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Research Article

Early Reversal of Hepatic Encephalopathy in Patients with Advanced Liver Disease with and without Branched Chain Amino Acids (BCAA)

Adeel Riaz,[1] Shaheryar Nazim[2]

and Maryam Shahid[3]

[1]Department of Medicine, Services Hospital, Lahore
[2]Department of Medicine, Services Hospital, Lahore
[3]Fatima Jinnah Medical College, Lahore
Correspondence: Dr. Adeel Riaz (House Officer),
Cell: 03334632286, Email: adeelqureshi86@gmail.com

ABSTRACT

Objectives: Compare the frequency of early reversal of hepatic encephalopathy in patients with advanced liver disease with and without BCAA.

Methodology: This study was conducted at Services Hospital, Lahore during 2013-14 we enrolled 100 cases (50 in each group) with Hepatic encephalopathy grade III or IV and Spleenomegaly & coarse liver on ultrasonography between 30-60 years of either sex, we excluded those cases with Serum bilirubin >5mg/dl, upper GIT bleed, Co morbidities i.e. History of Diabetes mellitus, Hypertension, Ischemic heart disease or Chronic kidney disease. Informed consent was taken from each attendant. Risks and benefits were explained. Demographic information including name, age, & address was taken from attendant and kept confidential. Grade of hepatic encephalopathy was established clinically on the day of admission and then daily on next 3consecutive post admission days. Subjects were assigned in to two groups by non probability randomly using random tables. Group I was given conventional therapy for hepatic encephalopathy along with intravenous BCAA 1000ml once daily while Group II was only on conventional therapy. All data collected from patients given BCAA and those not given BCAA and changes in grades of hepatic encephalopathy was recorded.

Results: Majority of the patients in both groups i.e. 44%(n=22) in Group-A and 52%(n=26) in Group-B between 41-50 years, mean and sd was calculated as 43.98+3.76 and 44.32+3.02 respectively, 66%(n=33) in Group-A and 58%(n=29) inGroup-B were male while rest of 34%(n=17) in Group-A and 42%(n=21) in Group-B were females, comparison of early reversal of hepatic encephalopathy in patient with advanced liver disease with and without BCCA which shows 64%(n=32) in Group-A and 26(n=13) in Group-B while rest of 36%(n=18)in Group-A and 74%(=37) in Group-B had no early reversal, p value was recorded as 0.00 which shows significant difference in both groups.

Conclusion: Comparison of frequency of early reversal of hepatic encephalopathy in patients with advanced liver disease with and without BCAA reveals that early reversal of hepatic encephalopathy is achieved in patients treated with BCAA

Keywords: Advance liver disease, hepatic encephalopathy, early reversal, branched chain amino acids

INTRODUCTION

Hepatitis B virus & hepatitis C virus infections contribute to the global public health threats confronting most developing countries, where health care systems lack the safety measures necessary to avert the risks of infection and public awareness about the modes of transmission is insufficient.[1,2] Chronic liver disease and cirrhosis result in about 35,000 deaths each year in United States.[3] Porto systemic encephalopathy is a serious complication of chronic liver disease.[4] It is a state of disordered central nervous system function resulting from failure of the liver to

detoxify noxious agents of gut origin due to hepatocellular dysfunction and Porto systemic shunting.[5]The spectrum ranges from day & night reversal and mild intellectual impairment to coma.[5]Malnutrition is an important complication & an important prognostic indicator of clinical outcome (survival rate, length of hospital stay & quality of life) in patients with cirrhosis.[6] According to one study BCAA (branched chain amino acids) have apromising role in early reversal of hepatic encephalopathy & decreases the unnecessary burden on health care resources.[7] The study shows that in group I (receiving standard treatment), 11 patients out of 44 of grade IV encephalopathy showed improvement to grade I in lessthan 3 days (25%) compared to 26 (56.5%) of in group II (receiving BCAA in addition to standard treatment). 8 patients showed improvement in 3-9 days (8.8%) & 11 (23.9%) of in group II. 25 patients showed improvement in more than 9 days (56.8%) & 9 patients (19.56%) in group II.[7]

In another study, hospital stay in group I patients (not given BCAA) in comparison with group II (given BCAA) was >7 days; group I = 8 patients 33.3% & group II = 0 patients. 8 patients from group II while only 1 patient remained hospitalized for 14 days (Group I 33.3% & group II 14.2%). 16 from group I (66.7%) & 6 from group II (25.0%) remained for >14 days.[8]

As this is a new emerging concept that BCAA are effective in early reversal of hepatic encephalopathy, only few studies have been done and no meta-analysis has been carried out yet in Pakistan.

METHODOLOGY

This study was conducted at Services Hospital, Lahore during 2013 to 2014 we enrolled 100 cases (50 in each group) with Hepatic encephalopathy grade III or IV and Spleenomegaly & coarse liver on ultrasonography between 30-60 years of either sex, we excluded those cases with Serum bilirubin >5mg/dl, upper GIT bleed, Co morbidities i.e. History of Diabetes mellitus, Hypertension, Ischemic heart disease or Chronic kidney disease.Informed consent was taken from each attendant. Risks and benefits were explained. Demographic information including name, age, & address was taken from attendant and kept confidential. Grade of hepatic encephalopathy was established clinically on the day of admission and then daily on next 3consecutive post admission days. Subjects were assigned in to two groups by non probability randomly using random tables. Group I was given conventional therapy for hepatic encephalopathy along with intravenous BCAA 1000ml once daily while Group II was only on conventional therapy. All data collected from patients given BCAA and those not given BCAA and changes in grades of hepatic encephalopathy was recorded.

