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Research Progress on Small Intestinal Bacterial Overgrowth in Liver Cirrhosis: From Diagnosis via Methane and Hydrogen Breath Tests to Clinical Management

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Abstract

In this paper, the author has tried to present a systematic review of the current research developments on the topic of small intestinal bacterial overgrowth (SIBO) in liver cirrhosis, focusing on its pathophysiology, non - invasive diagnosis, and its impact on patient outcomes. It discusses the mechanisms by which the changes in the intestinal environment consequent to cirrhosis promote abnormal bacteria growth in the small intestine by a synthesis of recent basic and clinical evidence. In addition, it discusses the mechanisms where the increased intestinal permeability, inflammation, and bacterial translocation worsen the progression of diseases and complications. It also evaluates the applicability, limitations, and optimization plans of the hydrogen breath test of this category of patients. The existing evidence indicates that SIBO is strongly common among the patients with cirrhosis and is closely associated with the level of disease and its complications manifested as hepatic encephalopathy, infections, and nutritional disorders. Meanwhile, hydrogen breath test is one of the main screening tools that are suitable to be utilized on cirrhotic patients. To sum up, SIBO has an important role in the course of cirrhosis and emergence of related issues, and it has probable potential in the early identification of high - risk patients and treatment recommendations.

Keywords

Breath hydrogen test; Cirrhosis; Small intestinal bacterial overgrowth; Diagnosis.

1. Introduction

Small intestinal bacterial overgrowth (SIBO) is a clinical syndrome that is characterized by an abnormally high number of cells and/or changes in the microbial flora in the small intestine [1]. It is typically characterized by a sequence of non - specific gastrointestinal symptoms, including- abdominal distension, diarrhea, abdominal pain, steatorrhea and malnutrition [2]. In physiological conditions, the bacterial load of the small intestine is usually below 103 CFU/mL. However, in case of improper colonization and growth of the colonic - type bacteria within the small intestine, fermentation of the luminal materials prematurely occurs leading to a loss of the absorption of fat and deficiency of proteins, minerals and vitamins [3]. Along with the recent developments in the gut microbiome studies over the recent years, SIBO has gained recognition as an extremely relevant pathological element of several systemic

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illnesses, such as irritable bowel syndrome, liver cirrhosis, and anxiety - depressive illnesses, chronic obstructive pulmonary disease [4]. SIBO incident and course is an essential factor in worsening liver damage. There is an indication supported by epidemiological studies that even though the prevalence of SIBO in general population is not especially high, the prevalence is much greater among patients with gastrointestinal motility disorders, structural anomalies, bile acid metabolic disruption, or immune dysfunctions.

A meta -analysis on the relationship between SIBO and liver cirrhosis found that the favorable frequency of SIBO in patients with cirrhosis is between 34.8 and 47.1% [5]. In addition, patients exhibiting SIBO have a 6.83 fold increased likelihood of getting cirrhosis than non - SIBO patients and this is largely higher than the rate in healthy controls [6]. This high rate suggests that SIBO is not just a mere coincidence with cirrhosis. In their place, these intestinal - obtained pathological alterations could be a critical mechanistic linkage in hepatic inflammation and fibrosis development.

The liver cirrhosis leads to intestinal motility arrest and congestion of the gastrointestinal system which consequently alters the structure and activity of the intestine. At the same time, a decrease in the amount of bile acids directly and indirectly results in the dysbiosis of gut microbiota [7], which is expressed as a decrease in the diversity of the microbiome and individual species, over -cultivation of harmful species, and uncoordinated metabolic activity of the microbiome [8]. Within such an unequal environmental context, the small intestine, which constitutes the transitoric area between the stomach and the colon is especially sensitive to the unnatural bacterial colonization. This weakness is explained by a decrease in peristalsis, decrease in the flow of bile, the violation of the barrier of the gastric acid, and the edema of the mucosa in connection with portal hypertension, which eventually leads to SIBO.

Bacterial proliferation of the small intestine has the potential of triggering the gut-liver axis by generating endotoxins, ammonia and various pro-inflammatory mediators and therefore, inducing or exacerbating systemic inflammatory reactions. This has been greatly associated with hepatic encephalopathy, spontaneous bacterial peritonitis, ascites as well as an increased risk to infection [9]. SIBO in patients with cirrhosis, thus, can no longer be viewed as a comorbid condition whereas it is increasingly viewed as a decisive factor that influences disease progression and clinical prognosis.

