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Research Article

PROPHYLACTIC EFFECT OF ACARBOSE FOR HEPATIC ENCEPHALOPATHY AMONG DIABETIC PATIENTS WITH LIVER CIRRHOSIS

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ABSTRACT

Objective: Prophylactic effect of Acarbose for hepatic encephalopathy among diabetic patients with liver cirrhosis.
Methodology: It was a randomized controlled, double blind clinical trial conducted in duration of one year at Holy Family hospital, Rawalpindi. Patients with diagnosis of cirrhosis along with DM were enrolled and randomly allocated to the two different treatment groups. Detailed history, physical examination and biochemical measurements were recorded. Patients underwent treatment either with lactulose plus Acarbose and lactulose alone treatment efficacy was recorded at the end of treatment in terms of prevention of hepatic encephalopathy.
Results: The mean age was 45±13.7years. Majority were male 130 (61.9%) males. Mean duration of cirrhosis was 3.35±3.3 year. Mean duration of DM was 6.27±3.7 years. On comparison of efficacy between two treatment groups, out of 105in groups, efficacy was found to be in (96.4%) patients among lactulose plus Acarbose group and (80.0%) patients in lactose group respectively with significant P-value (0.014).
Conclusion: Acarbose plus lactulose group found to be more effective as prophylactic agent to deal with hepatic encephalopathy than lactulose alone group.

INTRODUCTION

Liver cirrhosis is a serious and generally irreversible disease. It was the 12th leading cause of death in United States.[1] Hepatic encephalopathy (HE) is an acute hepatic complication of liver cirrhosis. HE is manifested by complex neuropsychiatric features after exclusion of any other explainable cause including organic brain diseases.[2]. Manifestations of HE in cirrhosis includes psychomotor dysfunction, impaired memory, increased reaction time, sensory abnormalities, poor concentration and in severe forms, coma.[3] These complications may ultimately lead to the death of the patients.[4] HE has profound effects on patients with cirrhosis, leading to frequent life disruptions, poor quality of life and extensive use of health care resources.[5,6] Increased systemic level of neurotoxins such as ammonia produced by protein breakdown by proteolytic bacteria are thought to be the major cause of HE and the most commonly used therapy for treatment and prevention is use of non-absorbable disaccharides, such as lactulose.[7,8]

Acarbose is a novel hypoglycemic agent acting through the inhibition of glucose absorption in the gut.[9] It acts by inhibition of α-glucosidase in small intestine hydrolyzing oligosaccharides, trisaccharides and disaccharides into glucose and other monosaccharide in small intestine.[10] Inhibition of this enzyme system reduces the rate of digestion of complex carbohydrates. At the same time, it promotes the sacchrolytic intestinal flora at the expense of proteolytic flora.

In a recent trial on 61 patients the efficacy of Lactulose to prevent hepatic encephalopathy was found to be 80.32%.[9] This study is to find prevention of HE in Diabetic patients with liver cirrhosis with use of Acarbose along with Lactulose. This is an agent that has the advantage of being a drug that can also improve glycemic control in these patients. So if we determine the role of this drug in prevention of hepatic encephalopathy then Acarbose will have definite advantage over other conventional treatments i.e., Lactulose alone, in diabetic patients with cirrhosis if we considered it in the prophylaxis

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and treatment of HE. Consequently, the prognosis and survival of these patients can be improved.

Experimental Section

Methodology

This was a randomized controlled trial conducted in Medical unit - I, center of liver and digestive diseases, Holy Family Hospital, Rawalpindi. Non-probability consecutive sampling was used to collect the sample from the target population. A sample of 210 patients, calculated using proportions 80.32% and 93.33% in combination versus alone treatment group, with 5% level of significance and 80% power of the study. Cirrhotic patients of both gender and age ranging from 15 years to 60 years who presented in hepatic encephalopathy (Grade 2) and had DM (BSF>200mg/dl) were included in this study. Patients with following known precipitants of HE (gastrointestinal hemorrhage and placement of a porto systemic shunt or a trans jugular intrahepatic porto systemic shunt) within 3 months of screening visit, CRF (creatinine level > 2mg / dL), diabetic Ketoacidosis and non ketotic hyperosmolar coma, hypoglycemia, inflammatory bowel disease, colonic ulceration, partial intestinal obstruction, and patients predisposed to intestinal obstruction, an electrolyte abnormality (serum sodium < 125mmol / L, serum calcium > 2.5 mmol / L, serum potassium < 2.5 mmol / L), active spontaneous bacterial peritonitis were excluded.

Experimental design and grouping

A written informed consent was obtained from the patients or their legally authorized representatives prior to enrolling them. Patients were randomly divided into 2 groups by using computer generated random number table. Lactulose alone was given to one group and Acarbose 100 mg (TDS) with each main meal along with the Lactulose was given to the other group. Glycemic control in both groups was achieved by using subcutaneous Insulin injections. Use of intra luminal and systemic antibiotics was allowed in equal doses in both groups. The baseline investigations including Fasting Blood sugar, serum electrolytes, serum bilirubin, renal function and urine complete examination were performed. During the study period, the daily protein intake of all patients was maintained at 40-60 grams per day. Patients were followed up for 8 weeks on monthly basis. During the follow up visit complete history and physical examination was conducted and HE episode in past month was diagnosed or ruled out.

