Functional disorders in patients with inflammatory bowel diseases

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Summary

The occurrence of so-called functional symptoms in patients affected by organic diseases in some instances represents a clinical challenge for physicians. Coexistence of organic and functional symptoms often occurs, and the overlap is complex as the weight of the two components varies in different patients and from time to time in the same patient, in relation to activity and remission of the underlying organic disease. This review will attempt to summarize the available information on occurrence and treatment of functional symptoms in patients with inflammatory bowel disease and provide clues for optimizing therapeutic strategies.

KEY WORDS: irritable bowel syndrome, inflammatory bowel diseases, ulcerative colitis, Crohn’s disease, functional disorders.

Occurrence of functional symptoms in inflammatory bowel disease

The absence of ongoing intestinal inflammation in inflammatory bowel disease (IBD) should lead to remission of abdominal symptoms. Unfortunately this is not the case in a large proportion of patients with inactive IBD. This discrepancy has been attributed to the existence of “functional” disorders which may coexist with, or be associated to, IBD. Symptoms compatible with the diagnosis of irritable bowel syndrome (IBS) are more frequently observed in IBD compared with healthy controls, with a prevalence 2-3 times higher in ulcerative colitis (UC) and 3-4 times higher in Crohn’s disease (CD) (1, 2). This occurs, as expected, more often in patients with active disease (66%), but similar figures (57%) have been documented in patients considered to be in remission (3). The most common functional symptoms are IBS-like, but an increased occurrence of reflux has also been reported (2). GERD-like symptoms are present 62 to 72% of UC and CD patients, respectively, and in 50% of controls. The perception of “severe” heartburn is not associated in IBD patients with increased occurrence of documented reflux episodes, suggesting that the difference results from other factors. IBD patients behave, in this respect, in the same way as IBS patients do, showing a considerable overlap between GERD and other functional disorders (4).

Role of anxiety and depression

The occurrence of upper and lower GI tract symptoms, and their severity, in IBD are significantly associated with altered Short Form 36-item Health Survey scores (SF-36). Those underscores measuring general health and physical component summary were the most severely affected ones. Similar findings are reported in the same patients, using the Health Survey Hospital Anxiety and Depression Scale (HADS). Number and severity of IBS-like symptoms parallel HADS scores, values exceeding 8 being associated with a 78% risk of functional symptoms, compared to 22% in those with lower scores. Clear-cut depression, when present, further increases the probability of functional symptoms, which are reported by about 90% of these subjects (3).
The quality of life (QOL) shows a strict inverse correlation with both SF-36 and HADS. Moreover, illness perceptions considering IBD a severe, chronic, recurrent disease, as well as an emotion-centered attitude, lead to ineffective coping and inadequate adjustment to disease (5). All these data apparently suggest that functional symptoms in IBD should be first addressed with a psychosocial approach, aimed at improving symptoms and QOL. Unfortunately, clinical results have been far less satisfactory than could be anticipated. The combination of mindfulness meditation with aspects of cognitive behavioral therapy, the so-called multi-convergent therapy, led to minor improvement in a group of IBD patients with IBS-type symptoms and/or high perceived stress levels (6). Similarly, adding cognitive behavioral therapy to the standard pharmacological approach was only marginally effective in a randomized controlled trial (7). Only young patients, with recent diagnosis of IBD and pre-existing psychological problems profited from the combination therapy and improved QOL at 6 months. Relatively stable, pre-existing psychological characteristics of IBD patients, such as the sense of coherence, also influence the outcome of strategies aimed at favoring effective coping (8). All the above-mentioned evidence supports the complex interplay between psychological factors and functional symptoms, in patients with UC and CD.

**Subclinical inflammation**

Another line of evidence indicates that persisting, subclinical inflammatory changes may still be present in those patients with IBD in clinical and endoscopical remission, who meet the Rome III criteria for IBS. Recent studies have shown that presence or absence of functional symptoms identifies quite different subgroups of IBD patients. Those with IBS-like symptoms have higher HADS and lower IBD-Q scores, which is consistent with the above-mentioned data (9). However, these patient are characterized by significantly higher calprotectin levels (591 +/- 171 mg/kg vs 229 +/- 83 mg/kg), suggesting undetected, ongoing subclinical inflammation.

