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Review Article

The management of patients awaiting liver transplantation

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The aims of monitoring patients accepted for a liver transplant are to maintain and, where possible, improve health, monitor and treat complications of chronic liver disease (Table 1).[1,2] Whilst on the liver transplant waiting list, patients may deteriorate as a result of disease progression, or develop complications associated with the underlying liver disease, either of which may result in removal from the waiting list or a worse outcome following surgery.

The prevention and management of the complications of end-stage liver disease, such as variceal bleeding, ascites, spontaneous bacterial peritonitis (SBP), hepatorenal syndrome (HRS) and hepatic encephalopathy are well described elsewhere.[1–5]

Table 1 Monitoring of liver transplant candidates

General well-being
Nutritional state
Detection of complications of cirrhosis
Ascites
Renal impairment
Varices
HCC development
Portal vein thrombosis
Malnutrition
Immunization
Psychological support
Retention of consent

GENERAL CARE

For both patients and candidates, the time on the waiting list is one of great stress and uncertainty. Clinicians need to be aware of this and ensure that in addition to physical care, attention is also paid to the psychological care of the candidates and their family during this uncertain time.[6]

Consent for surgery is usually taken prior to registration on the waiting list. However, before a graft is available, it is prudent to ensure that the candidate appreciates the risks of transplantation and re-affirms his/her consent. Furthermore, if the candidate has indicated that he/she does not wish to receive an extended criterion graft, then they should be offered the opportunity to change their mind.

Along with general assessment, we believe that transplant candidates should have regular (every 3–6 months) ultrasound examination as portal vein thrombosis may develop without clinical symptoms. Although such thrombosis should not preclude transplantation, it is helpful for the surgeon to be aware of this complication prior to surgery.

MONITORING FOR COMPLIANCE

Alcohol-associated liver disease is a major indication but liver transplantation and most centres demand that the recipients should remain abstinent from alcohol. Monitoring for compliance with abstinence should be done according to the agreed protocols. We recommend that there should be measurement of alcohol, breath, blood or urine, at each clinic visit and the patient and his/her family be questioned as to the use of alcohol. The uses of surrogate markers, such as variations in levels of gamma-glutamyl transpeptidase or mitochondrial AST or carbohydrate-deficient transferring are probably not sufficiently robust to trigger a response to non-compliance. In most units, non-compliance will result in suspension, either permanently or transiently, from the list. It is recognised that such screening is not completely foolproof and should not be undertaken without the agreement of the patient.

For those where use of legal (such as smoking) or illegal substances (such as heroin or other agents) is of concern, screening should also be undertaken. Time on the waiting

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list can be used to encourage participation in smoking cessation programmes.

VARICES

Endoscopic assessment of varices will be done during the work-up: in those with small varices and Child–Pugh class B/C disease, or with moderate and large varices, primary prophylaxis with a non-selective β-blocker (such as propranolol, nadolol or carvedilol) is usually prescribed (unless there are specific contraindications).[7] For patients who do not tolerate β-blockers or who have contraindications to treatment, variceal ligation should be offered.[8] There is no evidence that those on β-blockers have a worse outcome during or after anaesthesia.

Variceal bleeding, which may develop and occur despite prophylaxis, should be treated, as in the non-transplant candidate with prompt resuscitation with intravenous fluid and blood transfusion, use of terlipressin, prophylactic antibiotics and endoscopic ligation or sclerotherapy. Tamponnade should be used only when endoscopic measures are not effective. Possible triggers for the bleeding, such as infection (in particular SBP), portal vein thrombosis and the development of Hepatocellular carcinoma (HCC), should be considered.

A Transjugular Intrahepatic Portosystemic Shunt (TIPS) is effective in patients not responding to pharmacological and endoscopic treatment and should be considered early.[16] Although, there are reports of migration and embedded stents making liver transplantation more difficult and complex,[9] recent long-term data have shown that survival is not affected by the insertion of a TIPS.[10] The stent should be more than 1 cm proximal to the hepatic vein–caval junction and not extend beyond the portal bifurcation.

The patient should be suspended from the liver transplant waiting list until he/she has overcome the bleed. Sclerotherapy prior to transplantation has been associated, in our experience with para-oesophageal abscess formation in the post transplant period.

ASCITES

Patients with ascites should be given a low salt diet, aiming at a sodium intake of 70–90 mmol per day and care must be taken that the dietary restriction does not lead to exacerbation of malnutrition; also diuretics such as spironolactone combined with furosemide should also be given. Spironolactone can be started at 200 mg/day and increased up to 800 mg/day; furosemide is started at 40–80 mg/day and increased in parallel with the spironolactone. Weight and renal function should be monitored closely to detect renal impairment and electrolyte disturbance. Weight loss > 750 g/day, serum sodium < 125 mmol/L or an increase in serum creatinine or urea indicate a need for a reduction in the dose of the diuretic non-responsive or large ascites can be safely treated by paracentesis. TIPS can be safely be used in transplant recipients.

SPONTANEOUS BACTERIAL PERITONITIS

Spontaneous bacterial peritonitis (SBP) may develop up to 30% in patients with ascites. The high mortality can be reduced by early diagnosis and treatment. Intravenous antibiotics should be started if the polymorphonuclear leucocyte count in the ascitic fluid is more than 250/mm^3 (0.25×10^9/L). The use of a 20% albumin infusion at 1.5 g/kg at diagnosis and a repeat infusion on day 3 at 1 g/kg can reduce the risk of renal failure and mortality. Long term prophylactic antibiotics should be given to those who have had one episode of SBP and in those with low protein levels (1.5 g/L);[11] norfloxacin, ampicillin and co-trimoxazole are also effective. Although long-term use of antibiotics may be associated with the development of resistance, this is not a major problem in the liver transplant candidate.

HEPATORENAL SYNDROME (HRS)

Type 1 HRS occurs acutely and is usually triggered by events such as SBP, gastrointestinal bleeding or inappropriate use of dugs and other agents (such as non-steroidal anti-inflammatory drugs or some contrast media).

Type 2 HRS usually runs a more chronic course, often with moderately impaired but stable renal function. Terlipressin in combination with adequate intravascular filling with albumin is the treatment of choice for HRS but other treatment options such as midodrine and octreotide, or TIPS may be effective. Rarely, Renal Replacement Therapy (RRT) is required. If RRT is required for more than 6 weeks or if there is evidence of intrinsic renal disease, a combined liver and kidney transplant should be considered.

Hyponatraemia

Hyponatraemia is associated with a poor prognosis pre-transplant and may preclude transplantation if serum