Review Article

Narrative review of nutritional characteristics and supportive treatment of hepatitis B virus-related liver diseases

Weizhen Weng[1], Xiaohua Peng[2], Chang Gao[1], Youpeng Chen[1]

[1]Department of Infectious Diseases, The Seventh Affiliated Hospital of Sun Yat-sen University, Shenzhen, China; [2]Digestive Medical Center, The Seventh Affiliated Hospital of Sun Yat-sen University, Shenzhen, China

Contributions: (I) Conception and design: W Weng, Y Chen; (II) Administrative support: Y Chen; (III) Provision of study materials or patients: W Weng, X Peng, C Gao; (IV) Collection and assembly of data: X Peng; (V) Data analysis and interpretation: W Weng, Y Chen; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Youpeng Chen. Department of Infectious Disease, 628# Zhenyuan Road, Seventh Affiliated Hospital of Sun Yat-sen University, 510000, Shenzhen, China. Email: youpeng.chen@163.com.

Abstract: The liver is an important metabolic and synthetic organ of the human body. When liver injury and function decline, abnormal metabolism of various nutrients and different degrees of malnutrition may occur, and many studies have confirmed that malnutrition can affect the therapeutic effect and prognosis of patients with chronic liver disease. We searched PubMed, the CNKI, and relevant meeting abstracts (2008 to April 2020) for randomized trials and some relevant reviews that assessed nutritional status and supportive treatment in patients with hepatitis B virus-related liver diseases. Searches were limited to human studies and English-language publications. The main keywords used for the search were nutrition, liver disease and hepatitis B. Citation lists of retrieved articles were manually screened to ensure sensitivity of the search strategy. The study suggests that malnutrition is common in patients with liver disease, since metabolism is diverse in different stages of HBV related liver disease, details of nutritional support are different. The occurrence of malnutrition is closely related to the occurrence, development and prognosis of liver disease. Malnutrition plays an important role in the development of liver disease. Appropriate nutritional intervention can improve the prognosis of HBV related liver disease.

Keywords: Hepatitis B virus; liver disease; nutrition

Received: 21 September 2020; Accepted: 24 December 2020; Published: 30 December 2020.
doi: 10.21037/dmr-20-140
View this article at: http://dx.doi.org/10.21037/dmr-20-140

Introduction

The liver is an important metabolic and synthetic organ of the human body, which has the functions of metabolism, detoxification, bile secretion, synthesis and storage, immune defense, hematopoiesis and blood storage. Among them, the metabolism of carbohydrates, protein and fat, the absorption and storage of vitamins and trace elements all need the participation of the liver. When liver injury and function decline, abnormal metabolism of various nutrients and different degrees of malnutrition may occur, and many studies have confirmed that malnutrition can affect the therapeutic effect and prognosis of patients with chronic liver disease (1,2). HBV does not kill hepatocytes directly. The immune response induced by HBV is the main mechanism leading to hepatocyte injury and inflammatory necrosis. China is a large country with patients of hepatitis B virus. There are a large number of patients with chronic hepatitis B, hepatitis B virus related cirrhosis and liver failure. Malnutrition is a common and important complication of chronic liver disease, and the incidence rate can be as high as 50% to 90%. Child-Pugh score is a scoring system used to assess the prognosis of chronic liver disease, mainly cirrhosis, to predict operative mortality and the need for liver transplantation. It is calculated according to hepatic encephalopathy, ascites, total bilirubin, albumin,

and INR.

The study suggests that 81% of hospitalized patients with liver cirrhosis have protein-energy malnutrition. The incidence of malnutrition in cirrhotic patients with Child-Pugh (CHILD) grade A and B was 21% to 40%, and 70% to 90% for patients with liver cirrhosis of grade C. 90% of patients with chronic liver failure were malnourished (3-6). The occurrence of malnutrition is closely related to the occurrence, development and prognosis of liver disease.

This article reviews the nutritional metabolism and nutritional support treatment of patients with hepatitis B virus-related liver diseases.

We present the following article in accordance with the Narrative Review reporting checklist (available at http://dx.doi.org/10.21037/dmr-20-140).