RESULTS

Age distribution of the patients was done which shows majority of the patients in both groups i.e. 44%(n=22) in Group-A and 52%(n=26) in Group-B between 41-50 years, followed by 30%(n=15) in Group-A and 26%(n=13) in Group-B between 51-60 years, while 26%(n=13) in Group-A and 22%(n=11) in Group-B were recorded between 30-40 years of age, mean and sd was calculated as 43.98+3.76 and 44.32+3.02 respectively. (Table No. 1). Gender distribution of the patients was done which shows 66%(n=33) in Group-A and 58%(n=29) in Group-B were male while rest of 34%(n=17) in Group-A and 42%(n=21) in Group-B were females.(Table No. 2)

Comparison of early reversal of hepatic encephalopathy in patient with advanced liver disease with and without BCCA which shows 64%(n=32) in Group-A and 26(n=13) in Group-B while rest of 36%(n=18)in Group-A and 74%(=37) in Group-B had no early reversal, p value was recorded as 0.00 which shows significant difference in both groups. (Table No. 3)

Table 1: Age Distribution of The Patients (n=100)

Age(in years)	Group-A (n=50)		Group-B (n=50)	
30-40	13	26	11	22
41-50	22	44	26	52
51-60	15	30	13	26
Total	50	100	50	100
Mean and sd	43.98+3.76		44.32+3.02	

Table 2: Gender Distribution of The Patients(n=100)

Gender	Group-A (n=50)		Group-B (n=50)	
Male	33	66	29	58
Female	17	34	21	42
Total	50	100	50	100

Table 3: Comparison of Early Reversal Of Hepatic Encephalopathy in Patients with Advanced Liver Disease with and without BCAA(n=100)

Early reversal	Group-A (n=50)		Group-B (n=50)	
Yes	32	64	13	26
No	18	36	37	74
Total	50	100	50	100

P value=0.000

DISCUSSION

Understanding the pathophysiology of a disease is essential to develop effective treatments, although relying on pathophysiology can lead to fallacious treatments. The unknown pathogenesis of hepatic encephalopathy makes it difficult to find effective treatments, although some treatments have proven very effective before the pathophysiological mechanism were known, e.g., citrus fruit for scurvy.[9]

Previous observations in yeast suggested that the branched-chain amino acids (BCAAs) leucine, isoleucine, and valine might be potential candidates in promoting survival.[10]

Whether branched-chain amino acids are of benefit to patients with hepatic encephalopathy has been debated intensively.[11-16] Two comprehensive reviews published around the same time reached very different conclusions.[11,12] Naylor et al meta-analysed the results from randomised trials and concluded that branched-chain amino acids increased recovery rates from acute hepatic encephalopathy but had uncertain effects on mortality.[11] Erikkson and Conn performed a narrative review scrutinising each study for its strengths and weaknesses and concluded that the majority of trials provided little evidence that branched-chain amino acids were of benefit to patients with acute, chronic, or minimal hepatic encephalopathy.[12] Although Naylor et al reached quantitative results through meta-analyses, they did not assess and incorporate the quality of the included trials in the results or interpretation of the meta-analyses. In accordance with Naylor et al, we found that branched-chain amino acids seemed to improve encephalopathy in our overall analysis. However, in accordance with Erikkson et al[12,14] this effect was seen only in low-quality trials. The effect in the overall analysis most likely reflects bias because of the low methodological quality.[17-20] At present, there is insufficient evidence to recommend branched-chain amino acids for hepatic encephalopathy.

However, we evaluated the efficacy of BCAAs in the treatment of HE in addition to conventional treatment options so as to reduce the mortality as well as duration of indoor stay in patients of HE.The results of the study reveal that early reversal of branched chain amino acid in hepatic encephalopathy was significantly higher in (Branched Chain Amino Acid group) by showing 64%(n=32) in Group-A and 26%(n=13) in Group-B. These findings are in agreement with Afzaal S who demonstrated that the 56.6% of patients of hepatic failure from grade-*IV* to grade I, who were infused with branched chain amino acids[21]as compared to 25% improvement who were on conventional treatment after 3 day treatment.[21]

According to our study, branched chain amino acids (BCAA) had a role in early reversal of hepatic encephalo-pathy in chronic liver disease. Tangkijvanich P et al had shown similar results in their study that the branched chain amino acids had lead to reversal of hepatic encephalopathy in mean duration of 56.8 hours.[22]

In several studies, branched chain amino acids were found to decrease the duration of hospital stay.[23.] Similar results were found in our study though we did not include it in our data analysis but our observations show similarity.

Andrea Fabbri et al concluded that the results of the two largest, long-term studies, the use of branched-chain amino acids in the treatment of chronic encephalopathy may only be proposed for patients with advanced chronic liver disease,[24] which further supports the results of our study because the patients of hepatic encephalopathy with chronic liver disease were selected for the

study and were administered BC-AA. The results of the study also justifies the hypothesis of the study that "Branched chain amino acids are effective in reversal of hepatic encephalopathy when compared with placebo".

CONCLUSION

Comparison of frequency of early reversal of hepatic encephalopathy in patients with advanced liver disease with and without BCAA reveals that early reversal of hepatic encephalopathy is achieved in patients treated with BCAA.

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