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LETTERS TO THE EDITOR

Hepatic encephalopathy in patients with liver cirrhosis: Is there a role of malnutrition?

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Abstract

Hepatic encephalopathy (HE) is a common complication in patients with liver cirrhosis but its pathogenesis remains incompletely understood. Malnutrition is commonly encountered in patients with liver cirrhosis and it has been reported to affect the quality of life of this group of patients. Experimental studies suggest that low energy intake and poor nutritional status may facilitate the development of HE but there are scarce data on the potential role of malnutrition in HE in patients with liver cirrhosis. Two recently published studies have evaluated the potential role of malnutrition in the development of HE in cirrhotic patients with conflicting results. In this letter to the editor we briefly present the results of the two studies as well as potential reasons for the conflicting results reported.

Key words: Hepatic encephalopathy; Liver cirrhosis; Malnutrition

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TO THE EDITOR

The pathogenesis of hepatic encephalopathy (HE), a common complication of liver cirrhosis, remains incompletely understood but it is probably multifactorial in most cases[1]. Malnutrition is also commonly encountered in patients with cirrhosis and it has been reported to have an effect on health related quality of life[2]. Although experimental studies suggest that low energy intake and poor nutritional status may facilitate the development of HE[3], there are scarce data on the potential role of malnutrition in HE in patients with liver cirrhosis.

Recently Soros *et al*[4] performed a study investigating the potential role of malnutrition and hypermetabolism in HE in which 223 patients with non-alcoholic cirrhosis were enrolled. They were evaluated for the presence of HE according to the West Haven criteria and for malnutrition by means of body mass index (BMI), anthropometric measurements, and bioelectrical impedance analysis. Energy metabolism was also assessed by means of indirect calorimetry. Eighty-five (38%) out of 223 patients had no clinically evident HE, 123/223 (55%) had HE grade 1 and 15/223 (7%) had HE grade 2 or 3. Neither metabolic variables or BMI nor fat free mass or muscle mass differed significantly in patients with HE grade 1-3 from those without HE. In multivariate analysis none of these parameters was found to be independently related to HE. The authors concluded that malnutrition or catabolism does not seem to be independent risk factors for the presence of HE in patients with liver cirrhosis[4].

Recently, we performed a prospective study evaluating HE in 128 patients with liver cirrhosis of various etiologies[5]. HE was evaluated by means of the West Haven criteria and two psychometric tests (number connection test A and B). HE was defined as overt HE according to the West Haven criteria and/or number connection test A and/or B > 3 standard deviations of the general population. Nutritional status was evaluated with BMI and anthropometric measurement as well as estimation of recent weight change. Malnutrition was defined as anthropometric measurement below the 5th

percentile according to standard values for the general population and/or BMI < 20 kg/m^2 and/or weight loss ⩾ 5%-10% in the previous 3-6 mo. The presence of diabetes mellitus was also assessed with fasting glucose measurement. Forty percent of our patients were malnourished, 26% had diabetes, and 34% had HE. Patients with malnutrition suffered more frequently from HE compared to those without malnutrition (46% *vs* 27%, $P = 0.031$) , but there was no difference in age, etiology, or severity of liver cirrhosis. In multivariate analysis, the time needed to perform number connection test A was independently correlated to age, severity of cirrhosis expressed as the Child-Pugh score, diabetes and malnutrition[5]. This is in agreement with a previous study showing that diabetes mellitus is associated with HE in patients with hepatitis C cirrhosis[6].

In the paper of Soros *et al*[4], they did not report how many patients had diabetes mellitus. However, the risk of diabetes mellitus has been reported to be increased in patients with cirrhosis due to hepatitis C[7] and the majority of patients enrolled in the study of Soros *et al*[4] (56%) had viral cirrhosis[4]. It is therefore unknown whether the patients with HE had a higher proportion of diabetes compared with the patients without HE. This might have had an effect on the median BMI in the two groups as diabetes is more prevalent in patients with increased BMI, thus accounting for the lack of difference in median BMI between patients with HE and those without HE[4]. In fact, the BMI of patients with HE ranged from 14.5 to 36.3 kg/m^2 as compared to 17.5-28.4 kg/m^2 in those without HE[4]. Furthermore, in our study, recent weight change was included in the definition of malnutrition[4] whereas in the study of Sörös *et al* no definition of malnutrition was provided[4]. Interestingly we found that although patients with and without low fat or muscle mass did not differ in number connection A performance times, a recent weight loss was related to longer performance times [81 s (51) *vs* 54 s (32), $P = 0.001$][5]. It is therefore conceivable that deterioration in nutritional status, rather than nutritional status itself, may be of great importance for cognitive dysfunction in patients with liver cirrhosis. Finally, another factor that may, at least in part, explain the differences between the results of the two studies[4,5] is that we also included patients with minimal HE in our analyses[5] whereas as Soros *et al*[4] included only patients with clinically overt HE in their study.

In conclusion, methodological differences regarding the definitions of HE and malnutrition as well as the assessment of the role of diabetes mellitus in cognitive dysfunction may explain the differences in the results of the two studies[4,5]. As both studies had limitations mentioned by their authors[4,5] and the pathophysiology of HE is complex, it is clear that further studies are warranted to fully delineate the potential role of malnutrition in cognitive dysfunction in patients with liver cirrhosis.

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