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Irritable bowel syndrome and chronic constipation: Fact and fiction

Massimo Bellini, Dario Gambaccini, Paolo Usai-Satta, Nicola De Bortoli, Lorenzo Bertani, Santino Marchi, Cristina Stasi

Massimo Bellini, Dario Gambaccini, Nicola De Bortoli, Lorenzo Bertani, Santino Marchi, Gastrointestinal Unit, Department of Gastroenterology, University of Pisa, 56124 Pisa, Italy

Paolo Usai-Satta, Gastrointestinal Unit, P. Brotzu Hospital, 09124 Cagliari, Italy

Cristina Stasi, Department of Experimental and Clinical Medicine University of Florence, 50134 Florence, Italy

Cristina Stasi, Epidemiological Observatory, Regional Health Agency of Tuscany, 50141 Florence, Italy

Author contributions: Bellini M designed the review, wrote and revised the manuscript; Gambaccini D, De Bortoli N and Bertani L wrote the manuscript; Marchi S revised the manuscript; Usai-Satta P and Stasi C wrote and revised the manuscript.

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Correspondence to: Cristina Stasi, MD, PhD, Dipartimento di Medicina Sperimentale e Clinica, Università degli Studi di Firenze, Largo Brambilla, 3, 50134 Firenze, Italy. cristina.stasi@gmail.com
Telephone: +39-55-7947154
Fax: +39-55-7947154

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Abstract

Irritable bowel syndrome (IBS) and functional constipation (FC) are the most common functional gastrointestinal disorders. According to the Rome III Criteria these two disorders should be theoretically separated mainly by the presence of abdominal pain or discomfort relieved by defecation (typical of IBS) and they should be mutually exclusive. However, many gastroenterologists have serious doubts as regards a clear separation. Both IBS-C and FC, often associated with many other functional digestive and non digestive disorders, are responsible for a low quality of life. The impact of the media on patients' perception of these topics is sometimes disruptive, often suggesting a distorted view of pathophysiology, diagnosis and therapy. These messages frequently overlap with previous subjective opinions and are further processed on the basis of the different culture and the previous experience of the constipated patients, often producing odd, useless or even dangerous behaviors. The aim of this review was to analyze the most common patients' beliefs about IBS-C and CC, helping physicians to understand where they should focus their attention when communicating with patients, detecting false opinions and misconceptions and correcting them on the basis of scientific evidence.

Key words: Irritable bowel syndrome; Chronic constipation; Functional constipation

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Core tip: The media often suggests a distorted view of pathophysiology, diagnosis and therapy of irritable bowel syndrome and chronic constipation. These messages frequently overlap with previous subjective opinions and are further processed on the basis of the different culture and the previous experience of the constipated patients, often producing odd, useless or even dangerous behaviors. The aim of this review was to analyze the most common patients' beliefs regarding these disorders, helping physicians to understand where they should focus their attention when communicating with patients, detecting false opinions and misconceptions and correcting them on the basis of scientific evidence.

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STATE OF THE ART

Irritable bowel syndrome (IBS) and functional constipation (FC) are the most common functional gastrointestinal disorders. They negatively affect quality of life and are associated with a significant economic burden related to direct and indirect annual health-care costs^[1,2].

Most gastroenterologists, mainly on a scientific basis, use the Rome III Criteria^[3] (Figure 1), which divide non organic constipation into functional constipation (FC) and IBS-C. These two different categories are theoretically separated mainly by the presence of abdominal pain or discomfort relieved by defecation (typical of IBS) and they should be mutually exclusive: in FC abdominal pain and discomfort are not included in the definition. In clinical practice the situation is somewhat different and many gastroenterologists have serious doubts about clearly separating these two disorders^[4-7].

Population-based studies carried out in North America reveal that between 1.9% and 27.2% of individuals experience constipation, with most estimates ranging from 12% to 19%^[8]. These different values are probably due to the fact that constipation is a symptom rather than a disease, susceptible to different and subjective interpretations of a real or imagined disturbance of bowel function^[9]. This generates many different definitions, some focusing on the interval between defecations (number of weekly defecations), and others reflecting the sensation of difficult defecation or incomplete bowel movements, with an objective assessment of stool consistency being rarely used in clinical practice^[10]. A recent

meta-analysis shows an IBS prevalence of 11.2%. The prevalence varied according to the countries and criteria used to define IBS. The lowest prevalence appeared in South Asia (7.0%) and the highest in South America (21%). Women are at a slightly higher risk of both CC and IBS than men^[11].