Statistical analysis

Data analysis was done using SPSS version 20. Chi square test was applied to compare efficacy in two treatment groups. P-value<0.05 was significant.

RESULTS

The mean age of patients was 45.75±13.72 years. There were 130 (61.9%) male and 80(38.1%) females in the study. Mean duration of cirrhosis was 3.36±3.36 while mean duration of DM was 6.27±3.79.

On comparison between two groups efficacy was found to be in 96 patients (91.42%) in lactulose plus Acarbose group while it was found to bein 84 patients (80.0%) in Lactose grouponly with P-Value (0.01).

Table1 Comparison of Efficacy in Both Treatment Group

S.No	Treatment group	Efficacy		P value
		Yes (n=180)	No (n=30)	
1	Lactulose plus Acarbose	96(91.4%)	09(8.6%)	0.014
2	Lactulose alone	84(80%)	21(20%)	0.014

There was no significant difference in male in both treatment groups (p-value 0.124), while there was a significant difference in female in both treatment groups (p-value 0.02). A significant difference in patients who were more than 50 years, in both treatment groups (p-value 0.04). No significant difference in people less than 50 years (p-value 0.07).There was significant difference in patients who have diabetes less than 3 years (p-Value 0.04) or who have diabetes from more than 3 years (p-Value 0.04).

Table 2 Comparison of Efficacy According to Gender, Age and Duration of Diabetes

		Treatment group	Efficacy		Pvalue
			Yes	No	
Gender	Male	Lactulose plus Acarbose	53(93%)	04(7%)	0.124
		Lactulose alone	62(84.9%)	11(15.1%)	
	Female	Lactulose plus Acarbose	43(89.6%)	05(10.4%)	0.021*
		Lactulose alone	22(68.8%)	10(31.3%)	
Age	Age<50 year	Lactulose plus Acarbose	56(94.9%)	03(5.1%)	0.077
		Lactulose alone	61(85.9%)	10(14.1%)	
	Age>50 year	Lactulose plus Acarbose	40(87%)	06(13%)	0.036
		Lactulose alone	0(0%)	0(0%)	
Duration of Diabetes	< 3 year	Lactulose plus Acarbose	35(85.4%)	06(14.6%)	0.045*
		Lactulose alone	16(64%)	09(36%)	
	>3 year	Lactulose plus Acarbose	61(95.3%)	03(4.7%)	0.038*
		Lactulose alone	68(81.9%)	15(18.1%)	

DISCUSSION

HE imposes a formidable burden on the patients and their families. Repeated episodes are debilitating, require repeated hospitalizations and render the patient incapable of performing activities of daily life.[11]an increase in the frequency and severity of such episodes predict an increased risk of death.[12]

Although hyper-ammonia has been implicated, the exact pathogenesis of HE remains elusive.[3]The aim of treatment has been to reduce the gut-derived ammonia, increased ammonia clearance and control of precipitating factors.[13] Lactulose has been the standard of care while oral antibiotics have been effective only to be associated with toxic effects when used on long-term basis.[14, 15]

Increased systemic level of neurotoxins such as ammonia produced by protein breakdown by proteolytic bacteria are

thought to be the major cause of HE and the most commonly used therapy for treatment and prevention is use of non-absorbable disaccharides, such as lactulose.[7,8]

The prevention of episodes of HE is an important goal in the management of decompensated cirrhosis since symptoms of HE are associated with decreased ability to take care of activities of daily living,[1] poor nutrition, frequent hospitalizations which put a financial burden on the family and a poor quality of life. This study showed that the use of acarbose plus lactulose is more efficacious than lactulose alone. Lactulose has been found to be effective in the prevention of overt HE. In this study by Sharma *et al*. patients were enrolled. Out of those 125 patients, 19% patients in lactulose group developed episodes of HE in comparison to 46.8% in placebo group over 14 months.

Acarbose is a novel hypoglycemic agent acting through the inhibition of glucose absorption in the gut[9]. It acts by inhibition of α-glucosidase in small intestine hydrolyzing oligosaccharides, trisaccharides and disaccharides into glucose and other monosaccharide in small intestine.[10] Inhibition of this enzyme system reduces the rate of digestion of complex carbohydrates. At the same time, it promotes the sacchrolytic intestinal flora at the expense of proteolytic flora. As a result, there is less protein breakdown by proteolytic bacteria and resulting ammonia production is reduced by the use of Acarbose. This lowering of ammonia production prevents the development of HE in cirrhotic patients taking Acarbose. In our study efficacy of lactulose to prevent HE was 90%. While the efficacy of control group (acarbose alone) was 80%. In a recent trial on 61 patients the efficacy of Lactulose to prevent hepatic was found to be 80.32%.[9]

These findings are in contrast to the multicenter trial published by Bass *et al*. which showed no relative reduction in risk of HE.[16] This difference is due to a number of factors, one of which could be the etiology leading to cirrhosis. A greater number of patients in the trial mentioned above were suffering from alcohol induced cirrhosis, an etiology more common in the west than in our part of the world. Patients enrolled in this study had cirrhosis secondary to viral hepatitis mostly hepatitis C followed by hepatitis B as the next most common cause.

