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Review Article

A Dilemma for *Blastocystis*: Asymptomatic or Symptomatic Infection in Humans

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Abstract

Blastocystis presents a great challenge to parasitologists and clinicians to determine whether it is truly an enteropathogen or not and treatment is required if it is observed in symptomatic patients, because even without any treatment patient recovery and improvement has been noted. *Blastocystis hominis* is the most common protozoan parasite found in patients with gastrointestinal symptoms and also in healthy individuals. Communities with poor hygiene, lack of safe water supply and proper sewage system show a higher prevalence. Although its distribution was almost equal in a study; 53.6% asymptomatic and 46.4% symptomatic, but in a different study from Turkey, 70.2% of patients were found symptomatic. According to some reports, in children *Blastocystis* infection should be considered as a prominent causative agent of gastrointestinal disturbances. *B. hominis* has been established as a probable causal agent in patients of Irritable Bowel syndrome. Several issues about this parasite such as the clinical relevance, pathogenicity and the need for treatment are much debated and still unresolved. Metronidazole appears to be the most effective drug for treatment of *Blastocystis* infections despite some evidence for treatment failure. In such circumstances, nitazoxanide and TMP-SMX may be considered as second choice of drugs.

Keywords: *Blastocystis; B. hominis; Blastocystis hominis; Irritable Bowel syndrome; Metronidazole; Nitazoxanide*

Abbreviations

IBS: Irritable Bowel syndrome; TMP-SMX: Trimethoprim-Sulfamethoxazole

Introduction

Blastocystis spp. are considered as a highly controversial parasite because it has been variably remarked as a commensal and pathogen in humans. Clinicians and parasitologists have for decades wondered whether to consider it as a truly enteropathogen or not and whether treatment is required if it is observed in symptomatic patients, because even without any treatment patient recovery and improvement has been noted. Treatment is needed in most of patients due to persistence of symptoms, though it is associated with self-limiting condition [1,2].

Blastocystis spp. are worldwide distributed, especially in tropical and subtropical regions. As compared with developed countries, developing countries have a higher prevalence and also it widely varies in different regions of the same country. Communities with poor hygiene, lack of safe water supply and proper sewage system show a higher prevalence. However, infection is reported in all communities and different socioeconomic groups [3-6]. Despite of being one of the most common human intestinal parasites in the developing countries, current knowledge about this protozoan is incomplete and contradictory. Several issues about this parasite such as the clinical relevance, pathogenicity and the need for treatment are much debated and still unresolved [7].

This review discusses issues of *Blastocystis* in gastrointestinal disorders, its clinical relevance and diagnosis, and also provides a brief overview of antimicrobials used to target this organism.

Clinical Significance

Blastocystis is worldwide distributed and often reported as the most common intestinal protozoan. *B. hominis* is the most common in humans, has a higher prevalence (30 - 50%) in developing countries as compared to developed countries (1.5 - 10%) [3,4]. This high prevalence is related to poor hygiene, and consumption of contaminated food or water in developing countries [8].

Although *Blastocystis* was first described approximately 100 years ago, its pathogenicity and clinical relevance remains controversial. Several researchers considered it as a commensal organism, others think it is pathogenic [4,5,9]. There is lack of certain opinion to whether patients have *Blastocystis* infection are symptomatic or not. The distribution was almost equal in a study; 53.6% asymptomatic and 46.4% symptomatic [10]. But not like most research, in a study from Turkey, 70.2% of patients were found symptomatic [8]. According to some reports, in children *Blastocystis* infection should be considered as a prominent causative agent of gastrointestinal disturbances. In some studies, from different countries of world, the prevalence rates of *Blastocystis* infection among pre-school children were reported as 25% in Jordan and 18.9% in Venezuela; among the primary school children, they were 6.7% in Libya, 13.5% in Thailand, 16% in Venezuela and 22.4% in Colombia [11].

B. hominis as a causative agent of intestinal diseases has not yet been conclusively shown, but it has been associated with gastrointestinal disturbances such as nausea, vomiting, flatulence, discomfort, cramps, diarrhoea, abdominal pain, and is also linked to irritable bowel syndrome (IBS). Fever, urticaria and anorexia has also been reported in some cases [4,5,9]. It may cause acute, or chronic illness with symptoms persisting for several years. Travelers, immigrants, those living with poor sanitation, and people in close contact with animals are susceptible to *Blastocystis*- associated disorders. In immunocompetent as well as in immunocompromised patients, a significant correlation between *Blastocystis* and gastrointestinal symptoms was detected [4,9,12].

