Bile Acid Diarrhoea

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Contributor: Evette Hillman

Bile acid diarrhoea (BAD) is a widespread gastrointestinal disease that presents as chronic watery diarrhoea as well as bloating and abdominal pain. This condition is often misdiagnosed as irritable bowel syndrome and is estimated to affect 1% of the United Kingdom population alone. BAD is associated with excessive bile acid synthesis secondary to a gastrointestinal or idiopathic disorder (also known as primary BAD). Current treatment includes diet changes and bile acid sequestrant medication.

Keywords: bile acid diarrhoea ; irritable bowel syndrome ; SeHCAT scan ; Bile Acid Sequestrants

1. Overview

Bile acid diarrhoea (BAD) (previously referred to as bile acid malabsorption or bile salt malabsorption) is a condition that predominantly presents as chronic watery diarrhoea as well as bloating and abdominal pain [1]. A recent survey by Walters et al. (2020) observed that 86% of participants experienced frequent bowel movements, often more than 6 times a day [2]. In a different survey, Bannaga et al. (2017) reported that many BAD patients often experience tiredness, low energy levels and a lack of concentration [3]. Sufferers reported the negative impact BAD had on their social life and ability to work (which could lead to the loss of employment), and over 90% also felt a negative impact on their mental health. Although this condition is not life-threatening, the survey revealed that depression, isolation, helplessness and low self-esteem are very common among patients living with BAD, often leaving individuals housebound [3]. While the exact figures are not known, it is estimated that up to 1% of the population in the United Kingdom (UK) have primary BAD [4]. If non-primary BAD patients are included, this potentially results in an excess of 700,000 individuals in the UK alone [5]. Smith et al. (2000) estimated that over one-third of patients diagnosed with irritable bowel syndrome (IBS) actually suffer from BAD [6]. Consequently, BAD could have a wide-reaching economic impact due to absence from work through sickness and the cost of continued care.

BAD has several different causes that fall under one of three types [7]:

- Type I, when the ileum is damaged due to inflammation or surgical removal.
- Type II, is idiopathic and is also known as “primary BAD”.
- Type III, results from another disease or condition (such as gallbladder removal).

In 2009, Walters et al. proposed that primary BAD (type II) was not a result of reduced or impaired absorption but in fact resulted from unregulated bile acid synthesis [8]. Studies demonstrated that patients with BAD had significantly higher levels of 7α-hydroxy-4-cholesten-3-one ((C4), a bile acid precursor) and significantly lower levels of fibroblast growth factor 19 ((FGF19), a hormone that down-regulates bile acid synthesis) compared with healthy individuals [8]. Similarly, the authors also showed that patients with secondary BAD (type I and III) had lower levels of FGF19 in their blood serum compared with that in healthy subjects [8][9][10]. This excessive bile acid synthesis results in the insufficient absorption of bile acids in the ileum, causing the increased transit of bile acids into the colon. High levels of bile acid in the colon trigger a rise in water secretion to combat irritation, which prevents stool from properly forming in the lumen, leading to diarrhoea. Several studies have reported the importance of bile acids in a number of gut-related diseases [11]. Despite these observations, the cause of low serum levels of FGF19 and the consequent excess bile acid synthesis remains widely unknown.

2. Diagnosis

The selenium-75-homocholic acid taurine (SeHCAT) scan (a nuclear medicine test) is considered the gold standard for diagnosing BAD, as it has high sensitivity and specificity [12]. The parameters for diagnosing BAD are: less than 5% bile acid retention indicates severe BAD; between 5 to 10% bile acid retention indicates moderate BAD, and between 10 to 15% bile acid retention indicates mild BAD [4]. Despite the SeHCAT scan giving the highest diagnostic accuracy for BAD, it is not widely used or licensed in many countries (including the United States of America (USA)). In the absence of a SeHCAT scan, doctors often prescribe bile acid sequestrant medication as the response to treatment can provide a diagnosis. Bile acid sequestrants bind to excess bile acids with a high affinity preventing irritation in the large intestine. Frequently treatment for BAD is not administrated because it is often misdiagnosed as diarrhoea predominant IBS (IBS-D) due to the similarity in the clinical presentation of both diseases. Indeed, Bannaga et al. (2017) reported that 44% of respondents had experienced symptoms for more than five years before diagnosis, with a range of between one and thirty years [3]. IBS is a multifactorial spectrum disease, which can be triggered by both environmental and genetic factors, although the exact cause of IBS is widely unknown [13]. There is no accepted diagnostic test for IBS; however, as mentioned, there is one for identifying BAD. IBS is not to be confused with inflammatory bowel disease (IBD), which presents as chronic inflammation on the GI tract.

3. Treatment

Current treatment for BAD includes diet changes and medication; however, these only treat the symptoms and do not treat the cause of the disease. Physicians advise a diet with a reduced-fat intake of 40 g of fat per day [14]. To date, there have been no randomised trials that have evaluated different dietary regimes with BAD sufferers. Instead, observational studies seem to suggest that low-fat diets are beneficial. Low-fat diets are thought to result in reduced bile acid synthesis and could alter the microbiome, all leading to less severe symptoms in some cases [15][16][17]. Current treatment guidelines for BAD have not significantly improved since the 1960s, and sequestrants can have adverse effects such as constipation, bloating, nausea and abdominal pain (especially when combined with other medications) [18][19]. The pathophysiology of BAD is not fully understood, and, to date, a clinically effective cure remains elusive.

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