Both IBS-C and CC are often associated with functional digestive and non digestive disorders^[12-16]. In particular, IBS-C patients show a higher prevalence of psychological disorder, a higher rate of depression and anxiety and a lower quality of life than patients with IBS-D^[17].

The impact of the media on the perception of these topics is often disruptive because it proposes a distorted view of these disorders. This message frequently overlaps with previous subjective opinions and is further processed on the basis of the different culture of our patients, often producing odd, unhelpful or even dangerous behaviors. The aims of this review were to analyze the false beliefs of IBS-C and CC patients, which are influenced by a wide variety of factors, both internal to the patients themselves as well as the external media messages. Moreover, we will lay out a framework to help us understand where the clinicians should focus the patients' attention when communicating with them.

I underwent a barium enema/colonoscopy and they found my colon longer than normal; they told me it's the reason why I'm constipated and it would be better to shorten it. Could we cut a good piece away?

For the first time, Sir Arbuthnot Lane in the early 1900s formulated a theory according to which colonic kinking and/or an excessively long colon could cause fecal stasis, favoring intestinal absorption of water and toxins and leading to a systemic dysfunction. Consequently, colon bypass or total colectomy were suggested for indications ranging from lassitude to epilepsy^[18]. By the 1920s, surgical treatment of intestinal stasis had progressively fallen into disfavor. In fact, there is very little evidence to support either procedures aimed at shortening the colon of patients which is elongated but not dilated (dolichocolon), or indeed any surgical operations designed to straighten colonic kinks or intestinal loops, except in the presence of a volvulus causing an acute bowel obstruction). Actually no study has correlated colon length with colonic transit^[19].

Nowadays, if a surgical approach to the colon is suggested, it is a total colectomy. This is reserved for only very few cases. These are the most severe and refractory cases of constipation, in which imaging techniques and manometric findings have shown the presence of colonic inertia, usually linked to neuropathy and/or myopathy involving the whole colon^[20]. In these cases a very careful preoperative evaluation is mandatory to verify the real indication for colectomy, as is confirmed by a recent Italian study^[21]: 450

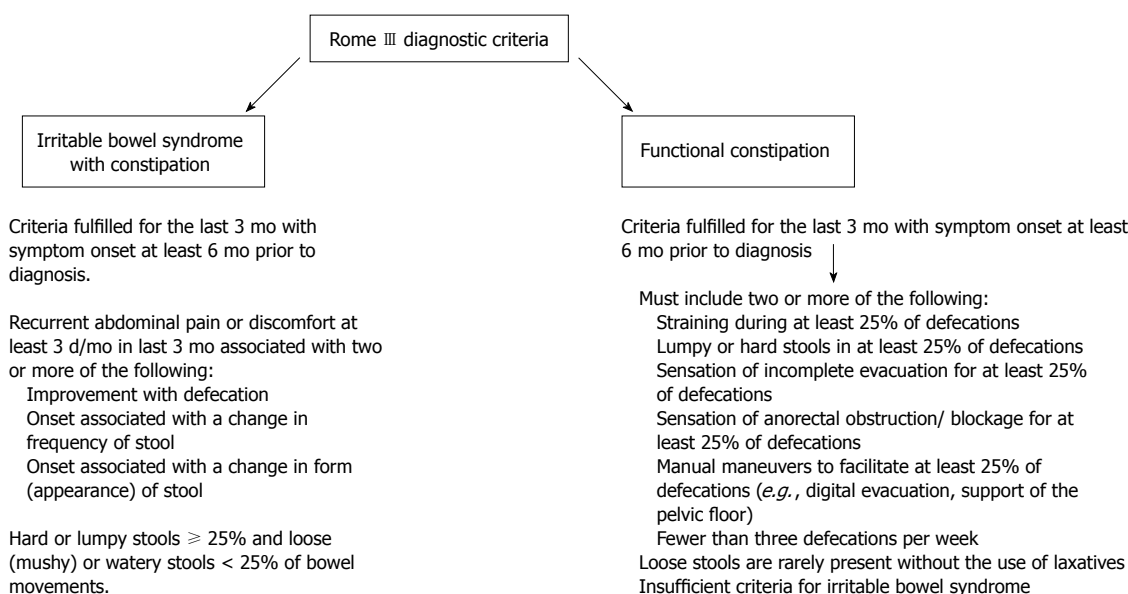


Figure 1 Rome III criteria for irritable bowel syndrome and functional constipation.

patients with chronic constipation were evaluated and 33 patients with a diagnosis of slow-transit constipation that had not improved with medical or rehabilitative treatment - after a meticulous assessment of colonic motility, they underwent colectomy. All patients except one had a positive outcome of the colectomy, thus improving their quality of life.

