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Effectiveness of the bowel management program in children with constipation secondary to anorectal malformation

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ABSTRACT

Introduction: in Mexico, approximately 1 000 children each year are born with anorectal malformation (ARM). Despite surgical correction, those children present fecal function problems (60-70% have difficult to manage constipation). A Bowel Management Program (BMP) was implemented, which consists of initial rectal disimpaction, followed by administration of a stimulant laxative (sennosides), with favorable results. The objective of this study was to describe the effectiveness of the BMP in children with constipation secondary to ARM.

Material and methods: A descriptive, retrospective, transverse study to answer the question: how effective is the BMP in children with constipation secondary to ARM? Efficacy was evaluated by means of a construct with three variables (daily fecal evacuations, absence of fecal staining, and simple abdominal x-ray without fecal residue in rectum and left colon after evacuation). All children with surgically corrected ARM and constipation from two national referral centers for children with the condition were included.

Results: of 151 children with ARM monitored in outpatient service, only 67.33% had constipation. Of this group, 88.1% showed good response to the BMP. The average dose of sennoside was 8.45 mg/kg, 95% CI: 5.94-11.12 mg/kg (199.5 mg total dose; 95% CI: 139.50-259.50 mg). Abdominal cramp was the primary adverse effect reported (5.8%).

Discussion: use of sennosides had a positive impact on our patients' quality of life by achieving colonic and rectal emptying and preventing daily fecal staining.

Key words. constipation, anorectal malformation, bowel management program, sennosides.

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In Mexico approximately 1,000 children a year are born with anorectal malformation (MAR), based on the number of births reported in 2012 by Instituto Nacional de Estadística y Geografía (INEGI) and considering a global incidence of ARM of 1 per 5,000 live neonates.[1] Posterior sagittal anorectoplasty (PSARP) is a surgical treatment, introduced in the 1980s,[2] which preserves the anorectal muscular complex. However, this advantage notwithstanding, children with ARM who undergo the procedure continue to experience fecal function problems (constipation in 66% and incontinence in 25% of cases). The severity of these problems is expressed in a clinical spectrum; in other words, there are patients with varying degrees of fecal incontinence or constipation. Unfortunately those patients do not receive adequate postoperative monitoring and their quality of life is poor.[3]

In a responsible and humane manner, in the 1990s, the pediatric surgery group at the Long Island Jewish Medical Center in New York began treating patients suffering from postoperative constipation or fecal incontinence with the aim of improving their quality of life and integrating them in society. The first reports using the concept Bowel Managment Program (BMP) for children with fecal incontinence date from 1998, with success rates between 88 and 93%;[4] greatly exceeding results with other forms of treatment. The evolution of the BMP, which we translate into Spanish as "*Programa de Rehabilitación Intestinal*" (BMP) and today has moved to the Cincinnati Children's Hospital, by 2012 has shown success above 95%.[4,5]

In Mexico, for cultural, economic, and service-related reasons specific to local labor practices, this program has been modified from a regimen of clinical and radiological evaluation with daily adjustments in treatment to one with weekly adjustments. For this reason, the purpose of this article is to report on the effectiveness of this BMP in the pediatric population receiving care in Mexican hospitals with constipation secondary to ARM.

MATERIAL AND METHODS

An observational, descriptive, retrospective, transverse study was conducted to evaluate the effectiveness of the Bowel Management Program in treating constipation secondary to ARM at two domestic referral centers: Hospital para el Niño Poblano and Instituto Nacional de Pediatría. Data were included without gender distinction, from children with constipation and history of anorectal malformation, who attended all their medical appointments and complied with their BMP. The effectiveness of treatment was evaluated by means of a construct with 3 variables: 1) daily fecal evacuations; 2) absence of fecal staining (clinically clean, without involuntary discharge of fecal matter). In children without toilet training fecal staining was understood as intermittent discharge of fecal matter reported by parents; and 3) simple abdominal x-ray without fecal residue in rectum and left colon after evacuating. The three variables were indispensable to consider treatment successful. In addition, the dose of sennoside administered daily and type of anorectal malformations were analyzed. The inclusion period was from February 2012 through February 2013.

The BMP is divided in three stages:

1. Integral diagnosis: identification of type of ARM, characteristics of sacrum (to rule out hypoplasias or aplasias that might cause fecal incontinence) and perineum of patients (neoanus located in the anorectal muscular complex).

2. Treatment: a) rectal fecal disimpaction of the distal colon performed daily with enemas until a clean simple abdominal x-ray is ob-

tained (without fecal residue in the rectum or left colon); b) start of laxative therapy with sennosides administered daily in a single dose; the dose is modified weekly at the interview with the patient (for evaluation of records of evacuations and reporting of fecal staining) and by evaluation with simple abdominal x-ray until the BMP is successful. The adverse effects imputed to laxative therapy were recorded. The patients' usual diet was not modified, and they were asked only to respect a regimen of three meals a day.