Currently, a quantitative cultivation of duodenal aspirates retrieved endoscopically at the end of the proximal small intestine distal to the ligament of Treitz is the gold -standard technique of diagnosing SIBO with the bacteria count present in the culture of the duodenal aspirates considered positive when 105 CFU/mL[10]. Nonetheless, the scope of conventional endoscopy is limited, and this feature, combined with its invasive nature, inappropriate reproducibility, and technical complexity make the latter approach difficult to implement on a wide scale in the routine clinical practice and, therefore the application of it is limited dramatically.

Conversely, the hydrogen breath test (HBT) has been one of the most commonly used diagnostic tools in the diagnosis of SIBO in clinical and scientific settings due to the non - invasiveness, simplicity, and high reproducibility [11]. The HBT is based on the principle that the hydrogen or methane is produced due to fermentation of carbohydrates by the bacteria in the small intestine. The gases so taken up are carried in the blood and the excess gas is released in the lungs. Therefore, the indirect indication of the overgrowth of bacteria in the small intestine is demonstrated by the measurement of changes in gas concentrations in the exhaled gases. Despite the continuing controversy of the diagnostic thresholds and values of interpretation, the usefulness of HBT in cirrhotic groups has gained increasing attention particularly in epidemiological screening, risk stratification, and therapeutic surveillance.

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Even so, some gaps still remain in the current body of literature on SIBO when compared to liver cirrhosis. SIBO clinical implications in relation to various phases of cirrhosis and between various cirrhosis - related complications have not been synthesized. Moreover, the translation of the evidence - based findings on the hydrogen breath test results to the practice-based tools to support clinical management and make therapeutic decisions is still under-evidence - based consensus.

In this regard, this paper aims to set out to thoroughly review the current developments of the study on SIBO among liver cirrhosis patients. Some special consideration will be placed on the diagnostic use of the hydrogen and methane breath tests and the implication of the tests on the clinical management. It aims at offering a theoretical foundation of future mechanistic research and development of personalised therapeutic plans.

2. Pathophysiological Correlation between Liver Cirrhosis and Small Intestinal Bacterial Overgrowth

2.1 Mechanisms through Which Cirrhosis - Associated Factors Contribute to the Progression of Small Intestinal Bacterial Overgrowth

SIBO among patients with cirrhosis of the liver is not a coincidental phenomenon, but the result of the interplay between various pathophysiological changes. The hemodynamic deviation which is the most important in cirrhosis, portal hypertension provokes ischemic circumference of the gastrointestinal mucosa and hypoxia, congestion of the intestinal wall with venous vessels, edema of the mucosa, and microcirculatory disturbances. These alterations destabilize the integrity of the intestinal barrier and increase intestinal transit time, thus creating a favorable condition of abnormal gastric colonization in the small intestine [12]. The studies have also shown that with increasing hepatic functional impairment, as indicated by Child - Pugh classes, the occurrence of small intestinal motility disorders increases, indicating that there exists a positive relationship between hepatic functional impairment and the risk of SIBO [13].

Disturbed gastrointestinal motility can be regarded as the most significant direct predisposing element of SIBO in patients with cirrhosis. Autonomic dysfunction is also a common condition with liver cirrhosis and consists of sympathetic hyperactivity, and parasympathetic suppression that slowly affects the digestive system. Research has stated that about 3/4th of the liver disease complex patients having autonomic neuropathy manifest through delayed gastric emptying [14]. Furthermore, the cirrhotic patients have a low frequency of migrating motor complexes in the small intestine and extended oroceal transit period, which enables the pathogenic colonization of colonic bacteria in the proximal small bowel [15]. The presence of intestinal mucosal edema caused by ascites and hypoalbuminemia further worsens the motility the faults and establishes a combined structural and functional environment which enhances bacterial overgrowth.

In addition, disruptions in bile acid metabolism have a critical part in SIBO related to cirrhosis. In addition to their common effect of lipid digestion, bile acids have strong antimicrobial properties in the intestinal lumen [16]. Through decreased bile acid production and impaired enterohepatic circulation in cirrhotic patients, this antibacterial barrier is weakened in the small intestine and allows a change in the microbial community composition away toward endotoxin -producing species. Moreover, bacterial deconjugation of the bile salts may increase the inactivation of bile acids and subsequently, increase the further bacterial proliferation and amplify a positive feed back loop that is self-enhancing [17].

