

Conservative and Novel Treatment Options for Fecal Incontinence

Dan Carter*

Department of Gastroenterology, Chaim Sheba Medical Center, Ramat Gan, Israel

*Corresponding author: Dan Carter MD, FEBGH. Department of Gastroenterology, Chaim Sheba Medical Center, Ramat Gan, Israel, Tel: 97235302197; Fax: 9723530 3160; E-mail: dr.dancarter@gmail.com

Rec date: Mar 14, 2015; Acc date: May 16, 2016; Pub date: May 21, 2016

Copyright: © 2016 Carter D. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Fecal incontinence (FI) in adults is a troublesome condition that effects substantial portion of the population and represent a major social and economic burden. The first line of treatment involves conservative therapy and physical treatments. When these measures fail, other interventions are warranted. In the last few years, new emerging techniques for the treatment of FI have become available, including sacral neuromodulation, posterior tibial stimulation, acupuncture, internal anal sphincter augmentation, temperature controlled radiofrequency anal energy delivery and stem cell transplantation. This paper discusses the conservative and novel treatment options for FI.

Keywords: Fecal incontinence; Physical therapy; Sacral neurostimulation; Tibial stimulation; Bulking agents; Secca procedure

Introduction

Fecal incontinence [FI] is a chronic and disabling disorder defined as involuntary loss of solid or liquid feces due to the loss of the ability to confine the passage of fecal material through the anal. FI is often associated with social stigmata and a major negative impact upon the quality of life, psychological stress to the patient and his family, frequent loss of working days, frequent infectious and medical complications [1]. The reported prevalence of FI varies in different population based reports. Most studies published in the last 20 years report a prevalence of 2.2-7% in the general population [2,3]. More recently published study reported even higher prevalence rates of 8.3% in non-institutionalized adults [4]. FI is more common in the elderly (6-19%) [5,6]. Up to 50% of nursing homes residents suffer from FI [7,8], although the overall incidence of FI is thought to be underestimated in this group due to the association with fecal impaction and disimpaction episodes and significant neurological disorders leading to Institutilization. Underreporting of FI is common, mainly due to shame and embarrassment. Only 27% of women reporting FI had discussed the problem with their primary physician, and only 10% had received treatment for the problem [9]. Similarly, only 16% of women who reported post- partum FI looked for medical help during the episode of up to 2 years after delivery if there are persistent continence issues [10]. Increased mortality was reported to be associated with FI [11,12]. However, it is unclear whether increased mortality results from the FI, or from chronic illnesses associated with FI.

The etiology of FI is multifactorial and diverse. Table 1 summarizes the common etiologies leading to FI. In community surveys, diarrhea and other bowel symptoms as well as the burden of chronic illness are the most important risk factors for fecal incontinence [13-15]. Other independent risk factors for FI are current smoking, cholecystectomy, rectocele, stress urinary incontinence and high body mass index. Obstetric trauma to the anal sphincter is another risk factor for postpartum FI [16]. Third-degree and fourth-degree lacerations are strong risk factors for FI [17]. Instrumented [forceps and vacuum] deliveries increase the risk for FI by 1.5 [18]. However, in the general population, the median age of onset of FI is the seventh decade [19], and the available data indicates that obstetric trauma is not a major risk factor for FI occurring many decades after vaginal delivery in women. Moreover, similar rates of FI were reported in nulliparous and nulligravid women, and the incidence of FI was not found to rise significantly during pregnancy [20,21].

Bowel disturbances: Diarrhea and combined constipation and diarrhea [e.g., fecal impaction].

Anal Sphincter injury: Obstetric, iatrogenic

Systemic disease: Scleroderma

Pelvic floor pathology:Fistula, rectal prolapse, descending perineum syndrome

Anal sphincter Neuropathy: Diabetes mellitus, obstetric.

Neurological pathology: Dementia, CVA, brain and spinal cord tumors, multiple sclerosis.

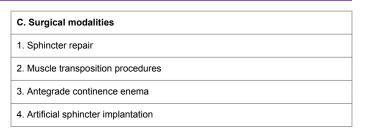
anorectic inflammation: Post radiation, Cohn's disease, Ulcerative colitis

Table 1: Main etiologies for FI.

Latrogenic FI is associated with surgery in the anorectal, perineal or pelvic area or post-pelvic irradiation. Internal sphincterotomy and peri-anal fistulotomy/fistulectomy have been shown to be associated with an FI incidence of up to 35% [22]. Pelvic irradiation has been shown to be connected to fecal urgency, diarrhea and flatulence [23,24]. Neurological disorders are another common cause for FI. Cerebrovascular accident is common neurological cause for FI, with a reported immediate and long-term FI prevalence of is 30% and 15%, respectively. Other neurological causes for FI include cerebral palsy, spinal cord injury, anoxic brain damage and multiple sclerosis.