The possible connection between inflammation, increased intestinal mucosal permeability and “functional” symptoms in IBD is further supported by a recent paper by Vivinus-Nebot reporting that paracellular permeability is increased and the expression of zonulin-1 and α-catenin are diminished (10). This pattern is shared by IBD patients with functional symptoms and IBS patients, focusing the attention on the relation between subclinical inflammation and visceral hypersensitivity. The two groups, however, differ in that the mucosal expression of TNF-α is increased in IBD, but not in IBS.

**Autonomic dysfunction**

Other factors play some role in inducing so-called functional symptoms. Psychologic comorbidity, overall increased number of symptoms, and need for hospitalization in IBD patients is related with autonomic dysfunction (11). Positivity of the sudomotor axon reflex test, the cardiovagal function test, the termoregulatory sweating test and the tilt test, all help diagnosing autonomic dysfunction, which should be suspected in female IBD patients presenting with syncope, paresthesia, anhidrosis or hyperhidrosis.

**Therapeutic considerations**

The main aim of therapy perceived by physicians and by the patients is not the same. Indeed, the disappearance of symptoms is not considered as a sufficient target by clinicians, who aim at deep remission in IBD patients. The same does not hold true for patients who primarily seek resolution of abdominal pain and normalization of bowel habits, irrespective of other factors (12).

**Pain**

Effective treatment of abdominal pain is central for patients, more so for those considered to be in clinical remission. In these patients, once microscopic inflammation has carefully been ruled out, some drugs may be taken into consideration, which are considered unsafe or not indicated during active disease. Antispasmodics and NSAIDs may thus have some role in individual patients. The same holds true for psychological support, favoring effective coping and adjustment to chronic illness, physical therapy or unconventional approaches, such as acupuncture (13, 14).
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FODMAPs and diet

The role of fermentable carbohydrates in triggering bloating, gaseousness and diarrhea is supported by rapidly increasing information in IBS. Dietary modifications, based on low FODMAP (Fermentable Oligo-, Di- and Mono-saccharides And Polyols) diets indeed proved effective in these patients (15).

Preliminary evidence suggests that low FODMAP diets may be of some use in IBD, improving functional symptoms, reducing gas production and fluid excretion in the gut (16, 17). Nonetheless, doubts concern the long-term effects of this approach, as a reduction of fermentable substrate reduces the intraluminal concentration of useful fermentation products, such as butyrate. It may also influence the microbiota, minimizing the prebiotic activity of FODMAP and leading to the expansion of potentially pro-inflammatory bacteria (15). Thus, the real role of FODMAPS-restricted diets in IBD still remains to be established (18).

Others dietary changes are undertaken by IBD patients, in many instances without consulting the attending physician. They consist in wheat-free/gluten-free diets in the absence of celiac disease, and the restriction of milk and dairy products, aimed at improving diarrhea, irrespective to the presence or absence of lactose malabsorption. Self-prescribed diets are often unbalanced and may lead to deficit of macro and micronutrients, primarily calcium, and favor osteoporosis (19).

Dietary advice plays at present only a minor part in published guidelines for the management of IBD. Thus, an increasing need exists for hard data on the use of food as a therapeutic or preventive tool in IBD (20).

Conclusions

In ulcerative colitis and Crohn’s disease, as well as other chronic organic diseases, functional symptoms should be always taken into consideration, more so when the organic disease is considered to be in remission. Conversely, symptoms which may be first classified as non-organic, may result from subclinical, undiagnosed inflammation. Psychological co-morbidity, anxiety and depression are significantly associated with chronic organic disorders and worsen QOL.

Thus, diagnostic workout and therapeutic approach should be individualized and targeted to the needs of single patients. Optimizing the efficacy of IBD therapy, more so during remission, does not only improve QOL, but favors adherence to pharmacological therapy and reduces the risk of relapsing disease.

References

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