Weakness of immune defense is another important but often ignored causative factor. Liver cirrhosis is linked to impaired proliferation of gut - related lymphoid tissue, lowered release of immune barrier elements like secretory immunoglobulin A and enzyme, and weakened

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innate immune reactions leading to a considerable decrease in the capacity of the small bowel to stop irrelevant translocation of bacteria [18]. In this case, acid - suppressive agents, such as proton pump inhibitors and H2 receptor antagonists, to weaken the gastric acidic barrier further exacerbate the problem and have been reported in several studies to be a highly correlated risk factor of SIBO [19].

2.2 Potential pathophysiological mechanisms by which SIBO participates in the progression of liver cirrhosis

SIBO mitigates the process of liver cirrhosis that is beyond the bowel lumen and spreads hepatic pathology throughout the gut - liver axis. SIBO plays a major role in the increase of intestinal permeability: bacterial excessive growth and its metabolic products affect the composition of the epithelial tight - junction proteins, creating a model of the leaky gut through which the other bacteria and endotoxins enter the mucosal barrier [20]. Endotoxins, bacterial DNA and other pathogen - associated molecular patterns then ultimately access the liver through the portal circulation triggering Kupffer cells and intrahepatic immune cells and activating NF - -kb signaling cascades through TLR - 4 and TLR - 2 receptor pathways. Chronic low -grade endotoxemia leads to a chronic inflammatory condition which promotes the activation of hepatic stellate cell and deposition of extra-cellular matrix thus hastening the development of liver fibrosis [21].

The deconjugation of the bile salts also causes further impaired absorption of lipids and the fat - soluble vitamins. At the same time, too much fermentation by small intestinal bacteria produces large amounts of gas, thereby resulting in bloating and pain in the abdomen, which, in turn, inhibits appetite and reinforces competitive intake of nutrients. These processes cause malnutrition, sarcopenia, and hypoalbuminemia among patients with cirrhosis with the ultimate result of causing an excessive nutritional imbalance [22]. Other studies also put forward that SIBO can be linked to more ethanol production endogenously and a higher level of oxidative stress therefore causing an extra metabolic load on the liver [23].

It has been shown that of patient samples with decompensated cirrhosis of various etiologies, neither the percentages of SIBO nor lactulose hydrogen breath test results are significantly different. Specifically, it is evident that the prevention of SIBO in alcoholic cirrhosis is no less than that in viral cirrhosis, which implies that the evolution of SIBO is not firmly linked to the source of liver cirrhosis.

2.3 The interaction between the two and its association with cirrhosis-related extrahepatic complications

These mechanisms have a vicious cycle of effects at the clinical level, whereby SIBO is promoted by cirrhosis, systemic inflammation, and portal hypertension are exacerbated by SIBO, and the reverse of the change occurs. Liater the appearance of SIBO, there is an increased number of ammonia -producing intestinal bacteria among the patients with cirrhosis. Within the setting of defective hepatic clearance, this leads to hyperammonemia and oxidative stress thus triggering or worsening hepatic encephalopathy. It has been shown in a meta - analysis that SIBO is strongly associated with hepatic encephalopathy with the risk of SIBO in patients with hepatic encephalopathy compared with those without encephalopathy being 4.43x, indicating that SIBO is most likely to be one of the precipitating factors [24].

It has been found that SIBO facilitates bacterial translocation, whereas, the growth of non - dominant intestinal flora can produce excessive endotoxin that may mediate mechanical and mucosal damage of the gut directly or indirectly, which has a pathologic basis to spontaneous bacterial peritonitis and systemic infections. The systemic inflammatory state of SIBO in cirrhotic patients is associated with the substantial increase in concentrations of serum

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lipopolysaccharide - binding protein, which is particularly evident in cirrhotic patients with decompensated cirrhosis [25].

Altogether, SIBO is not only a complication of an intestinal dysbiosis that is associated with cirrhosis but also a significant factor that predetermines the further development of the diseases and the appearance of their complications. This bidirectional pathophysiological interaction can be better understood to be a strong theoretical framework in determining high - risk cirrhotic patients in terms of hydrogen breath testing, and apply specific therapeutic changes.