3. Monthly follow-up to avoid relapse is performed when a patient has shown clinical and radiological improvement, ensuring that the dose of sennoside is maintained and continues to have suitable effectiveness (a minimum follow-up time of 3 weeks was considered adequate).

RESULTS

One hundred and fifty-one patients with ARM with ages from 7 months to 19 years and 3 months were included; one patient was excluded from the analysis on finding, in the initial evaluation, a neoanus outside the anorectal muscular complex requiring additional posterior sagittal surgery.

Sixteen patients (10.66%) did not require drug therapy because they presented fecal continence with daily evacuations without fecal staining and abdominal x-rays without fecal residue in rectum or left colon; 33 patients (22%) had fecal incontinence and 101 (67.33%) presented constipation.

In the initial part of the BMP all the constipated patients received enemas for fecal disimpaction, which were administered rectally, daily in doses of 20 mL/kg (saline solution) given in a single application for 3 to 7 days. Then they started drug therapy with stimulant laxatives (sennosides).

Eighty-nine of the 101 patients (88.1%) included in the BMP showed effectiveness (daily fecal evacuations without fecal staining or accidents and post-evacuation simple abdominal x-rays without fecal residue) at the end of an average 3 weeks' follow-up. Twelve of the 101 patients (11.9%) included in the BMP did not show favorable clinical or radiological response, with persistent fecal residue in the rectum or left colon in post-evacuation simple abdominal x-rays, as well as fecal staining (Table 1). We found no statistically significant difference in relation to the effectiveness of treatment between the different types of anorectal malformation (χ^2 $p = 0.12$).

The average daily dose of sennoside with which success was achieved in treatment was 8.45 mg/kg of body weight, 95% CI: 5.94-11.12 mg/kg (199.5 mg total dose; 95% CI: 139.50-259.50 mg). The minimum total dose required was 4 mg in a patient age 11 months (0.31 mg/kg) and the maximum daily dose administered was 1,309 mg in a patient age 11 years (59.05 mg/kg). To analyze any possible difference in the dose of sennoside administered by type of ARM, we performed a non-parametric Kruskal-Wallis test (given that the dose of sennoside administered did not show a normal distribution) and we found no statistically significant differences between the different groups (classified by type of ARM) (Table 2). Finally, we analyzed whether the dose was different for each age group and found that there was a statistically significant difference between them ($p = 0.042$) (Table 3).

The adverse effect reported by patients was abdominal cramp (5.8%), which was alleviated with paracetamol at the customary dose (10 mg/kg). Administration of sennoside was not changed until abdominal pain disappeared (which occurred in all cases in under one week) and if a patient required a ponderal increase in dosage, it was increased without complications.

Table 1. Distribution of patients by type of anorectal malformation and response to the program (sennosides) (n = 101)

Type of anorectal malformation		Effectiveness		Total
		no	Yes	
With rectoperineal fistula		6	41	47
	% of the total	5.9%	40.6%	46.5%
With rectovestibular fistula		2	18	20
	% of the total	2.0%	17.8%	19.8%
Without fistula		1	7	8
	% of the total	1.0%	6.9%	7.9%
With rectourethral bulbar fistula		0	11	11
	% of the total	.0%	10.9%	10.9%
With rectourethral prostatic fistula		0	4	4
	% of the total	.0%	4.0%	4.0%
Cloaca		0	3	3
	% of the total	.0%	3.0%	3.0%
Unknown		2	4	6
	% of the total	2.0%	4.0%	5.9%
With rectovesical fistula		0	1	1
	% of the total	.0%	1.0%	1.0%
Rectal atresia		1	0	1
		1.0%	.0%	1.0%
Total	Count	12	89	101
	% of the total	11.9%	88.1%	100.0%

χ^2 not significant (p = 0.12) for effectiveness of response to sennosides.

Table 2. Dose of sennoside between different types of anorectal malformation

	Type of malformation	N	Average
mg of sennoside	perineal	47	50.38
	vestibular	20	56.43
	w/o fistula	8	65.00
	urethral bulbar	11	34.05
	urethral prostatic	4	58.38
	cloaca	3	36.00
	unknown	6	59.17
	vesical	1	30.00
	rectal atresia	1	33.50
	Total	101	

Kruskal-Wallis test without statistically significant differences (p = 0.378)

Table 3. Dose of sennoside by age group

Age	N	mg of sennosides/day (average)
0 months - 1 year	3	35.00
1 - 2 years	14	38.39
2 - 3 years	13	39.77
3 - 4 years	10	49.70
4 - 5 years	8	42.69
5 - 6 years	8	50.94
6 - 7 years	5	56.00
7 - 8 years	6	31.83
8 - 9 years	5	66.80
9 - 10 years	6	69.33
> 10 years	23	66.28
Total	101	

Kruskal-Wallis test (p = 0.042).

DISCUSSION

Surgical treatment of children with ARM requires exhaustive knowledge of the anatomic and physiological details of the pelvic structures to obtain good functional outcomes in the area of fecal continence.

