EUROMEDITERRANEAN BIOMEDICAL JOURNAL
2022,17 (20) 89-94
(*FORMERLY: CAPSULA EBURNEA*)

Original article

OBSTRUCTED DEFECATION SYNDROME AND CHRONIC CONSTIPATION: CLINICAL AND SURGICAL ANALYSIS AND PSYCHOLOGICAL IMPLICATIONS

*Giovanni Tomasello [1 **], Dario Saguto [1 **], Salvatore Accomando ** 9, Benedetto Di Trapani [2,3], Carola Maria Gagliardo [4 **], Gessica Marceca [3 **], Marta Zanghì [6], Carlo Bargiggia [3,7], Simone Tomasini [3,7], Bernardo Molinelli [3,7], Antonio Ciulla [7], Claudio Missaglia [3,8], William Ra [1], Margherita Mazzola [1 **], Guido Zanghì [6], Francesco Carini [1 **]*

[**] *These authors contributed equally*

1. Institute of Human Anatomy and Histology, Department of Biomedicine, Neurosciences and Advanced Diagnostics, (BIND), University of Palermo, Italy.
2. Surgeon Chef, Unit of General Surgery, Casa di Cura Torina, Palermo, Italy.
3. AIDOP (Associazione Italiana Organi Pelvici), Italy.
4. Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties.
5. Clinical psychologist, Casa di Cura Torina, Palermo, Italy
6. Department of General Surgery and Medical Surgical Specialities, Policlinico V. Emanuele Hospital, University of Catania, Italy.
7. Unit of General Surgery, Casa di Cura Torina, Palermo, Italy.
8. Surgeon Chef, Unit of Coloproctology and Pelvic Floor, Casa di Cura Eretania, Vicenza.
9. Pediatrics Operative Unit, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (PROMISE), School of Medicine, University of Palermo.

ARTICLE INFO

Article history:
Received 20 Apr 2022
Accepted 27 Jun 2022
Published 19 Aug 2022

Keywords:
Chronic constipation, Obstructed Defecation Syndrome (ODS), STARR surgery, physical health, mental health.

ABSTRACT

Chronic constipation and Obstructed Defecation Syndrome (ODS) represent a high-incidence pathological status that severely compromise of Quality of Life (QoL). Our multidisciplinary study is aimed to investigate how the resolution of ODS by surgical technique can improve long-term clinical symptoms and the state of physical and mental health and QoL, focusing on the dual interaction between psyche and intestine Chronic constipation and Obstructed Defecation Syndrome (ODS) represent a high-incidence pathological status that severely compromise of Quality of Life (QoL). Our multidisciplinary study is aimed to investigate how the resolution of ODS by surgical technique can improve long-term clinical symptoms and the state of physical and mental health and QoL, focusing on the dual interaction between psyche and intestine. **S**tudy conducted on 50 patients of average age 56 years (range 22 -72), diagnosed with ODS and operated with STARR (Stapled Trans anal Rectal Resection) technique for rectal and hemorrhoidal prolapse at the Nursing home "Torina" of Palermo from 2018 since 2019. Before and after surgery, patients underwent psychological counseling, during which a questionnaire (Short form health survey SF-12) on their physical and mental health status and one for the Score of ODS symptomatology evaluation were administered. In ODS STARR surgical technique allows to improve clinical symptoms of patients, their physical and mental health and QoL. In these patients is essential a multidisciplinary study that investigates the dual interaction between psyche and intestine and how this affects patients' lives.

* *Corresponding author*: Dario Saguto, *dariosaguto@gmail.com*
DOI: 10.3269/1970-5492.2022.17.20
 ISSN: 2279-7165 - Available on-line at www.embj.org

EMBJ.ORG FOR YOUNG DOCTORS

EUROMEDITERRANEAN BIOMEDICAL JOURNAL
2022,17 (20) 89-94
(*FORMERLY: CAPSULA EBURNEA*)

1. Introduction

Constipation is a syndrome with high incidence in the world population, with prevalence in the female gender, that severely compromise of Quality of Life (QoL). It is classified in acute or chronic depending on whether the duration is less or more than three months respectively [1].

Obstructed defecation syndrome (ODS) is one of the most common causes of chronic constipation. It involves the recto-anal canal and is also classified into organic or functional depending on the cause.

In childhood, under two years of age, organic causes of constipation, due to aganglionosis such as Hirschsprung disease, Cystic Fibrosis or congenital malformations of the gut, like duplications, malrotations, and also imperforate anus, are prevalent.