Characteristics of nutrition and metabolism in patients with liver disease (Other Section)

Insufficient intake of nutrients

Insufficient intake of nutrients is an important cause of malnutrition in patients with liver disease. It mainly includes:

(I) Digestive tract symptoms such as nausea, vomiting and anorexia are obvious in patients with chronic liver disease, and the lack of trace elements such as magnesium and zinc lead to abnormal taste and affects appetite. At the same time, a large amount of ascites compression may occur in patients with decompensated liver cirrhosis and liver failure, which can lead to loss of appetite and increase of serum leptin levels, resulting in reduced food intake.

(II) Autonomic nerve disturbance leads to the weakening of gastrointestinal peristalsis, slowing down the absorption of nutrients, obvious abdominal distension and fullness, and further reducing food intake;

(III) The accumulation of metabolites in the body and the use of antibiotics and acid suppressants, leading to gastrointestinal dysfunction, gastrointestinal mucosal edema, intestinal flora imbalance, leading to the decline of digestion and absorption capacity of the body.

(IV) Some patients with jaundice have cholestasis and insufficient bile concentration, resulting in insufficient absorption of fat-soluble vitamins;

(V) Iatrogenic dietary changes, such as routine low-fat and light diet, sodium restriction and water restriction, lack of nutrition management after fasting of gastrointestinal bleeding, fasting in the morning, color ultrasound, gastroscopy and other fasting for a long time can lead to insufficient intake of nutrients.

Changes of energy metabolism in patients

Most of the patients with acute hepatitis are in a state of hyper metabolism, because the body is in a normal state before the onset of the disease, the acute course of the disease will not have too much impact on the nutritional status (7). The metabolism of patients with chronic liver disease is different in different diseases and stages, and hyper metabolism may occur in the early and acute stages of the disease.

Patients with high metabolism are more prone to weight loss and malnutrition, which may be related to hyper dynamic circulation and abnormal excitation of sympathetic nerve, which can affect the development and prognosis of the disease. Low metabolism is the result of self-adjustment of the body. The reduction of energy consumption helps to maintain the balance between intake and consumption and reduce the energy imbalance, which may be a response to body protection and conducive to the recovery of body function.

With the stable condition, the liver function of patients with chronic hepatitis B can return to normal, the nutritional status and energy metabolism are basically in the normal range, and most of the patients can be in the state of normal metabolism and low metabolism. Up to 80% of patients with liver cirrhosis have protein-energy malnutrition, and most of them are in a state of high metabolism, but compensatory cirrhosis and stable decompensated cirrhosis can show normal metabolism (8). Most of the patients with liver failure are in a state of stress and high metabolism, and their energy consumption is significantly increased, which may be related to systemic inflammatory reaction and multiple organ damage associated with liver failure (9).

Metabolism of three major nutrients

Glucose

The liver produces glucose through glycogen decomposition and gluconeogenesis to maintain normal fasting blood

glucose, and can maintain normal postprandial blood glucose by combining glucose in blood into liver glycogen, and at the same time degrade and clear glucose metabolism to maintain normal glucose metabolism. Patients with liver disease cannot maintain good blood glucose control function because of impaired liver function, and may have fasting hypoglycemia, impaired glucose tolerance and even hepatogenic diabetes.

The mechanisms of fasting hypoglycemia include: (I) liver cell necrosis leads to depletion of liver glycogen reserve; (II) decrease of glucose-6-phosphatase activity in liver cells. the remaining liver glycogen cannot be decomposed into enough glucose for the needs of the body; (III) the ability of the liver to convert non-glycogen into glycogen decreases and glucose cannot be supplied in time; (IV) when a large number of hepatocytes are necrotic, the inactivation function of the liver to insulin is weakened; (V) endotoxemia can also cause disturbance of liver energy metabolism.

The mechanisms of impaired glucose tolerance are as follows: (I) the ability of hepatocytes to absorb and deal with glucose is decreased, and the inactivation effect of liver against insulin hormones (glucagon and growth hormone) is weakened; (II) the insulin receptor is abnormal and insulin resistance occurs. Hepatogenic diabetes may occur in some patients (10).

