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Hepatic encephalopathy verified by psychometric testing and EEG in cirrhotic patients: Effects of mesocaval interposition shunt or sclerotherapy

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Abstract

Background. The aim of this randomised prospective study was to evaluate hepatic encephalopathy after mesocaval inter-position shunt operation and after repeated endoscopic sclerotherapy. *Methods.* Forty-five patients with bleeding oesophageal varices due to liver cirrhosis were randomised to the two treatment groups, 24 to the shunt group and 21 to the sclerotherapy group. The patients were evaluated preoperatively regarding blood tests, hepatic encephalopathy as measured by electro-encephalogram with spectral analysis and by a battery of psychometric tests. The direction of portal flow in the shunt group was investigated by shunt phlebography and ultrasonography with Doppler. During follow-up the same investigations were performed twice at median 6.7 and 14.7 months after operation. *Results.* No statistically significant difference was found during follow-up regarding blood tests and electroencephalography with spectral analysis. Although the preoperative psychometric tests showed that the shunt group performed significantly better than the sclerotherapy group, the first follow-up showed that the shunt group performed statistically worse than the sclerotherapy group in seven of the tests: Synonyms (measuring verbal ability), Block Design Test (measuring visuo-spatial ability), Memory for Design Test, Error Score (measuring memory function), Revised Visual Retention Test, correct answers and the same test error answers (measuring visuo-spatial memory, ability and immediate memory), Digit Symbol Test (measuring perceptual ability) and Trial Making Test B (measuring cognitive motor abilities). *Conclusions.* Patients treated by mesocaval interposition shunt showed a progressive general reduction in psychometric performance compared with patients treated with repeated sclerotherapy, in whom a general intellectual improvement was observed. This finding corresponds to the reverse direction of the preoperative portal flow to a hepatofugal pattern at first follow-up and at 12 months among two-thirds of the patients.

Key Words: *Hepatic encephalopathy, psychometric tests, EEG, mesocaval interposition shunt, sclerotherapy*

Introduction

All treatments of bleeding oesophageal varices other than liver transplantation aim to control the symptoms arising from the persistent underlying hepatic disorder. Generally these varices are associated with an alcohol-induced cirrhosis of the liver. Besides life-threatening gastrointestinal bleeding, the hepatic encephalopathy (HE) that frequently occurs in this situation is a major clinical problem both in the short term and the long term.

Oesophageal varices are usually treated either by endoscopic sclerotherapy or by portosystemic shunting of blood. The influence of these therapies on the development of HE has not been adequately scruti-nised. Results from several studies display considerable differences; the reason may be differences in treatment modalities as well as in evaluation techniques. Various degrees of HE have been reported to appear in 16–77% of patients after shunt surgery and in 7–12% after sclerotherapy [1–4]. In a meta-analysis of comparisons of a selective shunt, the distal spleno-renal shunt (DSRS) and sclerotherapy, it was concluded that the overall risk for development of chronic HE was slightly increased after DSRS in non-alcoholic patients, while there was no increased risk after DSRS in the studied groups as a whole [5]. A new shunt procedure has been introduced in recent years, the transjugular intra-hepatic portasystemic shunt (TIPS). The incidence of HE arising as a result of the TIPS procedure is be-tween 15 and 25% [6], a higher incidence than after sclerotherapy [7].

We initiated this study to investigate whether or not portosystemic shunting would result in more

pronounced HE than sclerotherapy; mesocaval interposition shunt (MIS) was used as the surgical alternative to endoscopic sclerotherapy (ST). This procedure acts as a complete shunt, because with time it totally siphons off the portal venous perfusion [8]. In an earlier report [9] of a prospective randomised trial comparing MIS and repeated ST as regards rebleeding and encephalopathy, we found no differences between the incidence of HE within 3 years of MIS. In that study we analysed the total scores of all psychometric tests in the two treatment groups. Using a more sophisticated method to analyse the data from the psychometric test results, which is described in the present study, we found several important changes in the development of HE between the shunt and the sclerotherapy group.

