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Neurological recovery after liver transplantation: a prospective study of 22 patients

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Abstract A group of 22 liver transplantation patients were examined pre- and postoperatively using clinical neurological, neurophysiological and neuroradiological methods. After the operation improvement was observed in neurological symptoms, and in neuropsychological and neurophysiological test results. Our study shows that liver recipients have a high prevalence of nervous system dysfunction and that successful transplantation is followed by significant improvement.

Key words Neurological complications
Liver transplantation

Introduction

Hepatic encephalopathy is a common neurological syndrome in cirrhotic patients waiting for liver transplantation. After transplantation new neurological complications emerge in about 20% of patients [1]. The spectrum of postoperative neurological events includes vascular complications, central nervous system infections, central pontine myelinolysis, myelopathy, cyclosporine-induced encephalopathy and peripheral nerve injuries [2, 3]. Some of these complications may be subclinical and pass undiagnosed if careful neurological examinations are not carried out. We examined prospectively liver transplantation patients both pre- and postoperatively in order to see whether there is a need for comprehensive neurological evaluation.

Patients and methods

Between January 1986 and May 1991 52 liver transplantations were performed in adults at Helsinki University Hospital. A neurological examination was performed on 32 nonalcoholic patients of whom 28 proceeded to transplantation. Six of them died before the second neurological examination 6–12 months postoperatively. The remaining 22 patients, 20 women and 2 men, who were examined both pre- and postoperatively form the basis for our study. Their mean age was 48 years (range 31–65 years). All patients had cirrhosis (grade III or IV) established by liver biopsy, and 18 had primary biliary cirrhosis. The duration of liver disease before transplantation varied from 2 to 16 years. Four patients underwent retransplantation because of rejection.

A thorough clinical neurological examination was carried out. Neuropsychological tests included the Wechsler adult intelligence scale (WAIS), the Wechsler memory scale (WMS) and recollection scale (WMS%), visuomotor tracking by trail-making tests, resistance to mental interference by Stroop tests and a quality of life scale. Each patient served as his or her own control. The findings were compared with results relating to a control group of 53 healthy subjects, 41–50 years old. Electroneuromyography (ENMG) was performed by a neurophysiologist. An MRI scan of the brain using an Acutscan MR imager operating at 0.02 T was carried out.

Immunosuppression was undertaken initially with a triple drug regimen of methylprednisone, azathioprine and cyclosporine. All the examinations mentioned above were repeated 6–12 months after the transplantation. Student's paired *t*-test and the Chi-squared test were used to assess the significance of the findings.

Results

Table 1 shows that both muscle strength and the subjective feeling of physical incompetence improved postoperatively. Preoperative neuropsychological tests revealed decreased intellectual ability compared with healthy controls. The neuropsychological test results generally improved, with only one patient, who had a thalamic haemorrhage, showing a clear deterioration (Table 2). After transplantation, three patients showed new focal changes on the MRI scan which were located in the so-called watershed area of the white matter, suggesting that they were of vascular origin. Preoperatively, three patients had brain atrophy and eight others developed brain atrophy postoperatively. One patient suffered from intracerebral haemorrhage of non-aneurysmic origin 13 days postoperatively. The ENMG results improved in 13 patients (62%) postoperatively. In three patients (14%) the ENMG results deteriorated and clinical symptoms of neuromyopathy were also present in these patients.

Discussion

Patients who survived after liver transplantation for 6–12 months were postoperatively well-adjusted both physically and neuropsychologically and experienced an improved quality of life. The most likely reasons for the preoperative neurological complaints in our patients were hepatic encephalopathy and polyneuropathy associated with liver disease. Postoperatively, neurotoxicity of immunosuppressive drugs, particularly that of cyclosporine, was responsible for most of the complaints. Two of the four patients who underwent retransplantation also had neuromyopathy and lesions in the white matter of the brain detected by MRI. However, the neuropsychological test results improved in both of them. Retransplantation patients are bound to receive higher doses of immunosuppressive drugs for longer periods and are therefore at greater risk of neurotoxic effects. The aetiology of the new white matter changes in our patients was obscure. Their location suggested an ischaemic origin, but no intraoperative or immediate postoperative cardiovascular complications were noticed in these patients.

To sum up, liver transplantation patients have a high frequency of nervous system dysfunction both pre- and postoperatively. Persisting but silent white matter changes may develop during or after the operation. Without a careful preoperative examination it would be difficult to determine whether the neurological findings are related to the transplantation procedure. Therefore, we recommend a preoperative clinical neurological evaluation for all candidates for liver transplantation.

Table 1 Subjective neurological symptoms before and 6–12 months after liver transplantation ($n = 22$)

Symptom	Before	After	*P*-value
Mental dysfunction	7 (32%)	1 (5%)	n.s.
Memory impairment	6 (27%)	2 (9%)	n.s.
Physical dysfunction	14 (63%)	3 (14%)	<0.001
Muscle weakness	10 (45%)	3 (14%)	<0.05
Headache	2 (9%)	6 (27%)	n.s.

Table 2 Neuropsychological test results in 22 patients before and 6–12 months after liver transplantation and in 53 healthy controls (mean + SD). Stroop C and Trail B are expressed using a reversed scale

Test	Before	After	Controls
WAIS PS	95.7 ± 19.0	106.9 ± 11.6**	109 ± 12.9
WMS	104.2 ± 18.9	110.3 ± 23.7	118 ± 15.6
WMS %	85.3 ± 10.9	79.1 ± 0.1	91 ± 9.1
Trail B	167.7 ± 141.7	122.1 ± 57.9	101 ± 46.0
Stroop C	144.5 ± 59.5	115.6 ± 51.7***	110 ± 24.6
Quality of life	34.0 ± 28.1	69.0 ± 20.2**	

** $P < 0.01$, *** $P < 0.001$ for significance of the differences after the operation

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