Constipation is the most relevant sequela in patients with ARM (64.5% of our population in follow-up vs. 61% reported in the literature).[6] It must be recognized early and treated aggressively to prevent fecal retention from causing a sigmoid megacolon because it promotes a vicious cycle of greater dilation with diminished colonic-rectal mobility and exacerbation of constipation.[1] Highly prolonged constipation can lead to fecal impaction, overflow evacuations (fecal pseudoincontinence), fecal staining, and the resulting psychological and social repercussions.

Constipation in patients with ARM is multicausal; damage to the extramural innervation of the rectum (pelvic splanchnic nerves and parasym-

pathetic innervation due to atypical anatomical development) when performing posterior sagittal anorectoplasty may be one of the pathological mechanisms; however, other factors are known such as hypoplasia of the development of the levator ani muscle (striated), reduced anorectal barrier pressure due to diminished density of the external anal sphincter and reduced rectal sensitivity to distinguish solids from liquids and gases. Nevertheless, the main factor to consider in this group of patients is, perhaps, rectal dilation with the resulting slow propulsion waves, significantly prolonged colonic transit with diminished propagating contractions, due probably to alterations in the nerve plexus of the intestinal wall (hypoganglionosis, neuronal dysplasia, desmosis, and deficiency of Cajal cells evidenced by reduced intensity of reaction to monoclonal antibodies in smooth muscle, mainly in layers of circular muscle in cases of hypertrophy; markedly diminished immune reaction to neuron-specific enolase, vasoactive intestinal peptide, and nuclear protein SP-100).[7]

In our clinical practice the use of osmotic laxatives (polyethylene glycol and lactulose) permits colonic emptying and prevents fecal impaction; however, they did not have a meaningful impact on these patients' quality of life due to their failure to prevent frequent fecal staining, compromising their fecal continence. At the colon and rectum clinics pf Centro Colorrectal para los Niños de México y Latinoamerica and Instituto Nacional de Pediatría (over the last 30 and 18 months, respectively) use of sennosides in treating constipation secondary to ARM has improved our patients' quality of life, with practically no adverse effects.

In clinical practice there are no studies that evaluate the use of stimulant laxatives (specifically sennosides) in this particular group of patients. Knowing the pathophysiology of constipation, we think they stimulate colonic and rectal movements which trigger fecal emptying without compromising the mechanism of continence because they do not alter the consistency of evacuations, and consequently improve patients' quality of life.

Stimulant laxatives increase intestinal motility with reduction of intestinal transit. This group includes anthraquinones and diphenylmethane derivatives.[8] This group includes the sennosides, picosulfate sodium, and bisacodyl. There are articles that report their innocuousness and efficacy; however, the evidence of their effectiveness is insusficient.[9]

The sennosides are derivatives of the anthraquinones. The sennosides and cascara sagrada (*rhamnus purshiana*) are the most accessible sources of anthraquinone laxative. Sennoside is obtained from the dried flakes or pods of *Cassia acutifolia* or *Cassia augustifolia*, and are, in essence, prodrugs. Following oral administration they are absorbed poorly by the small intestine. In the colon they produce, by bacterial action, elimination of sugar (D-glucose or L-rhamnose) and reduction to antrol, releasing the active forms which are absorbed in moderate degree; the absorbed material can be excreted in bile, saliva, breast milk, and urine. They stimulate colonic motility. Their active metabolite (aglycone) acts as a local irritant on the colon and stimulates Auerbach's plexus to produce peristalsis. The onset of action occurs between 6 and 24 hours following oral administration. They can cause melanosis coli (melanotic pigmentation) of the mucosa of the colon, which is benign and usually reverts between 4 and 12 months after discontinuing the medication.[8]

The effectiveness of the Bowel Management Program (BMP) for children with sequelae (fecal incontinence and constipation) of ARM, at the first global colorectal center: the Cincinnati Children's Hospital Medical Center (CCHMC) is 95%.[5]

We, evaluating exclusively the group of patients with secondary constipation and modifying evaluation from a daily to a weekly regimen, achieved 88.1% effectiveness; this has been possible due to systematization of the program, use of sennosides (stimulant laxatives), and the dedication of our personnel, but above all to the multidisciplinary efforts and improved physiopathological understanding of constipation in this particular group of patients with ARM. The pediatric population with this condition has benefited directly, with improved quality of life.

Finally, we do not consider recommending a ponderal dose, or a daily dose of sennosides for treating constipation in children with ARM, given that in age group analysis the values did not show a normal distribution. There were cases with significant extreme values in each group possibly because of the varying severity of constipation due to type of anorectal malformation, age at the time of surgical correction, presence of megarectum, etc., but we can affirm that effectiveness was observed in treating constipation in children with anorectal malformation using sennosides, that the ponderal dose was different in each of the patients, and that it must be modified in follow-up medical consultations based on the patient's response.

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