laxatives for many years.

Joo et al. compared changes observed during barium enemas in patients with chronic constipation in a group that used stimulant laxatives with radiographs in a group that did not.

They concluded that long-term stimulant laxative use results in anatomical changes in the colon characterized by loss of haustral folds, a finding that suggests neuronal injury or damage to colonic longitudinal muscle caused by these agents [11]. However, literature reviews of recent years indicate a lack of evidence of harmful effects of laxatives on the colon, and therefore the appropriateness of treatment with stimulant laxatives, even in the long term, should be reconsidered in the treatment of patients with constipation [12].

Review articles do not analyze articles themselves but rather rely on the opinions of the authors of the published papers. For example, all articles by pediatric surgeons using high doses of senna, like the article under review, state that "clinical studies confirm the long-term safety and efficacy of senna, with side effects generally limited to mild abdominal cramps and dermatologic reactions associated with prolonged skin contact with stool after application" [1]. These statements have influenced recommendations of recent years. However, just as review authors find no convincing evidence that senna causes colon damage, there is also no evidence that senna is harmless, especially at high doses and over long periods of use.

Analysis of the results of treatment of chronic constipation in children with high doses of Senna.

Complications of high dose senna use include abdominal cramps, vomiting, or fecal incontinence, which are resolved with a change in laxative or a switch to rectal enemas. More concerning is the formation of perineal blisters, which occur with inconsistent or high senna dosages (60 mg/day) and is associated with nighttime incontinence and prolonged contact of feces with the skin [13]. The pathogenesis of these symptoms requires detailed analysis.

1. The formation of perineal blisters. Firstly, if blisters form on the skin due to toxic substances in the stool, one can imagine the damage to the colonic mucosa, which lacks a protective epidermis. Secondly, the claim that feces remain in prolonged contact with the perineal skin in children over 5 years of age is questionable. However, feces undoubtedly remain in contact with the colonic mucosa for a significantly longer period, from the moment when it entered the colon until defecation. This suggests that senna is a toxic substance and damages the colon to a greater extent than the perineal skin.

2. **Melanosis coli.** Can pediatric surgeons' claims that Senna does not cause colon damage to be considered valid if they have never published the results of colonoscopy or rectal mucosal biopsy? The assertion that a dark pigmentation of the colonic mucosa is usually reversible after

discontinuation of the drug in no way denies the fact that after acquiring normal coloration, irreversible pathological changes remain in the colon, such as impaired haustration [11].

3. The effect of senna on the enteric nervous system. With prolonged use of significant doses of Senna, irritable colon syndrome occurs when, in response to increased pressure in the colon, instead of peristalsis, as described by the Bayliss-Starling intestinal law [14], severe spasms occur. A barium enema reveals a narrow-left colon with loss of haustration [15,16] **(Figure 2).**

