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Transplantation

Hypoalbuminaemia in brain-dead donors for liver transplantation

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Liver transplantation has become established as the treatment of choice for most patients with end-stage liver disease and is performed on a routine basis in most major centres throughout the world. The majority of donors for liver transplantation are brain-dead cadaver donors following either a severe head injury or a massive intracranial haemorrhage.

Potential liver donors undergo a rigid screening process before being accepted. This includes a thorough clinical examination to assess the haemodynamic status of the donor and to exclude any overt evidence of liver disease. Blood samples are also taken for viral studies to exclude HIV infection and hepatitis B and C infection, and for liver function tests to exclude liver disease or liver injury.

Over the years we have noted that our liver donors often had low serum albumin levels, although this has not been formally documented. A review of the literature revealed that hypoalbuminaemia associated with severe head injury has been documented previously. However the impact of brain death on serum albumin levels has not been studied previously. The present study was therefore undertaken to document serum albumin levels in brain-dead cadaver donors.

Patients and methods

We retrospectively reviewed the charts of the 37 brain-dead patients referred to the organ transplant unit at Groote Schuur Hospital in 2001 and 2002 as potential donors for liver transplantation.

All potential donors were assessed, investigated and managed according to standard protocols. The assessment consisted of taking an in-depth history from the family and doing a thorough physical examination of the donor to exclude any serious illnesses in the past, use of any medication that could compromise the liver, and any psychosocial behaviour that could potentially place the recipient at an increased risk of acquiring certain transmissible diseases. Periods of haemodynamic instability in relation to the injury were also noted. The investigations included blood tests for blood group, full blood count, viral studies for HIV, hepatitis B and C and cytomegalovirus (CMV), and renal and liver function tests. The latter included serum aspartate transaminase (AST), alanine aminotransferase (ALT), alkaline phosphatase, gammaglutaryl transferase (GGT), total protein, albumin and bilirubin levels.

The donors were carefully monitored to ensure adequate ventilation and haemodynamic stability. Intravenous fluids were administered according to urine output and haemodynamic status. Occasionally inotropic support was required for haemodynamic instability.

The charts of the patients were reviewed and demographic data, cause of brain death, time of the injury, time of certification of brain death, use of inotropic support, and biochemical and haemotological data were recorded. The results were analysed statistically using STATA corp 2001 statistical software

Results

The 37 potential donors for liver transplantation referred to the organ transplant unit at Groote Schuur Hospital between January 2001 and December 2002 were included in the study. There were 22 males and 15 females with an average age of 27.8 ± 10.7 years (range 3 - 52 years). The mean height of the patients was 1.73 ± 0.1 m (range 0.9 - 2.0 m) and the mean weight was 69.6 ± 19.5 kg (range 15 - 120 kg). Fifteen patients were blood group A, 15 were blood group O, 5 were blood group B and 2 were blood group AB.

The causes of brain death are shown in Fig. 1. In the majority of cases brain death was trauma related. The cause of brain death was a motor vehicle accident in 30% of cases, assault in 16%, a gunshot wound to the head in 16% and a fall in 8%. In only 30% of the patients was the brain death related to a cerebrovascular accident (CVA).

The time between the injury/CVA and referral to the organ transplant unit is shown in Fig. 2. The majority of patients were referred more than 20 hours after the injury/CVA. Only 9 patients were referred within 10 hours, and 9 patients were referred more than 30 hours after the injury/CVA.

The time since certification of brain death and referral to the organ transplant unit is shown in Fig. 3. In 22 patients the blood tests had been undertaken within 10 hours of certification of brain death. In 7 patients the blood tests had been undertaken more than 20 hours after certification of brain death.

The serum electrolyte levels are shown in Table I. Serum sodium, potassium, urea, creatinine, calcium, and glucose levels were all within the normal range.