Materials and methods

Patients

This study, which started in January 1980 and closed in December 1989, was carried out at the Surgical Department, University Hospital, Lund. Informed consent was obtained from each patient and the study was approved by the ethical committee for human studies at Lund University.

The patients all had bleeding oesophageal varices due to liver cirrhosis, histologically verified by pre-operative thick-needle biopsy, and portal hypertension. The criteria for inclusion in the study were (1) age between 20 and 75 years, (2) the bleeding source should be oesophageal varices verified endoscopically, (3) presence of portal hypertension, (4) the diagnosis of liver cirrhosis as proven histologically.

After emergency treatment of the bleeding varices with sclerotherapy, the patients were randomised into two elective treatment groups. Randomisation to the two treatment groups was done for patients fulfilling the inclusion criteria after they had been stratified according to Child's class. The randomisation was done by using closed envelopes. The results of the psychometric tests and EEG were not included in the randomisation procedure. Forty-five patients were included in the study, comprising 32 men and 13 women with a median age of 54 years (range 31–68). Twenty-four patients (19 men and 5 women) were randomised to mesocaval interposition shunt and 21 patients (13 men and 8 women) to sclerotherapy. During the same period, 180 other patients with bleeding oesophageal varices were treated with repeated ST, 36 were treated by MIS and 15 with a portacaval shunt.

All Child's classes were represented: 15% of patients belonged to Child's class A, 56% to Child's B and 29% to Child's C. As earlier studies on shunting procedures have not given conclusive results regarding outcome in Child's C patients compared to B patients, there seemed no reason to exclude Child's class C patients.

No statistical differences in the distribution of age, sex, albumin levels or Child's classification could be found between the two groups. Fourteen patients (67%) in the sclerotherapy group and 19 patients (81%) in the shunt group had a history of alcohol abuse.

Methods

Mesocaval interposition shunt was created by placement of a 14-mm PTFE, polytetrafluoroethylene graft (Gore-Tex®, WL Gore & Associates Inc. Medical Products, Flagstaff, AZ, USA) between the superior mesenteric vein and the inferior vena cava. Sclerotherapy was performed at flexible endoscopy with repeated injections of polidocanol 10 mg/ml (Aethoxysclerol®, Chemische Fabrik Kreussler & Co., GmbH, D-6200, Wiesbaden-Biebrick, Germany) both submucosally and paravariceally until the varices were eradicated.

All patients in the study underwent evaluation of cerebral activity by EEG with spectral analysis and with 12 different psychometric tests before randomisation to either of the two treatment groups.

Following a decision by the ethical committee, the patients in the ST group were not investigated with invasive radiological techniques to study portal flow. Thus the portal flow was only investigated in the MIS group. Portal flow was examined preoperatively by the use of conventional angiography and during follow-up by shunt phlebography, later (1984) replaced by ultrasonography [10]. The latter technique was first performed with Diasonic DRF 12 equipment, later with a Toshiba 90 and after 1986 with a Toshiba 100 Doppler Duplex.

The preoperative work-up procedure also included a routine blood chemistry screening. The same blood tests were monitored in all controls during follow-up. The following blood tests were analysed: haemoglobin (g/l), platelet count (10^9/l), activated thromboplastin time (APTT), normotest (NT), a liver failure test sensitive to small reductions of vitamin K, bilirubin (μmol/l), alkaline phosphatase (ALP; mkat/l), glutamyltransferase (GT; mkat/l), aspartate-amino-transferase (ALAT; mkat/l), creatinine (mkat/l), amylase (mkat/l), albumin (g/l) and urea (μmol/l). The tests were analysed according to the routine methods used in the Department of Clinical Chemistry, Lund University Hospital, Lund.

