Can Patients Who Develop Cerebral Death in Fulminant Liver Failure Despite Liver Transplantation Be Previously Forseen?

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ABSTRACT

Background. The outcome of medical treatment is worse in fulminant liver failure (FLF) developing on acute or chronic ground. Recently, liver transplantations with the use of living and cadaveric donors have been performed in these diseases and good results obtained. In this study, we aimed to present the factors affecting the recovery of cerebral functions after liver transplantation in hepatic encephalopathy (HE) developing in FLF, to identify irreversible patient groups and to prevent unnecessary liver transplantation.

Methods. In Inonu University's Liver Transplant Institute, 69 patients who made an emergency notice to the National Coordination Center for liver transplantation owing to FLF from January 2012 to December 2015 were included in the study. Patients were divided into 2 groups. Group 1 consisted of 52 patients who underwent liver transplantation and recovered normal brain function, and group 2 had 17 patients who underwent liver transplantation and did not recover normal brain function and had cerebral death. All patients were evaluated before surgery for clinical encephalopathy stage, light reflex, and convulsions. Groups were compared and assessed according to age (>40, 10–40 and <10 years), body mass index, etiologic factor, preoperative laboratory values, transplantation type, mortality, and encephalopathy level. Multivariate analysis was done for specific parameters.

Results. Prothrombin time (PT), international normalized ratio (INR), and total bilirubin values were significantly different between the groups. There was no significant difference between the groups regarding ammonia and lactate levels. There was a statistically significant difference between the groups regarding sodium and potassium levels from serum electrolytes. However, the averages of both groups were within normal limits. pH and total bilirubin levels were meaningful for multivariate analysis.

Conclusions. HE reversibility, mortality, and morbidity are important in patients with HE who undergo liver transplantation. Therefore, West Haven clinical staging and serum INR, PT, and total bilirubin level may be helpful in predicting the reversibility of FLF patients with HE before liver transplantation. It was determined that West Haven encephalopathy grading is important in determining the reversibility of

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HE after transplantation in FLF; especially the probability of reversibility of stage 4 HE decreases significantly. High PT and INR levels, hyperbilirubinemia, and serum sodium and potassium concentrations were risk factors for the reversibility of HE in this study.

THE ONLY treatment option for end-stage liver disease is liver transplantation [1]. The outcome of medical treatment is worse in fulminant liver failure (FLF) developing on acute or chronic ground. Nowadays, liver transplantations with live and cadaveric donors have been performed in these diseases and good results obtained [2]. In these patients, there are several parameters that determine the prognosis: hepatic encephalopathy (HE) grade, prothrombin time (PT), international normalized ratio (INR), sodium and potassium levels. HE grade, one of these parameters, is important. In the present study, we aimed to present the factors affecting the recovery of cerebral functions after liver transplantation in HE developing in FLF, to identify irreversible patient groups and to prevent unnecessary liver transplantation.

METHODS

In Inonu University's Liver Transplant Institute, 168 patients who made an emergency notice to the National Coordination Center owing to FLF from January 2012 to December 2015 were retrospectively examined, and 68 of these underwent liver transplantation and were included in the study. Patients were divided into 2 groups: Group 1 consisted of 52 patients who underwent liver transplantation and recovered normal brain function, and group 2 had 17 patients who underwent liver transplantation and did not recover normal brain function and had cerebral death. Cerebral death was diagnosed by the cerebral death committee of our hospital.

All patients were evaluated for clinical encephalopathy stage, light reflex (LR), and convulsions before liver transplantation. Transplantation decision was made according to the King's College criteria in adult patients and clinical and laboratory evaluations of related specialists in pediatric patients. Groups were compared and assessed according to age (adult [>16 years] and pediatric [≤16 years]), body mass index (BMI), etiologic factor, preoperative laboratory values, transplantation type, mortality, and encephalopathy level. Parameters that were meaningful ($P < .2$) were evaluated in multivariate analysis.

After the data were saved in an Excel (Microsoft) file, they were analyzed with the use of SPSS version 17.0. If constant variables were homogeneous, they were evaluated as mean ± SD. Heterogeneous distributions were reported as median and range. Percentages were used as descriptive statistics in the categorized variables. In the comparison of the groups, Student t test was preferred in the presence of constant variables. The Fisher exact test was used if the expected frequency in the classified data was <5, and the chi-square was used if the expected frequency was ≥5. P was considered to be statistically significant for values <.05.

RESULTS

All patients were LR positive. Two patients underwent confusion and they were lost owing to cerebral death after liver transplantation.

There was no statistical significance regarding age between group 1 and group 2. No significant statistical difference was found regarding the BMI of the patients. There was no statistically significant difference between the groups in terms of etiologic factor ($P < .90$). Of the 69 patients we worked with, 39 were children and 30 adults; 38 of the patients were male and 31 female; 34 patients underwent live-donor liver transplantation and 35 cadaveric liver transplantation. Mortality was 19% for those recovering brain functions, whereas mortality for those who did not recover brain functions was 100%. When patients were evaluated according to the level of clinical encephalopathy, it was observed that as the level of clinical encephalopathy increased, the rate of cerebral death increased. Also in this study, there was a statistically significant difference regarding clinical encephalopathy level and irreversibility of brain functions ($P < .05$; Table 1).

There was no statistical difference between groups regarding magnesium and calcium levels from serum

Table 1. Demographic Features of Groups

Parameter	Group 1	Group 2	Total	*P* Value
Age group				.73
Children	30 (77%)	9 (23%)	39	
Adults	22 (73%)	8 (27%)	30	
Age group				.55
<10 y	24 (80%)	6 (20%)	30	
10–40 y	21 (75%)	7 (25%)	28	
>40 y	7 (64%)	4 (36%)	11	
Body mass index, kg/m^2	20.8 ± 5.8	21.8 ± 6.7		.57
Etiology				.90
Cryptogenic	27	23	35	
Viral (HAV, HBV, CMV)	11	4	15	
Toxic (drug, fungus, unknown)	9	4	13	
Wilson	3	1	4	
Other (Budd-Chiari, post-hepatectomy)	2	0	2	
Sex				.18
Male	31 (82%)	7 (18%)	38	
Female	21 (68%)	10 (32%)	31	
Transplantation type				.18
Live	28 (82%)	6 (18%)	34	
Cadaver	24 (69%)	11 (31%)	35	
Mortality				.001
Alive	10 (19%)	17 (100%)	27	
Not alive	42 (81%)	0 (0%)	42	
Encephalopathy grade				.003
Grade 2	14 (78%)	4 (22%)	18	
Grade 3	37 (84%)	7 (16%)	44	
Grade 4	1 (14%)	6 (86%)	7	

Abbreviations: HAV, hepatitis A virus; HBV, hepatitis B virus; CMV, cytomegalovirus.