Management Patterns of Hepatic Encephalopathy: A Nationwide Survey in India

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Introduction and aim: **Hepatic encephalopathy (HE) is a common complication of cirrhosis. There is no standard practice for its management. This survey was done to determine the diagnostic and therapeutic practices of physicians treating patients with HE in patients with cirrhosis.** ***Material and method:*** **We designed a 21-item questionnaire, which was given to physicians working in academic and non-academic institutes and regularly treating patients with HE.** ***Results:*** **Of 500 printed questionnaires, we received 451 questionnaires [323 (72%) general physicians and 128 (28%) gastroenterologists] from academic and non-academic institutes. Commonest precipitating event of HE was upper gastrointestinal bleed (47%), constipation (18%) and spontaneous bacterial peritonitis (12%). Arterial ammonia was always measured at admission by 156 (35%) physicians, never measured by 128 (28%) and sometimes by 167 (37%). Prophylactic antibiotics were used by 54% of physicians on the day of admission irrespective of any precipitating event, and 13% used antibiotics only if cultures were positive while others used antibiotics only if patient needs intubation or had variceal bleed as the cause of precipitation of HE. Disaccharides remained the mainstay of treatment in the management of HE and were always used by 87% (n = 391) followed by LOLA (n = 297, 66%) and rifaximin (n = 276, 61%). Combination of therapy was used by 84% of respondents. Lactulose enema was used in patients with HE by 280 (62%) physicians and was thought to be as good as giving lactulose by mouth or nasogastric tube in the treatment of HE. Regarding the recovery of HE with the present mode of therapy, of 451 responses, only 11% (n = 49) got 90–100% response to present therapy for the recovery of HE, while 70–90% response was seen by n = 152 (34%) and 50–70% response was seen by n = 183 (41%). Lactulose was prescribed as secondary prophylaxis agent more by gastroenterologists than non-gastroenterologists (76% vs 41%, P = 0.001). Similarly, rifaximin was more prescribed by gastroenterologists at discharge compared to non-gastroenterologists (32% vs 17%, P = 0.001).** ***Conclusion:*** **Non-absorbable disaccharides are the most commonly prescribed treatment for HE and for secondary prophylaxis of HE. Combination of therapy (lactulose and LOLA or lactulose and rifaximin) was commonly used by treating physicians. (J Clin Exp Hepatol 2015;5:199–203)**

Hepatic encephalopathy (HE) is a challenging clinical complication of liver dysfunction with a wide spectrum of neuropsychiatric abnormalities that range from mild disturbances in cognitive function and consciousness to coma and death.[1,] The prevalence of overt HE at the time of diagnosis of cirrhosis is 10–14% in general, 16–21% in those with decompensated cirrhosis and 10–50% in patients with transjugular intrahepatic portosystemic shunt (TIPS).[2–4] The cumulated numbers indicate that overt HE will occur in 30–40% of those with cirrhosis at some time during their clinical course and in the survivors in most cases repeatedly. The pathogenesis of HE in cirrhosis is complex and multifactorial, but a key role is thought to be played by circulating gut-derived toxins of the nitrogenous compounds, most notably ammonia. Therapeutic treatment options for HE are currently limited and have appreciable risks and benefits associated with their use. Management of HE primarily involves avoidance of precipitating factors, limitation of dietary protein intake and administration of various ammonia-lowering therapies such as non-absorbable disaccharides and select antimicrobial agents.[5] Non-absorbable disaccharides, such as lactulose, have traditionally been regarded as first-line pharmacotherapy for patients with HE. Rifaximin is a novel antimicrobial agent with a wide spectrum of activity that has shown promise as an alternative antimicrobial treatment option for HE.[6–9] Several clinical trials have compared rifaximin to the disaccharides, lactulose and lactitol and the antimicrobial neomycin. Rifaximin appears to be at least as effective as conventional drug therapy and has been associated with fewer adverse effects due to its limited systemic absorption. Patients with recurrent HE episodes despite lactulose use benefit from the addition of rifaximin, which decreases the frequency of recurrent HE episodes and related hospitalizations.[10–12]

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Abbreviations: HE: hepatic encephalopathy; TIPS: transjugular intrahepatic portosystemic shunt
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In most countries, Internists and Gastroenterologists are the primary doctors who take care of patients with HE. However, there is no standard treatment protocol in most countries for the management of HE. We conducted a nationwide survey in India amongst Internists and Gastroenterologists to know their management practices in patients with HE and cirrhosis.