EEG

EEG was recorded with a 16-channel Siemens-Elema electroencephalograph (time constant 0.3 s, low pass filter 70 Hz). Quantitative frequency analysis was made from four bipolar channels symmetrically placed over precentral and parietal areas denoted as (F3-C3; C3-P3; F4-C4; C4-P4) using a Fast Fourier Transform (FFT) algorithm (Brain-Lab program, Digital on a PDP 11/03 computer). An average FFT spectrum

Table I. Psychometric tests

Test	Reference	Measures	Good performance
Synonyms	15	Verbal ability	High score
Figure Classification Test	15	Logic inductive ability Non-verbal reasoning functioning	High score
Block Design Test	16	Visual spatial capacity	High score
Memory for Design Test	17	Memory functioning	Low score
Revised Visual Retention Test	18	Memory functioning	Low score
Paired Associates Test	19	Memory functioning	High score
Digit Symbol Test	16	Perceptual ability	High score
Dot Test	20	Perceptual ability	Low score
Trial Making Test (TMT)	21	Perceptual ability	Low score
Colour Word Test (CWT)	22	Intellectual flexibility	Low score
Cylinder Board Test (Cyl)	23	Psychomotor capacity High score	
Reaction Time		Psychomotor capacity Low score	

from a total 10 min of EEG recording was calculated (sampling frequency 240 Hz). The EEG power within the delta and theta ranges ($=0.5$–8 Hz) from all four channels divided by the total power (0.5–25 Hz) was used as an index of EEG pathology (LFP, low frequency power ratio). The higher the value of the LFP ratio, the more severe the HE [11,12]. The results of the EEG measures are expressed as LFP ratio scores.

To calculate the median value for normal persons, a control group ($n=26$) was randomly selected from the population register among subjects without a history of cerebral disorder. Neurological examination of these subjects did not reveal any signs of CNS abnormality or any evidence of alcoholism. The control group consisted of 12 women and 14 men, median age 61 years (SD 47). There was no statistically significant difference between the control group and the two treatment groups according to age. The median LFP ratio of the control group was 41, SD 53.

Psychometric tests

The psychometric tests used to evaluate cognitive functions are listed in Table I [13–23]. The results of the psychometric tests are all expressed in raw scores, i.e. the values obtained from the original recordings.

The control group for psychometric testing consisted of 22 healthy male industrial workers with no evidence of alcoholism. The median age of the control group was 62 years (range 36–67). There was no statistically significant difference between the control group and the MIS and ST groups according to age.

Follow-up

Follow-up was scheduled at 4 months postoperatively and then annually; the tests were repeated as before. Among the MIS group of 24 patients, 5 were not investigated with psychometry and EEG and 2 patients could not be completely investigated during follow-up. Among the ST group of 21 patients, 1 was not investigated and 2 were not completely investigated.

Due to several administrative and other factors there were considerable variations in the time between operation and the first and second follow-up. The median postoperative interval until the first follow-up was 7.4 months (range 2.5–15), and until the second follow-up 14.7 months (range 10–26.7). Further follow-up could not be statistically analysed.

Data management

There were data losses in EEG and neuropsychological tests. For example, preoperative EEG data were available in 18 patients later treated with MIS and in 6 patients later treated with ST. At the first follow-up there were 17 MIS patients and 7 ST patients with EEG data, and at the second follow-up 16 MIS and 7 ST patients with EEG. Complete EEG data on every occasion were obtained in 12 MIS patients and 2 ST patients. As another example, results from the psychological test 'Synonyms' were available before treatment in 18 MIS and 18 ST patients, at first follow-up in 17 MIS and 13 ST patients and at second follow-up in 15 and 13 patients. Complete results from the Synonyms were obtained for 14 MIS patients and 10 ST patients. Complete data from all tests on all three occasions were available for 6 MIS and 2 ST patients.

To achieve a sufficient number of similar subjects with complete observations for statistical analysis tests, the scores from the first and second follow-ups were averaged. If only one observation was available this score was used instead of the average. The new variables created in this way are called 'postoperative' thereafter.