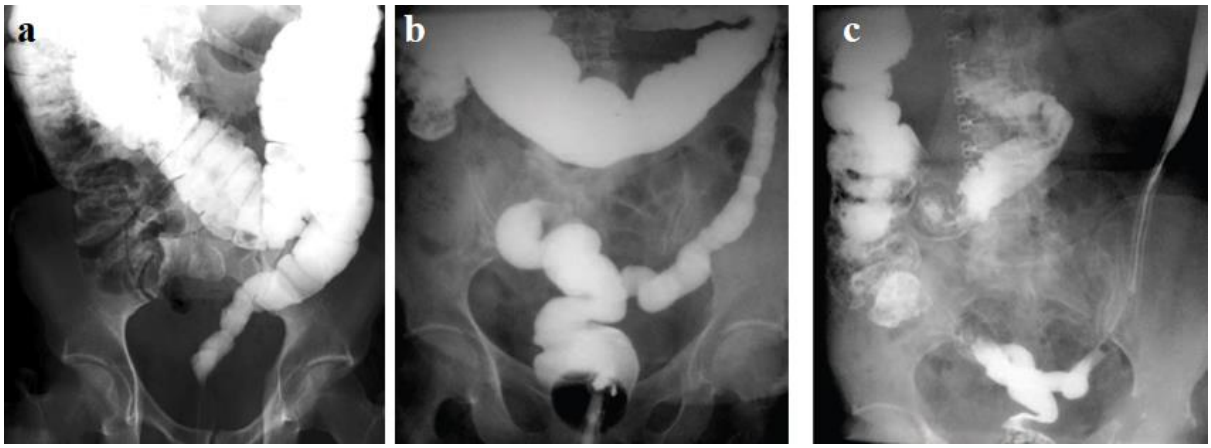

Figure 2. (a) From the article by Bischoff et al., with the caption under the figure: "Contrast enema showing a spastic rectosigmoid after prolonged use of a phosphate-based enema [15]. The rectum is markedly constricted. **(b-c)** An elderly woman had been taking the usual recommended doses of stimulant laxatives for many decades. In recent years, small volumes of stool impacted in the left colon caused her excruciating pain, because of which she often had to go to the hospital. When filled, narrowing of the left half of the colon with the absence of haustration is determined **(b)**. After emptying, the left side of the colon is spasmodic **(c).** Her life was restored to normal after a colostomy on the ascending colon [16].

Hypertonic sodium phosphate enemas sometimes cause hyperphosphatemia with severe consequences, but colon damage has not been described. Meanwhile, in the article where this radiograph was presented, the authors state: "We increase the amount of laxative (usually a senna derivative) on a daily basis, taking daily abdominal films, until we find the dosage that provokes a complete emptying of the colon as radiologically demonstrated" [15].

In 2021, Peña et al. described 22 patients who complained of severe colicky abdominal pain during cleansing enemas, as well as a gradual increase in the time required for fluid to be expelled. Contrast studies revealed marked dilation of the right colon and spastic stenosis of the left colon. They were unable to find descriptions of similar symptoms after enema use and

concluded: "An intriguing and, to our knowledge, previously unreported complication of chronic enema use is presented" [17].

Just because something happens after something else doesn't mean it caused by this other. In other words, if an enema causes pain, it doesn't mean the enemas caused colon damage. Cleansing enemas have been used for a long time and very often, so the authors should have wondered why no similar observations have been published yet. I pointed out to the authors and readers of the journal Pediatric Surgery that the changes described in Peña's article were due to the use of high doses of Senna [18]. Thus, long-term use of high doses of Senna has proven what had been in doubt: long-term use of high doses of Senna irreversibly damages colon function, likely by destroying the enteric nervous system.

Discussion

The study was conducted in Colombia, but the contribution of co-authors A. Peña and A. Bischoff is not declared. Obviously, full consistency of representations is implied. The article and literary reference lack an understanding of the pathological anatomy and physiology of diseases accompanied by chronic constipation. For example, it is stated that "Constipation in patients with anorectal malformations is multifactorial but often includes an anatomic component that may partially account for treatment response" [1]. There is no information in this phrase. Of the total number of patients (75), 16 (21%) had ARMs with a perineal fistula. In these patients, severe constipation is explained by the results of posterior sagittal anorectoplasty (PSARP). After the work of Stephens, it was known that ARM with visible fistulas has a normally functioning anal canal [19]. A cutback procedure, which transects the ectopic anus along with the subcutaneous portion of the external anal sphincter, leads to complete recovery. In the article by Kyrklund et al., constipation among patients (33 vs. 3% in controls; $p < 0.0001$) declined significantly with age [20]. Constipation can be completely avoided (1) if surgery is performed before the development of megarectum, (2) if skin grafting, which leads to stenosis of the neoanus, is avoided. Browne urged: "No attempt should be made to suture the raw surfaces thus produced, and after a month or two they will be covered with supple and satisfactory new skin" (after cutback) [21]. The formation of elastic tissue prevents the development of stenosis, as the anus can expand with age. During PSARP, to approach the rectum the puborectalis muscle (PRM), which plays a crucial role in fecal continence, is transected. The deep and superficial portions of the external anal sphincter (EAS) are transected. The internal anal sphincter (IAS), which accounts for 50% of fecal continence, is

removed under the name the "rectal pouch", and the bloodless and denervated rectum is brought down in its place. The levator plates, which normally open the anal canal during defecation to reduce resistance to the passage of feces, are separated from the rectum. During wide tissue dissection, invisible nerve branches that provide reflex communication between all pelvic organs are severed. As a result of this procedure, the normally functioning anal canal is transformed into a perineal fistula. All patients after pull-through surgery experience chronic constipation and fecal incontinence to varying combinations.

