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Research Article

Comparison of efficacy between rifaxamin and IV metronidazole in the treatment of hepatic encephalopathy

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ABSTRACT

Objective: To compare the efficacy between rifaxamin and IV metronidazole in the treatment of hepatic encephalopathy.

Material and methods: This was comparative study which was conducted at Department of MedicineBahawal Victoria Hospital, Bahawalpur from July 2016 to December 2016 over the period of 6 months. Total 120 patients of hepatic encephalopathy either male or female, having age range from 40-60 years were selected. Rifaxamin (550mg B.D) was given to patients of group A by nasogastric tube and metronidazole IV 500mg 8 hourly was given to patients of group B.At day 7 efficacy of the both drugs was assessed.

Results: This study was consisted on 120 patients of hepatic encephalopathy. Mean age of the patients was 49.43 ± 6.866 years, mean age in group A was 49.37 ± 6.757 years and mean age in group B was 49.50 ± 7.029 years.

Out of 60 patients of group A (Rifaxamin group), efficacy of treatment was noted in 14 (23.33%) patients and out of 60 patients of group B (Metronidazole group), treatment was found effective in 45 (75%) patients. Significantly higher rate of efficacy was noted in patients of group A as compared to group B with p value 0.000.

Conclusion: In this study efficacy of treatment was significantly higher in patients managed with Metronidazole as compared to patients managed with Rifaxamin. Statistically significant association of efficacy with age and gender are noted.

Keywords: Hepatic encephalopathy; Lactulose; Neomycin; Non-absorbable disaccharides; Rifaximin

INTRODUCTION

Hepatic encephalopathy describes a wide spectrum of often-reversible neuropsychiatric abnormalities that occur in patients with acute or chronic liver disease.[1-2] Often, the term "portal-systemic encephalopathy" is used to emphasize the failure of the liver to detoxify toxins that escape from the intestine. These toxins thus bypass the liver and enter the systemic circulation, causing the primary or secondary changes in brain neurochemistry that produce symptoms of hepatic encephalopathy. This metabolic disorder is characterized by reversibility, which suggests a lack of persistent structural lesions in the brain.[3]Hepatic encephalopathy can be develop due to many factors which include gastro-intestinal bleeding, infections, constipation, electrolyte imbalance (hyponatremia, hypokalemia), hypoglycemia, Medicines (sedative-hypnotics, opiates). It is imperative to identify one of these factors so that prompt treatment given to get patient out of encephalopathy.[4-5]The present standard of care

in the management of HE is directed at decreasing the accumulation of ammonia in the hope of altering the induction of glutamate neurotoxicity and the consequent increased tone of the GABA-A receptor system in the brain.[6] Several agents have been used to address this complication of end-stage liver disease.[7]

The antibiotic neomycin tends to be effective during acute exacerbations of the syndrome, whereas metronidazole has become quite favorable for preventing HE. However, all these agents are fraught with drug related side effects and/or therapeutic compliance.[8]Rifaximin is a derivative of rifamycin that acts by inhibiting bacterial RNA synthesis. Rifaximin is virtually unabsorbed after oral administration and exhibits broad spectrum antimicrobial activity against both aerobic and anaerobic gram-positive and gram-negative microorganisms within the gastrointestinal tract.[9] Many studies reported that rifaximin decreases ammonia plasma levels and improves the symptoms related to HE in patients with liver cirrhosis.[10]Rifaximin has a favorable profile in terms of tolerability and side effects.[11]

Patients of hepatic encephalopathy presents as medical emergency and needs immediate management. Our study is designed to find out the comparative efficacy of rifaximin versus metronidazole in these patients. Rifaximin is non-absorbable antibiotic as compared to metronidazole. we want to bring this drug in my routine practice.

OPERATIONAL DEFINITION

Hepatic encephalopathy: Hepatic encephalopathy is defined as a spectrum of neuropsychiatric abnormalities (personality changes, (depressed level of consciousness, deterioration of GCS from 15/15 to 8/15) intellectual impairment (disoriented and confused) in patients with liver dysfunction, (deterioration of liver function tests such as bilirubian>1mg/dl, ALT >40U/L, increased prothrombin time difference from control >4 seconds, decreased albumin <3.5g/dl) after exclusion of brain disease (meningitis, encephalitis, cerebrovascular accident, malignancy).

Efficacy: Efficacy is defined as improvement inneuropsychiatric abnormalities (personality changes (GCS 15/15), intellectual impairment in patients with liver dysfunction (Bilirubin <1mg/dl, ALT <40u/l, prothrombin time difference from control <4 seconds and serum Albumin >3.5g/dl, and a depressed level of consciousness after exclusion of brain disease (meningitis and encephalitis, cerebrovascular accident, malignancy, by CT scan brain and lumber puncture).

MATERIAL AND METHODS

This was comparative study which was conducted at Department of MedicineBahawal Victoria Hospital, Bahawalpur from July 2016 to December 2016 over the period of 6 months.

Inclusion Criteria:

- Patients of hepatic encephalopathy grade 3 and 4 (as operational definition).
- Both male and female.
- Age from 40 to 60 years.

Exclusion Criteria:

- Patients with brain disease. (meningitis, encephalitis, cerebrovascular accident, malignancy by CT scan, CSF examination and MRI brain)
- Diabetic ketoacidosis and renal failure. On history and lab investigation.
- Patients with septicemia. (On history and complete blood count.)