I do not eat citrus fruits because they cause constipation

It is a common belief that citrus fruits have constipating effects and could display a positive action in diarrheic syndromes. On the contrary, they are rich in pectin, which is an indigestible carbohydrate commonly contained in the cellular wall of the vegetal tissues. It is a soluble fiber representing a not negligible amount (0.5%-3.5%) of the fresh weight of the citrus fruits and particularly it represents about 30% of the fresh weight of the peel of citrus fruits^[22]. For more than fifty years^[23] pectin has been shown to be an adjuvant in controlling constipation. So actually citrus fruits can be useful in the treatment of constipation and in absolutely no way do they worsen it.

Furthermore, citrus fruits, like in general other plant products, contain water, sorbitol, fructose, fiber, and phytochemicals. The only fruit that is not recommended for a constipated patient is the banana, especially if unripe: an unripe banana contains 100-250 mg tannins/100 g and has a high amylase-resistant starch content (tannin acid reduces small intestinal secretions and inhibits peristalsis). This fruit can therefore have a constipating effect^[24].

My neighbor is constipated like me. She takes a small pill at bed time and everything is fine! Why doesn't the same happen to me?

Many people think that constipation is a single disease. Actually it is a complex multifaceted syndrome

involving many different causes (Table 1). Moreover, the term "primary constipation" itself hides different conditions, such as irritable bowel syndrome with constipation (IBS-C), functional constipation, functional defecation disorders and rectal hyposensitivity (Figure 1).

IBS-C, based on the Rome Criteria^[3], is defined as a recurrent abdominal pain or discomfort at least 3 d per month in the last 3 mo associated with 2 or more of the following: (1) improvement with defecation; (2) onset associated with a change in frequency of stool; and (3) onset associated with a change in form (appearance) of stool. The stools are hard or lumpy (Bristol Stool Form 1-2) \geq 25% and loose (mushy) or watery (Bristol Stool Form 6-7) \leq 25% of bowel movements, in the absence of use of antidiarrheals or laxatives.

Functional constipation, on the other hand, is a functional bowel disorder that presents as persistently difficult, infrequent, or seemingly incomplete defecation, which do not meet IBS criteria. Usually, there is no demonstrable physiological abnormality.

Functional defecation disorders are characterized by paradoxical contraction or inadequate relaxation of the pelvic floor muscles during attempted defecation (dyssynergic defecation) or inadequate propulsive forces during attempted defecation (inadequate defecatory propulsion)^[25] (Table 2).

Rectal hyposensitivity is a relatively new disorder defined by Gladman *et al.*^[26] as an elevation beyond the normal range in the perception of at least one of the sensory threshold volumes during anorectal manometry. In a population of 1351 patients with anorectal symptoms, rectal hyposensitivity was present in 23% of patients with constipation, 10% of patients with fecal incontinence and in 27% of patients with incontinence associated with constipation.

Table 1 Secondary causes of constipation

Drugs	Opiates, anticholinergics, antidepressants, anticonvulsants, calcium channel blockers
Endocrine and metabolic diseases	Hypothyroidism, hypercalcemia, diabetes, porphyria
Neurological diseases	Parkinson's disease, multiple sclerosis, spinal cord injury, autonomic neuropathy
Psychiatric disorders	Depression, eating disorders, obsessive disorders
Gastrointestinal diseases	Bowel obstruction, aganglioni, myopathies, neuropathies, megacolon/megarectum, anal atresia, anal stenosis

Therefore, rectal hyposensitivity can be considered as an important cause of constipation.

