CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187
http://doi.org/10.5281/zenodo.4395036

Avalable online at: http://www.iajps.com *Research Article*

EVIDENCE-BASED CLINICAL PRACTICE GUIDELINES FOR LIVER CIRRHOSIS

[1]Dr Ali Imran,[2]Dr Rimsha Sehar, [3]Dr Syeda Gul-e-Najaf

[1]MBBS, King Edward Medical University, Lahore.

[2]MBBS, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur, Azad Kashmir.

[3]MBBS, D.G Khan Medical Collge, Dera Ghazi Khan.

Article Received: October 2020 **Accepted:** November 2020 **Published:** December 2020

Abstract:

Liver disorders are curable at the early stages of onset of disease. After that it may be life threatening. Liver cirrhosis is a late stage of scarring (fibrosis) of the liver caused by many forms of liver diseases and conditions such as hepatitis and chronic alcoholism. Each time liver is injured whether by disease, excessive alcohol consumption or another cause like gastrointestinal bleeding and portal hypertension, hepatorenal syndrome, ascites, Hepatic encephalopathy, liver transplant it tries to repair itself. Anticoagulation therapy is proposed for patients with acute-onset or progressive portal vein thrombosis.

Corresponding author:

Dr. Ali Imran,

MBBS, King Edward Medical University, Lahore.

QR code

Please cite this article in press Ali Imran et al, ***Evidence-Based Clinical Practice Guidelines For Liver Cirrhosis.,*** *Indo Am. J. P. Sci, 2020; 07(12).*

INTRODUCTION:

Liver cirrhosis is a serious cause of death not in developed countries but worldwide. It is a diffuse hepatic process characterized by fibrosis and structurally abnormal nodules, representing the final histological change for a variety of chronic liver diseases. A decrease in the frequency of hepatitis C virus (HCV) infection as a major cause of cirrhosis and an increase in the number of non-B, non-C type cirrhosis. Cirrhosis is not a single disease entity, but has some serious complications, which enhances the disease prognosis. With continuous hepatocyte destruction and collagen deposition, the liver is shrunken in size and distorted in shape, forming multiple nodules of liver cells separated by broad fibrotic bands, which disturbs intrahepatic blood circulation and induces portal hypertension with extensive portocarval shunts. The major complications of cirrhosis, such as ascites, gastroesophageal varices, renal and cardiac disturbances and hepatic encephalopathy, occur mainly as a consequence of portal hypertension and hyperdynamic circulation and their hemodynamic and metabolic effects. These were world premiere comprehensive guidelines for liver cirrhosis, because the former American or European clinical practice guidelines for cirrhosis were divided into several themes that is, hepatitis C, hepatitis B, portal hypertension, alcoholic liver diseases, hepatic encephalopathy and ascites/hepatorenal syndrome (HRS), and not directed as a whole causes of liver cirrhosis.

Diagnosis of liver cirrhosis

On the characteristics of the patients, basic information on the cause of liver cirrhosis and from physical examination first gives a clue to the suspected diagnosis. Liver biopsy has been used for ages for the effective diagnosis of liver cirrhosis. Liver biopsy is an invasive procedure and has some limitations, including interobserver variation and sampling error. Although several noninvasive diagnostic methods have appeared, the selected methods includes the evaluation of tissue stiffness by transient elastography, determination of fibrosis scores based on several blood tests, liver biopsy and a morphological assessment with other imaging tools is useful for the diagnosis of liver cirrhosis in practice. An ideal simple noninvasive method should be further sought in the combination of numerous blood markers and imaging modalities.

Nutritional therapy

A evening snack of 200 kcal such as a and branched-chain amino acid ,rice ball, increasing body protein content, liquid nutrient, and branched-chain amino acid (BCAA) or enriched supplementation improves nocturnal fasting by improving nutritional status[1], and diminishes protein and fat oxidation.[2] It suppresses the serum free fatty acid levels[3] and recovers energy metabolism [4] at 1 week intake of good diet and serum albumin levels and nitrogen were balanced in the duration of 3 months.[5]Although its effect on survival rate has not been reported, it improves health-related quality of life.[6] These nutritional effects help cirrhotic patients having refractory ascites and undergoing repeated paracentesis[7] and also effective for those patients having hepatocellular carcinoma (HCC) and are receiving chemoembolization.[8]

Risk Factors

Risk factors contributes to liver cirrhosis are**:**

- Hepatitis B.
- Hepatitis C.
- Alcohol drinking.
- Infected blood transfusion.
- Obesity.
- Diabetes.
- Liver disturbance.
- Genetic predisposition.
- The family history of hematemesis.