The management of FI is often difficult, requires multiple interventions and may be extensive. Usually several treatment modalities are implemented, with a limited rate of success, before satisfactory results can be reached. Generally speaking, conservative modalities include lifestyle changes, reduction of diarrhea aggravating or rectal urgency inducing substances, urge suppression techniques and anti-diarrheal agents (Table 2). Medical management is largely directed toward symptom relief when the causes of FI cannot be easily diagnosed or treated. Other conservative treatment options include mechanical anal closure by the use of an anal plug and physical therapy that augments the anal sphincter tone. The overall reported improvement rates of the conservative treatment modalities approach 25% [25]. When conservative therapy fails, other therapeutic possibilities should be implemented. These include sacral neuromodulation [26], posterior tibial stimulation [27], acupuncture [28], internal anal sphincter augmentation [29], temperature controlled radiofrequency anal energy delivery [30] and stem cell transplantation [31]. Surgical therapeutic possibilities include sphincter repair, muscle transposition procedures supplemented by electrical stimulation, antegrade continence enema and artificial sphincter implantation [32]. This paper will focus on the non-surgical therapy options for FI.

A. Conservative modalities
1. Lifestyle habit modification
i. Weight loss
ii. Exercise
iii. Cessation of smoking
2. Dietary approach
i. Caffeine restriction
ii. Sodium and protein restriction
iii. Lactose restriction
iv. Adequate fluid intake
v. Fiber supplementation
vi. Dietary timing manipulation
vii. Avoidance of aggravating food
3. Avoidance of diarrhea aggravating drugs
4. Medications:
i. Anti-diarrheal drugs
ii. Phenylpherine gel
5. Physical therapy
i. Biofeedback
ii. Pelvic floor muscle training
iii. Electrical simulation
6. Anal Plug
B. Novel modalities
1. Sacral neuromodulation
2. Posterior tibial nerve stimulation
3. Acupuncture
4. Internal anal sphincter augmentation
5. Temperature controlled radiofrequency anal energy delivery
6. Stem cell implantation



Page 2 of 7

Table 2: Treatment options for fecal incontinence.

Treatment Modalities

Lifestyle Management

Obesity was found to be a risk factor for FI in various epidemiological studies, probably due to an increase in the intrabdominal pressure as well as due to pelvic organ prolapse [33,34]. Although dietary interventions have not shown significant difference in the severity of FI [35], bariatric surgery was found to improve FI severity in selected cases [36]. However, these results were dependent upon the selected procedure, with gastric bypass procedures actually worsening the FI severity as compared with gastric banding procedures, irrespective to the amount of weight loss [37]. Current smoking was found to be another potentially risk factor for FI, irrespective of the diagnosis of chronic obstructive lung disease [15]. Decreased rectosigmoid transit time and decreased rectal compliance may explain this phenomenon [38]. The effects of dietary modification have been examined previously. A self-designated dietary modification was reported to be useful in reliving FI symptoms in up to one third of the general population [39] and in 67% of an elderly cohort [40]. The main dietary modification approaches include avoidance of putative substances that could worsen FI [e.g., caffeinated foodstuff, spicy food] and increase flatus [e.g., cabbage]. Other strategies that improve FI related quality of life include the skipping of meals [41]. As FI can occur due to fecal impaction and constipation, adequate intake of fluid to prevent constipation is advised. Interestingly, lower levels of consumption of protein and sodium were more common in FI population [41,42]. Low fiber intake was also reported in FI patients [43], with lower fiber intake rates being 2.5 times more common in overweight women with FI [44]. Although fiber is used for constipation, it can also alleviate mild chronic diarrhea by absorbing water and increasing stool bulk and possibly by creating the perception of decreased stool fluidity. Though fiber consumption can exacerbate incontinence, this may be related to the type of fiber, with insoluble fiber being related to FI exacerbation [45].

Medical therapy

Medical treatment targeting chronic diarrhea and constipation has a major role in the treatment of FI, as bowel disturbances were found to be a major risk factor for the development of FI [46]. Therefore, medical treatment may focus on improving stool consistency, augmentation of the rectal evacuation and enhancement of anal sphincter function.

Three different anti-diarrheal medications can be used for FI: loperamide, diphenoxylate and codeine. All three decrease intestinal motility and stabilize stool consistency to a more controllable form. Loperamide is a synthetic opioid with an excellent safety profile and no central nervous effects. It acts by decreasing small intestinal transit and by enhancing the anal pressure at rest and squeeze, therefore reducing the frequency of bowel movements as well as the volume of the stool [47]. It may also reduce the recto anal inhibitory reflex and enhance rectal sensation [48]. Codeine and diphenoxylate have a similar bowel effect, but additional side effects that may limit their use. In a meta-analysis, the anti-diarrheal drugs were found to be more effective for the preservation of fecal continence than placebo [49]. Loperamide and codeine were more effective than diphenoxylate in keeping a higher percentage of stools solid and had fewer adverse effects [50]. The useful effect of prebiotics and probiotics in chronic diarrhea is well documented. However, hardly any research has been performed on the use of these agents in FI. Disappointing results were achieved in a group of patients who underwent colonic surgery due to colorectal cancer, where the use of probiotics did not change considerably the daytime defecation frequency, nighttime defecation frequency or the Wexner Incontinence Score [51].