While after the age of two, functional causes are more common like in adulthood. Among the most common functional causes is the pelvic floor dyssynergy, while organic causes include all diseases of the recto-anal canal that can mechanically impede the transit of feces, including, for example, neoplastic diseases, mucous prolapses, hemorrhoids, etc. (ref. 2).

The obstruction or narrowing of the lumen of the anorectal canal prevents the transit of feces and consequently their expulsion, making the subject constipated until the obstacle is removed. It is characterized by the feeling of an obstacle to evacuation with incomplete emptying, tenesmus, intended as grieving pain of the anal sphincter accompanied by a continuous stimulus to evacuate, prolonged evacuation effort and the need to resort to manual maneuvers.

These symptoms should be present in at least 25% of evacuations, for a period of not less than three months, in combination with a frequency of less than three times a week [3].

The therapeutic treatment of ODS coincides with that of chronic constipation. A radical approach to the resolution of the ODS from organic cause is represented by surgery: colon-rectal resection in neoplastic pathologies while STARR (Stapled Trans-anal Rectal Resection) technique in rectal prolapse and rectocele. The STARR technique aims to restore the anatomical and physiological continuity of the most distal tract of the gastrointestinal tract [4].

Given the succession of numerous studies in the literature concerning the interaction between the psyche and enteric nervous system[5], and how this may represent an etiology and / or concomitant cause and / or worsening of constipation, this study proposes a multidisciplinary approach dedicated to patients with ODS.

2. Methods

Our retrospective study was conducted on a sample of 50 patients aged 22 to 72 years (22 males (44%) with an average age of 53 years and 28 females (56%)) with an overall average age of 55 years (SD $\pm$ 10.4) operated at the "Nursing home Torina" of Palermo, with the collaboration of AIDOP ONLUS, from 2018 to 2019. Patients presented diagnoses of ODS due to internal rectal prolapse, rectocele and hemorrhoidal rectal prolapse. These patients underwent STARR surgery and put in follow-up. Before the surgery and 4 weeks after surgery the patients underwent psychological counseling: in order to detect the health status (self-reported) of subjects with ODS diagnosis, a standardized and validated questionnaire SF-12 (Short form health survey SF-12) was administered, as shorter form than the more extensive SF-36 (Short form health survey SF-36). The SF-12 questionnaire allows to describe the health of a group of people through two synthetic indices calculated on 12 items. The index called Physical Component Summary (PCS), concerns the physical state, while the Mental Component Summary (MCS) measures the mental state. The dimensions of the SF-12 are: physical activity [PF], role and physical health [RP], role and emotional status [RE], mental health [MH], physical pain [BP], general health [GH], vitality [VT] and social activities [SF] [6].

The data were, subsequently, processed through the statistical software Minitab (v.19) through the use of the statistical test *"Paired T-test"* ($\mu_{post} - \mu_{pre} \neq 0$) to evaluate the differences between PCS-12 and MCS-12 pre- and post- surgery. The statistical test "One Sample T-test" was used to evaluate the differences between post-operative PCS-12 and MCS-12 from the PCS-12 and MCS-12 indices provided by the ISTAT database of 2017 with reference to the health status of the Italian population [7].

For the evaluation of the ODS symptomatology, and therefore the clinical evaluation of how the symptomatology had or had not changed as a result of the intervention, the Score for the evaluation of ODS was used. This 6 items-questionnaire was administered in two different phases: first phase, during visits prior to the planning of the intervention; second phase, after the surgery (follow-up) at 4 weeks. For the analysis, answers to the questions administered in the second questionnaire have been transformed into dichotomous variables the results of the questionnaire; the McNemar *Chi-squared test* was used to test the difference between the dichotomous answers of the pre-operative and post-operative questionnaire.

3. Results

The sum of the scores obtained from the items of the SF-12 questionnaire administered allows to build the physical health index PCS-12 and the mental health index MCS-12 before and after the surgery (results in Table 1).

* *Corresponding author*: Dario Saguto, *dariosaguto@gmail.com*
DOI: 10.3269/1970-5492.2022.17.20
 ISSN: 2279-7165 - Available on-line at www.embj.org

Group	Indexes	μ_{pre}	μ_{post}	p-value
Overall	**PCS-12**	37.7 (SD ± 11.2)	50.9 (SD ± 8.0)	<0.001
	MCS-12	37.7 (SD ± 14.3)	47.1(SD ± 14.1)	<0.001
Females	PCS-12	34.1 (SD ± 10.7)	49.3(SD ± 9.1)	<0.001
	MCS-12	34.6 (SD ± 13.2)	47.1(SD ± 14.7)	=0.001
Males	PCS-12	42.2 (SD ± 10.4)	53.0(SD ± 5.8)	<0.001
	MCS-12	41.5 (SD ± 15.1)	47.0(SD ± 13.8)	=0.062

Table 1. Physical health index PCS-12 and mental health index MCS-12 pre- and post- surgery.