Protein

When the body is in a state of high metabolism, the synthesis and decomposition rate of protein metabolism is obviously accelerated, and the decomposition rate is higher than the synthesis rate, which further aggravates protein malnutrition. At the same time, in patients with severe liver function damage, the liver synthetic albumin function decreased, resulting in hypoalbuminemia, ascites production, plasma colloid osmotic pressure affected and the transport and absorption of some hormones and trace elements (11). The deficiency of branched chain amino acids in patients with liver dysfunction can accelerate the catabolism of muscle protein, reduce the synthesis of albumin, and decrease the ratio of branched chain amino acids to aromatic amino acids, which is related to the occurrence of hepatic encephalopathy (12).

Lipids

The decline of liver synthetic function leads to the decrease of blood lipid indexes such as serum total cholesterol, triglyceride, high-density lipoprotein cholesterol, low density lipoprotein cholesterol and apolipoprotein in patients with liver disease (7).

Vitamins and trace elements

Due to liver function damage leading to reduced intake, malabsorption and other reasons, there is often a lack of vitamins and trace elements, which leads to physiological disorders and aggravates the progression of malnutrition and liver disease. The deficiency of vitamins and trace elements is different in different degrees of liver injury, the contents of zinc, calcium, magnesium and iron in serum can decrease in different degrees, while the content of copper accumulates (13-15). The absorption of fat-soluble vitamins A, D, E and K can be caused by cholestasis, which should be supplemented. There is a parallel relationship between the high level of vitamin B12 and the degree of hepatocyte damage. Daily intake of 150 to 200 grams of fresh vegetables and fruits can supplement patients' requirements for most vitamins and trace elements, but for patients with severe liver diseases who do not eat enough, multivitamin preparations can be considered. At the same time, attention should be paid to the supplement of various trace elements. As the degree of element deficiency varies from person to person, it should be evaluated regularly before and after supplementation to prevent the aggravation of liver fibrosis caused by blind supply of some elements such as iron, manganese, copper, etc. (16,17).

Nutritional status of patients with hepatitis B related liver disease

Acute hepatitis B virus hepatitis

Before the onset of acute hepatitis, the body is mostly in a normal state. The acute course of disease has little effect on the nutritional status, and most of them are in a high metabolic state. Some patients with anorexia, nausea, vomiting and other gastrointestinal symptoms are obvious, so the intake can be significantly reduced. At this time, attention should be paid to meet the increased energy metabolism needs of patients, and at the same time, excessive nutrition supply should be avoided to cause damage to various organs of the body (7).

Chronic hepatitis B virus hepatitis

The liver function of patients with chronic hepatitis B is basically normal in the stable stage, most of them are in low metabolism or normal metabolism. Generally, there is no need for artificial nutrition support. Carbohydrates are the

main functional substances, and supply adequate protein, vitamins and trace elements (18).

Hepatitis B cirrhosis

Malnutrition often occurs in patients with cirrhosis. PEM was found in 81% patients with cirrhosis in some research. Malnutrition rates were found in patients with cirrhosis of Child A and B (21–40%) and at stage Child-Pugh C (70–90%). Most patients with cirrhosis are highly metabolic and consume increasing. If patients receive insufficient nutrition, they often appear weight loss and protein consumption increase, resulting in protein-energy malnutrition (8).

Total energy consumption of patients with cirrhosis was approximately 1.3–1.4 times as much as resting energy consumption and its daily total energy intake suggested differently in different body conditions. European Society of Enteral Nutrition recommends daily energy intake of 30–35 kcal/kg, European Association of liver diseases recommends that non obese individuals consume ≥35 kcal/kg daily capacity, while patients with malnutrition suggest that patients with malnutrition may be reduced to 25 kcal/kg. Protein intake recommended high quality protein [1.2–1.5 g/(kg·d)] to maintain nitrogen balance and reduce incidence of muscle reduction. Meanwhile attention should be paid to the application of branched chain amino acids preparations reducing the ratio of branched amino acids/aromatic amino acids reducing hepatic encephalopathy or other neurological complications. Carbohydrate intake recommended 2–3 g/(kg·d). Patients with cirrhosis often exist glucose metabolism disorders, and excessive glucose intake may aggravate liver dysfunction. if patients have impaired glucose tolerance, extra insulin is needed. Restricted fat intake <1 g/(kg·d) in patients without oral fat intake. Supplementation of fat emulsion by enteral or parenteral nutrition may appropriately increase metabolizable medium and long chain fat emulsion to avoid increasing liver burden (19,20).