Another therapeutic option is the augmentation of the anal sphincter pressure by topical administration of phenylephrine, a $\alpha 1$ adrenergic agonist. Phenylephrine acts by increasing the internal anal sphincter tone, and therefore increasing the resting anal pressure. Phenylephrine was found to be effective in improving continence symptoms and achieving full continence [52-54]. However, a recently published placebo controlled study did not find significant benefits to another $\alpha 1$ -adrenoceptor agonist [55]. Similarly, clonidine [an a2-adrenergic agonist that can inhibit gastrointestinal motor activity by presynaptically inhibiting acetylcholine release from nerves in the myenteric plexus and at the neuromuscular junction] failed to alter bowel symptoms, fecal continence, or anorectal functions in women with urge-predominant FI. Among patients with diarrhea, clonidine increased stool consistency, with a borderline significant improvement in fecal continence [56].

Fecal impaction may result in FI due to the relaxation of the internal sphincter in response to the pressure induced by the fecal load. Lower anal squeeze pressure, reduced integrity of the sphincter and of the pelvic musculature, impaired anorectal sensation and neurogenic abnormalities may all promote incontinence in the presence of fecal impaction [57]. Therefore, constipation should be avoided by the use of adequate fluid and fiber intake. When these measures fail, the use of laxatives, stool softeners and tap water enemas should be considered. The attainment of rectal emptying was found to reduce FI rates in elderly nursing home residents with FI related to fecal impaction [58]. Patient with FI related to evacuation and post defecatory incontinence may benefit from daily water irrigation to evacuate stool. Various types of apparatus may be used for colonic irrigation, including a mechanical pump [59], a stoma irrigation system [60] and specially designed anal irrigation equipment [61].

Anal plug and anal insert device

The anal plug consists of a special intra-anal device that acts as a physical barrier that enables continence. Historically used only for patients with a neurological problem, today it is used for FI of any etiology. The anal plug is a simple and inexpensive treatment that can reduce incontinence and FI related problems, provided the plug is tolerated and used persistently. Continence was well controlled in close to 40% of patients who tolerated the device in two studies, although compliance was poor [62,63]. Polyurethane anal plugs (Conveen, Coloplast) were found to be more useful than the polyvinyl alcohol plug [Med. SSE system, Germany] [64]. In a Cochrane review published recently, that included four studies with a total of 136

Page 3 of 7

participants, data suggested that if tolerated, anal plugs can be helpful in preventing incontinence [65].

The anal insert device is a single-use, soft silicone self-inserted anal device. This device seals the top of the anal canal and helps prevent leakage of stool [66]. Satisfying results were obtained in 77% of users that achieved a \geq 50% reduction in incontinence frequency.

Physical therapy

Biofeedback, sphincter exercise and electric stimulation can be performed as an adjunct to other modalities of treatment or when other conservative therapeutic measures fail to improve the incontinence [66]. Biofeedback is a therapeutic process based on operant conditioning, where a specific body function that is only poorly perceived during normal conditions is measured by a technical device and demonstrated to the subject. The subject can improve the relevant function by the power of understanding. Biofeedback techniques may be directed on enhancement of the voluntary conditioning of the external anal sphincter when the rectum is full [67]. Other techniques concentrate on discrimination of smaller rectal volumes, therefore reducing the delay between sensation and external anal muscle contraction [68]. External anal sphincter contraction enhancement can also be targeted during biofeedback [69]. The external anal muscle and the puborectalis muscle are striated muscles, therefore amenable to pelvic floor muscle training. By contracting the external anal and the puborectalis muscles while keeping the abdominal muscle relaxed, enhancement of the strength and the endurance of the muscles as well as improvement of the rectal emptying can be achieved. Based upon the available data [70-74], no single method of biofeedback or exercises gives any benefit over any other method, but biofeedback or electrical stimulation may offer an advantage over exercises alone if patients have previously failed to respond to other conservative management. Biofeedback treatment combined with pelvic floor exercises is usually the first line option for FI that is not responding to dietary and medical therapy. Virtually all FI patients referred for less conservative measures have undergone this form of therapy [68].

Sacral neuromodulation

Since the introduction of sacral neuromodulation (SNS) for the management of FI in 1995 by Matzel [75], it has gained popularity as a less invasive approach for FI (when compared to the surgical methods). SNS is well recognized method for controlling FI when conservative treatment modalities fail. In SNS, electrodes are inserted close to sacral nerves and continuously pulsed by a battery-operated stimulator. The procedure is usually performed in two phases: first, electrodes are inserted into the sacral foramina to identify an electrode location that causes a contraction of the external anal sphincter. Temporary stimulation is applied for 2-3 weeks to determine whether there is at least a 50% reduction in FI frequency. If this trial is successful, a permanent stimulator is implanted beneath the skin. On an intention to treat basis, the success rates ranged between 54-63% [76]. In a US multicenter trial, 5 years after permanent SNS implantation, 36% of the subjects reported complete continence and 89% were considered a therapeutic success [77]. SNS is useful both in intact anal sphincters and in defected anal sphincters [78-80]. The most common complications are pain and infection at the insertion site, which occur in up to 11% [81]. In 2011 SNS was approved for the treatment of FI by the United States Food and Drug Administration (FDA). In a Cochrane review including six crossover trials and two parallel group trials, SNS was found to improve continence in a proportion of patients with fecal incontinence [82]. SNS should be offered after conservative treatments, have failed [83].

