

DIET IN CHRONIC HEPATITIS C

E. Rusu^{1,2}, *AD Dragomir*², *G. Radulian*^{1,2}

¹ University of Medicine "Carol Davila"

² National Institute of Diabetes, Nutrition and Metabolic Diseases "Prof. N. Paulescu"

Abstract

The liver plays a major role in metabolism and has a number of functions in the body, including carbohydrate metabolism (gluconeogenesis, glyco-genolysis, glycogenesis), protein and lipid metabolism and detoxification. The liver stores a multitude of substances, including glucose (in the form of glycogen), triglycerides, vitamin A (1-2 years supply), vitamin D (1 - 4 months supply), vitamin B12, iron, and copper.

To be defined as chronic hepatitis, a patient must have at least 6 months of hepatitis or biochemical and clinical evidence of liver disease with unsolved hepatic inflammation found on biopsy procedures.

Hepatitis C (HCV) is a major cause of acute hepatitis and chronic liver disease,

including cirrhosis and liver cancer. Globally, an estimated 170 million people are chronically infected with HCV and 3 to 4 million persons are newly infected each year. HCV is spread primarily by direct contact with human blood. The major causes of HCV infection worldwide are the use of unscreened blood transfusions, and the re-use of needles and syringes that have not been adequately sterilized. About 80% of newly infected patients progress to develop chronic infection.

Cirrhosis develops in about 10% to 20% of persons with chronic infection, and liver cancer develops in 1% to 5% of persons with chronic infection over a period of 20 to 30 years.

Keywords: diet, chronic hepatitis C

Background

Healthy eating is a significant factor in reducing the risk of developing a variety of chronic conditions^{6,9}.

Eating adequate amounts of essential nutrients, coupled with energy intake in balance with energy expenditure, is essential to maintain health and to prevent or delay the development of obesity or malnutrition.

Nutrition care should be a component of the total health care provided to persons infected with HCV.

Persons infected with HCV do not need to follow specific dietary restrictions unless they

have advanced liver disease or some other condition that require dietary modification, such as diabetes, dyslipidemia or celiac disease. Adjustments in macronutrients, electrolytes, fluids, vitamins and minerals may be indicated in these circumstances.

About 80% of newly infected patients progress to develop chronic infection³¹. Cirrhosis develops in about 10% to 20% of persons with chronic infection, and liver cancer develops in 1% to 5% of persons with chronic infection over a period of 20 to 30 years³¹.

Risk factors for rapidly progressive disease include²³:

- male gender
- age > 40 years at time of infection
- daily alcohol consumption of > 50 g/day
- obesity
- type 2 diabetes
- associated medical conditions such as: alcoholic liver disease, hepatitis B viral infection
- HIV co-infection
- persistent elevation in serum ALT concentration
- active cirrhosis on liver biopsy

Importance of a Healthy Body Weight

Because weight-related problems can adversely affect health, patients with chronic HCV should be advised to achieve and maintain a healthy weight by adopting healthy eating and activity patterns.

Studies have identified that BMI > 25 kg/m² is associated with hepatic steatosis, which leads to more severe fibrosis^{12,32}.

The published data suggest that: (1) hepatic steatosis is present in about 50% of patients with HCV infection; (2) the association of HCV and steatosis is genotype-specific; (3) steatosis contributes to the progression of fibrosis in HCV-related liver disease; (4) NAFLD adversely affects the viral response rates to anti-HCV therapy; and (5) the concomitant presence of NAFLD and HCV infection possibly leads to an increased risk of hepatocellular carcinoma^{4, 21, 25, 27}.

Patients with both hepatitis C and obesity-related nonalcoholic fatty liver disease are at greater risk for more advanced liver disease. According to a new study²⁰, obese patients chronically infected with HCV and treated

with combination drug therapy may have better outcomes if the underlying abnormalities caused by excessive fat tissue are corrected.

Protein energy malnutrition is common in patients with chronic liver disease and can lead to weight loss. HCV increases basal metabolic rate in non-cirrhotic patients²⁴. Malnutrition (either under- or overweight) negatively affects nutritional status, quality of life and survival.