The numbers of patients with complete neuropsychological preoperative and postoperative test results were eight for the MIS group and seven for the ST group. These sample sizes were considered inadequate to be representative of the whole groups. Thus, a 'core material' was derived comprising those tests with the highest number of common patients with complete preoperative and postoperative test results. A maximum of four missing observations within a test was allowed. The core material defined in this way consisted of 16 MIS and 16 ST patients with results from a

core of 14 neuropsychological tests preoperatively and as averages of first and second follow-ups (or estimates from one of them) postoperatively.

There were 5 women of median age 51.4 years (range 46.4–56.4) and 11 men of median age 50.9 (range 40–61.8) in the MIS group. In the ST group there were 6 women of median age 43.7 years (range 33.4–54) and 10 men of median age 56.8 (range 48.5–64.9). There was no statistical difference in age or gender distribution between the core material and the other patients (core material: $n = 32$, median age 51.5 years, range 41.5–61.5; other patients: $n = 13$, median age 54.0 years, range 43.3–64.7; $df = 43$; $t = 0.75$; $p = 0.46$), (core material: 11 women, 21 men; other patients: 3 women and 10 men; $df = 1$; $df = 1$; $\chi^2 = 0.15$; $p = 0.70$).

Statistics

Non-parametric statistical methods were applied as far as possible. Fisher's exact probability test and the Mann–Whitney U-test were used for testing differences between the treatment groups regarding data on the nominal and ordinal scale levels, respectively. Analysis of variance, repeated measures, was applied in testing differences between the two treatment groups over time. The statistical computations were performed by the computer program Statview (Abacus Concepts Inc., Berkely, CA, USA). The rejection limit for the null-hypothesis was set to 0.5. All tests were two-tailed.

Results

No patient died during follow-up. Median follow-up was 14.7 months, range 5 days–8 years.

Blood tests

There were no statistically significant differences between the MIS and the ST groups during follow-up.

Anti-encephalopathic drugs

About half the patients in each treatment group received drugs with a known effect on the development of encephalopathy. There was no systematic treatment with lactulose and/or paromomycin, and the treatment was evenly spread in the two treatment groups, except at first follow-up in the sclerotherapy group, in whom more drugs were administered.

Recurrent bleeding

During follow-up there was one patient in the MIS group who had to be transfused with 1–3 units of blood at first and second follow-up (median 14.7 months). In the ST group three patients were transfused up to the first follow-up with 1–3 units, three patients with 4–6 units and two patients with 7–9 units. Up to the second follow-up two patients were transfused with 4–6 units, one patient had 7–9 units and three patients received

>10 units of blood. The differences at the first and the second follow-up were statistically significant (Fisher's exact test, $p = 0.0073$ and 0.039, respectively).

Hospitalisation because of overt HE

Two patients in the MIS group developed overt HE and were hospitalised for treatment. One patient had a period of heavy alcohol intake 2 years postoperatively and developed liver coma. After treatment with lactulose he recovered. The other patient was taken to hospital 3 years postoperatively with signs of encephalopathy, he also suffered from a psychiatric disorder and was found to have an excessive concentration of lithium in the blood, besides liver insufficiency. He too recovered after lactulose treatment.

Neuropsychological findings

Only 3 of 13 patients in the rest of the original material had preoperative neuropsychological test results, so no meaningful statistical calculations could be performed between the core material and the rest of the material.

There was no significant difference in any neuropsychological test score between the MIS and ST groups using the Mann–Whitney U-test in the core material.

Significant changes between preoperative and postoperative results were found (according to ANOVA, repeated measures), for the Synonyms, Block Design Test, Memory for Design Test-error scores and the Digit Symbol test (Table I). Significant interactions between groups and order of occasions were found in the tests Synonyms, Memory for Design Test, error scores, Revised Visual Retention Test, correct answers and error scores and Digit Symbol (Table I).

According to the classification guidelines proposed by Guilford [24], 62 of a possible maximum of 105 correlation coefficients (*rho*) between the core neuropsychological tests before operation were moderate or high.