For patients with hepatic encephalopathy, high protein intake is one of the causes of hepatic encephalopathy. Protein intake is often prohibited in clinical practice, which can aggravate protein-energy malnutrition and affect the prognosis and recovery of the disease. ISHEN consensus does not require strict intake of proteins associated with hepatic encephalopathy. It suggested that only mild hepatic encephalopathy could not limit or consider 0.5 g/(kg·d) high quality protein, which could be increased after symptom controlled. If severe hepatic encephalopathy occurs, the protein intake can be temporarily stopped for several days. After the disease is improved, a small amount of protein (10–20 g/d) is added, and the principle is that it does not exceed the load that patients can tolerate. For patients with recurrent hepatic encephalopathy, protein intake was recommended for more tolerant vegetable proteins (e.g., asparagus, broccoli, oats, spinach, broccoli), whey protein (egg, milk) and reduce animal protein intake. Because vegetable protein contains less methionine and aromatic amino acids, while contains more arginine, aspartate and glutamate, which is beneficial to reduce blood ammonia (21-24).

Hepatitis B liver failure

Patients with liver failure are acute and severe manifestations of chronic hepatitis B. Clinical treatment measures are mainly comprehensive support treatment and prevention of complications. Malnutrition is often easily ignored. On the basis of comprehensive medical treatment, reasonable diet should be actively provided to maintain the stability and balance of nutrients, so that patients can pass through the critical stage of the disease tend to recover.

Patients with liver failure are often in stress and high metabolism, but some patients are in low metabolism, which may be related to the condition at different stages of liver failure.

Daily total energy intake of 35–40 kcal/(kg·d), 60–70% of energy comes from carbohydrates. Protein recommended 1.2–1.5 g/(kg·d), with the premise of supporting protein synthesis and metabolism and not inducing hepatic encephalopathy.

Glucose intake at 120–180 g/d, insufficient intake will produce negative nitrogen balance, further increase protein consumption. When patient recovers, we should try to increase protein diet and then appropriately reduce glucose. Bear in mind that glucose intake should not exceed 250 g/d. Excessive glucose can lead to fat synthesis and fat accumulation in liver. Fat intake should be <1 g/(kg·d), because liver failure exhaustion patients cannot fully utilize fatty acid. Avoid excessive fat drop in parenteral nutrition to prevent accumulation of liver inside. If the disease course is too long, we can use medium and long chain fat emulsion appropriately (9,25,26) when appropriate (*Table 1*).

Nutritional intervention of hepatitis B associated liver disease

Nutritional screening, nutritional assessment and nutritional intervention should be carried out at the first visit of each patient and dynamically monitored. According to different

Table 1 Suggestion of nutrition intake

	Metabolism state	Energy intake	Protein intake	Carbohydrate intake	Lipid intake
Acute HBV hepatitis	Mostly high	Higher than normal	As usual	As usual	As usual
Chronic HBV hepatitis	Normal or low	As usual	As usual	As usual	As usual
HBV related cirrhosis	mostly high	30–35 kcal/kg, reduced to 25 kcal/kg in obesity	1.2–1.5 g/(kg·d), avoid hepatic encephalopathy	2–3 g/(kg·d), add insulin for impaired glucose tolerance	Oral: unlimited, intravenous: <1 g/(kg·d), adequate medium and long chain fat emulsion
HBV related liver failure	Mostly high	35–40 kcal/(kg·d)	1.2–1.5 g/(kg·d), even less when hepatic encephalopathy occurs	2–3 g/(kg·d), avoid hypoglycemia	Oral: unlimited, intravenous: <1 g/(kg·d), even less when insulin resistance occurs

disease stages, different intervention time was adopted. For patients with stable chronic hepatitis, regular follow-up and monitoring of nutritional status is needed. Usually, they need no nutritional intervention unless nutritional insufficiencies are detected. For patients with acute hepatitis, liver cirrhosis and liver failure who are admitted into hospitals, nutritional status should be evaluated as soon as possible, and intervention should be carried out before malnutrition occurs.