Posterior tibial nerve stimulation

Posterior tibial nerve stimulation [PTNS] was introduced as a treatment modality for FI in 2003 [84]. The procedure is carried out with a needle inserted posterior and superior to the medial malleolus and then connected to a pulse stimulator. The PTNS is technically simple, with relative low costs due to the use of reusable stimulator and simple percutaneous needles. Contraindications for the use of PTNS are few, mainly coagulopathy and local neuropathy. The optimal regimen for PTNS is unclear, and various treatment regimens had been reported, including bilateral stimulation [85] and different frequencies of treatment. However, the transcutaneous technique was found to be superior to percutaneous stimulation [86]. A recently published systematic review concluded that multiple low-quality studies showed improvement in FI after PTNS, however high quality studies are missing, and therefore meaningful outcome measures that would further establish the utility of PTNS for FI are missing [87]. In another double-blind randomized controlled trial of percutaneous tibial nerve stimulation versus sham electrical, PTNS did not show significant clinical benefit over sham electrical stimulation in the treatment of FI [88]. Therefore, the evidence for the efficacy of PTNS is limited, and PTNS should not be recommended for patients with FI at this time.

Acupuncture

Acupuncture treatment for FI was reported in few studies, with 50-85% reduction in FI episodes [28,89,90]. The reported regimens consist of a 10 weeks treatment followed by maintenance therapy after 1-3 month. During the treatment, the needles are inserted over the sacrum or the perineal area and stimulated for 30 minutes. Increase in the internal anal sphincter tone, elevated sensory threshold and increases rectal capacity was reported after acupuncture [28]. Further studies are needed for the evaluation of the efficacy of this strategy.

Internal anal sphincter bulking agents

Internal anal sphincter [IAS] dysfunction can be caused by structural damage to the internal anal muscle [during delivery or anal dilatation] or due to dysfunction with intact internal anal muscle [e.g. due to radiotherapy or age related]. Treatment modalities toward IAS dysfunction are currently limited. Injectable agents can potentially improve FI by a mechanical closure of the anal cushions or by providing an adequate lining that can plug the anal orifice while the IAS tonically constricts. In ideal terms, an injectable material should be biocompatible, non-immunogenic, non-allergenic, and easy to inject, and produce long term results [91]. Vast numbers of materials were studied, including polytetrafluerthlene, autologous fat, silicone products, bovine collagen treated with gluteraldehyde, carbon beads, hydroxyapatite ceramic microspheres, hyaluronic acid, cross linked procine dermal collagen and cross linked polyacrylamide. A Cochrane review published in 2013 overviewed 5 randomized trials with a total of 382 patients [92]. Most studies demonstrated only short term efficacy. Lately, long term efficacy of stabilized hyaluronic acid/ dextranomer [NASA DX, Solesta, Salix Pharmaceuticals, and Raleigh, USA] was demonstrated in a prospective multicenter study, with 59% reduction in FI episodes and significant reduction in incontinence episodes. Similarly, the number of incontinence free days and the quality of life increased in the study group [29].

Temperature controlled radiofrequency anal energy delivery

Page 4 of 7

The Secca procedure involves the delivery of radiofrequency energy into the anal canal. The procedure is performed using moderate sedation and a specially designed applicator. The energy is delivered through 4 needles in four quadrants of the anal canal. Allegedly, the SECCA procedure improves FI by the mechanism of tissue damage, remodeling, scarring and contraction of the anal canal [93]. The reported outcomes of this procedure varied widely from 6-84% in various unrandomized studies [94]. However, a recently published study reported disappointing outcomes at 1 and 3 years post procedure [95].

Stem cell transplantation

Stem cell transplantation is an experimental method, studied mainly in animal models. This method involved intramuscular injection of stem cells in order to induce muscle differentiation and growth, and therefore improve muscle functioning. Only one human study has been published to date, involving 10 women with post-delivery external anal damage [31]. Anal squeeze pressures did rise significantly at 1 month and 6 months post-injection, but not at 12 months. However, at 12 months, the Wexner incontinence score and overall quality of life scores had improved significantly.

Summary and Recommendations

Fecal incontinence is a distressing symptom that significantly decreases the quality of life and may cause isolation and embracement. Therefore effective treatment modalities are warranted. Fortunately, patients have increasing number of conservative and minimally invasive treatment options. As the treatment of FI may be difficult, combination of various treatment modalities is possible. Table 3 summarizes the success rate of the main conservative treatment options in fecal incontinence. Recent guidelines published by national societies of gastroenterology and surgery [96,97] suggest initial treatment strategy encompassing dietary modifications, skin care, and pharmacologic agents to modify stool delivery and liquidity, as the regulation of transit and stool consistency are priorities in the management of FI. Pelvic floor rehabilitation should be offered to patients who do not respond to conservative measures. Minimally invasive procedures such as injectable anal bulking agents may have a role in patients with FI due to internal sphincter malfunction who do not respond to conservative therapy. Sacral neuromodulation should be offered to patients who failed conservative measures. Further surgical treatment [outside the context of this review] can be suggested to those patients who do not respond to more conservative measures.

Further research is required in order to examine the effects of combined minimal invasive therapeutic modalities on fecal incontinence.