There are as yet no specific criteria that can differentiate the subtypes of chronic constipation based on anamnesis^[25]. Also performing a full assessment of defecation using specific tests (e.g., anorectal manometry, colonic transit time and defecography) may not be enough to distinguish these different conditions^[4-6]. However, a careful attempt to understand the pathophysiological mechanisms underlying the constipation of each patient is mandatory in order to suggest an effective therapy. This should be strictly tailored to each individual patient and therefore different from one patient to another. Therefore, it is not at all unusual that a drug effective in one patient does not work in another.

Bowel frequency bothers me: I don't have a bowel movement every day!

The frequency of bowel movements is usually considered a "key point" for the diagnosis of chronic constipation and IBS-C, but it is neither a sufficient nor a necessary issue^[3]. A decrease in bowel frequency usually prompts the patient to define her/himself as suffering from constipation. However, according to the Rome III criteria, the item "fewer than three defecations per week" must be accompanied by at least one of the other five characteristics in at least 25% of the defecations^[3] (Figure 1).

In clinical practice it is mandatory to explain to the patients that most normal people have a bowel frequency ranging from 3 times a day to 3 times a week and that it is not necessary to have a bowel movement every day.

The term "constipation" often has different meanings for patients and physicians^[6,27] and it is necessary to understand what exactly patients mean with "bowel movements". Sometimes both patients and physicians consider bowel movements simply as attempts at defecation or the defecation of small, unsatisfying, pieces of feces which oblige patients to go to the toilet many times a day. It is a gross mistake to consider this to be an increase in bowel frequency, possibly indicating a diarrhea. This is simply "fragmented defecation", typical of many constipated patients, especially of those affected with obstructed defecation. Moreover, some patients do not consider "bowel movement" when they use enemas or suppositories and this can cause a misunderstanding

with their physician. It is important to investigate all attempts to defecate so as to better understand what exactly patients mean.

I'm too constipated: I'll get colon cancer, sooner or later!

Prospective cross-sectional surveys and more recent meta-analysis demonstrate no increase in the prevalence of colorectal cancer in patients or individuals with constipation. The significant association observed in case-control studies may be related to a combination of poor study quality and recall bias among enrolled patients. When patients undergo colonoscopy for constipation as a main indication of the procedure the diagnosis of colorectal cancer is less common than in patients undergoing colonoscopy for other gastrointestinal symptoms. Therefore, the use of lower GI investigations to exclude colon cancer in patients presenting with constipation, in the absence of other "red flags", should be discouraged^[28-30].

If I haven't got my bowel movement every day I feel like a wet rag!

Constipated patients often refer fears linked to an undefined and unspecified concept of poisoning. They often imagine that fecal stasis has systemic effects and a range of intestinal and extra intestinal manifestations such as feelings of a bitter taste in the mouth, dyspepsia, headache and tiredness, etc. This is likely related simply to a delayed intestinal transit time^[19].

There is no scientific evidence to support the idea that there are diseases related to fecal stasis associated with the mechanisms of self-intoxication. The lack of specific symptoms and the improvement related to the act of defecation (more typical for mechanical effects and not for systemic effects) has led the scientific community to abandon the hypothesis of such relationships^[18].

The presence of comorbidities associated with both constipation and IBS-C (psychiatric disorders, fibromyalgia, headache, sleep disturbance, dyspareunia, recurrent urinary infections) have been confirmed by many studies^[16,31]. Psychiatric and extra intestinal comorbidity impacts on the quality of life and bowel symptom burden in functional GI disorders^[32].

The relationship with the brain-gut axis is not completely understood. Probably, the dysbiosis caused by constipation induces slight inflammation, due to altered barrier dysfunction, and a release of pro-inflammatory cytokines, with consequent dysregulation

of the brain-gut and gut-brain axes^[33-35].

My stools are like a sausage, a Havana cigar, a snake, fettuccini, a tubular tire, small black olives...

Fecal consistency is often overlooked in the anamnesis, both because of patient's embarrassment and because of the variability and the subjectivity of their descriptions (a great many bizarre and surprising metaphors are frequently heard in our surgeries...)^[27]. However, fecal consistency is an important clue to the transit time and must be clarified both in the clinical practice of prescribing a tailored and efficacious therapy and also within a clinical research setting. With this purpose in mind the Bristol scale offers a valuable aid in order to avoid errors related to excessively vague and subjective descriptions or to patient's recall bias, and its use should be encouraged in everyday practice^[36,37].