The differences in performance were most pronounced in tests assessing visuo-spatial memory ability, the Revised Visual Retention Test and the Memory for Design Test. In a previous investigation, these particular tests differentiated well between patients with mild dementia caused by chronic toxic encephalopathy due to organic solvents, and patients with moderate-severe dementia caused by cerebrovascular diseases or presenile dementia of Alzheimer's type [25]. The results from the preoperative testing thus indicate that the ST patients had more pronounced HE than the MIS patients.

At the 12-month follow-up psychometric testing, however, the MIS patients performed statistically worse than the ST patients in 3 of the 15 test variables: Synonyms, Block Design Test and Colour Word Test (Table II). The p value for follow-up was also statistically significant, at 0.030 (Table II). Furthermore, the MIS patients performed worse than the ST patients in

Table II. ANOVA (repeated measures) of neuropsychological test results preoperatively (Pre) and postoperatively (Post) in the core material between the MIS and ST groups

	df	F	p	Group	M±SD Pre	M±SD Post	n
Synonyms							
A Group	1,30	0.00	0.96	MIS	19.8±5.4	20.1±4.9	16
B Order	1,30	7.87	0.009**	ST	18.9±7.7	20.8±7.0	16
AB	1,30	4.60	0.04*				
Figure Classification							
A Group	1,30	0.21	0.65	MIS	18.4±4.4	17.6±4.6	16
B Order	1,30	0.04	0.85	ST	16.7±5.5	17.8±5.5	16
AB	1,30	2.05	0.16				
Block Design Test							
A Group	1,28	0.09	0.77	MIS	19.6±6.5	20.4±6.6	16
B Order	1,28	4.56	0.042*	ST	18.2±6.8	20.3±7.3	14
AB	1,28	0.90	0.35				
Memory for Design Test, Error Scores							
A Group	1,27	0.41	0.53	MIS	4.71±4.5	4.71±4.5	14
B Order	1,27	4.94	0.035*	ST	6.87±5.0	4.73±4.9	15
AB	1,27	4.94	0.035*				
Revised Visual Retention Test, Correct Answers							
A Group	1,30	0.24	0.62	MIS	6.13±2.1	5.50±1.6	16
B Order	1,30	0.10	0.75	ST	5.13±1.5	5.94±1.9	16
AB	1,30	5.89	0.021*				
Revised Visual Retention Test, Error Answers							
A Group	1,29	0.08	0.78	MIS	6.00±4.4	7.13±3.5	15
B Order	1,29	0.09	0.77	ST	6.94±3.5	5.50±3.4	16
AB	1,29	6.38	0.017*				
Paired Associates, Correct Answers							
A Group	1,30	0.10	0.76	MIS	20.4±4.7	20.5±4.0	16
B Order	1,30	0.35	0.56	ST	20.6±5.4	21.3±4.6	16
AB	1,30	0.28	0.60				
Digit Symbol							
A Group	1,30	0.23	0.64	MIS	34.1±11.8	34.8±10.1	16
B Order	1,30	8.29	0.0073**	ST	34.0±12.4	39.1±15.4	16
AB	1,30	4.70	0.038*				
Dot Test, Time							
A Group	1,30	0.01	0.92	MIS	486±113	477±104	16
B Order	1,30	0.91	0.35	ST	495±103	476±145	16
AB	1,30	0.11	0.74				
Dot Test, Errors							
A Group	1,29	0.02	0.90	MIS	14.5±11.6	12.9±8.0	15
B Order	1,29	0.65	0.43	ST	14.7±11.8	13.7±9.0	16
AB	1,29	0.03	0.86				
Colour Word Test, Time							
A Group	1,29	0.01	0.93	MIS	145±50	150±49	15
B Order	1,29	0.05	0.83	ST	151±64	148±73	16
AB	1,29	0.78	0.38				
Cylinder Board, Right Hand							
A Group	1,30	1.05	0.31	MIS	70.7±10.7	68.3±9.5	16
B Order	1,30	0.19	0.66	ST	63.8±16.9	65.3±17.2	16
AB	1,30	3.04	0.09				
Cylinder Board, Left Hand							
A Group	1,26	0.03	0.87	MIS	63.4±9.6	62.4±8.9	14
B Order	1,26	0.00	0.98	ST	61.8±12.0	62.7±12.7	14
AB	1,26	0.66	0.43				
Cylinder Board, Difference							
A Group	1,26	0.01	0.93	MIS	6.29±5.2	5.00±3.6	14
B Order	1,26	1.13	0.30	ST	5.57±3.7	5.46±3.6	14
AB	1,26	0.81	0.38				
Reaction Time, Median							
A Group	1,29	0.67	0.42	MIS	1.60±0.74	1.73±0.86	15
B Order	1,29	1.11	0.74	ST	1.94±0.93	1.88±0.92	16
AB	1,29	0.85	0.37				