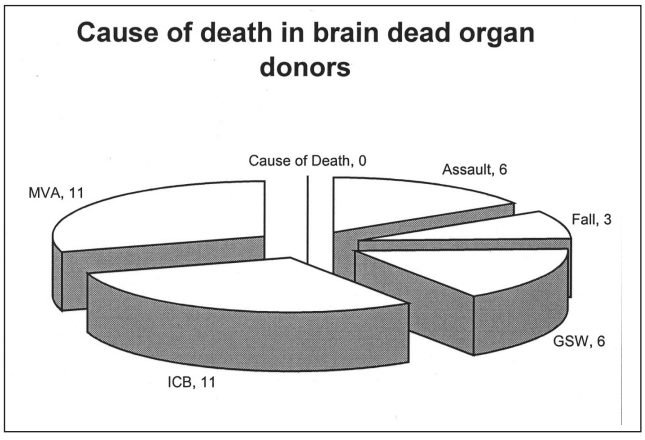

Fig. 1. Causes of brain death in potential donors for liver transplantation.

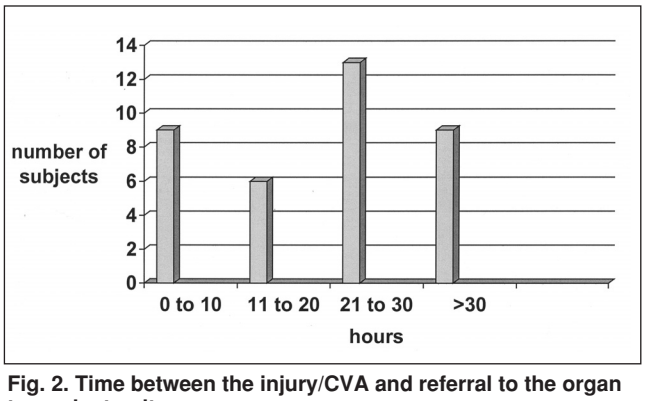

Fig. 2. Time between the injury/CVA and referral to the organ transplant unit.

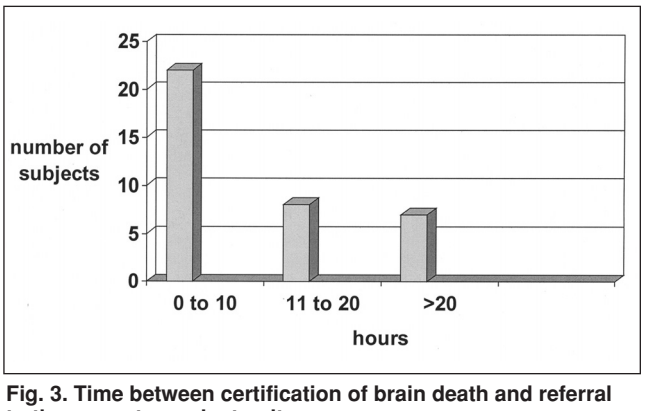

Fig. 3. Time between certification of brain death and referral to the organ transplant unit.

The results of liver function tests are shown in Table II. The serum alkaline phosphatase, GGT, ALT, AST, lactate dehydrogenase and total bilirubin were all within the normal range. However the mean total protein was 49.4 ± 41 and the mean serum albumin 23.3 ± 7.4, both of which were significantly below the normal range. The distribution of the protein levels is shown in Fig. 4. Only 2 patients had total protein levels within the normal range. The distribution of the serum albumin levels is shown in Fig. 5. Only 1 patient had a serum albumin level in the normal range.

Seventy per cent of the patients had received inotropic support to maintain haemodynamic stability. The mean serum albumin level in the patients who received inotropic support was 22 g/l compared with 25 g/l in the patients who did not receive inotropic support ($p > 0.05$) (Fig. 6).

