

Is IBD a Different Disease in Elderly Population?

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Abstract

Inflammatory bowel diseases (IBD) are idiopathic inflammatory disorders that are becoming always more prevalent in western society. The incidence of IBD in elderly population is expected to increase because of ageing and because IBD have nowadays a minimal impact on life span. Data on clinical presentation and natural history, outcomes and therapeutic strategies are limited. Comorbidities and polypharmacy make the management of these diseases in the elderly more challenging compared to younger patients. This mini-review will focus on recent knowledge of epidemiology, natural history, clinical characteristics and therapeutic strategies of this fragile IBD population

Keywords: *Inflammatory Bowel Diseases (IBD); Ulcerative Colitis (UC); Crohn's Disease (CD)*

Introduction

The incidence and prevalence of ulcerative colitis (UC) and Crohn's disease (CD) is increasing worldwide and the ageing of population makes IBD in elderly people a rising problem [1,2]. We, as clinicians, can face two different scenarios: patients with IBD diagnosed during a younger age who become older and people diagnosed with IBD after the age of 65 years. Almost 25 - 30% of IBD patients are over 60 years old. Among them 15% received diagnosis later in life and 20% reached the old age even though they had an IBD diagnosis early in life [3,4]. Incidence in this sub-setting of patients is 8/100.000/year for UC [5] and 4/100.000/year for CD [6]. When we compare elderly onset with children and adult onset we can find several differences in clinical presentation, course of disease, complications and therapeutic strategies. Unfortunately, clinical studies are lacking on this subject because old people are rarely included in clinical trial [7].

Natural history and clinical characteristics

It is well known that the natural history of IBD in the elderly is less aggressive when compared to younger IBD patients [8,9]. If we look at the clinical presentation in CD, colic localization is more common and disease activity seems to be milder with a more stable clinical course; strictures and fistulas are unusual, inflammatory phenotype is predominant and it tends to remain stable during time. Diarrhea, abdominal pain and anemia tend to be less frequent but weight loss, bloody diarrhea, fever and, paradoxically, constipation are common signs and symptoms at onset [10]. In elderly patients with UC, the first manifestation of disease may be serious or atypical [11]. Distal localization is more frequent and tends to remain stable, with only 16% of patients showing disease extension over time [12]. Flares are less frequent but that can be much more severe than in children and adult IBD population [13]. Extra intestinal manifestations are not related to the age of IBD-onset, so prevalence in the elderly is similar to adult population [14,15]. It is important to highlight that in IBD population and in particular in the subgroup of the elderly, there are some pathological condition mimicking IBD typical symptomatology. Misdiagnosis is a frequent cause of diagnostic delay in IBD, especially in the elderly onset and it may have a negative impact on disease outcomes in terms of complications with and increase morbidity in this subgroup of patient [15]. Differential diagnosis with symptomatic colonic diverticula, ischemic colitis, iatrogenic colitis (antibiotics and NSAID), infections, microscopic colitis and post-actinic colitis is re-

quired [13]. Diverticular disease is common in elderly people (40 - 60%) and bleeding from diverticula is the most common complication mimicking IBD [16]. Moreover, abscesses, perforations and fistulas formation make differentiation with CD complicated as well as a form of diverticular colitis (SCAD) which can mimic CD of the colon [17]. Ischemic colitis usually presents with skip areas, usually typical for CD, and with sudden abdominal pain and bloody diarrhea (symptoms that are typical for UC) [18]. Infective colitis with bloody diarrhea can be confused often with UC and in particular differential diagnosis is necessary with particular forms of infectious colitis such as *Clostridium Difficile*, *Shigella*, *Campylobacter*, *Salmonella* and *Escherichia coli* O157:H7. Typically, this kind of colitis is associated with fever and sudden onset of symptoms but diagnosis is easy with stool culture [19].

Diagnostic work up is similar to the one used in young and adult IBD population but some procedures should be performed with caution in the elderly because of possible comorbidities. Older patients that underwent invasive procedures have more anesthesiological risk, especially for enteroscopy and colonoscopy. Moreover, abdominal RMN is contraindicated in patients with metallic prosthesis or defibrillators. It is also for these reasons that, as initial procedures, proctosigmoidoscopy with biopsies is an alternative for colonoscopy and abdominal TC is the alternative for abdominal RMN for the small bowel assessment. Elderly patients with IBD are seldom enrolled in clinical trials, and that's the reason why there are no evidence based guidelines. It should always bear in mind that elderly people are different for physiology, functional state, comorbidities and poly-therapies and so any therapeutic strategy should be evaluated in terms of risk-benefit ratio, monitoring any possible adverse event [20]. Elderly patients with IBD often tend to be institutionalized and it is estimated that 25% of the admissions for IBD-related complication concern patients with an age more than 65 years. Older patients have a major risk for malnutrition, anemia, hypovolemia and need for blood transfusion. Moreover, they usually have usual longer hospital stays especially after surgery [21,22]. Finally, elderly patients, in particular the institutionalized ones, have a major thrombotic risk because of the active disease and because of hypo mobility and dehydration. Malnutrition is a frequent problem in many patients with IBD, but this phenomenon is impressive in elderly IBD patients because of their physiology and their major risk of nutritional deficiencies. Specific diets are used to prevent or reduce symptoms and complications of IBD in particular micronutrients deficiencies, IBD-like symptoms, prevention of intestinal occlusion, dyspepsia, fat malabsorption and kidney stones prevention. In the elderly IBD patients iron deficiency is the most common micronutrients deficiency, but vitamin B12 and vitamin D are common deficiencies too. Moreover, vitamin D deficiency modify bone structure leading to osteoporosis.