DATA COLLECTION PROCEDURE:

Total 120 patients of hepatic encephalopathy grade 3, 4 was included in this study after scrutinized by inclusion criteria and after taking written consent from Institutional Review Board. Written consent was taken from every patient. Patients were randomly divided into two groups A & B. Rifaxamin (550mg B.D) was given to patients of group A by nasogastric tube and metronidazole IV 500mg 8 hourly was given to patients of group B. At day 7 efficacy of the both drugs was assessed as operational definition and noted on pre-designed proforma as Yes/No.

Demographic profile of all the patients was also noted on the proforma.

DATA ANALYSIS PROCEDURE:

The data was entered in SPSS V16 for statistical analysis. Quantitative variable like age was presented as mean ± SD, while qualitative variable like gender, efficacy (Yes/No) was presented in frequency and percentages. Chi-square test was applied to compare the frequency of efficacy in both groups. Stratification was done for age and gender. Post stratification. Chai-square test was applied to see the level of significance. P-values ≤ 0.05 was considered statistically significant.

RESULTS:

Total 120 patients (60 patients in each group) with HE were selected for this study. Mean age of the patients was 49.43 ± 6.866 years, mean age in group A was 49.37 ± 6.757 years and mean age in group B was 49.50 ± 7.029 years.Out of 60 patients of group A, efficacy of treatment was noted in 14 (23.33%) patients and out of 60 patients of group B, treatment was found effective in 45 (75%) patients. Significantly higher rate of efficacy was noted in patients of group A as compared to group B with p value 0.000. (Table 1) Two age groups were made age group 40-50 years and age group 51-60 years. In age group 40-50 years, out of 30 patients of group A, efficacy of treatment was noted in 8 (26.67%) patients and out of 30 patients of group B, efficacy was noted in 23 (76.67%) patients and the difference of efficacy between the both groups was significant with p value 0.000. In age group 51-60 years, efficacy of treatment was noted in 6 (20%) and 22 (73.33%) patients and the difference was statistically significant with p value 0.000. (Table 2)

Out of 39 male patients of group A and 31 male patients of group B, treatment was found effective in 11 (28.21%) patients and 21 (67.74%) patients. Difference of efficacy was significant with p value 0.001. Among the 21 female patients of group A and 29 female patients of group B, treatment was found effective in 3 (14.29%) patients and 24 (82.76%) patients and difference was statistically significant with p value 0.000. (Table 3)

Total 32 of group A and 32 patients of group B was found with grade 3 HE. Efficacy of treatment was found effective in 8 (25%) patients and 24 (75%) patients and the difference of efficacy was statistically significant with p value 0.000. Total 28 patients of group A and 28 patients of group B was found with grade 4 HE. Treatment was found effective in 6 (21.43%) patients and 21 (75%) patients and the difference was statistically significant with p value 0.000. (Table 4)

Table 1 Comparison of efficacy between both groups

Group	Efficacy		Total	P value
	Yes	No		
A (Rifaxamin)	14 (23.33)	46 (76.67)	60	0.000
B (Metronidazole)	45 (75)	15 (25)	60	

Table 2 Comparison of efficacy between both groups for age groups

Group	Efficacy		Total	P value
	Yes	No		
age groups 40-50 years				
A	8 (26.67)	22 (73.33)	30	0.000
B	23 (76.67)	7 (23.33)	30	
age group 51-60 years				
A	6 (20)	24 (80)	30	0.000
B	22 (73.33)	8 (26.67)	30	

Table 3 Comparison of efficacy between both groups for male/female patients

Group	Efficacy		Total	P value
	Yes	No		
Male patients				
A	11 (28.21)	28 (71.79)	39	0.001
B	21 (67.74)	10 (32.26)	31	
Female patients				
A	3 (14.29)	18 (85.71)	21	0.000
B	24 (82.76)	5 (17.24)	29	

Table 4 Comparison of efficacy between both groups for HE grades

Group	Efficacy		Total	P value
	Yes	No		
HE grade 3				
A	8 (25)	24 (75)	32	0.000
B	24 (75)	8 (25)	32	
HE grade 4				
A	6 (21.43)	22 (78.57)	28	0.000
B	21 (75)	7 (25)	28	

DISCUSSION

HE represents a challenging clinical complication of liver insufficiency and presents with a wide spectrum of neuropsychiatric symptoms that range from mild disturbances in cognitive function to coma.[12] The pathogenesis of this complex syndrome is thought to be multifactorial, but a key role is played by circulating gut-derived toxins such as ammonia.[13] With appropriate medical treatment, most clinical manifestations of HE are reversible when the precipitating factors are corrected.

Total 120 patients (60 patients in each group) with HE were selected for this study. Mean age of the patients was 49.43 ± 6.866 years, mean age in group A was 49.37 ± 6.757 years and mean age in group B was 49.50 ± 7.029 years.

Out of 60 patients of group A, efficacy of treatment was noted in 14 (23.33%) patients and out of 60 patients of group B, treatment was found effective in 45 (75%) patients. Significantly higher rate of efficacy was noted in patients of group A as compared to group B with p value 0.000.

In one study, rifaximin found effective in 22.1% cases for the treatment of hepatic encephalopathy.[14]In other study metronidazole found effective in 78% patients.[15]findings of

these studies are comparable with the findings of present study.

This was the first study which comparing the efficacy of rifaxamin and metronidazole for the treatment of hepatic encephalopathy grade 3, 4.

CONCLUSION

In this study efficacy of treatment was significantly higher in patients managed with Metronidazole as compared to patients managed with Rifaxamin. Statistically significant association of efficacy with age and gender are noted.

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