After comprehensive nutritional status assessment, definite metabolism status, combined with dietary habits and intake conditions, individualized nutritional support scheme was adopted for patients. After individualized nutrition support scheme was established, patients received oral intake, encouraged less food meals daily, 4–6 meals daily, and fasted hours during daytime should not exceed 4–6 h. We should monitor the patient's energy and protein consumption, and specific nutrition programs can be developed jointly with nutrition physicians. Promote pre-bedtime snacks, i.e., if you keep your daily intake unchanged, remove some energy until bedtime. It is suggested that nighttime snacks which composed of carbohydrates can improve glucose tolerance, decrease lipid metabolism and protein oxidation rate, increase carbohydrate energy supply ratio and improve metabolism state. Total energy of pre-sleep snack was 200 kcal, carbohydrate accounted for 70–80%, fat accounted for 20–30%, and fatty acid containing branched amino acids could recover albumin level and energy metabolism faster (27,28). If the digestive tract symptoms of patients are obvious, or the digestion and absorption are too poor to reach the target demand or the nutrient intake is not comprehensive enough, oral nutritional supplements (ONS) or enteral nutrition can be considered, and parenteral nutrition can be given if necessary.

Enteral nutrition

Enteral nutrition consists of three types: amino acid type, short peptide type and whole protein type. They can be divided into balance and disease applicable type according to nitrogen sources. Commercial preparations commonly used clinically are essential factors (amino acids type short peptide type) non-element type (whole protein type). Different enteral nutrition preparations should be selected according to age, gastrointestinal status, protein variation, lipid absorption, lactose tolerance disease and nutritional status etc., which can be combined with enteral nutrition program in patients with common system of nutrition. For patients with normal gastrointestinal function, we can choose whole protein preparation; patients with low gastrointestinal function should choose amino acid type or short peptide type preparations. Patients with liver diseases should choose low protein, high branched amino acids and low aromatic amino acid formulation formulations (29,30).

Digestive tract symptoms such as anorexia, nausea, vomiting, abdominal distension and diarrhea often occur in patients with liver diseases, especially in patients with end-stage liver diseases, or large amounts of ascites lead to eating difficulties, gastrointestinal function and intestinal flora disorder. Significantly, enteral nutrition can improve and maintain the structural and functional integrity of intestinal mucosal cells, maintain the growth of gastrointestinal inherent flora, stimulate the secretion of digestive juice and gastrointestinal hormones, promote gallbladder contraction and gastrointestinal peristalsis, which is of great significance to the recovery of intestinal function and the regulation of

flora (31,32).

The infusion of general enteral nutrition preparation is best by continuous infusion. In the first three days of the beginning, the intestinal tract needs to be gradually adapted to use low-dose, low-concentration and low-speed infusion, and then gradually increases. It can be considered to use 1/4 of the total amount on the first day, and the concentration is diluted 1 times. If the patient is well tolerated, the second day can be increased to 1/2 of the total demand, and the third day will be full. Infusion started at a slow rate of 25–50 mL/h, followed by an increase of 25 mL/h every 12–24 h at a maximum rate of 125–150 mL/h (29).

Some patients can cause nausea, vomiting, abdominal distension, abdominal pain, diarrhea and other digestive tract symptoms. If necessary, slow feeding speed can be considered to reduce the incidence of adverse reactions. Enteral nutrition should not be suitable or should be used cautiously in some cases. Such as those patients with complete mechanical intestinal obstruction, intestinal paralysis, intestinal bleeding, early inflammatory response to acute pancreatitis, allergies to enteral nutrition components, intractable diarrhea or vomiting, severe abdominal infection, severe digestion or poor absorption, early severe stress state, shock state, high flow jejunum fistula, etc.