From the "Paired T-test" with Null Hypothesis $\rightarrow H_0: \mu_{post} - \mu_{pre} = 0$ and Alternative Hypothesis $H_1: \mu_{post} - \mu_{pre} \neq 0$, the comparison of the overall indexes (male + female) PCS-12 and MCS-12 before and after the surgery shows a statistically significant difference (P<0.001) of both the physical and mental health.

By evaluating these indices separately for both sexes, the results of these tests show that both values of PCS-12 (P<0.001) and MCS-12 (P=0.001), in females are higher than before surgery with statistically significant results. In males alone, the post-operative PCS-12 index is statistically different than the pre-operative PCS-12 index (P<0.001), while the post-operative MCS-12 index is not significantly changed compared to the pre-operative MCS-12 index (P=0.062).

According to the latest ISTAT data updated to 2017, the national physical status index PCS-12 is equal to 51.2, while the mental status index MCS-12 is equal to 49.1 In our study, the post-operative indices correspond to 50.9 for PCS-12 and 47.1 for MCS-12. The "One-Sample T-test" $[H_0: \mu_{ISTAT} = \mu_{post}]$ was performed to verify the difference between our results and those in the ISTAT database (results in Table 2).

Indexes	μ_{ISTAT}	μ_{Post}	P-value
PCS-12	51.2	50.9	0.792
MCS-12	49.1	47.1	0.317

Table 2. Physical health index PCS-12 and mental health index MCS-12 of the Italian population, according to ISTAT data updated to 2017, and of post-operative patients.

Since both tests were not statistically significant, we can conclude that after the intervention there is no significant difference between the averages found in our study and the averages in the ISTAT database, so there is an adjustment after the intervention of the general state of health to the Italian national average.

From the questionnaire about the pre- and post-operative clinical evaluation of the ODS, it emerges that there is almost a statistically significant reduction in the use of laxatives (P=0.059), while there is a significant reduction in the use of enemas in post-operative (P=0.025). There is also a reduction in abdominal pain (P=0.001), tenesmus (P=0.001), incomplete sense of evacuation (P=0.002) and the recourse to manual maneuvers to promote evacuation (P=0.013), while from a statistical point of view, the evacuate effort is not significantly reduced (P=0.068).

The following table summarizes the results of McNemar's χ^2 tests conducted to assess significant differences between preoperative and postoperative questionnaire responses at 4 weeks after surgery (results in **Table 3**).

Questions	Pre-Op:		Post- Op:		p-value
	Yes	No	Yes	No	
Q1 – Use of laxatives	22	28	13	37	**0.059**
Q2 – Use of enemas	9	41	2	48	**0.025**
Q3 – Evacuate effort	41	9	33	17	0.068
Q4 – Incomplete sense of evacuation	27	23	37	13	**0.002**
Q5 – Abdominal pain / anorectal weight	40	10	16	34	**0.001**
Q6 – Anorectal Tenesmus	38	12	20	30	**0.001**
Q7 – Manual maneuvers to facilitate evacuation	19	31	8	42	**0.013**

Table 3. Pre- and post-operative results to questions about the clinical symptomatology of the ODS.

4. Discussion

Constipation is a syndrome characterized by the presence of symptoms attributable to disorders of the bowel. It represents a syndrome with high incidence in the world population and is classified as acute or chronic depending on whether the duration is less or more than three months respectively. Chronic constipation is further divided into functional or organic depending on whether an underlying cause is recognized or not. In cases of functional or idiopathic constipation (SF), according to the criteria of Rome III[(Ref. 8)] it is necessary to find the presence of at least two of the following symptoms:

- Frequency of the bowel less than three evacuations per week
- Evacuation effort in at least 25% of evacuations
- Hard or goat feces in at least 25% of evacuations
- Feeling of incomplete evacuation in at least 25% of evacuations
- Manual maneuvers facilitating emptying in at least 25% of evacuations.