Treatment modality	Success rate	Complication	Remarks
Lifestyle modification	Various results	Worsening of FI after gastric bypass	
Dietary Modification	One third	none	
Medications: Loperamide and codeine	50% improvement	Rare	

Topical phenylephrine	30% improvement	Rare	
Polyurethane anal plug	40% improvement	Intolerable at close to 50%	
Sacral neuromodulation	50-60% improvement	Infections	
Post Tibial Neuro- stimulation	Not beneficial		
Acupuncture	80-90% improvement		Uncontrolled studies
Bulking agents	60% improvement		Short and long term efficacy for hyaluronic acid
Secca Procedure	Not beneficial		

 Table 3: Success rate of the main conservative treatment options in fecal incontinence.

Acknowledgment

I would like to thank Prof. Ben Novis for the intellectual review of this work.

References

- Cotterill N, Norton C, Avery KN (2011) Psychometric evaluation of a new patient-completed questionnaire for evaluating anal incontinence symptoms and impact on quality of life: the ICIQ-B. Dis Colon Rectum 54: 1235-1250.
- 2. Drossman DA, Li Z, Andruzzi E (1993) U.S. householder survey of functional gastrointestinal disorders. Prevalence, sociodemography, and health impact. Dig Dis Sci 38: 1569-1580.
- 3. Nelson R, Norton N, Cautley E, Furner S (1995) Community-based prevalence of anal incontinence. JAMA 274: 559-561.
- 4. Whitehead WE, Borrud L, Goode PS, Meikle S, Mueller ER, et al. (2009) Fecal incontinence in US adults: epidemiology and risk factors. Gastroenterology 137: 512-517.
- 5. Johanson JF, Lafferty J (1996) Epidemiology of fecal incontinence: the silent affliction. Am J Gastroenterol 91: 33-36.
- 6. Teunissen TA, van den Bosch WJ, van den Hoogen HJ (2004) Prevalence of urinary, fecal and double incontinence in the elderly living at home. Int Urogynecol J Pelvic Floor Dysfunct 15: 10-13.
- 7. Dey AN (1997) Characteristics of elderly nursing home residents: data from the 1995 National Nursing Home Survey. Adv Data : 1-8.
- Nelson R, Furner S, Jesudason V (1998) Fecal incontinence in Wisconsin nursing homes: prevalence and associations. Dis Colon Rectum 41: 1226-1229.
- 9. Aitola P, Lehto K, Fonsell R, Huhtala H (2010) Prevalence of faecal incontinence in adults aged 30 years or more in general population. Colorectal Dis 12: 687-691.
- Lo J, Osterweil P, Li H, Mori T, Eden KB, et al. (2010) Quality of life in women with postpartum anal incontinence. Obstet Gynecol 115: 809-814.
- Nakanishi N, Tatara K, Shinsho F, Murakami S, Takatorige T, et al. (1999) Mortality in relation to urinary and faecal incontinence in elderly people living at home. Age Ageing 28: 301-306.
- 12. Alameel T, Basheikh M, Andrew MK (2012) Digestive symptoms in older adults: prevalence and associations with institutionalization and mortality. Can J Gastroenterol 26: 881-884.