Goals of Nutrition Intervention in Hepatitis C

The following are the general goals of nutrition intervention in liver disease. Their relative importance depends on the stage of disease (acute hepatitis, chronic hepatitis, cirrhosis, hepatic encephalopathy):

- to provide adequate energy and protein to facilitate hepatocyte regeneration
- to promote and maintain nitrogen balance, avoiding excess production of ammonia from endogenous or exogenous protein catabolism
- to avoid complications related to the role of the liver in intermediary metabolism
- of carbohydrate, lipids and protein
- to avoid fluid and electrolyte imbalance
- to provide adequate vitamins and minerals
- to use appropriate supplements when needed
- to treat or reduce symptoms or treatment side effects

- to prevent increased morbidity or death related to nutritional factors

Energy requirements

Energy requirements are the number of calories a person needs to achieve for certain weight goals — meaning to lose, gain, or maintain weight — in healthy individuals. People with chronic HCV have higher calories needs than normal because of the hepatitis viral load. If liver disease progresses to cirrhosis or decompensate cirrhosis, the calorie requirements increase even more to prevent undesired weight loss and malnutrition.

For patients with hepatitis C energy requirements are: 25 to 40 kcal/kg, based on dry weight or an adjusted ideal weight^{1, 19, 29} or add 20% to 40% to basal energy expenditure (BEE) using the Harris-Benedict equation^{2, 5, 10} in malnourished patients, energy needs are 1,5 to 1,75 X BEE or 35 to 45 kcal/kg.

Proteins

Proteins provide the building blocks for liver, immune, and muscle cells. Protein intake must be adjusted for body weight and medical conditions. The requirement of proteins in hepatitis C is estimated minimally at 1,0 to 1,2 g/kg/day and may range up to 1,5 g/kg if patients have cirrhosis²⁸.

More than 95% of patients with cirrhosis can tolerate a diet containing up to 1,5 g/kg/day of proteins, without risk of hepatic encephalopathy (HE)^{15, 22}.

In severely malnourished patients, supplements may be considered to meet protein requirements¹⁸.

In general, dietary proteins intake is limited only in patients with acute HE or refractory HE not attributable to other causes, such as gastrointestinal bleeding, infection, dehydration, lactulose non-compliance, or constipation¹¹.

Carbohydrates

People with liver disease should strive for a diet consisting of approximately 45-65% carbohydrates, with complex carbohydrates predominating.

Carbohydrates come from starches, grains, fruits, vegetables, and sugars. It is not necessary to limit grains, fruits, and vegetables, but more whole grains should be chosen.

Fibers

Requirements for hepatitis C are set at 38 g/day for men and 25 g/day for women aged 19 to 50 years⁷.

Lipids

The Acceptable Macronutrient Distribution Range (AMDR) for lipids is 20% to 35% of total energy intake for adults⁷.

For n-6 PUFA, the AMDR is 5% to 10% of energy, which is expected to meet the adequate intake (AI) for linoleic acid (17 g/day for young men and 12 g/day for young women). The AMDR for alpha-linolenic acid is 0,6% to 1,2% of energy, with up to 10% of the AMDR consumed as eicosapentaenoic acid (EPA) and/or docosahexaenoic acid (DHA); the AI is 1,6 g/day for men and 1,1 g/day for women.

In patients with cirrhotic liver, which does not produce enough bile acids to digest and absorb dietary fats, results fat malabsorption and diarrhea; in this case, specialized fats — medium-chain triglycerides - can be prescribed to supplement the diet.

Fluids

Fluid requirements are generally the same for people with HVC as they are for the general population. Most people need:

- urine output plus 500 mL/day
- 1 mL/kcal
- 35 or 30 mL/kg/day in adults 20 to 55 and 55 to 75 years of age, respectively³
- requirements are higher in those with diarrhea, fever, vomiting
- fluid restriction (1,0 to 1,5 L/day) may be necessary if ascites or peripheral edema are present²⁶.

Vitamins

Not much research is available on vitamin needs specific to patients with hepatitis C. In patients with cirrhosis vitamin deficiencies are common.

Fat-soluble Vitamins

Vitamin A deficiency may increase the risk of liver cancer but excess of vitamin A is toxic for the liver. The toxicity of vitamin A (retinol) is enhanced by ethanol; they share some metabolic pathways and may therefore be in competition for metabolism¹⁶.

Vitamin D is activated in the liver and can be compromised in cirrhosis.

Vitamin E has been shown to decrease oxidative stress, lower liver enzyme levels, and delay anemia associated with ribavirin treatment³⁰.

Vitamin K supplements prevent hepatocellular carcinoma recurrence.

Hydro-soluble Vitamins

An optimal and safe intake of **thiamine** for hepatitis C is unknown. The RDAs for healthy females and males are 1,1 g and 1,2 g, respectively. There have been no apparent reports of toxicity from excess consumption of thiamine from supplements.