TABLE I. SERUM ELECTROLYTE LEVELS AND RENAL FUNCTION IN BRAIN-DEAD DONORS FOR LIVER TRANSPLANTATION

Serum electrolytes	(mmol/l)
Na^+	**140.9 ± 8.8**
K^+	**4.0 ± 0.9**
Urea	**4.9 ± 2.1**
Creatinine	**97.9 ± 37.0**
Ca^{2+}	**1.5 ± 0.2**
Glucose	**16.4 ± 9.3**

TABLE II. LIVER FUNCTION TEST RESULTS IN BRAIN-DEAD DONORS FOR LIVER TRANSPLANTATION

Total protein	**49.4 ± 21 g/l**
Albumin	**23.3 ± 7.4 g/l**
Alk po4	**60.4 ± 44.8 IU/l**
GGT	**27.7 ± 26.6 IU/l**
ALT	**36.8 ± 31.4 IU/l**
AST	**54.6 ± 31.6 IU/l**
LDH	**534.3 ± 328.9 IU/l**
Conj. bilirubin	**3.6 ± 2.6 µmol/l**
Total bilirubin	**14.1 ± 9.4 µmol/l**

The effect of the cause of brain death on serum albumin levels is shown in Fig. 7. Serum albumin levels were significantly lower in the patients who had trauma (21 g/l) compared with the CVA patients (28 g/l) ($p < 0.05$).

There was no effect of the time since injury/CVA on serum albumin levels. The patients referred to the transplant unit within 20 hours of the injury/CVA had a serum albumin level of 23 g/l, compared with a serum albumin level of 25 g/l in the patients referred more than 20 hours after the injury/CVA ($p > 0.05$). Similarly, the patients referred within 10 hours of certification of brain death had a serum albumin level of 23 g/l, compared with a serum albumin level of 25 g/l in the patients referred more than 10 hours after certification of brain death ($p > 0.05$).

Discussion

In this study we have documented significant hypoalbuminaemia and hypoproteinaemia in brain-dead patients who had been referred to the organ transplant unit as potential donors for liver transplantation. The liver function tests are used as part of the screening process for the acceptability of potential brain-dead donors for liver transplantation. Many of the patients included in this study were eventually used as donors for liver transplantation. Therefore, although the liver function tests were used to screen the potential donor for evidence of liver disease, the low serum albumin levels were ignored when making the decision whether to use the donor as a liver donor or not. The impact of the hypoalbuminaemia on the outcome after liver transplantation remains unresolved and did not form part of this study.

In this study the serum albumin levels were not influenced by the cause of brain death, the use of inotropic support, the time since injury/CVA, and the time since the certification of brain death. In contrast, serum albumin levels were influ-

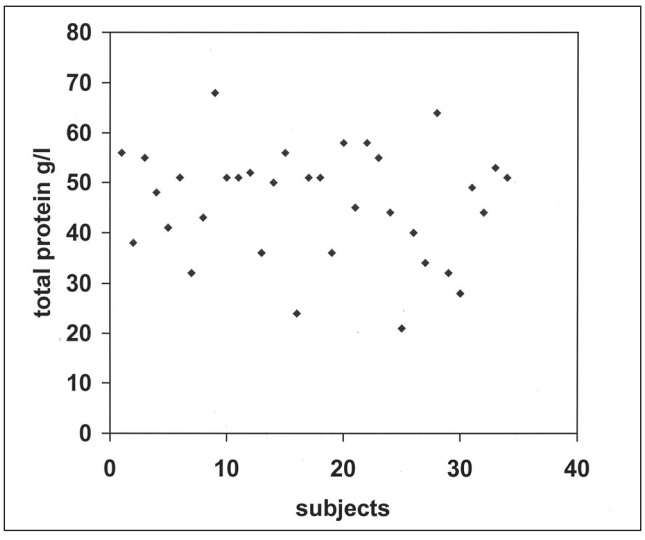

Fig. 4. Distribution of total serum protein levels.