Antiviral therapy for hepatitis B virus related cirrhosis

Antiviral therapy for hepatitis B includes nucleoside analogues (tenofovir, lamivudine, adefovir and entecavir) are recommended for such patients because they enhance sustained virological response and hepatitis B e antigen (HBeAg) , hepatitis B virus related cirrhosis and seroconversion in patients with hepatitis B virus.

Antiviral therapy for Hepatitis C related cirrhosis

Antiviral therapy for hepatitis C such as Interferon therapy is proposed for hepatitis C patients with compensated of hepatitis C related cirrhosis because it suppresses hepatocellular carcinoma (HCC) development and there is a possibility of an improvement in the prognosis of such patients.

Therapy for non-viral liver cirrhosis

Drinking alcohol is the main cause for non-viral cirrhosis, although drinking alcohol on alcoholic fibrosis needs to be clarified. Continued heavy drinking of alcohol was associated with poor survival of cirrhotic patients.[9] The mortality in patients with advanced alcoholic cirrhosis was extremely high with duration of 71 % for 5 years and 90 % for 15 years.[10] Continuous alcohol consumption and high age of more than 10 g ethanol per day were proposed for a

poor prognosis.[10] Corticosteroid therapy is proposed for patients with active autoimmune-hepatitis related cirrhosis because relief of fibrosis and improvement of prognosis are expected for the responders. Corticosteroid therapy is not proposed for patients with inactive autoimmune-hepatitis related cirrhosis because its effect is unknown. Fibrosis was progressed in 25 % of patients with long-term corticosteroid therapy and relieved in 53 % of patients.[11]

Gastrointestinal Bleeding and Portal Hypertension

In gastrointestinal bleeding and portan hypertension endoscopic injection sclerotherapy (EIS) is more useful than endoscopic variceal ligation (EVL) in preventing recurrence of esophageal varices. Endoscopic injection sclerotherapy is recommended for preventing recurrence because both the recurrence and the bleeding rates after endoscopic injection sclerotherapy are lower than the corresponding rates after endoscopic variceal ligation. Between these two groups, endoscopic injection sclerotherapy and endoscopic variceal ligation the eradication rate of esophageal varices was not significantly known, although the rate of recurrence of esophageal varices was higher in the endoscopic variceal ligation group than in the endoscopic injection sclerotherapy group.[12] Some studies concluded that endoscopic variceal ligation was ineffective as a prophylactic therapy, because both recurrence of portal hypertension and bleeding from oesophageal varices during the duration of 18 months follow-up period were observed more frequently in the endoscopic variceal ligation group than in endoscopic injection sclerotherapy group recurrence was about 56 % and 16 %, bleeding 20 % and 0 %). Endoscopic variceal ligation was proved to be no more effective than no treatment in preventing initial variceal bleeding than endoscopic injection sclerotherapy.[13] Endoscopic injection sclerotherapy was preferable in combination with endoscopic variceal ligation therapy as a means of preventing the recurrence of esophageal varices.[14]Some b-Blockers are known to be useful for primary prophylaxis of esophageal variceal bleeding. The combination of endoscopic therapy and b-blockers is proposed for secondary prophylaxis of esophageal variceal bleeding as it decreases rebleeding and mortality rate. A b- blocker like propranolol is proposed for management of portal hypertensive gastropathy because it is effective in relieving portal hypertensive gastropathy.

Ascites

Ascites is the abnormal buildup of fluid in the abdomen. Technically, it is more than 25 ml of fluid in the peritoneal cavity, although volumes greater than 1 liter may occur.

Symptoms

Symptoms may include

- Increased abdominal size.
- Increased weight.
- Abdominal discomfort.
- Shortness of breath.

The proper management of ascites begins with the optimal testing strategy for the differential diagnosis. Diagnostic paracentesis should include differential cell count, measurement of total protein and albumin concentration and cell count to rule out asymptomatic spontaneous bacterial peritonitis (SBP). Bacterial culture is also necessary if ascitic fluid infection is suspected. A salt-restricted diet is considered effective for mild to moderate ascites. A mild salt-restricted diet to maintain appetite is proposed for such patients. Although dietary salt has been restricted in European countries, this may cause protein malnutrition so it needs to be manage.[15] Contradictory results have been presented on the effect of salt restriction on the disappearance of ascites in patients taking diuretics.[16,17] The importance of an evening protein snack was stressed over salt restriction in survival of cirrhotic patients with refractory ascites.[18] A mild salt restriction (85–120 mmol/day) may be proposed to avoid appetite loss.