- Bharucha AE, Zinsmeister AR, Locke GR, Seide BM, McKeon K, et al. (2006) Risk factors for fecal incontinence: a population-based study in women. Am J Gastroenterol 101: 1305-1312.
- Bharucha AE, Seide BM, Zinsmeister AR, Melton LJ (2008) Relation of bowel habits to fecal incontinence in women. Am J Gastroenterol 103: 1470-1475.
- Bharucha AE, Zinsmeister AR, Schleck CD, Melton LJ (2010) Bowel disturbances are the most important risk factors for late onset fecal incontinence: a population-based case-control study in women. Gastroenterology 139: 1559-1566.
- Bols EM, Hendriks EJ, Berghmans BC, Baeten CG, Nijhuis JG, et al. (2010) A systematic review of etiological factors for postpartum fecal incontinence. Acta Obstet Gynecol Scand 89: 302-314.
- 17. Borello-France D, Burgio KL, Richter HE, Zyczynski H, Fitzgerald MP, et al. (2006) Fecal and urinary incontinence in primiparous women. Obstet Gynecol 108: 863-872.
- Pretlove SJ, Thompson PJ, Toozs-Hobson PM (2008) Does the mode of delivery predispose women to anal incontinence in the fi rst year postpartum? A comparative systematic review. BJOG 115: 421-434.
- 19. Bharucha AE, Fletcher JG, Melton LJ, Zinsmeister AR (2012) Obstetric trauma, pelvic floor injury and fecal incontinence: a population-based case-control study. Am J Gastroenterol 107: 902-911.
- McKinnie V, Swift SE, Wang W, Woodman P, O'Boyle A, et al. (2005) The effect of pregnancy and mode of delivery on the prevalence of urinary and fecal incontinence. Am J Obstet Gynecol 193: 512-517.
- Lukacz ES, Lawrence JM, Contreras R, Nager CW, Luber KM (2006) Parity, mode of delivery, and pelvic floor disorders. Obstet Gynecol 107: 1253-1260.
- Baeten LCG, Kuijpers HC (2007) Incontinence. In: Wolff BG, Fleshman JW, Beck DE (edn), The ASCRS Textbook of Colon and Rectal Surgery New York, NY. Springer 653-664.
- 23. Barraclough LH, Routledge JA, Farnell DJ (2012) Prospective analysis of patient-reported late toxicity following pelvic radiotherapy for gynaecological cancer. Radiother Oncol 103: 327-332.
- 24. Atherton PJ, Halyard MY, Sloan JA (2013) Assessment of patient-reported measures of bowel function before and after pelvic radiotherapy:an ancillary study of the North Central Cancer Treatment Group study N00CA. Support Care Cancer 21:1193-1199.
- Bharucha AE, Rao SS2 (2014) An update on anorectal disorders for gastroenterologists. Gastroenterology 146: 37-45.
- 26. Carrington EV, Evers J, Grossi U (2014) A systematic review of sacral nerve stimulation mechanisms in the treatment of fecal incontinence and constipation. Neurogastroenterol Motil 26: 1222-1237
- Thomas GP, Dudding TC, Rahbour G, Nicholls RJ, Vaizey CJ (2013) A review of posterior tibial nerve stimulation for faecal incontinence. Colorectal Dis 15: 519-526.
- 28. Scaglia M, Delaini G, Destefano I, Hultén L (2009) Fecal incontinence treated with acupuncture--a pilot study. Auton Neurosci 145: 89-92.
- 29. Mellgren A, Matzel KE, Pollack J, Hull T, Bernstein M, et al. (2014) Longterm efficacy of NASHA Dx injection therapy for treatment of fecal incontinence. Neurogastroenterol Motil 26: 1087-1094.
- 30. Efron JE (2004) The SECCA procedure: a new therapy for treatment of fecal incontinence. Surg Technol Int 13: 107-110.
- Frudinger A, Kolle D, Schwaiger W, Pfeifer J, Paede J, et al. (2010) Muscle-derived cell injection to treat anal incontinence due to obstetric trauma: pilot study with 1 year follow-up. Gut 59: 55-61.
- 32. Bleier JI, Kann BR (2013) Surgical management of fecal incontinence. Gastroenterol Clin North Am 42: 815-836.
- Melville JL, Fan MY, Newton K, Fenner D (2005) Fecal incontinence in US women: a population-based study. Am J Obstet Gynecol 193: 2071-2076.
- 34. Altman D, Falconer C, Rossner S, Melin I (2007) The risk of anal incontinence in obese women. Int Urogynecol J Pelvic Floor Dysfunct 18: 1283-1289.

Page 5 of 7

- 35. Markland AD, Richter HE, Burgio KL, Myers DL, Hernandez AL, et al. (2011) Weight loss improves fecal incontinence severity in overweight and obese women with urinary incontinence. Int Urogynecol J 22: 1151-1157.
- 36. Cuicchi D, Lombardi R, Cariani S, Leuratti L, Lecce F, et al. (2013) Clinical and instrumental evaluation of pelvic floor disorders before and after bariatric surgery in obese women. Surg Obes Relat Dis 9: 69-75.
- 37. Roberson EN, Gould JC, Wald A (2010) Urinary and fecal incontinence after bariatric surgery. Dig Dis Sci 55: 2606-2613.
- Scott AM, Kellow JE, Eckersley GM (1992) Cigarette smoking and nicotine delay postprandial mouth-cecum transit time. Dig Dis Sci 37: 1544-1557.
- 39. Bliss DZ, Fischer LR, Savik K (2005) Managing fecal incontinence: selfcare practices of older adults. J Gerontol Nurs 31: 35-44.
- Croswell E, Bliss DZ, Savik K (2010) Diet and eating pattern modifications used by community-living adults to manage their fecal incontinence. J Wound Ostomy Continence Nurs 37: 677-682.
- Hansen JL, Bliss DZ, Peden-McAlpine C (2006) Diet strategies used by women to manage fecal incontinence. J Wound Ostomy Continence Nurs 33: 52-61.
- 42. Bliss DZ, McLaughlin J, Jung J, Lowry A, Savik K (2000) Comparison of the nutritional composition of diets of persons with fecal incontinence and that of age- and gender-matched controls. Journal of Wound Ostomy and Continence Nursing 27: 90-97.
- Korula J (2002) Dietary fiber supplementation with psyllium or gum arabic reduced fecal incontinence in community-living adults. ACP J Club 136: 23.
- 44. Markland AD, Richter HE, Burgio KL, Bragg C, Hernandez AL, et al. (2009) Fecal incontinence in obese women with urinary incontinence: prevalence and role of dietary fiber intake. Am J Obstet Gynecol 200: 566.
- 45. Norton C, Chelvanayagam S (2004) Conservative management of faecal incontinence in adults. In: Norton C and Chelvanayagam S (edn), Bowel Continence Nursing. Beaconsfield Publishers 114-131.
- Roach M, Christie JA (2008) Fecal incontinence in the elderly. Geriatrics 63: 13-22.
- 47. Ruppin H (1987) Review: loperamide--a potent antidiarrhoeal drug with actions along the alimentary tract. Aliment Pharmacol Ther 1: 179-190.
- Musial F, Enck P, Kalveram KT, Erckenbrecht JF (1992) The effect of loperamide on anorectal function in normal healthy men. J Clin Gastroenterol 15: 321-324.
- 49. Omar MI, Alexander CE (2013) Drug treatment for faecal incontinence in adults. Cochrane Database Syst Rev 6: CD002116.
- 50. Palmer KR, Corbett CL, Holdsworth CD (1980) Double-blind cross-over study comparing loperamide, codeine and diphenoxylate in the treatment of chronic diarrhoea. Gastroenterology 79: 1272-1275.
- Ohigashi S, Hoshino Y, Ohde S, Onodera H (2011) Functional outcome, quality of life, and efficacy of probiotics in postoperative patients with colorectal cancer. Surg Today 41: 1200-1206.
- Carapeti EA, Kamm MA, Nicholls RJ, Phillips RKS (2000) Randomized, controlled trial of topical phenylephrine for fecal incontinence in patients after ileoanal pouch construction. Diseases of the Colon and Rectum 43: 1059-1063.
- 53. Cheetham MJ, Kamm MA, Phillips RK (2001) Topical phenylephrine increases anal canal resting pressure in patients with faecal incontinence. Gut 48: 356-359.
- 54. Park JS, Kang SB, Kim DW, Namgung HW, Kim HL (2007) The efficacy and adverse effects of topical phenylephrine for anal incontinence after low anterior resection in patients with rectal cancer. International Journal of Colorectal Disease 22: 1319-1324.
- 55. Siproudhis L, Graf W, Emmanuel A (2016) Libertas: A phase II placebocontrolled study of NRL001 in patients with faecal incontinence showed an unexpected and sustained placebo response. Int J Colorectal Dis.
- 56. Bharucha AE, Fletcher JG, Camilleri M, Edge J, Carlson P, et al. (2014) Effects of clonidine in women with fecal incontinence. Clin Gastroenterol Hepatol 12: 843-851.