Enteric probiotics

The liver is closely linked to the intestine through the portal vein, and exposure to gut microbiota and its metabolites can affect the liver of patients. The disorder of gastrointestinal hormone secretion in patients with end-stage liver disease leads to weakened gastrointestinal motility, intestinal wall edema, and decreased digestion and absorption capacity. It is easy to cause intestinal microecological imbalance and intestinal barrier function damage, which leads to intestinal bacterial translocation and endotoxemia, further aggravates the development of the disease and poor prognosis (33,34). Reasonable nutrition intervention can maintain intestinal barrier function and reduce intestinal flora disorder occurrence. Probiotics is a living bacterium preparation, which can regulate balance of intestinal flora and play beneficial role in organism. Currently commonly used kinds include *Lactobacillus*, *Bifidobacterium*, *Enterococcus*, *Bacillus*, and *Clostridium spp*. Intestinal probiotics could improve nutritional status of intestinal epithelial cells reduce intestinal permeability decrease bacterial translocation and endotoxemia increase hepatic ammonia clearance thereby reducing hepatic encephalopathy (35,36). But because there are trillions of resident bacteria in human colon bacteria may not be enough to replace all resident probiotics. Gastrointestinal peristalsis function decreased in patients with end stage liver disease and probiotics might not reach colon function. And antibiotics are widely used in end-stage liver disease patients, which may kill vulnerable probiotic species. Therefore, specific effective probiotic strains and therapeutic doses should be further studied.

Sarcopenia

Due to functional decline and metabolic abnormality, patients with liver diseases need prolonged bed rest, resulting in decreased exercise, together wiith insufficient energy or protein intake, often leading to decreased muscle weight, muscle strength loss, muscle quality damage, and changes in muscle structure and composition, which is called muscle deficiency syndrome (37). According to duration, it can be divided into acute muscle syndrome and slow muscle syndrome. Acute muscular syndrome occurs within 6 months, which may happen in acute hepatitis, acute or subacute hepatic failure. Chronic muscular disease has a duration of more than 6 months, commonly occurs in chronic liver cirrhosis and chronic liver failure. The factors related to muscle deficiency syndrome include anorexia, fasting leads to low intake, vomiting, diarrhea, resulting in decreased nutrient absorption and high metabolic status. Muscular reduction can increase mortality rate and risk of hepatic encephalopathy in cirrhotic patients (38). Prognosis of liver transplantation in patients with cirrhosis complicated with muscular cirrhosis is worse (39).

Currently potential therapeutic strategies for patients with cirrhosis and muscle deficiency syndrome include increasing calorie and protein intake, night snack, chain amino acid supply and exercise therapy etc. (40). Patients may exercise aerobic exercise or individualized anti-resistance exercise to maintain muscle strength, muscle mass and reduce further muscle loss. It is suggested that moderate intensity walk 30–40 minutes per week should be performed 3–4 times per week if permitted and combined with resistance training such as mild weight lifting and lower extremity resistance movement etc. (41). Muscle deficiency syndrome is complicated and simple diet intervention is insufficient. Further research on mechanisms may be helpful to develop more effective therapies for specific potential metabolic disorders.

Conclusions

Above all, hepatitis B associated liver disease, whether

acute chronic or end-stage liver disease, it's nutritional support therapy is extremely important. Early detection of abnormal nutritional metabolism and individualized rational nutritional support therapy are important for disease progression, prognosis, prevention and development of malnutrition. However, there are a lack of large scale clinical trials to verify these theories. Also, satisfied quantitative indicators and operability for patients at home are insufficient. Therefore, further researches such as RCTs and better quantitative indicators are needed.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at http://dx.doi.org/10.21037/dmr-20-140