3. Current Applications of the Hydrogen Breath Test in the Diagnosis of SIBO among Patients with Liver Cirrhosis

3.1 Principles of the Hydrogen Breath Test and Standard Interpretation Criteria for the Diagnosis of SIBO

Hydrogen breath test (HBT) is the most widely used currently non - invasive diagnostic tool of SIBO. It primarily includes two tests namely the glucose hydrogen breath test (GHBT) and the lactulose hydrogen breath test (LHBT) [26]. The theoretic rationale is that one exhalation by a human contains more than 500 gaseous species, of which nitrogen, carbon dioxide, carbon monoxide, methane (0% to 54%), hydrogen (0% to 86%), a large number of volatile organic substances, water vapor (metabolism of body fluids) and the oxygen absorbed but not metabolized being inhaled. Among them, only methane and hydrogen are a result of the fermentation of carbohydrates by the bacteria within the intestine and cannot be synthesized by human cells. When produced in the gut, the gases are then sucked into the blood to be later discharged through the lungs thus indirectly reflecting the bacteria load in the small intestine [26],[27].

In terms of the interpretation criteria, the main criteria used in studies today and by the international guidelines are the following: after the oral intake of 75 g of glucose or 10g of lactulose with water, an increase in breath hydrogen by 20ppm or more over the baseline in 90minutes or an increase in methane by 10ppm or more shall be considered an indication of a positive SIBO result [28].

The proximal jeunum rapidly carries out its absorption of glucose in a comprehensive way giving it great specificity. Nonetheless, glucose - based tests might not recognize distal SIBO, as only small quantities get to be absorbed in the distal small intestine. Comversely, lactulose is a non -absorbable carbohydrate which may pass along the whole small intestine and hence bacteria fermentation at the end parts of the small intestine. However, it is more likely to be affected by the intestinal motility and thus there is always a risk of false - positive results [29]. Jirapinyo et al. [30] used radiolabeled tracers to determine the time taken by lactulose to the cecum and found false - positive result of 27.8% using 90 -minute cutoff. As a result there are still a lot of controversy to do with the substrate transit time to the cecum and the diagnostic levels of hydrogen and methane.

3.2 Potential impacts of cirrhosis - associated physiological changes on the outcomes of hydrogen breath tests

Liver cirrhosis patients have a set of physiological alterations that can pose a significant obstacle to identifying the accuracy of SIBO by measuring hydrogen breath, which puts it at a high risk of being excluded as a diagnostic tool in the patient group. abnormal small intestinal transit and delayed gastric emptying, each of which is a common outcome of portal hypertension, have the potential to significantly change the time at which test substrates enter the small intestine or colon, therefore, changing the peaks in breath curves [31].

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A meta -analysis study has shown that, for cirrhotic patients whose undergoing evaluation of SIBO is performed, the percentage rate of LHBT is more prevalent than GHBT. Its pathophysiology is presumably linked to cirrhosis - related small intestinal dysmotility. Glucose only taken orally can be wholly absorbed before it reaches the segments with bacteria overgrowth thus giving false - negative results on GHBT [32].

In addition, edema of the intestinal wall and disruptions in microcirculation as a result of portal hypertension can alter the kinetics of gas absorption and excretion with the result of reduced or slowed peaks of breath hydrogen or methane, and therefore, making the interpretation of the results more ambiguous. Besides, cirrhotic patients usually come out with confounding variables which include; the long term use of acid - suppressive drugs, pre-exposure to antibiotics, and dietary modifications. Such variables have the potential to cause serious changes in gut microbial makeup and gas - generating structures, finally compromising the reproducibility and reliability of hydrogen breath testing [33].

3.3 Research Progress on Enhancing the Diagnostic Efficacy of the Hydrogen Breath Test in Patients with Cirrhosis

Several optimization techniques have been proposed to improve the diagnostic capacity of the hydrogen breath testing on liver cirrhosis patients in the recent years. To begin with, the co-detection of hydrogen and methane is considered to be able to significantly enhance the rate of SIBO detection [34]. There is a subgroup of patients whose major producer is methane and, therefore, only measuring hydrogen will be contra-indicative of diagnosis. Dual - gas analysis is more detailed analysis of the intestinal fermentation and allows to obtain combined interpretation with clinical background.In addition, proper pre - test preparation is important as it puts downward limit on measurement variability and increases accuracy. The patients should be advised to avoid fiber - rich foodstuffs and high - protein foods as a rule before a test and also to fast and avoid smoking at least 12 hours before a test [35].

Second, time efficiency in terms of sampling period and interpretation of breath curves have turned out to be the central areas of concern in modern studies. Other researchers have also suggested increasing the test duration and involve oro - cecal transit time, which enables distinction between early and late peaks to be dynamic rather than using fixed single - time - point thresholds, which reduces misclassification due to motility abnormalities [36]. Based on this, the implementation of cirrhosis - specific interpretative criteria or stratified diagnostic cut - offs should be seen as one of the promising avenues to enhance the accuracy of SIBO diagnosis in a group of patients.