Obstructed defecation syndrome (ODS) is one of the most common causes of chronic constipation. It involves the anorectal canal and is characterized by an obstruction or narrowing of the lumen of the anorectal canal such as to prevent the transit of feces and consequently expulsion making the subject constipated until the obstacle is removed. The ODS causes an abnormal defecation, characterized by a feeling of obstacle to evacuation with incomplete emptying, prolonged and excessive evacuation effort and the need to resort to manual maneuvers [1]. These symptoms should be present in at least 25% of evacuations, for a period of not less than three months, in combination with a frequency of less than three times a week. This can be caused by both functional and organic causes. Among the most common functional causes, there is the dyssynergy of the pelvic floor, while organic causes include all the diseases that occur in the anal canal and rectum that can hinder the transit of feces, interfering mechanically with the defecatory act, among which there is a strong representation of rectal prolapse but also carcinomas, rectocele, hemorrhoidal prolapse, etc. [(Ref.2)].

Internal rectal prolapse is one of the most frequent causes of ODS. In a study of 56 women with documented ODS in association with internal rectal prolapse, an increase in MMP-1 (Matrix metalloproteinase-1) and a decrease in TIMP-1 (TIMP metallopeptidase inhibitor-1) in the rectal submucosa was found, which could provide a hypothesis of clinical approach to the prevention of internal rectal prolapse and consequently of obstructed defecation. However, the scientific community has not yet fully investigated this aspect [9-10].

Another study carried out on 262 female patients divided into two groups, the first with fecal incontinence and the second with fecal incontinence in association with chronic constipation, showed in the incontinence-constipation group the significant presence of high Body Mass Index (BMI) and hypotonic sphincter suggesting a correlation between the increase in general adiposity and chronic constipation, once again emphasizing the importance of body composition in the development of diseases of the gastrointestinal tract [11].

The therapeutic treatment of ODS coincides with that of chronic constipation. In the first instance, it is important to correct eating habits by encouraging the intake of fiber and liquids; in cases of insufficient response, it is necessary to use laxatives (Polyethylene glycol)(Ref. 12) and probiotics to promote the regulation of the gut microbiota [13-15], not only in adults but also in pediatric patients [16]. Finally, a radical approach to the resolution of ODS from organic cause is represented by surgery [4]. Both in functional and organic form of ODS, another therapeutical option consists of pelvic floor rehabilitation (PFR). It can be adopted alone in functional cases and before and/or after surgery in the organic forms. PFR help to rehabilitee dysfunctional pelvic floor with a program of functional retraining to improve muscle strength and relaxation. In our patient we have suggested PFR after surgery. However, in this study we only focused on the clinical outcomes after performing the STARR surgical technique; we did not take into account the variable of pelvic floor rehabilitation as not all patients underwent it [17].

To date, due to the lack of specific studies on the argument, according to our knowledge there is still no integrated treatment that takes into account the psycho-enteric nervous system and ODS interaction.

The enteric nervous system (ENS), in fact, interacts with the central nervous system (CNS), in a bidirectional way [18]. Like the CNS, ENS is responsible for the production of serotonin (5-HT), a neurotransmitter known as the “good mood” molecule, also involved in other important intestinal functions, such as the regulation of peristalsis. The external stimuli received by the brain can generate an action of excessive stimulus to the production of serotonin or on the contrary block its action, evolving in this way in two possible outcomes: diarrhea (caused by an accelerated transit in the colon) or constipation (caused by a slowed transit in the colon) (Ref. 5). The ENS receives commands from the brain, but it is also able to send them (such as, for example, the sense of nausea and satiety), affecting the psychophysical well-being: this has allowed Gherson to define it "second brain" (Ref. 19). To this day, talking about defecation is still taboo. The psychoanalyst Sigmund Freud, in his theory on psychosexual development, pointed out how the child from the earliest years of life feels pleasure from the expulsion of feces and uses the control of the anal sphincters to express drives and/or conflicts [20]. A natural and pleasant act such as defecation can become difficult, painful or impossible for patients with ODS.

A further study highlights how psychological stress contributes to increased muscle tension in the pelvic floor - pelvic floor dyssynergy is implicated in ODS- and how stress-related psychological disorders can arise as a result of gastrointestinal disorders[5]. A study conducted on a sample of patients with colorectal disease shows that 66% of patients with obstructed defecation suffer from anxiety and/or depression, suggesting, therefore, a multidisciplinary approach for the study of these patients[21-22].