I have cited reliable data from available sources. Table 1 shows the long-term results after the cutback procedure and PSARP in patients with perineal fistula using the same assessment method, which was used before 1982. Ratings were deemed as “good” when normal fecal retention and absence of constipation were achieved, “fair” when patients required laxatives or enemas, and “poor” when fecal incontinence and/or uncontrollable constipation occurred.

Table 1. Comparison of treatment results after cutback (1-4) and after PSARP (A-D).

Authors	Good (%)	Fair (%)	Poor (%)
1. Nixon [22]	98	0	2
2. Ackroyd et al. [23]	85	15	0
3. Kyrklund et al. [20]	90	8	2
4. de la Fuente [24]	90	?	?
A) Schmiedeke et al [25]			≈ 60
B) Lombardi et al. [26]			≈ 61.4
C) Stenström et al. [27]			≈100
D) Abo-Halawa et al. [28]			?

The authors of the peer-reviewed article prescribed high doses of Senna for many years, causing suffering to patients and damaging colon function. The authors attributed the increase in Senna dose with age to weight gain. They state that the dose per unit of weight at the end of the study was the same as at the beginning. This interpretation is erroneous, as Senna is not absorbed in the bloodstream. The study ended in July 2023, but these patients continued taking high doses of Senna. From a pathological physiology perspective, Senna increases colon tone. The tone of the IAS, which is the thickened continuation of the circular muscle fibers of the rectum, also increases, causing obstruction to fecal evacuation. This necessitates increasing the dose of Senna to overcome the high IAS tone. Therefore, the increase is not due to weight gain, but to overcome the spasm of the IAS, which leads to a vicious circle. To determine the extent and frequency of the damage to the colon, it is necessary to study long-term results. More importantly, this harmful practice must be stopped immediately.

In this study, severe constipation after PSARP for ARM with perineal fistula indicates a poor outcome, confirming the comparative results shown in Table 1. Why did the authors use the worst of the two options to treat their patients? Why was Peña's "experiment," which contradicts scientific research, preferred over scientifically validated studies?

The authors state that "Idiopathic constipation includes several phenotypes, of which the subgroup most commonly refractory to management (and often seen in BMPs) is characterized by physiologically slow colonic transit, which may contribute to higher stimulant laxative requirements" [1]. The term “idiopathic constipation” indicates that the etiology and pathogenesis of the disease are unknown. It is impossible to apply pathogenetic treatment without understanding the causes and development of functional megacolon.

The etiology and pathogenesis of functional megacolon in children have been established. During the toilet training period, when a child is distracted or upset, he delays defecation. When he attempts to defecate after delaying defecation, he experiences severe pain because large-diameter stool had formed in the rectum. Because of the pain, they delay defecation again. This creates a vicious cycle, resulting in dilation of the rectum and the left half of the colon, т.е. megacolon [28]. Thus, "**megacolon**" is one of the main characteristics distinguishing it from other types of constipation.

Pathological physiology of the anal canal in patients with functional megacolon

Since the width of the anal canal during attempted defecation is smaller than the width of the stool, a strong peristaltic wave of the rectum cannot push a wide stool through the anal canal. But it causes stretching of the pelvic floor muscles, primarily the PRM. A weak PRM cannot prevent the passage of liquid stool through the anal canal, which is defined as encopresis. Since a stretched and weak PRM does not compress the upper part of the anal canal, the functional portion of the anal canal shortens, which is revealed by X-ray examination as a shortened anal canal. It is as if the rectum has descended toward the perineum. This condition is called descending perineum syndrome [30]. Manometric examination reveals that during rectal balloon dilation, which in healthy individuals leads to relaxation of the IAS and a decrease in anal canal pressure (rectoanal inhibitory reflex), in patients with megacolon, the anal canal contracts. This "paradoxical" contraction was believed to be the cause of fecal stagnation in the rectum. It had various names: anismus, spastic pelvic floor syndrome, obstructed defecation, anorectal outlet obstruction, etc. However, this interpretation of this phenomenon is incorrect. To induce the rectoanal inhibitory reflex in the dilated rectum, it is necessary to create the same