Niacin can be toxic to the liver in doses of 1 g per day. An optimal and safe intake of this vitamin for persons with hepatitis C is unknown.

Vitamin C offers antioxidant protection, but high doses can increase iron levels in the liver. An optimal and safe intake of vitamin C for persons with hepatitis C is unknown. The RDAs for healthy females and males are 75 mg and 90 mg, respectively.

Minerals

Trace elements should be supplemented when they are recognized as being deficient. Some results suggest that a low **iron** diet may be of benefit to some patients with hepatitis C. Long-term iron reduction therapy in patients with chronic hepatitis C may lower the risk of progression to hepatocellular carcinoma¹⁴.

Zinc deficiency is common in cirrhosis and may be involved in the development of encephalopathy²⁹.

Calcium deficiency may develop because of poor nutrition, malabsorption, or vitamin D deficiency.

Magnesium deficiency may occur, especially in persons taking diuretics.

Alcohol and coffee in hepatitis C

The consensus statement concerning management of hepatitis C released March 1997 from the National Institutes of Health, further warned about the dangers of excessive **alcohol** use in patients with hepatitis C. These recommendations stressed limitation of alcohol use to no more than one drink per day. Therefore, it would be unwise for patients with hepatitis C to drink alcohol in excess, and total avoidance of all alcohol intakes is recommended.

Coffee may have a protective effect against the development of hepatocellular carcinoma in patients with liver disease when consumed in quantities of three or more cups

per day. It is unclear which compound in coffee causes this effect^{8, 13}.

Healthy eating requires the knowledge and ability to plan (which includes budgeting and meal planning), grocery shop and preparation of healthy meals. Many persons infected with HCV face additional challenges due to a limited budget, limited energy, nausea and food aversions.

Additional screening factors such as living environment (e.g. homelessness, home security), income and expenses and functional status can be linked to specific interventions that address problems. People at risk for malnutrition based on psychosocial or economic status should be referred to social service professionals for more complete evaluation and intervention.

REFERENCES

1. **American Dietetic Association, Dietitians of Canada:** *Manual of Clinical Dietetics*, 6th ed. ADA and DC, Chapter 29: Liver Disease. 2000; october

2. **American Dietetic Association, Dietitians of Canada:** *Manual of Clinical Dietetics*, 6th ed. ADA and DC, Chapter 41: Liver Transplant. 2000; october

3. **American Dietetic Association, Dietitians of Canada:** *Manual of Clinical Dietetics*, 6th ed. ADA and DC, Chapter 1: Nutrition Assessment of Adults. 2000; october

4. **Castera L, Hezode C, Roudot-Thoraval F, et al.** Effect of antiviral treatment on evolution of liver steatosis in patients with chronic hepatitis C: indirect evidence of a role of hepatitis C virus genotype 3 in steatosis. *Gut*. 2004;53:420-424.

5. **Corish C:** Nutrition and liver disease. *Topics Clin Nutr* 1997; 55:17-20

6. **Food and Nutrition Board, Institute of Medicine:** Dietary Reference Intakes for Energy,

Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients). [prepublication version], Washington, DC: National Academy Press. 2002. www.nap.edu/catalog/10490.html

7. **Food and Nutrition Board, Institute of Medicine:** Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients). [prepublication version], Washington, DC: National Academy Press. 2002. www.nap.edu/catalog/10490.html

8. **Gelatti U, Covolo L, Franceschini M, Pirali F, Tagger A, Ribero ML, et al.** Coffee consumption reduces the risk of hepatocellular carcinoma independently of its aetiology: a case-control study. *J Hepatol* 2005;42(4):528-34.

9. **Health and Welfare Canada:** *Nutrition Recommendations: The Report of the Scientific Review*

Committee. Ottawa: Minister of Supply and Services Canada, 1990

10. Hasse J, Weseman B, Fuhrman MP et al: Nutrition therapy for end-stage liver disease: a practical approach. *Support Line* 1997; 19:8-15

11. J, Weseman B, Fuhrman MP et al: Nutrition therapy for end-stage liver disease: a practical approach. *Support Line* 1997; 19:8-15

12. Hu KQ, Kyulo NL, Esrailian E, Thompson K, Chase R, Hillebrand DJ, et al. Overweight and obesity, hepatic steatosis, and progression of chronic hepatitis C: a retrospective study on a large cohort of patients in the United States. *J Hepatol* 2004;40(1):147-54.