Pathogenicity of *Blastocystis* which is a debatable topic has stimulated interest among researchers to study the epidemiological and molecular aspects of this parasite. In various studies, it has been shown that there is association between its pathogenicity, with genotypic characteristics and serious illnesses like Irritable Bowel Syndrome as well as colorectal cancer [13]. Role of *B. hominis* as an etiological agent of gastrointestinal disorder has been linked to symptoms such as chronic diarrhea and functional gastrointestinal disorder i.e. Irritable Bowel syndrome (IBS) which manifests with recurrent abdominal pain associated with changes in bowel habit [14,15].

B. hominis has been established as a probable causal agent in patients of Irritable Bowel syndrome [16]. Prevalence of *B. hominis* as a causal agent of IBS varies with geographical region ranging from 2.6% to 100% [16-18]. In Indian subcontinent, clinical studies on IBS so far have been reported in few studies with a prevalence of 4% to 4.2% [19,20].

Morphology

Blastocystis is highly refractile appearing like fat granules and often not identified since it is not looked for. The sizes are variable since it has different morphological forms [7]. Four different morphological forms have been described i.e. vacuolar, granular, cystic and amoeboid [4]. The vacuolar and amoeboid forms are most commonly observed in fecal specimens [21]. The amoeboid form would resemble a leukocyte. The organism is anaerobic, so it easily dies on a slide [7]. In fecal specimens, *B. hominis* is brightly refractile and of widely variable in diameter (4 - 15μ) and contains visible mitochondria and sometimes a vacuole [22].

Diagnosis

Diagnosis is routinely made by detecting characteristic forms of the protozoan in fecal specimens. Sometimes it may be difficult to identify the parasites in wet mounts. Lugol's iodine mount and permanent stained preparations of fecal smears with acid-fast, trichrome, Field's and Giemsa are the most useful methods. Among these, trichrome is the most commonly used, and the most sensitive stain com-

pared with other stains [4,5]. Previous epidemiological studies suggested that *Blastocystis* spp. rapidly multiplies in a culture medium with serum supplementation after 24 - 48 h of cultivation [23]. It is a strict anaerobe and requires the presence of bacteria for growth. Optimal growth of this organism occurs at 37°C at neutral pH [21]. Recently, molecular diagnostic techniques have been used in the diagnosis of this parasite, and the Real-Time PCR is found to be highly sensitive and specific for *Blastocystis* infection [24-26].

Treatment

In instances where treatment is required, metronidazole is the most commonly prescribed antibiotic. It is prescribed in different dosage regimens ranging from 250 mg to 750 mg 3 times a day, to 1.5 grams per day for 10 days. It may be used alone or in combination with other drugs like paromomycin or cotrimoxazole [4,14,28]. Large scale treatment trials are lacking as a result of this uncertainty surrounding of its pathogenic role. Despite the self-limiting nature of this infection, treatment of symptomatic patients is often warranted [11,29]. Recent data suggests that *Blastocystis* infection causes symptoms frequently. Therefore, treatment should be limited to patients with persistent gastrointestinal symptoms subsequent to a complete work up for alternative infections [30]. In symptomatic patients, studies reporting therapeutic improvement concomitant with parasite clearance substantiates the pathogenic role of the organism and hence, treatment required [4,31,32].

TMP-SMX has also been shown to have good effects on the clinical symptoms and the cure rate in patients with *Blastocystis* infection. In some reports, it is considered to be better than metronidazole in the treatment without the side-effects [33]. Nitazoxanide, a 5-nitro thiazole, broad spectrum anti-parasitic drug is also found to have potent activity against *Blastocystis* infection [34-36]. Metronidazole treatment failures in Blastocystis infection may well respond to nitazoxanide [27,36]. *Saccharomyces boulardii* is a non-pathogenic yeast, has proven effective in gastrointestinal disorders with predominant inflammatory conditions, indicating its supportive role in management of symptomatic Blastocystis infection [30,37].

Conclusions

Blastocystis hominis is the most common protozoan parasite found in patients with gastrointestinal symptoms and also in healthy individuals. In several studies, it has been shown that it is a common protozoan infection with varying levels of pathogenicity. This parasite is worldwide distributed, especially in tropical and subtropical countries. *Blastocystis* has a wide variety of reservoirs, and these make people more vulnerable to the infection. A comprehensive parasitological examination must be carried out in all symptomatic and asymptomatic individuals to understand the real prevalence of the disease. A number of drug treatment options are available for symptomatic *Blastocystis* infections. Metronidazole appears to be the most effective drug for treatment of *Blastocystis* infections despite some evidence for treatment failure. In such circumstances, nitazoxanide and TMP-SMX may be considered as second choice of drugs. Treatment should be instituted if the diarrhoea and other gastrointestinal symptoms are persistent and no other causative pathogen is identified in fecal samples.

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Conflict of Interests

All the authors declare that there are no conflicts of interest related to this review article.

Informed Consent

Consent was obtained from all individual participants included in the presentation of review article.

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