Hepatorenal Syndrome

Terlipressin with the infusion of albumin was proposed for patients with type 1 hepatorenal syndrome because 46 % of them improve with this type of therapy. Combination of treatment with midodrine, albumin infusion and octreotide improves the survival of patients with type 1 and type 2 hepatorenal syndrome. Albumin infusion and norepinephrine infusion is proposed for patients with hepatorenal syndrome because they are as effective as midodrine, albumin infusion and octreotide. Two types of hepatorenal syndrome have been discussed as type 1 is a rapidly progressive acute renal failure defined by a doubling of the initial serum creatinine level to greater than 2.5 mg/dL in less than 2 weeks.[19] Type 2 hepatorenal syndrome is characterized by moderate renal failure as initial serum creatinine level increase from 1.5 to 2.5 mg/dl) in patients with refractory ascites, showing a steady or slowly progressive course.[19] Several metaanalyses concluded that terlipressin showed higher efficacy in reversing renal function than placebo in type 1 hepatorenal syndrome patients receiving albumin infusion.[20-22] Some patients in them was also reported survival improvement with terlipressin therapy.[21,22]A study

revealed that the regimen of midodrine, albumin infusion and octreotide was significantly improved short-term survival and renal function in both type 1 and type 2 hepatorenal syndrome.[23] A study showed that norepinephrine is as safe and effective as terlipressin, but is less expensive in the treatment of type 1 and type 2 hepatorenal syndrome.[24,25,26]Albumin and norepinephrine were proposed because norepinephrine is the only drug approved by the National Health Insurance. The International Club of Ascites recently proposed a revised consensus recommendation where an increase in initial serum creatinine level greater than two fold from the baseline without a response to withdrawal of diuretics and volume expansion with albumin (1 g/kg) for 2 days is considered as type 1 hepatorenal syndrome.[27] This revision was in the expectation of a better therapeutic effect by early diagnosis. Liver transplant is recommended for both type 1 and type 2 hepatorenal syndrome if indicated.

Hepatic Encephalopathy

Protein-restricted diets are not proposed for long-term management of cirrhotic patients because they may enhance protein breakdown and worsen the prognosis of cirrhotic patients. Normal protein diet was recommended because a low-protein diet was proved to cause higher protein breakdown as compare to diets with a normal protein content. This type of protein is metabolically more adequate and tolerable for cirrhotic patients with episodic hepatic encephalopathy.[28] Protein restricted diet does not confer any benefit to patients during an episode of encephalopathy.[29] Disaccharides are recommended for patients with hepatic encephalopathy because they improve the parameters and relieve the symptoms of hepatic encephalopathy. Randomized controlled trials showed nonabsorbable disaccharides such as lactulose that improve the parameters of hepatic encephalopathy.[30,31] Nonabsorbable disaccharides seemed to reduce the risk of no improvement in patients with hepatic encephalopathy but they showed no significant effect on mortality compared with no intervention and placebo.[32] Lactulose the disaccharides appears to have the most beneficial effect on minimal hepatic encephalopathy, followed closely by symbiotic and probiotics.[33]

Liver Transplant

Survival rates were increased by liver transplant, its indication should be carefully evaluated in each patient.[34]In almost 12,966 patients it is analyzed that on the waiting list for liver transplant and reported that significant progression in survival benefit was demonstrated. Antiviral therapies are recommended for viral cirrhosis patients receiving a liver transplant because they are useful for management of recurrent hepatitis B virus and hepatitis C virus. Introduction of antiviral therapy for liver transplant, 67 % of patients had hepatitis B with the duration of 3 years, and survival rate was about 68 % for 1 year and 44 % for 3 years.[35]After liver transplant for hepatitis C virus cirrhosis, 20–40 % of patients was progressed to allow grafting for cirrhosis within the duration of 5 years. The rate of their decompensation was about more than 60 % for 3 years and 40 % for 1 years.[36] Although nucleoside analogues are useful for preventing hepatitis B virus reoccurrences, the reoccurrences rate was lowest in patients who received nucleoside analogue prophylaxis (6.6 %) and hepatitis B immunoglobulin as compared to those receiving hepatitis B immunoglobulin prophylaxis alone (26.2 %) and nucleoside analogue prophylaxis alone (19.0 %).[37] In hepatitis C, antiviral therapy slows disease progression [235]. Ribavirin therapy with peginterferon-a2b for 48 weeks led to survival rate was about 18.5 %of F3–F4 fibrosis patients and 48 % of F0–F2 fibrosis patients. Fibrosis progression by one or more stages was noticed 54 % of treated F3–F4 fibrosis patients and 26 % of treated F0–F2 fibrosis patients and 70 % of untreated F0–F2 fibrosis patients.[38]