Therefore, thanks to questionnaires administered before and after the intervention of STARR, to which our 50 patients were subjected, we wanted to adopt a multidisciplinary approach to the patient, evaluating clinical outcomes not only from a medical-surgical point of view, but also psychological. In this case, thanks to the SF-12 questionnaire, we evaluated the physical and mental health status of the patients before and after the intervention, the symptoms of the ODS, and how the psychological aspect could influence it.

The comparison of the overall indexes PCS-12 and MCS-12 before and after the surgery shows a statistically significant improvement of both the physical and mental health (Tab.1), with improvement especially in being able to carry out regular physical and daily activities and in work.

Most of the interviewees said that the emotional state with depressed or anxious mood would have caused just a worse performance at work. On the contrary in the last 4 weeks most of the patients stated that they had been in a calm and serene mood and with more energy, without their state of health had negatively affected personal relationships, unlike pre-operative. This, in fact, underlines how the ODS determines a serious involvement of the psychic state and how this in turn has negatively influenced the normal activities in the patient's life. What said above is also confirmed by ISTAT data about Italian status of general health, from which we noticed an adjustment of the general state of health in our patients after the intervention to the Italian national average.

However, by evaluating these indices separately for both sexes, the results of these tests show that both values of PCS-12 and MCS-12, in females are higher than before surgery, with statistically significant results. In males alone, instead, the post-operative PCS-12 index is statistically higher than the pre-operative PCS-12 index, but the post-operative MCS-12 index is not significantly changed. We have interpreted this finding on women as a greater influence of the psychological component on their health status and at the same time as a greater variability of the psychological component too, in this case positively on QoL after surgery. Effectively, a female preponderance in depression is universal and substantial. The expression of both depression and anxiety reflects the impact of gonadal steroid changes in women [23]. On the contrary, in men a less variability of the psychological component.

From the questionnaire about the pre- and post-operative clinical evaluation of the ODS, it emerges that there is a slightly statistically significant reduction in the use of laxatives, while there is a very significant reduction in the use of enemas in post-operative. There is also a reduction in abdominal pain, tenesmus and the recourse to manual maneuvers to promote evacuation, incomplete sense of evacuation and the recourse to manual maneuvers to promote evacuation, while from a statistical point of view, the evacuate effort is not significantly reduced (Table 3).

Therefore, the following results highlight how surgery has improved from a clinical point of view the overall health status of patients affected by ODS, understood as both physical and mental, and therefore also QoL. From what we discussed previously, about the mutual interaction between psyche and intestine, we think that it is the surgical act that determines a positive change in the clinical symptomatology and psyche and that vice versa a psyche with a serene mood can in turn determine a reduced perception of the symptomatology over time.

Therefore, with reference to the purpose of our study, these results suggest us how the study of "complex" patients through a multidisciplinary approach can not only allow us to take care of them at 360 degree, but also to highlight all the different facets that affect and determine their state of health, and can further deepen the psychopathological dynamics to the scientific community.

5. Conclusions

Numerous physio-pathological mechanisms insist in constipation and ODS. In its organic forms, several studies confirm the importance of the surgical approach, especially the safety of the STARR technique, where possible, in cases of rectocele and rectal and hemorrhoidal prolapses.

With surgery we have obtained a significant reduction of the use of laxatives and enemas post-operatively, decreased abdominal pain, tenesmus and recourse to manual maneuvers to promote the evacuation.

The improvement of the clinical condition leads to an overall improvement in the health status of the patients, as both physical and mental, especially in being able to perform regular physical activities and work. This clearly improves the QoL of the patients, whose mood goes from a state of pre-operative depression to calm and serene in post-operative. The improvement of the psyche in turn improves and reduces the perception of clinical symptoms in post-operative and makes us assume that it participates in the continuation of these benefits over time. The integration of the psychological approach therefore allows us to obtain an integrated vision of the patient and therefore of the treatment in its entirety. Finally, it allows us to study the dual interaction between psyche and intestine. However, in order to better deepen this aspect, further prospective studies are needed.