Doctor, do we really need to do a rectal examination? I'm a bit embarrassed to have rectal examination...

Digital rectal examination (DRE) is the most commonly used method to clinically assess anal tone although there is a lack of consensus in the current literature with regards to its accuracy and reliability. A comparison of DRE findings by an experienced gastroenterologist alongside objective ano-rectal manometry to establish anal tone reported DRE to be of low specificity and sensitivity and too inaccurate to use as a clinical finding^[38]. Many patients consider DRE bothersome or are afraid of feeling pain or more often than not are ashamed of undergoing this kind of medical examination. However, DRE is strongly recommended to verify if there is any fecal impaction in the rectum and to detect any early form of rectal cancer^[39] or benign diseases such as polyps, hemorrhoids (internal), anal fistula (low or high), rectal prolapse, etc.^[40,41]. Recent data have shown that DRE is performed in only 56% of Italian gastroenterological consultations^[16].

Doctor, you suggested a lot of annoying tests: aren't there too many of them? Are they really necessary for my constipation?

Gut functional disorders should be diagnosed using the Rome criteria^[3], but in clinical practice they are frequently dealt with by means of an exclusion criteria approach that takes into account the exclusion of organic diseases (alarm signs)^[42].

The presence of alarm features alerts the clinician to the possibility of an organic, rather than a functional disease process, and usually signals the need for testing in order to rule out an underlying organic disorder. These alarm features include rectal bleeding, weight loss, iron- deficiency anemia, nocturnal symptoms, and a family history of certain organic diseases such as colorectal cancer and inflammatory bowel disease^[43]. Their presence may indicate the

need for colonoscopy, colon-CT, or barium enema to exclude the presence of organic lesion or an associated disease^[20,43-45].

In patients without alarm symptoms, a "step-by-step" diagnostic approach is suggested, even if it frequently overlaps with life-style changes or a pharmacological treatment to resolve symptoms.

In patients with unsolved, recurrent signs and symptoms haematological, faecal and radiologic or instrumental approaches are considered necessary and advised^[20,43,44].

Integrated information coming from anorectal (sometimes gastrojejunal and/or colonic) manometry, Rx defecography and colonic transit time are often necessary because, up to now, no test has resulted in being completely exhaustive in assessing the pathophysiological mechanisms of defecation. Indeed, none of them studies defecation in normal conditions, but uses catheters, probes, different contrast media or simply in a position (usually left lateral position) not normally used in daily normal defecation. Last but not least, it should be considered that patients undergoing these tests are generally requested to simulate defecation, which is such an intimate and private act, in front of doctors, nurses and technicians. This can generate obvious embarrassment, hindering proper conduct and reducing the reliability of a single test: using more than one test can reduce errors and improve the quality of the assessment of the defecatory pattern^[20,44].

In Figure 2 we report a diagnostic flow-chart approach to chronic constipation.

Could physical activity help me to have more satisfying defecation?

It is well known that people who undertake more physical activity have a lower prevalence and a better control of constipation. There is some evidence that bowel function can correlate to physical activity, but other factors may very well be involved. For instance, in the elderly many cofactors such as diet, medications, cognitive and psychological condition are likely to play a role and physical activity is only a part of a multifaceted and multidisciplinary therapeutic approach. On the other hand, in the young severely constipated patients physical activity probably does not improve bowel function^[19,43].

My bowel function and abdominal pain are worse after eating food! I usually drink a lot of water but I don't feel better. I eat a lot of fibers and drink plenty of liters of water every day to improve my bowel function but I'm quite unsatisfied.

Patients with IBS-C and CC commonly believe that specific dietary products contribute to their symptoms while other foods could prevent the same disturbances. Most patients increase the use of dietary fiber to regularize bowel function and to reduce meteorism