Treatment

Therapeutic approach is similar in elderly patients with IBD and people with younger age at presentation of the disease, but the speed of response may be slower and there are specific factors that may increase the risk of negative outcomes in elderly IBD patients [23]. Elderly patients are more fragile and more complicated because of comorbidities and polypharmacy [24]. Polypharmacy is common in this setting, with 22% of patients taking more than 5 different medications and 94,7% taking more than 3 medications [25]. This has the potential to increase the risk of drug interactions and it is well known that polypharmacy and complex dosing regimens reduce the rate of adherence to prescribed therapy [10] leading to disease flares, increased costs, hospitalization and low quality of life [26,27]. When facing with an active disease in an elderly patient, it is important to choose the most appropriate therapeutic approach: current guidelines don't differentiate between elderly and younger patients and the management should take in account potential benefit and risk, on an individual basis.

5-ASA (mesalamine): Oral and topical mesalamine is used to induce and keep remission in UC; data are not so impressive for CD, but it is used for colonic CD too. The favorable safety profile and relatively unusual side effects suggests that this drug may be preferred by elderly patients over other treatment [23]. In elderly IBD patients mesalamine is used in 84% of UC patients and 80% of CD patients. Oral and topical combo therapy is particularly efficacy in ulcerative proctitis [28]. Adherence to therapy is a common problem in the elderly; topical formulations can be problematical for elderly people to use, and compliance can be reduced because of number and shape of capsules, frequency of administration and adverse events such as vomiting, nausea, abdominal pain, headache, rash, nephrotoxicity and leucopenia [29]. Nephrotoxicity is a well-known adverse event of mesalamine but there is no data that clarify if the risk of toxicity is related to age and a systematic review on this topic suggested that renal reaction may be idiosyncratic rather than dose and age related [30].

Corticosteroids: Corticosteroids are commonly used to induce clinical remission in moderate to severe IBD [28]; adverse events are serious and common in elderly IBD patients (osteoporosis, cataracts and glaucoma, diabetes, hypertension, infections) and, moreover,

aging patients treated with steroids are at significantly increased risk for developing mental status changes. Despite data demonstrating high rates of adverse events with steroids, the “perceived safety” and perceived concern about immunosuppressive drugs or biologics contribute to the widespread use of corticosteroids in the elderly [25]. Corticosteroid therapy should be used only to induce remission and current IBD guidelines recommend tapering once clinical remission is achieved. In case of steroid dependency, which is defined as the inability to discontinue or reduce dosage of systemic steroids, it is mandatory a change in therapeutic strategy to reduce steroid exposure [31]: immunosuppressive medication (thiopurines and methotrexate) and/or biological medication (anti-TNF α , anti-integrins and anti-interleukin) is required so far.

Immunosuppressive medication: In the elderly IBD population type and efficacy of immunosuppressive drugs is the same as the young and adult population, but because of the characteristics of these fragile patients the use of these drugs presents some peculiarities. Thiopurines and methotrexate use remains quite low (6% and 1% respectively) and this is likely to be due to the risk of severe adverse effects and requirement for blood test monitoring (frequent adverse events include leucopenia, transaminase increase, allergic reaction nausea, pancreatitis, increased risk of non-melanoma skin cancer [32] and NHL [33]. Thiopurines moreover have a large spectrum of drug interaction (coumarin derivatives and allopurinol above all) requiring dose adjustments [34].

Biological agents: The role of anti-TNF α and anti-integrin in inducing remission and in the natural history modification of IBD is well established [28,35]. Unfortunately IBD onset in the elderly is a sub optimal predictive factor of efficacy of these drugs as highlighted in a recent observational retrospective study [8] where anti-TNF α therapy in elderly IBD patients showed a significantly lower rate of short term clinical response (68% vs 89% in younger patients) and a higher risk of severe adverse events, including severe infections and mortality [36]. It should be taken in consideration that combination therapy with an immunosuppressant can contribute to this trend and so monotherapy should be preferred in patients requiring anti-TNF α therapy. Preliminary results show a good safe profile for anti-integrin therapy in young and adult population but in the elderly too [37] and for this reason vedolizumab therapy should be considered a first line therapy especially in moderate to severe UC patients with high risk for neoplastic and infective disease [20]. Ustekinumab, a monoclonal antibody of interleukin 12 and 23 was recently approved for moderate to severe CD, but there is limited information related to its use in the elderly.

Surgery: Surgery remains a therapeutic option for all IBD patients who failed medical treatment [38]. Studies report low rate of total colectomy (0 - 2,1%) and segmental colectomy (0 - 4%) in elderly IBD patients. Elderly UC patients were less likely to undergo surgery compared to younger UC patients (5,9 vs 18,2%) [39]. However, if UC is severe, early colectomy is recommended for elderly patients in order to reduce complications [40]. The surgical technique has little influence on post-operative outcome. In UC restorative proctocolectomy with ileo-anal pouch is the technique of choice at all ages (pouch failure rates similar in young, adult and elderly patients). In CD patients the necessity of surgery appears to be lower with a higher age at the onset of disease. As it happens for medical treatment even for surgery there may be significant incidence of complication in the post-operative period in older IBD patients: age, type of admission, nutritional status and comorbidities are associated with increased post-operative mortality [41] and for this reason general health conditions should be carefully evaluated possibly referring to a multidisciplinary care for a more optimized disease management [42].

Conclusions

Management of IBD in elderly people is challenging: it takes more time to diagnosis, misdiagnosis is common because of several diseases that may mimic IBD, treatment in this fragile population is difficult and often suboptimal because of comorbidities, reduced adherence to therapies and cognitive decline, but above all management requires personalization for a good balance between risks and benefits. Data in the elderly IBD patients are still lacking and only future prospective studies with clear end points will help decision making and improve outcomes.

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