



Treatment of diverticular disease, targeting symptoms or underlying mechanisms

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Abstract

Diverticular disease (DD) is a highly prevalent disease in western industrialized countries that encompasses a complex set of disorders. Because of its complexity and heterogeneity, both from a pathogenic and a clinical point of view, the management of this disease represent a challenge in clinical practice. This review aims to analyze and summarize the most recent evidence on the medical strategies for DD, considering separately the different stages of the disease, from prevention of diverticula formation to treatment of acute diverticulitis and prevention of recurrences. Based on some evidence, dietary fiber is useful to prevent diverticula formation and in diverticulosis, with no pharmacological treatment in these settings. Treatment of symptomatic uncomplicated diverticular disease as well as primary prevention of acute diverticulitis is based on probiotics, fibres, mesalazine and rifaximin, individually or as combination therapy, although a standard approach has not yet been defined. On the contrary, in acute diverticulitis (AD) recent acquisitions have clarified and standardized the role of systemic antibiotics, reserving its use only to complicated forms and in selected cases of uncomplicated disease. Secondary prevention of AD is essentially based on mesalazine and rifaximin but, despite promising results, no strong evidence have been produced. To date, grey areas remain in the medical management of DD.

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Introduction

Diverticular disease (DD) is a complex and heterogeneous condition that is not merely represented by acute diverticulitis (AD) but is characterized by different clinical scenarios, ranging from asymptomatic diverticulosis to acute episodes of inflammation and severe complications [1].

In the United States, DD is the eighth most important gastrointestinal (GI) disease in terms of healthcare costs [2], and AD is a relevant cause of hospitalization and mortality—with increasing prevalence among the general population in industrialized countries [3].

Taking into account the complexity of the disease, the wide spectrum of manifestations, the social and economic burden, it is essential to devise appropriate therapeutic strategies and correct management.

Several guidelines have been produced in recent years but the therapeutic aspects of DD have not been completely defined. In addition, in clinical practice, very often empirical and sometimes inappropriate choices are made.

The aim of the present review is to summarize the evidence emerged in the last few years.

In our opinion, the DD therapy should focus on the following goals (Figure 1):

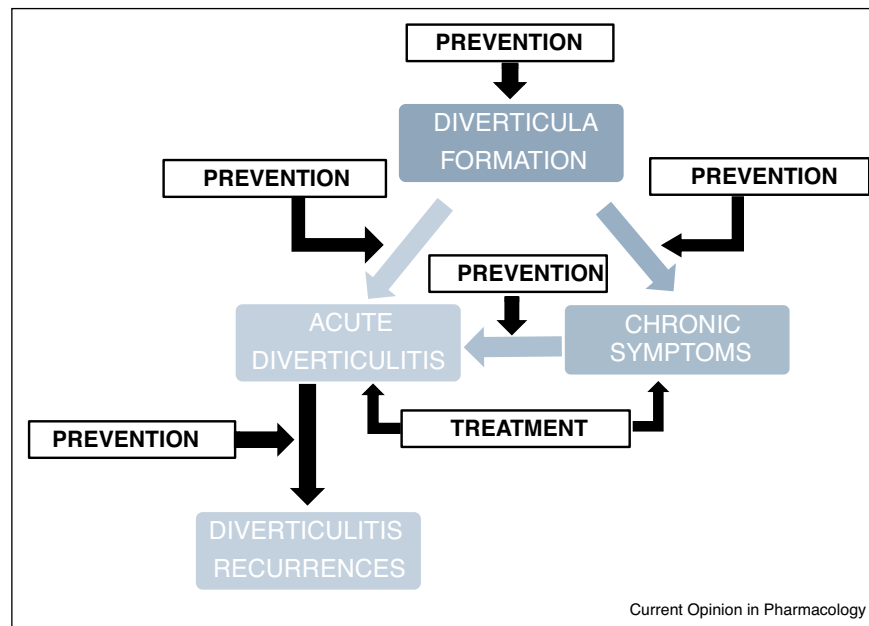
- Prevention of diverticula formation;
- Prevention and treatment of chronic GI symptoms;
- Prevention of AD and its complications (primary prevention);
- Treatment of AD;
- Prevention of AD recurrence (secondary prevention)

Considering this approach, pharmacologic strategies should be targeted to treat both the pathophysiological mechanisms of the different stages of DD and its chronic symptoms.

Formation of diverticula

Considering the high prevalence of diverticulosis in the general population (up to 65% of people aged 65 years and over) [4] and the likelihood of having AD (about 1–4% of

Figure 1



Main strategies of the pharmacologic treatments in DD. Prevention strategies aim to prevent diverticula formation, development of chronic symptoms and acute diverticulitis (first episode or recurrences, primary and secondary prevention respectively). Treatments aim to relief chronic symptoms and resolve acute diverticulitis.

subjects) [5], it seems reasonable to adopt measures to prevent mucosal herniation and formation of diverticula.

Traditionally, diverticulosis has been considered the result of constipation secondary to dietary habits typical of industrial countries—that is poor in fiber and rich in refined food, with consequent increase in colonic pressure and delay in colonic content transport, according to the model proposed by Painter *et al.* [6]. Taking into account this physio-pathological setting, a high fiber intake should be encourage to favor increasing stool weight thus reducing transit time [7].

An adequate fiber intake has been estimated by the Academy of Nutrition and Dietetics to amount to 25/38 g daily for adult women and men, respectively, to reduce the risk of several chronic conditions, including digestive ones. In the United States, the mean intake is 17 g/day, and only 5% of population meets the above criteria [8].

However, in the last years, the fiber hypothesis has been challenged. A recent cross-sectional, colonoscopy-based study, failed to find any association between low dietary fiber intake and diverticulosis, comparing the highest quartile to the lowest (mean intake 25 versus 8 g/day). Contrary to commonly assumptions, the authors did not describe a positive association between lower bowel movements or hard stool and diverticulosis [9].

Prevention and treatment of lower chronic GI symptoms

Disorders due to symptomatic uncomplicated diverticular disease (SUDD) consist of recurrent lower abdominal pain or discomfort associated to changes in bowel habit. In a past research [10] in a large cohort of men, the risk to develop symptomatic disease was reduced in subject with high daily consumption of fiber (relative risk (RR) = 0.58; 95% CI 0.41, 0.83; P for trend = 0.01 for men in the highest compared with the lowest quintile of dietary fiber), particularly for cellulose fiber, which is naturally present in high percentage in vegetables and fruits rather than in cereals. On the contrary, a high consumption of red meat and total fat increased the risk of symptoms.

The management of chronic symptoms remains uncertain [11,12] and a definitive algorithm has not been established. The pathogenesis of symptoms in SUDD is complex and partially overlaps with that of the irritable bowel syndrome (IBS). The therapeutic strategies commonly utilized act on the underlying mechanisms considered responsible of symptoms pattern (Figure 2).

Fibers are considered an option for the treatment of recurrent lower GI symptoms although the mechanisms underlying their therapeutic benefit are not completely known.

In 2012 Ünlü *et al.* made a systematic review of the literature regarding the use of dietary fiber in SUDD

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