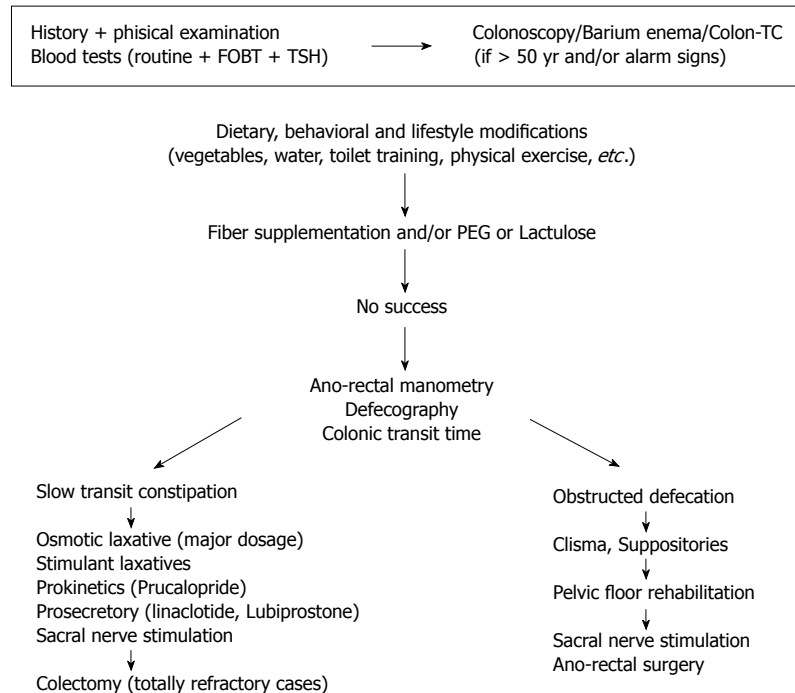


Figure 2 Multi-step management of chronic constipation. After a careful history and some blood tests, if there are no alarm signs and the patient is < 50 years old the first line approach encompasses a correction of lifestyle and dietary habits (on the contrary a colonic morphological assessment by using colonoscopy or barium enema or colon-CT is advisable). If the results are not satisfying, fiber supplementation and/or therapy with polyethylene glycol (PEG) or lactulose are advisable. Should there be unsatisfactory results, “second line” drug therapy, using saline or stimulant or softening laxatives, could be suitable and, possibly using or adding the new drugs with a prokinetic or prosecretory effect (prucalopride, lubiprostone, linaclotide). At this step performing some diagnostic “second level” exams (e.g., anorectal manometry and/or defecography and/or colonic transit time) should be taken into account. Pelvic floor rehabilitation and subsequently anorectal surgery or sacral nerve stimulation should be considered on the basis of the results of the “second level” exams. Colectomy represents the “last resort” and should be suggested only for patients with “inertia coli” only after performing also colonic and gastrojejunal manometry. FOBT: Fecal occult blood test.

and pain. There is some evidence that patients taking soluble fiber (psyllium, guar) have significant symptom relief, whereas insoluble fiber (bran) shows no clinical benefit and actually may worsen symptoms in many cases^[45]. The impairment of symptoms after an increase in dietetic fiber can also be due to the kind of constipation. It is well known that patients with dyssynergic defecation or with severe slow transit constipation can meet more severe symptoms after heavy fiber supplementation because it can further slow down colonic transit or it simply increases the amount of feces in the rectum, which the patient is not able to empty^[46]. Another common conviction is that constipation can be improved by drinking a considerable amount of water. Many patients force themselves to drink more than 2 L of water a day. Data currently available do not suggest that stool consistency and frequency of evacuation can be significantly modified by increasing fluid ingestion by more than 2 L a day^[47].

Furthermore, patients often associate their complaints with the ingestion of foods containing fructans, galactans, lactose, fructose, sorbitol, xylitol, and mannitol (fermentable oligo-di-monosaccharides and polyols; FODMAPs), which mainly increase abdominal bloating and distension^[48]. Patients with IBS, but without celiac disease, may reach satisfactory symptom control with a gluten-free diet^[49]. Because of

conflicting evidence regarding dietary implications in functional disorders, only a double-blind food-specific challenge will discriminate between a true and a false food-sensitivity in IBS patients.

I sometimes take a lot of PEG but I don't get good results. Why does my cousin have good defecation after drinking a coffee and eating a kiwi at breakfast?

Patient skepticism characterizes the relationship with medical professionals. Patients with IBS-C and functional chronic constipation (CC) are often not satisfied with the treatment they are receiving and actively, and sometimes compulsively, seek information on possible alternatives.

The main source of information to obtain knowledge and to know how to deal with the disease is the general practitioner, the pharmacist, but also friends and relatives and the mass media (magazine, TV, the Internet, etc.). The gastroenterologist is often at the end of the queue of this informative process.