- 57. Rao SS, Welcher KD, Leistikow JS (1998) Obstructive defecation: a failure of rectoanal coordination. Am J Gastroenterol 93: 1042-1050.
- Chassagne P, Jego A, Gloc P, Capet C, Trivalle C, et al. (2000) Does treatment of constipation improve faecal incontinence in institutionalized elderly patients? Age Ageing 29: 159-164.
- 59. Crawshaw AP, Pigott L, Potter MA, Bartolo DC (2004) A retrospective evaluation of rectal irrigation in the treatment of disorders of faecal continence. Colorectal Dis 6: 185-190.
- Gosselink MP, Darby M, Zimmerman DD, Smits AA, van Kessel I, et al. (2005) Long-term follow-up of retrograde colonic irrigation for defaecation disturbances. Colorectal Dis 7: 65-69.
- 61. Gardiner A, Marshall J, Duthie G (2004) Rectal irrigation for relief of functional bowel disorders. Nurs Stand 19: 39-42.
- 62. Van Winckel M, Van Biervliet S, Van Laecke E, Hoebeke P (2006) Is an anal plug useful in the treatment of fecal incontinence in children with spina bifida or anal atresia? J Urol 176: 342-344.
- 63. Bond C, Youngson G, MacPherson I, Garrett A, Bain N, et al. (2007) Anal plugs for the management of fecal incontinence in children and adults: a randomized control trial. J Clin Gastroenterol 41: 45-53.
- 64. Pfrommer W, Holschneider AM, Löffler N, Schauff B, Ure BM (2000) A new polyurethane anal plug in the treatment of incontinence after anal atresia repair. Eur J Pediatr Surg 10: 186-190.
- 65. Deutekom M, Dobben AC (2015) Plugs for containing faecal incontinence. Cochrane Database Syst Rev 7: CD005086.
- 66. Lukacz ES, Segall MM, Wexner SD (2015) Evaluation of an Anal Insert Device for the Conservative Management of Fecal Incontinence. Dis Colon Rectum 58: 892-898.
- 67. Heymen S, Scarlett Y, Jones K (2009) Randomized controlled trial shows biofeedback to be superior to alternative treatments for fecal incontinence. Dis Colon Rectum 52: 1730-1737.
- MacLeod JH (1987) Management of anal incontinence by biofeedback. Gastroenterology 93: 291-294.
- Miner PB, Donnelly TC, Read NW (1990) Investigation of mode of action of biofeedback in treatment of fecal incontinence. Dig Dis Sci 35: 1291-1298.
- Engel BT, Nikoomanesh P, Schuster MM (1974) Operant conditioning of rectosphincteric responses in the treatment of fecal incontinence. N Engl J Med 290: 646-649.
- Norton C, Chelvanayagam S, Wilson-Barnett J, Redfern S, Kamm MA (2003) Randomized controlled trial of biofeedback for fecal incontinence. Gastroenterology 125: 1320-1329.
- 72. Fynes MM, Marshall K, Cassidy M, Behan M (1999) A prospective, randomized study comparing the effect of augmented biofeedback withsensory biofeedback alone on fecal incontinence after obstetric trauma. Diseases of the Colon & Rectum 42: 753-761.
- 73. Schwandner T, König IR, Heimerl T, Kierer W, Roblick M, et al. (2010) Triple target treatment (3T) is more effective than biofeedback alone for anal incontinence: the 3T-AI study. Dis Colon Rectum 53: 1007-1016.
- Matzel KE, Stadelmaier U, Hohenfellner M, Gall FP (1995) Electrical stimulation of sacral spinal nerves for treatment of faecal incontinence. Lancet 346: 1124-1127.
- 75. Thin NN, Horrocks EJ, Hotouras A, Palit S, Thaha MA, et al. (2013) Systematic review of the clinical effectiveness of neuromodulation in the treatment of faecal incontinence. Br J Surg 100: 1430-1447.
- Hull T, Giese C, Wexner SD, Mellgren A, Devroede G, et al. (2013) Longterm durability of sacral nerve stimulation therapy for chronic fecal incontinence. Dis Colon Rectum 56: 234-245.
- Jarrett ME, Dudding TC, Nicholls RJ, Vaizey CJ, Cohen CR, et al. (2008) Sacral nerve stimulation for fecal incontinence related to obstetric anal sphincter damage. Dis Colon Rectum 51: 531-537.
- 78. Melenhorst J, Koch SM, Uludag O (2008) Is a morphologically intact anal sphincter necessaryfor success al. Is with sacral nerve modulation in patients with faecal incontinence? Colorectal Dis; 10: 257-262
- 79. Brouwer R, Duthie G (2010) Sacral nerve neuromodulation is effective treatment for fecal incontinence in the presence of a sphincter defect,