CONCLUSION:

From the above study we get to know that liver cirrhosis is curable at its early stages, although after ages or prolonged disease however it is incurable. Chronic liver disease if remains untreated for longer period of time it may be fatal. After different stages if liver disease remains untreated it may be irreversible causing death. Liver transplant is although a good option in liver cirrhosis however liver has power to regenerate itself.

REFERENCES:

1. Plank LD, Gane EJ, Peng S, et al. Nocturnal nutritional supplementation improves total body protein status of patients with liver cirrhosis: a randomized 12-month trial. Hepatology. 2008;48:557–66.
2. Chang WK, Chao YC, Tang HS, et al. Effects of extra-carbohydrate supplementation in the late evening on energy expenditure and substrate oxidation in patients with liver cirrhosis. JPEN J Parenter Enteral Nutr. 1997;21:96–9.
3. Yamauchi M, Takeda K, Sakamoto K, et al. Effect of oral branched chain amino acid supplementation in the late evening on the nutritional state of patients with liver cirrhosis. Hepatol Res. 2001;21:199–204.
4. Yamanaka-Okumura H, Nakamura T, Takeuchi H, et al. Effect of late evening snack with rice ball

on energy metabolism in liver cirrhosis. Eur J Clin Nutr. 2006;60:1067–72.
5. Nakaya Y, Okita K, Suzuki K, et al. BCAA-enriched snack improves nutritional state of cirrhosis. Nutrition. 2007;23:113–20.
6. Yamanaka-Okumura H, Nakamura T, Miyake H, et al. Effect of long-term late-evening snack on health-related quality of life in cirrhotic patients. Hepatol Res. 2010;40:470–6.
7. Sorrentino P, Castaldo G, Tarantino L, et al. Preservation of nutritional-status in patients with refractory ascites due to hepatic cirrhosis who are undergoing repeated paracentesis. J Gastroenterol Hepatol. 2012;27:813–22.
8. Takeshita S, Ichikawa T, Nakao K, et al. A snack enriched with oral branched-chain amino acids prevents a fall in albumin in patients with liver cirrhosis undergoing chemoembolization for hepatocellular carcinoma. Nutr Res. 2009;29:89–93.
9.Borowsky SA, Strome S, Lott E. Continued heavy drinking and survivalinalcoholiccirrhotics.Gastroenterology.1981;80:1405–9.
10. Bell H, Jahnsen J, Kittang E, et al. Long-term prognosis of patients with alcoholic liver cirrhosis: a 15-year follow-up study of 100 Norwegian patients admitted to one unit. Scand J Gastroenterol. 2004;39:858–63.
11. Czaja AJ, Carpenter HA. Progressive fibrosis during corticosteroid therapy of autoimmune hepatitis. Hepatology. 2004;39:1631–8.
12.Svoboda P, Kantorova I, Ochmann J, et al. A prospective randomized controlled trial of sclerotherapy vs ligation in the prophylactic treatment of high-risk esophageal varices. Surg Endosc. 1999;13:580–4.
13.Triantos C, Vlachogiannakos J, Armonis A, et al. Primary prophylaxis of variceal bleeding in cirrhotics unable to take betablockers: a randomized trial of ligation. Aliment Pharmacol Ther. 2005;21:1435–43.
14. Iso Y, Kawanaka H, Tomikawa M, et al. Repeated injection sclerotherapy is preferable to combined therapy with variceal ligation to avoid recurrence of esophageal varices: a prospective randomized trial. Hepatogastroenterology. 1997;44:467–71.
15. Moore KP, Aithal GP. Guidelines on the management of ascites in cirrhosis. Gut 2006;55;Suppl 6:vi1-12.
16. Gauthier A, Levy VG, Quinton A, et al. Salt or no salt in the treatment of cirrhotic ascites: a randomised study. Gut. 1986;27:705–9.
17. Bernardi M, Laffi G, Salvagnini M, et al. Efficacy and safety of the stepped care medical treatment of ascites in liver cirrhosis: a randomized controlled clinical trial comparing two diets with different sodium content. Liver. 1993;13:156–62.
18. Sorrentino P, Castaldo G, Tarantino L, et al. Preservation of nutritional-status in patients with refractory ascites due to hepatic cirrhosis who are undergoing repeated paracentesis. J Gastroenterol Hepatol. 2012;27:813–22.
19. Salerno F, Gerbes A, Gines P, et al. Diagnosis, prevention and treatment of hepatorenal syndrome in cirrhosis. Gut. 2007;56:1310–8.
20. Fabrizi F, Dixit V, Messa P, Martin P. Terlipressin for hepatorenal syndrome: a meta-analysis of randomized trials. Int J Artif Organs. 2009;32:133–40.
21. Sagi SV, Mittal S, Kasturi KS, Sood GK. Terlipressin therapy for reversal of type 1 hepatorenal syndrome: a meta-analysis of randomized controlled trials. J Gastroenterol Hepatol. 2010;25:880–5.
22. Gluud LL, Christensen K, Christensen E, Krag A. Terlipressin for hepatorenal syndrome. Cochrane Database Syst Rev. 2012;(9):CD005162.
23. Skagen C, Einstein M, Lucey MR, Said A. Combination treatment with octreotide, midodrine, and albumin improves survival in patients with type 1 and type 2 hepatorenal syndrome. J Clin Gastroenterol. 2009;43:680–5.
24. Alessandria C, Ottobrelli A, Debernardi-Venon W, et al. Noradrenalin vs terlipressin in patients with hepatorenal syndrome: a prospective, randomized, unblinded, pilot study. J Hepatol. 2007;47:499–505.
25. Singh V, Ghosh S, Singh B, et al. Noradrenaline vs. terlipressin in the treatment of hepatorenal syndrome: a randomized study. J Hepatol. 2012;56:1293–8.
26. Ghosh S, Choudhary NS, Sharma AK, et al. Noradrenaline vs terlipressin in the treatment of type 2 hepatorenal syndrome: a randomized pilot study. Liver Int. 2013;33:1187–93.
27.Angeli P, Gines P, Wong F, et al. Diagnosis and management of acute kidney injury in patients with cirrhosis: revised consensus recommendations of the International Club of Ascites. Gut. 2015;64:531–7.
28. Cordoba J, Lopez-Hellin J, Planas M, et al. Normal protein diet for episodic hepatic encephalopathy: results of a randomized study. J Hepatol. 2004;41:38–43.
29. Plauth M, Cabre E, Riggio O, et al. ESPEN Guidelines on Enteral Nutrition: liver disease. Clin Nutr. 2006;25:285–94.
30. Sharma BC, Sharma P, Agrawal A, Sarin SK. Secondary prophylaxis of hepatic