4. Therapeutic Strategies and Future Research Directions for Liver Cirrhosis Complicated by SIBO

4.1 Potential Influence of SIBO on the Overall Prognosis of Patients with Liver Cirrhosis

All current data in this topic point in one direction, that SIBO is strongly associated with poor prognosis in patients of liver cirrhosis. Several studies based on the concept of hydrogen breath testing have indicated that the incidence of SIBO increases correspondingly with increased Child - Pugh classes and Model for End - Stage Liver Disease (MELD) scores. Furthermore, SIBO has an independent relationship with the severity of the disease in multivariate analyses, which suggests that it is not only a manifestation of intestinal dysbiosis but can potentially be the cause of future hepatic degradation [19],[25],[37].

Being an important part of gut - liver axis dysfunction, SIBO encourages the production of endotoxins and ammonia, increases the intestinal permeability, and activates systemic inflammatory reactions, thereby contributing to the emergence of numerous key cirrhosis -

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associated complications. One of them, in particular, is its correlation with hepatic encephalopathy (HE): Patients who are positive in SIBO are found to have markedly greater chances of developing and re-developing hepatic encephalopathy. Besides, some studies proved that SIBO interventions are potentially effective to improve neurocognitive functioning and recurrence rates, which proved SIBO to be a possibly alterable factor of cirrhosis treatment [38].

Moreover, SIBO was linked to malnutrition, hypoalbuminemia and sarcopenia. It also increases the risk of spontaneous bacterial peritonitis and systemic infections by increasing the likelihood of bacterial translocation, thus further worsening the issue of hepatic cirrhosis progression. All in all, SIBO among cirrhotic patients presents a steady association to the level of the disease rate, the burden of comorbidities, and the poor clinical prognosis. It is thus important to consider it as a significant biological indicator of gut - liver axis malfunction and prognostic risk. Early diagnosis and specific treatment of SIBO could contain significant prospects of enhancing long-run performance of patients with liver cirrhosis.

4.2 Comprehensive Intervention Strategies for Cirrhosis Complicated by SIBO

Clinical outcomes can be improved in liver cirrhotic patients through the treatment of SIBO through various mechanisms. These processes include the normalization of the intestinal microbial environment, the increased luminal motility, the recovery of the intestinal mechanical barrier, and the increase of the metabolism of bile acids. Antibiotics still remain the foundation of treatment regimens. An example of the common agents used is the rifaximin, tetracyclines, Vancomycin, metronidazole and aminoglycosides, which are majorly predatory on both aerobic and anaerobic Enterobacteriaceae family. Rifaximin is also one of these antibiotics that are widely used in patient with SIBO and cirrhosis because it has high intraluminal efficacy, low levels of systemic absorption and good safety profile.

A five - year follow - up report carried out by Vlachogiannakos et al. [39] suggested that the non - absorbable antibiotic rifaximin was significantly effective in reducing the occurrence of such complications as hepatic encephalopathy, variceal bleeding as well as spontaneous bacteriogenic peritonitis among patients with alcoholic cirrhosis. This is probably done by the elimination of intestinal bacteria that have the ability to produce urease and the consequent decreasing in the level of ammonia synthesis. Short - term treatment can also be done using other agents such as neomycin, metronidazole, and ciprofloxacin. However, the long-term administration is associated with the risks of antimicrobial resistance and adverse effects. The use of rotational antibiotic regimens has also been reported to be providing a better therapeutic effect in comparison against single - agent therapy.

The microecological modulation has become another important adjunctive therapy method over the past few years. Probiotics, Prebiotics and Synbiotics Microbiota -targeted preparations may help prevent the development of SIBO by promoting the growth of beneficial microbes, disrupting the growth of pathogenic species, recovering the integrity of the intestinal barrier and reducing inflammation. Research has also revealed that a combination probiotic therapy decreases positivity of the hydrogen breath test and alleviates the clinical symptoms of liver cirrhosis patients [40].

With respect to dietary intervention, it can be reduced by limiting the consumption of fermentable carbohydrates and a low - FODMAP diet may help in the limitation of bacterial substrates. Nonetheless, its support regarding its long term applicability in cirrhotic populations is poor [41]. Also, transjugular intrahepatic portosystemic shunt (TIPS) can modify the pathophysiological process of cirrhosis [42], moderate hepatic portal pressure with the use of nonselective β - blockers could enhance the perfusion of intestines [43]. Prokinetic agents also improve small intestinal motility and decrease gastrointestinal

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permeability, shorten transit time, and abnormal bacterial stasis that could indirectly lower bacterial translocation and the risk of SIBO.