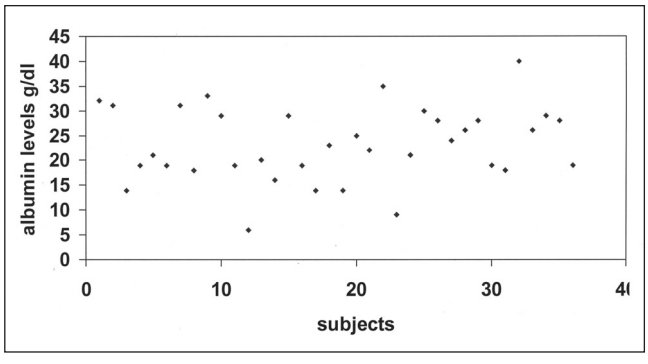

Fig. 5. Distribution of serum albumin levels.

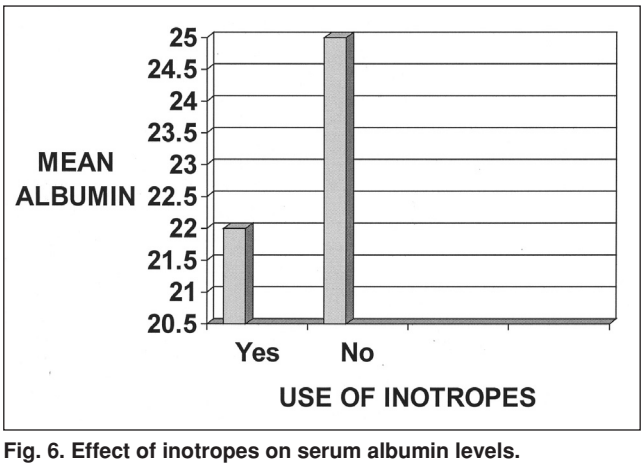

Fig. 6. Effect of inotropes on serum albumin levels.

enced by the cause of the brain death; the trauma-related brain-dead patients had significantly lower serum albumin levels.

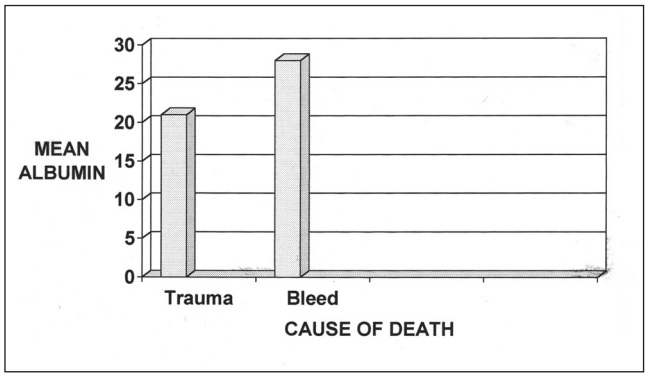

Fig. 7. Effect of the cause of brain death on serum albumin levels.

The precise cause of the low serum albumin levels following brain death remains unresolved. Hypoalbuminaemia has been documented previously in association with severe head injury.[1-4] The hypoalbuminaemia has been attributed to the hypermetabolism/hypercatabolism seen in these patients. Brain-injured patients are thought to have depressed serum albumin levels due to the negative nitrogen balance as part of the acute response to injury.[3] However, this does not explain why the patients who had sustained a CVA had low serum albumin levels since the injury would have been relatively minimal.

Hypoalbuminaemia in association with clinical brain death has not been documented previously. Furthermore the previous studies have all demonstrated the low serum albumin levels in patients with severe head injury. The present finding of hypoalbuminaemia following CVA has not been reported previously.

It is also interesting to note how soon after the head injury/CVA hypoalbuminaemia is detected. In 9 patients the hypoalbuminaemia was noted within 10 hours of the injury/CVA. The previous studies of head injury patients were undertaken beyond 24 hours. The majority of the patients in this study presented more than 10 hours after the injury/CVA. Further studies are required of the period immediately after the injury/CVA to determine how quickly the hypoalbuminaemia occurs.

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