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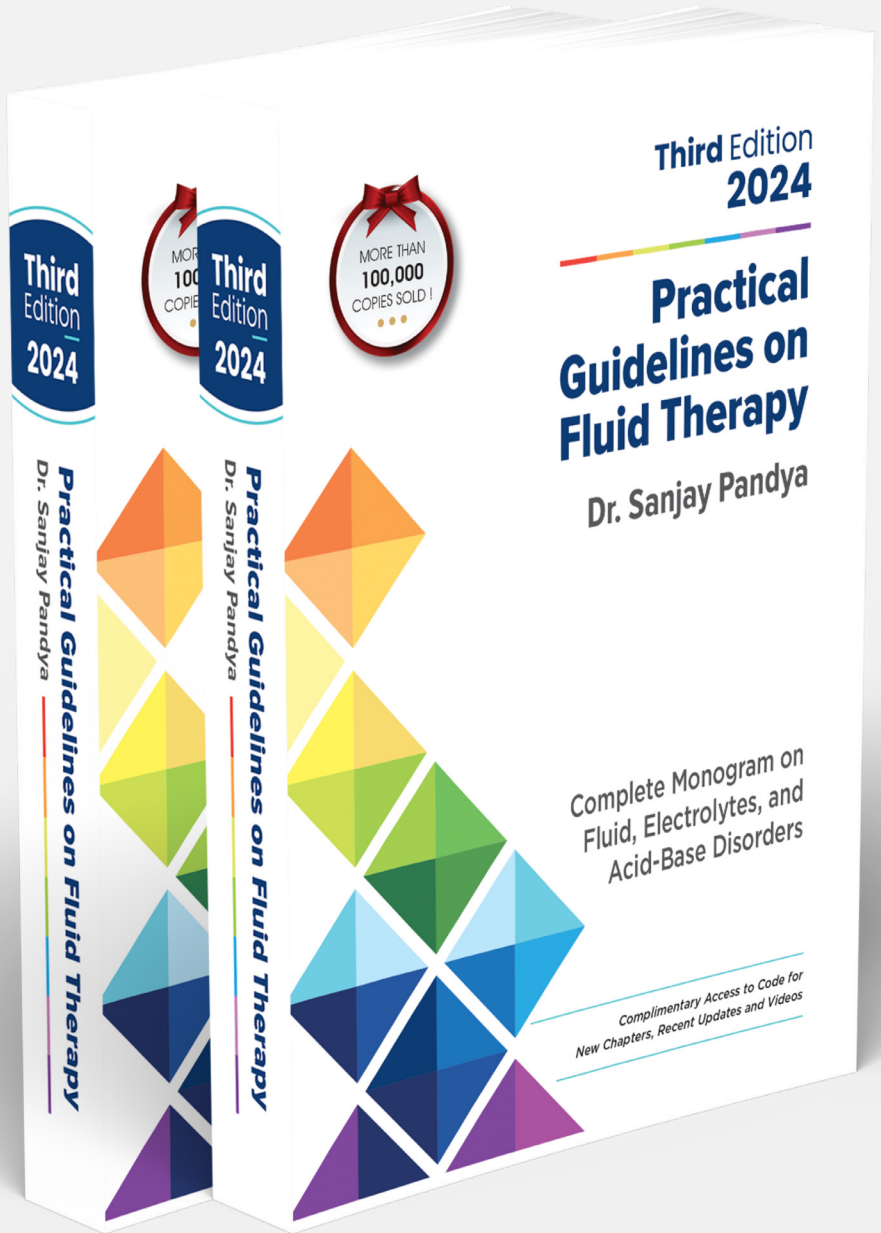
Chapter 36:

Hepatic Encephalopathy



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36 Hepatic Encephalopathy

Hepatic encephalopathy (HE) is a potentially reversible condition characterized by a spectrum of neurological or psychiatric abnormalities ranging from subclinical alterations to coma, which occurs as one of the many complications of decompensated liver disease or portosystemic shunting [1]. About 30 to 45% of patients with cirrhosis develop overt hepatic encephalopathy [2], which is associated with significant morbidity, mortality, high healthcare cost, and a huge burden on patients and their caregivers [3, 4].