encephalopathy: an open-label randomized controlled trial of lactulose versus placebo. Gastroenterology 2009;137:885–91.e1.
31. Sharma P, Agrawal A, Sharma BC, Sarin SK. Prophylaxis of hepatic encephalopathy in acute variceal bleed: a randomized controlled trial of lactulose versus no lactulose. J Gastroenterol Hepatol. 2011;26:996–1003.
32. Als-Nielsen B, Gluud LL, Gluud C. Non-absorbable disaccharides for hepatic encephalopathy: systematic review of randomised trials. BMJ. 2004;328:1046.
33. Shukla S, Shukla A, Mehboob S, Guha S. Meta-analysis: the effects of gut flora modulation using prebiotics, probiotics and synbiotics on minimal hepatic encephalopathy. Aliment Pharmacol Ther. 2011;33:662–71.
34.Merion RM, Schaubel DE, Dykstra DM, et al. The survival benefit of liver transplantation. Am J Transplant. 2005;5:307–13.
35.Samuel D, Muller R, Alexander G, et al. Liver transplantation in European patients with the hepatitis B surface antigen. N Engl J Med. 1993;329:1842–7.
36. Gane E. The natural history and outcome of liver transplantation in hepatitis C virus-infected recipients. Liver Transpl. 2003;9:S28–34.
37. Cholongitas E, Goulis J, Akriviadis E, Papatheodoridis GV. Hepatitis B immunoglobulin and/or nucleos(t)ide analogues for prophylaxis against hepatitis b virus recurrence after liver transplantation: a systematic review. Liver Transpl. 2011;17:1176–90.
38. Carrion JA, Navasa M, Garcia-Retortillo M, et al. Efficacy of antiviral therapy on hepatitis C recurrence after liver transplantation: a randomized controlled study. Gastroenterology. 2007;132:1746–56.