4.3 Limitations of Existing Therapies and Emerging Directions for Novel Interventions

The research on SIBO in patients with liver cirrhosis has increased significantly in recent years. However, the present treatment approaches are limited. SIBO has a tendency towards relapse and as has been noted, patients are often positively relapsed in breath tests and the symptoms recur within months following short course antibiotic therapy. This implies that the antimicrobial suppression is not sufficient in the long-term management of the disease. Additionally, overexposure to antibiotics can also further upset the balance of microbes present in the intestine, and increase the likelihood of development of resistant strains, increasing the likelihood of infection [44]. Also, most of the available research is constrained by small samples, and scarce large - scale prospective randomized controlled trials are specifically in cirrhotic population.

It is in this light that the subsequent research is progressively focusing on more narrowly focused microbiota - based therapies. Phage therapy as a targeted antimicrobial agent can potentially selectively deactivate the pathogenic bacteria with little harm to the commensal microbiome, and this may provide a new avenue of treatment of SIBO. Transplantation of fecal microbiota which reinstates the intestinal microbial homeostasis has demonstrated therapeutic benefits in reversing cirrhosis - related dysbiosis and is under consideration as a treatment approach to long-term management of SIBO [45]. As the multi - omics technologies advance, customized approaches to the gut - liver axis collaboration and targeted microbiome therapy are expected to be considered in subsequent research.

5. Discussion and perspectives

SIBO has a significant impact on the pathogenesis, evolution of liver cirrhosis and complication range. Pathological basis of SIBO are the portal hypertension, GI dysmotility, dysregulated bile acid metabolism and compromised immune functioning related to cirrhosis. On the contrary, SIBO worsens hepatic damage and portal hypertension by destabilising the intestinal barrier, leading to bacterial translocation, increasing systemic inflammation and increasing the production of ammonia.

In addition, SIBO is significantly linked to severity of the disease, hepatic encephalopathy, malnutrition and high risk of infection in cirrhotic patients. It is an important factor that determines prognosis as well as a possible target of therapy. Thus, screening and management of SIBO in high - risk groups (in particular, in patients with decompensated cirrhosis, repeat hepatic encephalopathy, unexplained malnutrition or increased susceptibility to infections) is extremely urgent.

Quantitative small intestinal aspirate bacterial culture is still the gold standard of diagnosing SIBO. But being an invasive exercise, it has limitations on technical complexity, high cost and failure to recreates the overall bacterial milieu. Comparatively, hydrogen breath testing portrays different strengths in determining the epidemiology of SIBO, their association with the severity of the disease and temporal changes and variation prior to and after therapeutic applications. Dual - gas detection, optimization of sample time, and improved interpretation of the curve have been recommended as some of the strategies that can improve its diagnostic performance in cases of cirrhosis. However, the discrepancies in substrate choice, study design and diagnostic cut points still exist, underscoring the need to come up with cirrhosis - specific standardized criteria. Particularly, the recent developments have brought about ingestible gas - sensing capsule endoscopy that is able to detect intestinal gases in real - time.

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This method is very sensitive in measuring hydrogen and at the same time locates the anatomical sites where gas is produced and this consequently improves the accuracy of diagnosis of SIBO further [46].

Whether SIBO is only an indicator of the severity of cirrhosis or it is a pathogenic agent on its own is not clear and the causal aspect of SIBO requires further explanation with prospective and mechanistic research. Also, the long - term prognostic outcomes of existing interventions, including antibiotics, probiotics, and fecal microbiota transplantation, the therapeutic value of integrative therapies between traditional Chinese and Western medicine are yet to be confirmed through high -quality randomized controlled trials.

6. Conclusions

The paper is a systematic review of the pathophysiological processes, diagnostic developments, and clinical data about SIBO in liver cirrhosis, in which the diagnostic significance of hydrogen breath testing and its possible implications are especially emphasized. Investigating the physiological peculiarities of cirrhotic patients and their diagnostics challenges, this paper will outline the current consensus and controversies in the field, and highlight the most important research and clinical practice directions in the future. The recognition of SIBO as a recognizable and modifiable pathological agent can offer new thinking on the accurate treatment and prognosic improvement of liver cirrhosis patients.

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