PATHOPHYSIOLOGY

The pathophysiology of HE is poorly understood, it is often multifactorial, and different abnormalities may be present at the same time, leading to the development of HE [5].

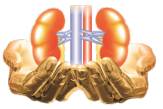
The various pathogenetic mechanisms proposed in the development of HE are [5, 6]:

- Neurotoxins (Ammonia, benzodiazepines, benzodiazepine-like compounds such as gamma-aminobutyric acid, and manganese deposition within the basal ganglia).
- Alteration in neurotransmission due to increased GABA - neurotransmitters and serotonin activity in HE.
- False neurotransmitters such as tyramine, octopamine, and beta-phenylethanolamines may compete with the normal catecholamine neurotransmitters.
- Altered brain energy due to impaired hepatic gluconeogenesis in the terminal stages of liver failure.
- The systemic inflammatory response may exacerbate the harmful effects of hyperammonaemia on the brain [7].
- Alterations of the blood-brain barrier contribute to an increased influx of varieties of neurotoxic substances into the brain, which may contribute to HE.

REFERENCES

1. Vilstrup H, Amodio P, Bajaj J, et al. Hepatic encephalopathy in chronic liver disease: 2014 Practice Guideline by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. Hepatology. 2014;60(2):715–35.
2. Romero-Gómez M, Boza F, García-Valdecasas MS, et al. Subclinical hepatic encephalopathy predicts the development of overt hepatic encephalopathy. Am J Gastroenterol 2001;96(9):2718–23.
3. Kabaria S, Dalal I, Gupta K, et al. Hepatic Encephalopathy: A Review. EMJ Hepatol. 2021;9(1):89–97.
4. García-Martínez R, Diaz-Ruiz R, Poncela M. Management of Hepatic Encephalopathy Associated with Advanced Liver Disease. Clin Drug Investig. 2022;42(Suppl 1):5–13.
5. Elwir S, Rahimi RS. Hepatic Encephalopathy: An Update on the Pathophysiology and Therapeutic Options. J Clin Transl Hepatol. 2017;5(2):142–151.
6. Ferenci P. Hepatic encephalopathy. Gastroenterol Rep (Oxf). 2017;5(2):138–147.
7. Shawcross DL, Davies NA, Williams R, et al. Systemic inflammatory response exacerbates the neuropsychological effects of induced hyperammonaemia in cirrhosis. J Hepatol. 2004;40(2):247–54.
8. Jaffe A, Lim JK, Jakab SS. Pathophysiology of Hepatic Encephalopathy. Clin Liver Dis. 2020;24(2):175–188.
9. Häussinger D, Dhiman RK, Felipo V, et al. Hepatic encephalopathy. Nat Rev Dis Primers. 2022;8(1):43.