Laxatives are the most widely used medications to improve bowel function both in IBS-C and CC. In particular, polyethylene glycol (PEG) is more effective than lactulose and stimulant agents in increasing stool frequency and improving stool consistency, and it is considered the first choice of treatment for CC^[20]. It should be taken on a regular basis, using it as an intestinal regulator and not to induce bowel

Table 2 Rome III diagnostic criteria for functional defecation disorders

Criteria fulfilled for the last 3 mo with symptom onset at least 6 mo prior to diagnosis
The patient must satisfy diagnostic criteria for functional constipation
During repeated attempts to defecate must have at least two of the following:
Evidence of impaired evacuation, based on balloon expulsion test or imaging
Inappropriate contraction of the pelvic floor muscles (e.g., anal sphincter or puborectalis) or less than 20% relaxation of basal resting sphincter pressure by manometry, imaging, or EMG
Inadequate propulsive forces assessed by manometry or imaging

movement, as a stimulant laxative. The starting dose, even a low dose, has to be progressively adjusted by the patient who has to find her/his own effective dosage. Generally speaking, the success of the constipation therapy is variable, depending on patients' age and compliance, duration of disease, impairment of colonic transit and/or pelvic floor, comorbidities and psychological disturbances. In the presence of only a partial clinical success or failure of traditional therapy, a second line treatment (prucalopride in CC and linaclotide in IBS-C and lubiprostone both in IBS-C and CC) is available today^[44-50]. In more severe cases of IBS-C and CC higher drug dosages than normal and/or combined therapies with laxatives with different mechanisms of action (e.g., osmotic plus stimulant drugs or osmotic plus prokinetic drugs or prokinetic plus secretagogue drugs) may be necessary.

I couldn't live without laxatives: I have become dependent on laxatives!

Some IBS/CC patients are "dependent" on laxatives to constantly maintain bowel movements without complaints. In most cases this addiction does not have a pharmacological basis, because most laxatives are not absorbed and none cross the blood brain barrier, but it is based only on psychological and behavioral factors^[51]. However, some patients, usually with psychiatric or psychological problems, abuse the use of laxatives for extended time periods. After stopping laxatives a "rebound constipation" does not seem to represent a real, frequent problem^[19].

Premature pharmacological tolerance can develop if there is prolonged treatment and this can represent another worry for constipated patients. Tolerance to laxatives has not been systematically studied in humans. However, tolerance (in particular to stimulant products) seems to occur in the most severely constipated patients for whom other products are ineffective. On the other hand, tolerance seems to be uncommon in the majority of cases^[19,51].

Can laxatives cause risks for my health?

Patients are obviously interested in the potential side effects of these products. Laxatives can determine

electrolyte disturbances or abdominal complaints such as abdominal pain and intestinal bloating. However, this can be minimized with an appropriate selection of the drug (osmotic laxatives are better than stimulant agents) and the tailored dose for a given patient. In particular, stimulant laxatives are preferred due to their rapid action even if, due to their mechanism of action, they tend to induce abdominal pain more frequently than osmotic laxatives^[19]. A typical fear of patients regards the risk of developing colorectal cancer after a chronic use of laxatives. Particularly pseudomelanosis coli, merely a pigmentation of the colon surface due to the accumulation of lipofuscin in macrophages as a consequence of the chronic use of anthraquinones, was considered in the past to be an expression of mucosal damage, should not in any way be considered as related to colon cancer^[52,53]. In general, constipation does not appear to be associated with an increased risk of cancer and there are no solid data supporting the idea that stimulant agents are a specific risk factor for colon cancer^[19].

A friend advised me to take herbal medications. What about the efficacy and safety of these products?

Another frequently asked question regards the use of herbal medication. Some IBS/CC patients consider this approach safer than traditional therapy. Herbal medications have been used in many countries for many centuries for the treatment of patients with constipation. Many patients underestimate the possible metabolic interaction of herbal products compared to the drugs they currently take, mistakenly presuming that all that is natural is beneficial, or at least harmless^[54]. Moreover, many of these "natural products" are bought by the patients without any medical prescription or supervision and without any information regarding their composition and origin. Indeed, there is a lack of controlled data supporting the safety and the efficacy of these treatments and no conclusive data are available regarding the possible toxicity of any herbal mixtures^[55,56].

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