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/dmr-20-140). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Juakiem W, Torres DM, Harrison SA. Nutrition in cirrhosis and chronic liver disease. Clin Liver Dis 2014;18:179-90.
2. Ghufran A. Nutrition in Chronic Liver Disease: A Point-of-Care Review. Nutr Clin Pract 2020;35:211-7.
3. Huynh DK, Selvanderan SP, Harley HA, et al. Nutritional care in hospitalized patients with chronic liver disease. World J Gastroenterol 2015;21:12835-42.
4. Dong LM, Li M, Li YH, et al. Analysis of Nutritional Status in Hospitalized Patients with Chronic Liver Cirrhosis. Medical Journal of Qilu 2016;31:219-220.
5. Shi HM, Cao X, Gu YJ, et al. Investigation on the Nutritional Status of Hospitalized Patients with Hepatitis Disease in Shanghai. Journal of Medical Research 2016;45:113-5.
6. Ding HL, Li Y. Analysis of NRS2002 screening in 296 inpatients with liver disease. Shandong Medical Journal 2016;56:80-3.
7. Hou W, Meng QH. Characteristics of nutritional metabolism and nutritional intervention in patients with liver disease. Beijing Medical Journal 2012;34:208-10.
8. Meng QH, Wang JH, Yu HW, et al. Resting energy expenditure and substrate metabolism in Chinese patients with acute or chronic hepatitis B or liver cirrhosis. Intern Med 2010;49:2085-91.
9. Meng QH, Hou W, Yu HW, et al. Resting energy expenditure and substrate metabolism in patients with acute-on-chronic hepatitis B liver failure. J Clin Gastroenterol 2011;45:456-61.
10. Zhu FY, et al. Pathogenesis of impaired glucose tolerance and hepatogenic diabetes mellitus in patients with liver cirrhosis. Chinese Journal of Clinical Gastroenterology 1999;11:142-4.
11. Storck LJ, Imoberdorf R, Ballmer PE. Nutrition in Gastrointestinal Disease: Liver, Pancreatic, and Inflammatory Bowel Disease. J Clin Med 2019;8:1098.
12. Chadalavada R, Sappati BR, Maxwell J, et al. Nutrition in hepatic encephalopathy. Nutr Clin Pract 2010;25:257-64.
13. Jamil Z, Arif S, Khan A, et al. Vitamin D Deficiency and Its Relationship with Child-Pugh Class in Patients with Chronic Liver Disease. J Clin Transl Hepatol 2018;6:135-40.
14. Chavez-Tapia NC, Cesar-Arce A, Barrientos-Gutierrez T, et al. A systematic review and meta-analysis of the use of oral zinc in the treatment of hepatic encephalopathy. Nutr J 2013;12:74.
15. Takuma Y, Nouso K, Makino Y, et al. Clinical trial: oral zinc in hepatic encephalopathy. Aliment Pharmacol Ther 2010;32:1080-90.
16. Zhao M. The research status of nutrition assessment and nutritional support in patients with cirrhosis. Chinese Journal of Gastroenterology and Hepatology