rectal pressure as normal, i.e., for this, a large-diameter balloon must be inflated in the rectum. In functional megacolon, only large volumes of air, sharply insufflated into the rectum, caused a slight decrease in pressure in the anal canal. However, several days after anal distension under anesthesia, the depth of anal pressure reduction after the introduction of standard volumes of air reached normal values [6]. The study by Keshtgar et al showed the physiological importance of functioning thickened IAS in the absence of RAIR (of non-relaxing IAS muscle) in severe constipation in children. They respond well to injection of botulinum toxin into the external anal sphincter muscles. Thickening of the IAS correlate significantly with the duration and severity of symptoms [31]. In 14 cases of idiopathic megacolon, which no medical treatment could alleviate, Duhamel performed partial sphincterectomy of the IAS. The structure of the IAS was abnormal. In most cases, the smooth muscle was dissociated by sclerosis and intimately mingled with striated muscle fibers. In some cases, there was even a complete absence of smooth muscle, which had been replaced by striated fibers that were more or less fibrotic. He recommends this treatment method, after which symptoms may disappear or significantly decrease [32]. In four (5%) of 79 children with long-standing chronic constipation who had not responded to medical treatment, Clayden and Lawson found a mild degree of anal stenosis with the formation of a filiform stricture at the mucocutaneous junction during anal canal dilation. This filiform stricture, located approximately 1 cm from the anal verge, accommodated only two fingers (instead of four) of the operator's hand [33]. The results of these studies show that, in addition to dilation of the rectum and colon, changes occur in the anal canal, which can impede bowel movements or cause constipation and megacolon in approximately 5% of patients with anal canal stenosis. Dilation of the anal canal under general anesthesia eliminates rigidity, restores the depth of the rectoanal inhibitory reflex, and, as demonstrated by the experience of the Belarusian Center for Pediatric Surgery, allows for the avoidance of surgical treatment.

Pathophysiology of the rectum and colon. Rectal dilation is always accompanied by dilation of the left half of the colon, where feces accumulate for more than three days. If constipation is diagnosed soon after the onset of symptoms, the use of polyethylene glycol leads to recovery. The later the diagnosis of constipation, the wider the rectum and other parts of the colon, and the sigmoid colon, which has a mesentery, is usually elongated. However, since the size of the anal canal and rectum increases with age, to promptly identify megacolon, it is necessary to compare the dimensions with the age norm [34,35]. I distinguish 3 degrees of megacolon depending on the integral characteristic of the size of the colon, which I determine using a

formula that includes the width of the rectum (cm) multiplied by the volume of the colon in milliliters of barium introduced up to the cecum, per centimeter of height of the patient [34]. The wider the colon is, the less effective the peristaltic wave, since it does not close the intestinal lumen. This leads to a slowing of transit. Furthermore, balloon dilation of the rectum results in a reflex slowing of transit in the jejunum, and ileum. Shafik suggested that under normal physiological conditions, the reflex suppresses intestinal transit, allowing the rectum time to empty [36]. Thus, transit slowing, although to varying degrees, is always observed with constipation. Grade 3 megacolon indicates severe damage to the colon, which is reflected by a slowing of transit using manometric or scintigraphic technique. This is a symptom, not a diagnosis, and not an indication for surgery. Grade 3 megacolon indicates that treatment may take several years, involving enemas, laxatives, anal distension, Botox injections, etc.

The authors of the peer-reviewed article used the seven-day treatment trial method described in the article by Bischoff et al. in patients with idiopathic constipation, which selects patients for rectosigmoid resection to reduce the Senna dose [3]. The trial-and-error protocol is followed during the one-week period until the abdominal film shows a clean colon. The goal is to reach the point where the patient adequately empties his/her colon on daily basis with radiologic confirmation. The dosage of Senna required to reach that point, is considered an objective measure of the magnitude of the patient's constipation. (on what basis?) Patients with extreme constipation who failed to pass stool, became distended, and vomited after receiving laxatives 10–15 times higher than the recommended dosage are considered “resistant to medical treatment” and are therefore candidates for a surgical treatment (on what basis?). Out of the 215 patients who underwent the laxative protocol, 41 (19%) ultimately underwent colonic resection. Fifty-two patients (24%) had follow-up for less than 30 days, therefore they considered them lost to follow-up. The mean follow-up for the remaining 163 patients was 329 days (range 31–2612 days) [2]. More than 10 years have passed since then, but the authors have not published the treatment results after conservative treatment and after surgery.