* $p < 0.05$.
** $p < 0.01$.

Table III. ANOVA (repeated measures) of EEG and Trail Making Test results in available patients with preoperative and postoperative results in the MIS and ST groups

	df	F	p	Group	M ± SD before	M ± SD after	n
EEG							
A Group	1,20	1.02	0.32	MIS	48.8 ± 17.5	59.4 ± 19.3	17
B Order	1,20	1.00	0.33	ST	46.4 ± 21.6	45.4 ± 15.3	5
AB	1,20	1.46	0.24				
Trail Making Test A							
A Group	1,22	0.54	0.47	MIS	56.6 ± 16.9	58.6 ± 23.0	13
B Order	1,22	0.19	0.67	ST	66.5 ± 28.5	61.1 ± 22.6	11
AB	1,22	0.86	0.36				
Trail Making Test B							
A Group	1,22	1.03	0.32	MIS	80.3 ± 21.7	93.1 ± 34.9	13
B Order	1,22	0.04	0.84	ST	114.7 ± 77.2	103.9 ± 74.7	11
AB	1,22	6.16	0.021*				

* $p < 0.05$.

an additional 10 test variables, although these differences were not statistically significant (e.g. in the Memory for Design Test).

To study the effects of the two different treatment methods, MIS and ST, we considered it important to evaluate patterns in psychometric test performances rather than performance in single tests. The general pattern of the test performance for ST patients was an improvement after treatment as opposed to the MIS patients' test performance, which deteriorated over time.

EEG findings

The preoperative LFP median was 46 (SD 62) for the MIS group ($n=17$), median 47 (SD 49) for the ST group ($n=5$) and median 41 (SD 53) for the control group ($n=26$). The postoperative medians were 58 (SD 69) for the MIS group ($n=17$) and median 37 (SD 35) for the ST group ($n=5$) (Table III).

HE in relation to portal flow

The preoperative evaluation of the 20 MIS patients showed hepatopetal flow in 16 (80%), hepatofugal flow in 2 (10%) and mixed flow in 2 (10%) patients. During first follow-up only three patients (16%) had preserved hepatopetal flow, in (84%) had the flow nine changed to hepatofugal. At the second follow-up, at 12 months, three patients (30%) had hepatopetal flow and seven (70%) had hepatofugal flow.

Discussion

Factors known to influence HE are the aetiology of cirrhosis, intake of alcoholic beverages, age over 60 years (as older patients are at greater risk of developing encephalopathy) and low serum albumin levels [6,11,26]. There were no significant differences between the two treatment groups in these aspects and no differences in liver function parameters between the MIS and the ST groups. Gitlin and associates reported elevations in liver parameters in their group of cirrhotic patients, but they could not find any correlation between biochemical and psychological tests [27].

Warren and his group [28,29] stressed the importance of hepatic portal perfusion in preventing postoperative HE; later studies [30–32] supported this hypothesis. Our findings are in agreement: portal flow did influence the development of HE.

The use of anti-encephalopathic drugs was evenly distributed in the two groups, except at the first follow-up time when the sclerotherapy patients received more drugs. This variable does not seem to influence the trend in deterioration of the three psychometric tests, as the ST group did better at both follow-up times.