2015;24:887-90.
17. Yu JC, Chen W, Jiang H, et al. Expert consensus on clinical application of multiple trace element preparations. Chinese Journal of Surgery 2018;56:168-76.
18. Fan CL, Wu YJ, Duan ZP, et al. Resting energy expenditure and glucose, protein and fat oxidation in severe chronic virus hepatitis B patients. World J Gastroenterol 2008;14:4365-4369.
19. Teramoto A, Yamanaka-Okumura H, Urano E, et al. Comparison of measured and predicted energy expenditure in patients with liver cirrhosis. Asia Pac J Clin Nutr 2014;23:197-204.
20. Prieto-Frias C, Conchillo M, Payeras M, et al. Factors related to increased resting energy expenditure in men with liver cirrhosis. Eur J Gastroenterol Hepatol 2016;28:139-45.
21. Bajaj JS, Lauridsen M, Tapper EB, et al. Important Unresolved Questions in the Management of Hepatic Encephalopathy: An ISHEN Consensus. Am J Gastroenterol 2020;115:989-1002.
22. Hamed A, Hamed A, Lambert K. Branched-chain Amino Acids for People with Hepatic Encephalopathy. Am Fam Physician 2020;101:Online.
23. Romeiro FG, Ietsugu M, Franzoni LC, et al. Which of the branched-chain amino acids increases cerebral blood flow in hepatic encephalopathy? A double-blind randomized trial. Neuroimage Clin 2018;19:302-10.
24. Maharshi S, Sharma BC, Sachdeva S, et al. Efficacy of Nutritional Therapy for Patients With Cirrhosis and Minimal Hepatic Encephalopathy in a Randomized Trial. Clin Gastroenterol Hepatol 2016,14:454-460.e3; quiz e33.
25. Guideline for diagnosis and treatment of liver failure (Version of 2018). Journal of Practical Hepatology 2019;22:164-71.
26. Chinese Society of Hepatology, Chinese Medical Association, Chinese Society of Gastroenterology, Chinese Medical Association. Clinical guidelines on nutrition in end-stage liver disease. Journal of Practical Hepatology 2019;22:624-35.
27. Hou W, Li J, Lu J, et al. Effect of a carbohydrate-containing late-evening snack on energy metabolism and fasting substrate utilization in adults with acute-on-chronic liver failure due to Hepatitis B. Eur J Clin Nutr 2013;67:1251-6.
28. Hanai T, Shiraki M, Imai K, et al. Late Evening Snack with Branched-Chain Amino Acids Supplementation Improves Survival in Patients with Cirrhosis. J Clin Med 2020;9:1013.
29. Consensus on clinical pharmacy of enteral nutrition (Version 2). Pharmacy Today 2017;27:361-71.
30. Chen LZ, Fei XF, Li L, et al. Formulation evaluation of enteral nutrition products. (J). Clinical Medication Journal 2019;17:43-6.
31. Shergill R, Syed W, Rizvi SA, et al. Nutritional support in chronic liver disease and cirrhotics. World J Hepatol 2018;10:685-94.
32. Hasse JM, Dicecco SR. Enteral Nutrition in Chronic Liver Disease: Translating Evidence Into Practice. Nutr Clin Pract 2015;30:474-87.
33. Giannelli V, Di Gregorio V, Iebba V, et al. Microbiota and the gut-liver axis: bacterial translocation, inflammation and infection in cirrhosis. World J Gastroenterol 2014;20:16795-810.
34. Ponziani FR, Zocco MA, Cerrito L, et al. Bacterial translocation in patients with liver cirrhosis: physiology, clinical consequences, and practical implications. Expert Rev Gastroenterol Hepatol 2018;12:641-56.
35. Albillos A, de Gottardi A, Rescigno M. The gut-liver axis in liver disease: Pathophysiological basis for therapy. J Hepatol 2020;72:558-77.
36. Woodhouse CA, Patel VC, Singanayagam A, et al. Review article: the gut microbiome as a therapeutic target in the pathogenesis and treatment of chronic liver disease. Aliment Pharmacol Ther 2018;47:192-202.
37. Anand AC. Nutrition and Muscle in Cirrhosis. J Clin Exp Hepatol 2017;7:340-57.
38. Bhanji RA, Moctezuma-Velazquez C, Duarte-Rojo A, et al. Myosteatosis and sarcopenia are associated with hepatic encephalopathy in patients with cirrhosis. Hepatol Int 2018;12:377-86.
39. Dimartini A, Cruz RJ, Dew MA, et al. Muscle mass predicts outcomes following liver transplantation. Liver Transpl 2013;19:1172-80.
40. Sinclair M, Gow PJ, Grossmann M, et al. Review article: sarcopenia in cirrhosis – aetiology, implications and potential therapeutic interventions. Alimentary Pharmacology & Therapeutics 2016;43:765-77.
41. Tandon P, Ismond KP, Riess K, et al. Exercise in cirrhosis: Translating evidence and experience to practice. J Hepatol 2018;69:1164-77.

doi: 10.21037/dmr-20-140
Cite this article as: Weng W, Peng X, Gao C, Chen Y. Narrative review of nutritional characteristics and supportive treatment of hepatitis B virus-related liver diseases. Dig Med Res 2020;3:51.