10. Montagnese S, Russo FP, Amodio P, et al. Hepatic encephalopathy 2018: A clinical practice guideline by the Italian Association for the Study of the Liver (AISF). Dig Liver Dis. 2019;51(2):190–205.
11. Hasan LZ, Wu GY. Novel Agents in the Management of Hepatic Encephalopathy: A Review. J Clin Transl Hepatol. 2021;9(5):749–759.
12. Bajaj JS, O'Leary JG, Lai JC, et al. Acute-on-Chronic Liver Failure Clinical Guidelines. Am J Gastroenterol. 2022;117(2):225–252.
13. Hoilat GJ, Suhail FK, Adhami T, et al. Evidence-based approach to management of hepatic encephalopathy in adults. World J Hepatol 2022;14(4):670–681.
14. 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(3):454–460.e3.
15. Faccioli J, Nardelli S, Gioia S, et al. Nutrition Assessment and Management in Patients with Cirrhosis and Cognitive Impairment: A Comprehensive Review of Literature. J. Clin. Med. 2022;11(10):2842.
16. Amodio P, Bemeur C, Butterworth R, et al. The nutritional management of hepatic encephalopathy in patients with cirrhosis: International Society for Hepatic Encephalopathy and Nitrogen Metabolism Consensus. Hepatology 2013;58(1):325–36.
17. Córdoba J, López-Hellín J, Planas M, et al. Normal protein diet for episodic hepatic encephalopathy: results of a randomized study. J Hepatol. 2004;41(1):38–43.
18. Maharshi S, Sharma BC, Srivastava S. Malnutrition in cirrhosis increases morbidity and mortality. J Gastroenterol Hepatol. 2015;30(10):1507–13.
19. Plauth M, Bernal W, Dasarathy S, et al. ESPEN guideline on clinical nutrition in liver disease. Clin Nutr. 2019;38(2):485–521.
20. Bianchi GP, Marchesini G, Fabbri A, et al. Vegetable versus animal protein diet in cirrhotic patients with chronic encephalopathy. A randomized cross-over comparison. J Intern Med. 1993;233(5):385–92.
21. Merli M, Iebba V, Giusto M. What is new about diet in hepatic encephalopathy. Metab Brain Dis. 2016;31(6):1289–1294.
22. Tsien CD, McCullough AJ, Dasarathy S. Late evening snack: exploiting a period of anabolic opportunity in cirrhosis. J Gastroenterol Hepatol. 2012;27(3):430–41.
23. Gluud LL, Dam G, Les I, et al. Branched-chain amino acids for people with hepatic encephalopathy. Cochrane Database Syst Rev. 2017;2017(5):CD001939.
24. Katayama K, Kawaguchi T, Shiraishi K, et al. The Prevalence and Implication of Zinc Deficiency in Patients With Chronic Liver Disease. J Clin Med Res. 2018;10(5):437–444.
25. Silva M, Gomes S, Peixoto A, et al. Nutrition in Chronic Liver Disease. GE Port J Gastroenterol. 2015;22(6):268–276.