The current study also differs from previous randomized studies, [16-18] in that it was conducted on an equal number of men and women, all of whom belonged to the same ethnic background. Patients were from diverse backgrounds including those in Russia, Canada as well as in the US and the trial was conducted at 180 investigative sites.[16]Thus, the difference in response could be because of the difference in the patients' population of gut micro flora. The gut flora changes with genetic makeup, diet and environmental factors.[19] Hence, the composition of gut flora varies from one ethnic group to the other.

CONCLUSION

Acarbose plus lactulose group found to be more effective as prophylactic agent to deal with hepatic encephalopathy than lactulose alone group.

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References

1. Mokdad AH, Forouzanfar MH, Daoud F, *et al*. Global burden of diseases, injuries, and risk factors for young people's health during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *The Lancet*. 2016;387(10036):2383-401.
2. Pinto C. Indian research on acute organic brain syndrome: Delirium. *Indian J Psychiatry*. 2010; 52:139–47.
3. Malaguarnera M. Acetyl-L-carnitine in hepatic encephalopathy. *Metab Brain Dis*. 2013; 28:193–9.
4. Cash WJ, McConville P, McDermott E,*et al*. Current concepts in the assessment and treatment of hepatic encephalopathy. *QJM Mon J Assoc Physicians*. 2010; 103:9–16.
5. Bajaj JS, Heuman DM, Wade JB, *et al*. Rifaximin improves driving simulator performance in a randomized trial of patients with minimal hepatic encephalopathy. *Gastroenterol*. 2011; 140:478–87.
6. Bughdad Khan, Zahidullah Khan, Jamalud Din, Hamza Khan, Muhammad Taimur Khan. Spectrum of factors precipitating hepatic encephalopathy in patients with liver cirrhosis *J Med Sci* 2011; 19:62-5.
7. Toris GT, Bikis CN, Tsourouflis GS, Theocharis SE. Hepatic encephalopathy: an updated approach from pathogenesis to treatment. *Med Sci Monit Int Med J Exp Clin Res*. 2011;1753–63.
8. Sharma BC, Sharma P, Agrawal A, Sarin SK. Secondary prophylaxis of hepatic encephalopathy: an open-label randomized controlled trial of lactulose versus placebo. *Gastroenterol*. 2009; 137:885–91.
9. Gentile S, Guarino G, Romano M, Alagia IA, Fierro M, Annunziata S, Magliano PL, Gravina AG, Torella R. A randomized controlled trial of acarbose in hepatic encephalopathy. *Clin Gastroenterol Hepatol*. 2005;3(2):184-91.
10. Zhu Q, Tong Y, Wu T, Li J, Tong N. Comparison of the hypoglycemic effect of acarbose monotherapy in patients with type 2 diabetes mellitus consuming an Eastern or Western diet: a systematic meta-analysis. *Clin Ther*. 2013; 35(6):880–99.
11. Bajaj JS, Wade Jb, Gibson DP, Heuman DM, Thaker LR, Sterling RK, *et al*. The multi-dimensional burden of cirrhosisand hepatic encephalopathy on patients and caregivers. *Am J Gastroenterol* 2011; 106:1646-53.
12. Oneykwere CA, Ogbera AO, Hameed L. Chronic liver disease and hepatic encephalopathy: clinical profile and outcomes.*Niger J Clin Pract* 2011; 14:181-5.
13. 13. Grønbaek H, Johnsen SP, Jepsen P, *et al*. Liver cirrhosis, other liver diseases, and risk of hospitalisation for intracerebral haemorrhage: a Danish population-based case-control study. *BMC Gastroenterol* 2008;8:16.
14. Mullen KD, Prakash RK. Management of covert encephalopathy. *Clin Liver Dis* 2012; 16:91-3.

15. Phongsamran PV, Kim JW, Cupo Abbott J, Rosenblatt A. Pharmacotherapy for hepatic encephalopathy. *Drugs* 2010; 70:1131-48.
16. Bass NM, Mullen KD, Sanyal A, Poordad F, Neff G, Leevy CB. Rifaximin treatment in hepatic encephalopathy. *N Engl J Med* 2010;362:1071-81.
17. Festi D, Mazzella G, Orsini M, *et al*.Rifaximin in the treatment of chronic hepatic encephalopathy; results of a multicenter study of efficacy and safety. *Curr Therapeut Res* 1993; 54:598-609.
18. William R, James OF, Warnes TW, Morgan MY. Evaluation of the efficacy and safety of Rifaximin in the treatment of hepatic encephalopathy: a double blind, randomized, dose-finding multi centre study. *Eur J Gastroenterol Hepatol* 2000; 12:203-8.
19. 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.

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