The authors do not recommend without justification: (1) tapering/deccreasing the dose since they believe that idiopathic constipation is a chronic, not curable, disease (no logical connection); (2) Botox injections for the management of idiopathic constipation (why?); (3) Myectomies are controversial procedures, frequently performed without scientific basis (contradicts the results described); (4) They believe that most patients do not need enemas to treat constipation (why?).

The statement that: "In our experience, Senna (used with much higher doses than those recommended in the literature) has revealed itself to be an effective and safe stimulant laxative" [1,3], as demonstrated above, is false, dangerous, and unacceptable from both a moral and legal standpoint, because there is no basis for recommending bowel resection 7 days after prescribing high doses of Senna, which causes intolerable pain due to spasm of both the colon and anal canal. Continuing treatment in those who have undergone this scientifically unsubstantiated experiment risks irreversible loss of function of the left colon. Surgery on children aged 11 months and older, when long-term conservative treatment yields better results, is inexplicable from a basic logical standpoint. Firstly, removal of the colon does not resolve the underlying problem in the anal canal. Secondly, it is known that surgery is followed by a temporary improvement in symptoms, followed by a relapse of symptoms [32, 37].

Compelling evidence that senna is a toxic product.

The above analysis of pediatric surgical units prescribing high doses of senna has demonstrated that senna damages colon function. A review of the literature indicates a broader range of toxic effects of senna on the body. Long-term use of anthraquinone laxatives contained in Senna is reported to cause morphological changes in the colonic muscular system, particularly the enteric nervous systems and smooth muscles. In addition, high doses of anthraquinones may inhibit hepatocyte proliferation, leading to cell shrinkage, vacuolization, mitochondrial membrane reduction, and hepatotoxicity. Excessive anthraquinones can also cause morphological changes in HK-2 cells inhibiting cell growth, block changes of the cell cycle and triggering apoptosis, which leads to nephrotoxicity in turn. Due to these safety and health concerns, the European Medicines Agency published a draft report on the evaluation of Folium Senna in 2017 (https://www.ema.europa.eu/en/medicines/herbal/sennae-fructus), stating that long-term administration of free anthraquinone-containing drugs (such as emodin and aloe-emodin) could lead to hyperpigmentation of the colon and cecum intestinal wall within 4–13 months. Due to toxicity, the daily dose and cycle length of anthraquinone-containing laxatives were limited and prohibited for children and breastfeeding women [cited in Long et al. 39]. The FDA Adverse Event after the Senna Reporting System (FAERS) for the period 2004 to 2024 found a significant increase in the number of reported adverse events during the study period, with the highest incidence observed in 2024 (n = 423). The most frequently reported system organ class was immune disorders (n = 1722), followed by gastrointestinal disorders and hypersensitivity reactions [40]. Plants of the genus Senna (formerly Cassia) have been implicated as the cause of a natural and experimental muscle degeneration syndrome, often

fatal in animals. Histological examination revealed necrosis of skeletal and cardiac muscle with flocculent degeneration and proliferation of sarcolemmal nuclei. This was recently described as an experimental model of mitochondrial myopathy in chickens chronically Senna occidentalis. Microscopic examination revealed, in addition to muscle-fiber atrophy, lipid storage in most fibers and a moderate amount of cytochrome oxidase-negative fibers [41]. Rabbits that received the ration containing 4% ground S. occidentalis seeds gained less weight ($p < 0.05$) and died in the third week. Histopathology revealed that the heart and liver were the main organs affected, with myocardial necrosis and centrolobular degeneration. There was a reduction in cytochrome oxidase activity in the glycogenolytic fibers, together with muscle atrophy, confirmed by the morphometric studies. Electron microscopy of the liver cells revealed dilated mitochondria, with destruction of the internal cristae [42]. Ten Nubian goats were given oral doses of the fresh fruits and leaves of Cassia senna at 1, 5, and 10 g/kg/day. Eight goats died within 30 days, and two others were slaughtered in a moribund condition on days 18 and 29 [43]. The rats that ate Senna occidentalis showed lethargy, weakness, recumbency, depression and emaciation. Two rats died during the experiment. Histopathological study showed fiber degenerations in the skeletal (Tibial, pectoral and diaphragm) and cardiac muscles. In the liver parenchyma, vacuolar degeneration was observed and, in the kidney, mild nephrosis in the proximal convoluted tubules. All these alterations occurred in a dose-dependent fashion. Moderate to severe degeneration and spongiosis in the central nervous system, especially in cerebellum. Electron microscopy revealed mitochondrial lesions in all analyzed tissues [44]. Extracts of S. obtusifolia in the study Doughri et al demonstrated a broad-spectrum of activity against both gram-positive and gram-negative bacteria and fungi [45]. Senna is also effective against helminths, leishmaniasis, and other parasites. A review of the literature shows that senna contains an ingredient with a non-selective toxic property that destroys any cells. A review article by Mnisi et al. showed that in experiments on mice, changes in internal organs were rarely detected after the use of Senna. Therefore, the authors concluded that "Toxicological assessments suggest relative safety at moderate doses." [46] This difference between some animals, including ruminants, and mice can be explained by the fact that in mice, as in humans, the toxic component generally does not penetrate the vascular system and therefore damages mainly the large intestine. In other animals, the poison is absorbed in the intestinal wall, penetrates the vascular bed, which leads to the destruction of internal organs.