References

1. Gallegos-Orozco JF, Foxx-Orenstein AE, Sterler SM, Stoa JM. Chronic constipation in the elderly. Am J Gastroenterol 2012; 107(1):18-25
2. Cavallaro PM, Staller K, Savitt LR, Milch H, Kennedy K, Weinstein MM, Ricciardi R, Bordeianou LG. The Contributions of Internal Intussusception, Irritable Bowel Syndrome, and Pelvic Floor Dyssynergia to Obstructed Defecation Syndrome. Dis Colon Rectum 2019; 62(1):56-62.
3. Bove A, D'Addetta V, Palone G, Paniccia T, Chiarini S, Lapergola A, Bongarzoni G. Symptoms of obstructive defecation syndrome: functional outcome after stapled haemorrhoidectomy. Ann Ital Chir 2016; (87):161-5.
4. Zehler O, Vashist YK, Bogoevski D, Bockhorn M, Yekebas EF, Izbicki JR, Kutup A. Quo vadis STARR? A prospective long-term follow-up of stapled transanal rectal resection for obstructed defecation syndrome. J Gastrointest Surg 2010; 14(9):1349-54.
5. Kiecolt-Glaser JK, Glaser R. Psychoneuroimmunology: can psychological interventions modulate immunity? J Consult Clin Psychol 1992; 60(4):569-75.
6. Apolone G, Mosconi P. The Italian SF-36 Health Survey: translation, validation and norming. J Clin Epidemiol 1998; 51(11):1025-36.
7. Istat. PCS-12 and MCS-12 indices in Healthy Population Available from: https://www.istat.it/it/archivio/207259 (Last Accessed 18/08/2022)
8. Russo M, Strisciuglio C, Scarpato E, Bruzzese D, Casertano M, Staiano A. Functional Chronic Constipation: Rome III Criteria Versus Rome IV Criteria. J Neurogastroenterol Motil 2019; 25(1):123-128.
9. Cao LL, Yu J, Yang ZL, Qiao X, Ye H, Xi CL, Zhou QC, Hu CC, Zhao CJ, Gong ZL. MMP-1/TIMP-1 expressions in rectal submucosa of females with obstructed defecation syndrome associated with internal rectal prolapse. Histol Histopathol 2019; 34(3):265-274.
10. Carter D, Bardan E, Maradey-Romero C. Clinical and physiological risk factors for fecal incontinence in chronically constipated women. Tech Coloproctol 2019; 23(5):429-434.
11. Giarratano G, Toscana C, Toscana E, Shalaby M, Sileri P. Stapled transanal rectal resection for the treatment of rectocele associated with obstructed defecation syndrome: a large series of 262 consecutive patients. Tech Coloproctol 2019; 23(3):231-237.
12. Mínguez M, López Higueras A, Júdez J. Rev Esp Enferm Dig. Use of polyethylene glycol in functional constipation and fecal impaction 2016; 108(12):790-806.
13. Russo M, Giugliano FP, Quitadamo P, Mancusi V, Miele E, Staiano A. Efficacy of a mixture of probiotic agents as complementary therapy for chronic functional constipation in childhood. Ital J Pediatr 2017; 43(1):24.
14. Messina M, Mazzola M, Carini F, Damiani P, Scardina AS, Tulone L, Milazzo V, Crapanzano F, Gagliardo C, Damiani P, Tomasello G. Oral microbiota: Characteristics, related pathologies, and future prospects. Int J Clin Dent 2020; 13(2): 73-179
15. Tomasello G, Sorce A, Damiani P, Sinagra E, Carini F. The importance of intestinal microbial flora (microbiota) and role of diet. Prog Nutr 2017; 19(3): 342-344
16. Koppen IJN, Broekaert IJ, Wilschanski M, Papadopoulou A, Ribes-Koninckx C, Thapar N et al. Role of Polyethylene Glycol in the Treatment of Functional Constipation in Children. J Pediatr Gastroenterol Nutr 2017; 65(4):361-363.
17. Wallace SL, Miller LD, Mishra K. Pelvic floor physical therapy in the treatment of pelvic floor dysfunction in women. Curr Opin Obstet Gynecol 2019; 31(6):485-493.
18. Mawe GM, Hoffman JM. Serotonin Signaling in the Gastrointestinal Tract: Functions, dysfunctions, and therapeutic targets, Nat Rev Gastroenterol Hepatol 2013; 10(8): 473–486.
19. Gherson MD. Il secondo cervello: gli straordinari poteri dell'intestino. UTET; 2017.

20. Lis A, Stella S. Manuale di psicologia dinamica. Il Mulino; 1999.
21. Pescatori M. Olistic approach to chronic constipation. Acta Chir Iugosl 2006; 53(2): 67-69.
22. Bouchoucha M, Mary F, Bon C, Bejou B, Airinei G, Benamouzig R. Sleep quality and functional gastrointestinal disorders. A psychological issue. J Dig Dis 2018; 19(2): 84-92.
23. Parker G, Brotchie H. Gender differences in depression. Int Rev Psychiatry 2010; 22(5):429-36.