26. Loomba V, Pawar G, Dhar KL, et al. Serum zinc levels in hepatic encephalopathy. Indian J Gastroenterol. 1995;14(2):51–53.
27. Takuma Y, Nouso K, Makino Y, et al. Clinical trial: oral zinc in hepatic encephalopathy. Aliment Pharmacol Ther. 2010;32(9):1080–90.
28. Chavez-Tapia NC, Cesar-Arce A, Barrientos-Gutiérrez 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.
29. Shen YC, Chang YH, Fang CJ, et al. Zinc supplementation in patients with cirrhosis and hepatic encephalopathy: a systematic review and meta-analysis. Nutr J. 2019;18(1):34.
30. Fallahzadeh MA, Rahimi RS. Hepatic Encephalopathy and Nutrition Influences: A Narrative Review. Nutr Clin Pract. 2020;35(1):36–48.
31. Hung TH, Tseng CW, Tsai CC, et al. Prognosis of hypoglycemia episode in cirrhotic patients during hospitalization. BMC Gastroenterol. 2021;21(1):319.
32. Scheiner B, Lindner G, Reiberger T, et al. Acid-base disorders in liver disease. J Hepatol. 2017;67(5):1062–1073.
33. Jiménez JV, Carrillo-Pérez DL, Rosado-Canto R, et al. Electrolyte and Acid-Base Disturbances in End-Stage Liver Disease: A Physiopathological Approach. Dig Dis Sci. 2017;62(8):1855–1871.
34. Musso CG, Juarez R, Glassock RJ. Water, electrolyte, acid-base, and trace elements alterations in cirrhotic patients. Int Urol Nephrol. 2018;50(1):81–89.
35. Katopodis P, Pappas EM, Katopodis KP. Acid-base abnormalities and liver dysfunction. Ann Hepatol. 2022;27(2):100675.
36. Mikkelsen ACD, Thomsen KL, Vilstrup H, et al. Potassium deficiency decreases the capacity for urea synthesis and markedly increases ammonia in rats. Am J Physiol Gastrointest Liver Physiol. 2021;320(4):G474–G483.
37. Zavagli G, Ricci G, Bader G, et al. The importance of the highest normokalemia in the treatment of early hepatic encephalopathy. Miner Electrolyte Metab. 1993;19(6):362–7.
38. European Association for the Study of the Liver. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. J Hepatol. 2018;69(2):406–460.
39. Fortune B, Cardenas A. Ascites, refractory ascites and hyponatremia in cirrhosis. Gastroenterol Rep (Oxf). 2017;5(2):104–112.
40. Alukal JJ, John S, Thuluvath PJ. Hyponatremia in Cirrhosis: An Update. Am J Gastroenterol. 2020;115(11):1775–85.
41. Sharma BC, Sharma P, Agrawal A, et al. Secondary prophylaxis of hepatic encephalopathy: an open-label randomized controlled trial of lactulose versus placebo. Gastroenterology. 2009;137(3):885–91, 891.e1.
42. Gluud LL, Vilstrup H, Morgan MY. Non-absorbable disaccharides vs placebo/no intervention and lactulose vs lactitol for the prevention and treatment of hepatic encephalopathy in people with cirrhosis. Cochrane Database Syst Rev. 2016;4:CD003044.
43. Morgan MY, Hawley KE, Stambuk D. Lactitol versus lactulose in the treatment of chronic hepatic encephalopathy. A double-blind, randomised, cross-over study. J Hepatol. 1987;4(2):236–44
44. Bass N, Mullen K, Sanyal A, et al. Rifaximin treatment in HE. N Engl J Med. 2010;362(12):1071–1081.
45. Sanyal A, Younossi ZM, Bass NM, et al. Randomised clinical trial: rifaximin improves health-related quality of life in cirrhotic patients with hepatic encephalopathy - a double-blind placebo-controlled study. Aliment Pharmacol Ther. 2011;34(8):853–61.
46. Eltawil KM, Laryea M, Peltekian K, et al. Rifaximin vs. conventional oral therapy for hepatic encephalopathy: a meta-analysis. World J Gastroenterol 2012;18(8):767–77.
47. Kimer N, Krag A, Møller S, et al. Systematic review with meta-analysis: the effects of rifaximin in hepatic encephalopathy. Aliment Pharmacol Ther 2014;40(2):123–32.
48. Bajaj JS, Barrett AC, Bortey E, et al. Prolonged remission from hepatic encephalopathy with rifaximin: results of a placebo crossover analysis. Aliment Pharmacol Ther 2015;41(1):39–45.
49. Patel VC, Lee S, McPhail MJW, et al. Rifaximin-α reduces gut-derived inflammation and mucin degradation in cirrhosis and encephalopathy: RIFSYS randomised controlled trial. J Hepatol 2022;76(2):332–342.
50. Sharma BC, Sharma P, Lunia MK, et al. A randomized, double-blind, controlled trial comparing rifaximin plus lactulose with lactulose alone in treatment of overt hepatic encephalopathy. Am J Gastroenterol. 2013;108(9):1458–1463.
51. Hudson M, Schuchmann M. Long-term management of hepatic encephalopathy with lactulose and/or rifaximin: a review of the evidence. Eur J Gastroenterol Hepatol. 2019;31(4):434–450.
52. Wang Z, Chu P, Wang W. Combination of rifaximin and lactulose improves clinical efficacy and mortality in patients with hepatic encephalopathy. Drug Des Devel Ther. 2018;13:1–11.
53. Fu J, Gao Y, Shi L. Combination therapy with rifaximin and lactulose in hepatic encephalopathy: A systematic review and meta-analysis. PLoS ONE 2022;17(4):e0267647.

KidneyEducation 

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