Rypins and colleagues [33] used a 10-mm portacaval shunt in their study. They could not find any support for the concept that portal pressure is important in the development of postoperative HE but rather the portal flow. In a later study from the same authors [32] comparing 8-mm grafts to 16-mm portacaval H grafts, hepatopetal flow was maintained in the 8-mm graft group during follow-up, which was not the case in the 16-mm group. They also found significantly greater encephalopathy-free survival for the smaller diameter graft group. Rikkers and co-workers obtained similar findings [3] when distal splenorenal shunt was compared with sclerotherapy; although hepatic portal perfusion was better after ST there was no major difference between the groups in terms of post-therapy psychoneurological function.

In both the MIS and the ST group we found a high incidence of preoperative encephalopathy. However, the results from the preoperative psychometric testing showed that the ST patients had more pronounced HE than the MIS patients at the onset of the study. The differences in test performances were more pronounced in tests previously known to differentiate well between mild and moderate-severe dementia. Using unbalanced repeated measurement of variance, we found that during follow-up the patients in the shunt group performed significantly worse in seven tests, which measure either verbal ability (Synonyms), visuo-spatial ability (Block Design Test and Revised

Visual Retention Test Correct/Error Answers), memory function (Memory for Design Test, Error Score), perceptual ability (Digit Symbol Test), cognitive motor abilities (Trial Making Test B) or intellectual flexibility (Colour Word Test). The other tests that evaluate reasoning function, memory function and psychomotor capacity showed no significant difference between the two treatment groups.

EEG with spectral analysis showed no significant difference between groups at follow-up. To evaluate hepatic encephalopathy in this group of patients at risk of developing encephalopathy, psychometric tests sensitive to diffuse global cognitive dysfunction should be used. Other studies that have evaluated encephalopathy after a distal splenorenal shunt (which acts as a selective shunt) [5] and TIPS (which acts as a total shunt) [7] have shown a somewhat more pronounced encephalopathy after shunting than after sclerotherapy.

In our study we used a 14-mm mesocaval interposition shunt as the surgical alternative to sclerotherapy. This shunt is a total shunt, as we found that almost all patients had hepatofugal portal flow after 12 months. Our findings are in line with the previously cited works: test performance in MIS patients deteriorated over time compared with that in ST patients, whose test performance improved over time. Using an MIS of smaller diameter (10 or 12 mm), Paquet and colleagues found that hepatopetal flow was preserved during a follow-up of about 4 years, with no case of chronic HE and <10% of acute HE [34].

Gitlin and associates [35] reported a 70% incidence of subclinical HE in a study of non-shunted and well compensated cirrhotic patients. They found three psychometric tests that could identify subclinical HE: the Digit Symbol Test, the Block Design Test and the Trailmaking Test. Srivastava and colleagues found a 66% incidence of subclinical HE in patients with cirrhosis and portal-systemic shunting, although there was no major impairment in fitness to drive [36]. According to Van der Rijt and associates [37], all known electrophysiological methods are non-specific for latent HE and no method is superior to EEG with spectral analysis.

In our previous analysis of this study with regard to rebleeding and surgical complication [9], the encephalopathy was assessed by psychometric tests and EEG analysis. Patients were scored and divided into three groups in a similar way to many other reports [3, 34]. In this analysis no difference could be observed in the encephalopathy rate between the two treatment arms. However, to evaluate shunting procedures as carefully as possible, we considered it important to perform a detailed analysis of all the test results. It became apparent that the shunted patients fared worse than the patients undergoing sclerotherapy.

In conclusion, in this prospective randomised study we found that patients treated with mesocaval interposition shunt show a progressive general reduction in intellectual capacity, which is not clinically evident but can be detected on psychometric testing, as opposed to patients treated with sclerotherapy, who show general intellectual improvement. The importance of these observations in relation to the development of clinically overt encephalopathy is not fully understood at the present time. We believe that it is important to make a detailed analysis of subclinical encephalopathy, evaluating shunting procedures in patients with portal hypertension and bleeding oesophageal varices.

Acknowledgements

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