pudendal neuropathy, or previous sphincter repair. Dis Colon Rectum 53: 273-278.

- Wexner SD, Hull T, Edden Y (2010) Infection rates in a large investigational trial of sacral nerve stimulation for fecal incontinence. J Gastrointest Surg 14: 1081.
- Thaha MA, Abukar AA, Thin NN, Ramsanahie A, Knowles CH (2015) Sacral nerve stimulation for faecal incontinence and constipation in adults. Cochrane Database Syst Rev 8: CD004464.
- 82. Maeda Y, O'Connell PR, Lehur PA, Matzel KE, Laurberg S; European SNS Bowel Study Group (2015) Sacral nerve stimulation for faecal incontinence and constipation: a European consensus statement. Colorectal Dis 17: O74-87.
- Shafik A, Ahmed I, El-Sibai O, Mostafa RM (2003) Percutaneous peripheral neuromodulation in the treatment of fecal incontinence. Eur Surg Res 35: 103-107.
- Thomas GP, Dudding TC, Nicholls RJ, Vaizey CJ (2013) Bilateral transcutaneous posterior tibial nerve stimulation for the treatment of fecal incontinence. Dis Colon Rectum 56: 1075-1079.
- George AT, Kalmar K, Sala S (2013) Randomized controlled trial of percutaneousversus transcutaneous posterior tibial nerve stimulation in faecal incontinence. Br J Surg 100: 330-338.
- Edenfield AL, Amundsen CL, Wu JM, Levin PJ, Siddiqui NY (2015) Posterior tibial nerve stimulation for the treatment of fecal incontinence: a systematic evidence review. Obstet Gynecol Surv 70: 329-341.
- Knowles CH, Horrocks EJ, Bremner SA (2015) Percutaneous tibial nerve stimulation versus sham electrical stimulation for the treatment of faecal incontinence in adults (CONFIDENT): a double-blind, multicentre, pragmatic, parallel-group, randomised controlled trial. Lancet. 10004: 1640-1648
- Bergström K, Carlsson CP, Lindholm C, Widengren R (2000) Improvement of urge- and mixed-type incontinence after acupuncture

treatment among elderly women - a pilot study. J Auton Nerv Syst 79: 173-180.

- Yang T, Liu Z, Liu Y (2003) Electroacupuncture at ciliao and huiyang for treating neuropathic incontinence of defecation and urination in 30 cases. J Tradit Chin Med 23: 53-54.
- 90. de la Portilla F (2014) Internal anal sphincter augmentation and substitution. Gastroenterol Rep (Oxf) 2: 106-111.
- 91. Politano VA (1982) Periurethral polytetrafluoroethylene injection for urinary incontinence. J Urol 127: 439-442.
- 92. Maeda Y, Laurberg S, Norton C (2013) Perianal injectable bulking agents as treatment for faecal incontinence in adults. Cochrane Database Syst Rev.
- Felt-Bersma RJ, Szojda MM, Mulder CJ (2007) Temperature controlled radiofrequency energy (SECCA) to the anal canal for the treatment of faecal incontinence offers moderate improvement. Eur J Gastroenterol Hepatol 19: 575-580.
- 94. Felt-Bersma RJ (2014) Temperature-controlled radiofrequency energy in patients with anal incontinence: an interim analysis of worldwide data. Gastroenterol Rep (Oxf) 2: 121-125.
- 95. Lam TJ, Visscher AP, Meurs-Szojda MM (2014) Clinical response and sustainability of treatment with temperature-controlled radiofrequency energy (Secca) in patients with faecal incontinence: 3 years follow-up. Int J Colorectal Dis 29: 755-761
- Vitton V, Soudan D, Siproudhis L (2014) Treatments of faecal incontinence: recommendations from the French national society of coloproctology. Colorectal Dis. 16: 159-166.
- 97. Wald A, Bharucha AE, Cosman BC, Whitehead WE (2014) ACG clinical guideline: management of benign anorectal disorders. Am J Gastroenterol 109: 1141-1157.

Page 7 of 7