13. Inoue M, Yoshimi I, Sobue T, Tsugane S, JPHC Study Group. Influence of coffee drinking on subsequent risk of hepatocellular carcinoma: a prospective study in Japan. *J Natl Cancer Inst* 2005;97(4):293-300.

14. Kato J, Kobune M, Nakamura T et al: Normalization of elevated hepatic 8-hydroxy-2'-deoxyguanosine levels in chronic hepatitis C patients by phlebotomy and low iron diet. *Cancer Res* 2001; 61(24):8697-8702

15. Korsten MA, Lieber CS: Nutrition in pancreatic and liver disorders. In Shils ME, Olson JA, Shike M (eds): *Modern Nutrition in Health and Disease*, 8th ed. Philadelphia, PA: Lea and Febiger, 1994:1066-1080

16. Leo MA, Lieber CS: Alcohol, vitamin A, and beta-carotene: adverse interactions, including hepatotoxicity and carcinogenicity. [Review] *Am J Clin Nutr* 1999; 69(6):1071-1085

17. Lindsay KL, Hoofnagle JH. Serologic tests for viral hepatitis. In Kaplowitz N, editor: *Liver and biliary diseases*, ed 2, Baltimore, 1996, Williams & Wilkins.

18. Marchesini G, Bianchi G, Rossi B, Brizi M, Melchionda N: Nutritional treatment with branched-chain amino acids in advanced liver cirrhosis. *J Gastroenterol* 2000; 35(Suppl 12):7-12

19. McCullough AJ, Teran JC, Bugianesi E: Guidelines for nutritional therapy in liver disease. In Klein ES (ed): *ASPEN Nutritional Support Practice*

Manual. Silver Springs, MD: American Society for Parenteral and Enteral Nutrition, 1998:12.1.12-11

20. Michael R. Charlton, Paul J. Pockros, Stephen A. Harrison. Impact of obesity on treatment of chronic hepatitis C, *Hepatology*, 2006;43:1177-1186.

21. Monto A, Alonzo J, Watson JJ, Grunfeld C, Wright TL. Steatosis in chronic hepatitis C: relative contributions of obesity, diabetes mellitus, and alcohol. *Hepatology*. 2002;36:729-736.

22. McCullough AJ, Teran JC, Bugianesi E: Guidelines for nutritional therapy in liver disease. In Klein ES (ed): *ASPEN Nutritional Support Practice Manual*. Silver Springs, MD: American Society for Parenteral and Enteral Nutrition, 1998:12.1.12-11

23. Marchesini G, Bianchi G, Rossi B, Brizi M, Melchionda N: Nutritional treatment with branched-chain amino acids in advanced liver cirrhosis. *J Gastroenterol* 2000; 35(Suppl 12):7-12

24. Piche T, Schneider SM, Tran A, Benzaken S, Rampal P, Hebuterne X. Resting energy expenditure in chronic hepatitis C. *J Hepatol* 2000;33(4):623-7.

25. Rubbia-Brandt L, Fabris P, Paganin S, et al. Steatosis affects chronic hepatitis C progression in a genotype specific way. *Gut*. 2004;53:406-412.

26. Runyon BA: Management of adult patients with ascites caused by cirrhosis. [Review] *Hepatology* 1998; 27(1):264-272

27. Sharma P, Balan V, Hernandez J, et al. Hepatic steatosis in hepatitis C virus genotype 3 infection: does it correlate with body mass index, fibrosis, and HCV risk factors? *Dig Dis Sci*. 2004;49:25-29.

28. Swart GR, Vandenberg JWO, van Vuure JK et al: Minimum protein requirements in liver cirrhosis determined by nitrogen balance measurements at three levels of protein intake. *Clin Nutr* 1989; 8:329-336

29. Teran FC, McCullough AF: Nutrition in liver diseases. In Gottschlich MM (ed): *The Science and Practice of Nutrition Support: A Case-Based Core Curriculum*. American Society for Parenteral and Enteral Nutrition. Dubuque, Iowa: Kendall/Hunt Publishing Company, 2001:537-552

30. Von Herbay A, Stahl W, Niederau C et al:
Vitamin E improves the aminotransferase status of patients suffering from viral hepatitis C: a randomized, double-blind, placebo-controlled study. *Free Rad Res* 1997; 27(6):599-605

31. Weekly Epidemiological Record. N° 49, 10 December 1999, WHO

32. Zarski JP, McHutchison J, Bronowicki JP, Sturm N, Garcia-Kennedy R, Hodaj E, et al. Rate of natural disease progression in patients with chronic hepatitis C. *J Hepatol* 2003;38(3):307-14.