Conclusion

1. Articles by pediatric surgeons (Bischoff, Levitt, Peña, Alzate-Ricaurte, Santos-Jasso, and their colleagues) who prescribe high doses of Senna, not recommended by pharmacists, do not contain scientific justification of diagnostic, therapeutic, or surgical methods. All references lack evidence, being either reviews or assumptions. The articles lack understanding of the pathological physiology of ARM and functional megacolon.

2. There is no logic in preferring posterior sagittal anorectoplasty for ARM with perineal fistula, which leads to severe constipation and fecal incontinence in patients, instead of the cutback procedure, which, by preserving the anal canal, prevents fecal incontinence, and mild constipation resolves over time.

3. An analysis of the article by Alzate-Ricaurte et al. showed that in most patients receiving high doses of Senna, the dose increase was due to spastic contractions of the rectum and anal canal, which interfered with defecation and necessitated a dose increase. The authors' interpretation is refuted by the facts they presented.

4. An analysis of articles claiming "Clinical studies support the long-term safety and effectiveness of Senna" revealed the exact opposite: patients suffered from cramping pain caused by damage to the neuromuscular regulation of the colon. This damage was proportional to the dose and duration of use. In some cases, irreversible loss of colon function was observed, consistent with irritable colon syndrome (not to be confused with irritable bowel syndrome). As a result of the loss of neuromuscular regulation, the colon responded to any increase in pressure with spasm instead of peristalsis, like congenital aganglionosis.

5. The authors claimed that "The cause of this condition (idiopathic constipation) is unknown," ignoring a long history of research and a well-developed theory. Instead of protracted efforts using various methods to empty the colon and reduce anal rigidity, they prescribed high doses of senna for 7 days, which were not recommended by the pharmacopoeia. As a result, 19% of patients ultimately underwent colonic resection to temporarily reduce their laxative dosage. Without studying the long-term results, they recommended this method while downplaying the complications. They dismissed the unbearable pain, which caused patients to refuse treatment, as mild spasms. Why did they choose this method over decades of experience using anal distension, conventional enemas, and laxatives recommended by the pharmacopoeia, which would have excluded surgical intervention?

6. The publication of these articles, which bear no relation to scientific research, is the result of the destruction of pediatric colorectal surgery, initiated by A. Peña with the support of his

co-authors. The scientifically unsubstantiated experiments on children, which he claimed were his experience, with supposedly good results, were never compared with other methods, and no long-term results were ever reported. The Krickenbeck classification, accepted by most of the shills, declared PSARP to be the ideal procedure. After its publication, all articles contradicting Pena's ideas were not published in children's magazines, as they did not correspond to Peña's experience. Thus, creating the impression of universal support and Peña's infallibility.

7. I call on the American pediatric surgical association to establish a commission to evaluate the legacy of Alberto Peña.

8. All parts of the Senna plant contain a toxic component that kills any cell upon contact. According to the FDA, using standard doses of senna-based laxatives dramatically increases adverse effects. Long-term use of high doses of Senna in children is dangerous to their health. This practice must be immediately discontinued and an independent panel of experts established to evaluate the results of this treatment.

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