MATERIAL AND METHODS

This survey was designed and initiated by the author (P.S.). A printed questionnaire was sent to participants identified from the membership lists of various physician societies. The questionnaire was divided into several sections: (1) participant information (place of practice and speciality, number of patients with cirrhosis and HE which were seen in a month); (2) precipitants of HE and treatment regimen used; (3) prophylaxis of HE if any used at the time of discharge; and (4) ways of increasing awareness among physicians.

STATISTICAL ANALYSIS

Data were expressed as mean ± S.D. For a comparison of categorical variables, chi-square and Fisher's exact tests were used, and for continuous variables, a Mann–Whitney test for unpaired data and a Wilcoxon rank sum test for paired data were used as appropriate.

RESULTS

Study Participants

Five hundred questionnaires were printed and distributed at random to various physicians who had completed 3 years of internal medicine training after graduation and had at least 3 years of experience in clinical practice. Similarly, questionnaire was given to specialists in gastroenterology who had 3 years of training in the field of gastroenterology after completing their internal medicine training. Of 500 printed questionnaires, 451 completed responses were collected manually by volunteers for this study from their working place, and hence, we had a good response rate of 90%. The characteristics of the surveyed physicians are listed in Table 1. Most physicians had a hospital-based practice and 60% were from non-teaching hospital.

Management of HE

The commonest precipitating event of HE was upper gastrointestinal bleed (47%), constipation (18%) and spontaneous bacterial peritonitis (12%). However, according to this survey, no cause could be elicited in 21% and infections other than spontaneous bacterial peritonitis was the cause of HE in only 2% (Figure 1).

Table 1 Baseline Characteristics of Physicians.

Parameters	*n* (%)
General physicians (M.D.)	323 (72%)
Gastroenterologists (M.D, D.M.)	128 (28%)
Place of work	
Teaching hospital	167 (37%)
Non-teaching hospital	284 (63%)
Number of cirrhosis patients with HE seen in a month	
1–5	270 (60%)
6–10	110 (24%)
>10	71 (16%)

M.D., Master in Internal Medicine; D.M., Master in Gastroenterology.

Prophylactic endotracheal intubation is not a routine practice even in patients with higher grade of HE (HE 3, 4) in patients with cirrhosis. Only 39% ($n = 174$) routinely intubate patients with grade 3 and 4 HE, while 61% ($n = 277$) did not intubate these patients and manage patients with constant strict supervision care. We did not find any difference between Gastroenterologists and Internists regarding prophylactic intubation of patients with grade 3 and 4 HE (38% vs 41%, $P = 0.08$). Similarly, there was no difference between physicians working in teaching vs non-teaching hospital regarding prophylactic endotracheal intubation in these patients (41% vs 37%, $P = 0.48$).

Arterial ammonia was always measured at admission by 156 (35%) physicians, never measured by 128 (28%) and sometimes by 167 (37%). We find significant difference between Gastroenterologists and Internists (40% vs 20%, $P = 0.01$) regarding the role of ammonia measurement during management of HE.

Management of Acute Episode of HE with Disaccharides, Rifaximin, LOLA and Combination Therapy

Prophylactic antibiotics were used by 54% of physicians on the day of admission irrespective of any precipitating event, and 13% used antibiotics only if cultures were positive, while others used antibiotics only if patient need intubation or had variceal bleed as the cause of precipitation of HE. Disaccharides remain the mainstay of treatment in the management of HE and were always used by 87% ($n = 391$) followed by LOLA ($n = 297$, 66%) and rifaximin ($n = 276$, 61%). Combination of therapy was used by 84% of respondents (Table 2). However, 378 respondents (84%) still believe that there should be more studies on combination therapy for the treatment of HE, while 38 (8%) were convinced with the present data available and further 8% were not sure of this combination therapy.