

ANAESTHESIA AND LIVER DISEASE – PART 2 ANAESTHESIA TUTORIAL OF THE WEEK 272

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QUESTIONS

Before continuing, try to answer the following questions. The answers can be found at the end of the article, together with an explanation.

1. Which of the following are considered standard monitoring in Child's B and C patients undergoing abdominal surgery?
 - a. Central venous pressure (CVP) monitoring
 - b. Arterial line monitoring
 - c. Oesophageal doppler monitoring
 - d. Temperature monitoring
2. Which inhaled anaesthetic agent is most suitable for use in patients with liver failure?
3. Which classification system is commonly used when considering a patient for liver transplantation?
 - a. Child's - Pugh
 - b. MELD
 - c. King's classification

INTRODUCTION

This tutorial builds on [ATOTW 270, Anaesthesia and Liver disease part 1](#). Part two examines the practicalities of anaesthetising patients with liver dysfunction and the impact of physiological changes associated with liver disease on anaesthetic techniques. We will also summarise the indications for liver transplantation and briefly discuss considerations for the anaesthetist when dealing with a post-transplantation patient.

ANAESTHESIA IN PATIENTS WITH LIVER FAILURE

Pre-operative assessment

The number of patients with liver dysfunction requiring surgery is on the rise. An estimated 1 in 700 patients admitted for elective surgery has abnormal liver enzyme levels. The risks of anaesthesia in this group are related to where the patient lies on the liver disease spectrum, from subclinical to end-stage liver disease. The range of symptoms present depends on whether the disease duration is acute or chronic. The extent to which liver disease results in other systemic dysfunction may be just as important as the manifestations of primary liver dysfunction in predicting outcome after surgery. Optimal preparation may decrease both peri-operative death and post-operative complications. In patients with cirrhosis, liver failure is the most common cause of postoperative death.

Pre-operatively a cause for the liver dysfunction should be sought where possible, not least to establish infective risk to health care workers. The risk-benefit of carrying out surgery needs to be carefully

considered once the patient has been fully assessed. Patients with liver disease have an inappropriate response to surgical stress due to both the loss of hepatic reserve capacity and other systemic derangement. Prediction of surgical risk is based on the degree of liver dysfunction, type of surgery and the preclinical status of the patient.

The Childs Pugh score can be used to estimate risk of peri-operative mortality, although it is of limited use as essentially all Childs B and C patients are high risk. Recent figures suggest patients with Childs A have 5-10% peri-operative mortality after abdominal surgery, compared to Childs B where it rises to 25-30% and Childs C where peri-operative mortality is >50% in all types of abdominal surgery.

Patients undergoing emergency surgery are at an even greater risk. The lack of opportunity to correct reversible factors such as electrolyte imbalance, coagulopathy and the clinical manifestations of portal hypertension such as ascites and encephalopathy all have an impact. The presence of malnutrition, sepsis and significant blood loss increase risks further still.

A thorough pre-operative assessment is essential. Common investigations include:

- Full blood count – to establish anaemia, thrombocytopenia or evidence of infection.
- Pro-thrombin time – as an indicator of hepatocellular function. Pro-thrombin time may also be raised due to vitamin K deficiency; This should be replaced pre-operatively where indicated.
- Baseline renal function – in patients with cirrhosis a creatinine in the normal range may indeed represent renal impairment.
- Identification and correction of electrolyte disturbances.
- ECG and echocardiography - to help establish ventricular function and the presence of cardiomyopathy, valvular lesions or raised pulmonary vascular pressure.
- Exercise ECG or stress echo – as previously discussed the chronic state of vasodilatation may mask ischaemia by limiting ventricular workload, stress testing may be useful where undiagnosed ischaemia is suspected.
- CXR or ultrasound imaging of chest - to establish the presence of effusions amenable to pre-operative drainage, may be helpful in optimising peri-operative respiratory function.
- Pulmonary function tests - may be useful as they are in other patient groups to help identify disease processes and stratify risk.

Pre-operative management includes addressing the primary features and secondary manifestations of liver disease to decrease the risk of perioperative complications or death. This includes optimisation of electrolytes, intravascular volume status, coagulation and infection status. Pre-optimisation may be best achieved by admission to a critical care bed, and this should be considered on a case by case basis. Pre-operative vitamin K and fresh frozen plasma (FFP) administration may in part correct the coagulation defect, and cryoprecipitate may also be required if the PT remains prolonged. Bleeding time reduction should be guided by levels, and may need prophylactic desmopressin (DDAVP) administration, platelet transfusion, thromboelastogram use and expert haematological advice. Tranexamic acid may also be helpful.

Ascites present at the time of surgery can lead to wound dehiscence, abdominal wall herniation and respiratory compromise secondary to diaphragmatic splinting. As such pre-operative diuresis or aggressive paracentesis may be required. Ascitic fluid removal either pre-operatively, or intraoperatively at laparotomy, can lead to significant fluid shifts and intravascular volume depletion, potentially precipitating cardiovascular collapse. Boluses of colloid, usually in the form of albumin replacement may be required depending on the volume of ascites removed.

Nutritional health should be addressed preoperatively wherever possible. Dietetic input and vitamin supplementation should occur as early as possible in the pre-operative process. Gastric emptying is often delayed in this population and as such aspiration is a greater risk, pre-medication with H₂ antagonists may be advisable.

Sedative premedication should be avoided as it may precipitate encephalopathy. Other identifiable causes of encephalopathy, such as infection, electrolyte dysfunction and gastrointestinal blood loss

should be avoided or treated where possible and lactulose administration may be required. It should be remembered that encephalopathy in the postoperative period of non-hepatic surgery is associated with greatly elevated postoperative mortality.

Intraoperative Management

Monitoring

Routine monitoring should be established pre-induction. Invasive monitoring by means of arterial line and CVP can be very helpful and is used almost universally when dealing with Childs B and C patients. Oesophageal doppler and trans-oesophageal echo (TOE) can be useful, but the presence of varices may preclude this. Use of a pulmonary artery catheter, or arterial waveform analysis techniques such as LiDCO or PiCCO are potential alternatives for cardiac output monitoring. All will provide information to aid the maintenance of intravascular volume and the need for vasopressors to maintain adequate perfusion pressures.

Monitoring of neuromuscular blockade, urine output, lactate, glucose, electrolytes and temperature, with active warming devices available, should all occur throughout the intra-operative period.

The potential for significant blood loss means large bore IV access is ideal. Warming of IV fluids and the availability of a rapid infusor is standard practise in these cases. Cell salvage should also be available where blood loss is likely to be significant.

The increased risk of infection in this group means aseptic technique must be scrupulous and antibiotic prophylaxis needs to be carefully considered. Depletion of glycogen stores may result in perioperative hypoglycaemia and a background infusion of dextrose may be required. N-acetylcysteine infusion in patients with fulminant hepatic failure may improve oxygen delivery and consumption and reduce base deficit.

Choice of anaesthetic agents

Anaesthetic choice should take into account alterations in protein binding of drugs secondary to decreased synthesis, an impairment of drug metabolism, detoxification and excretion, all acting to prolong drug half lives. The absorption, distribution, metabolism and excretion of anaesthetic agents, muscle relaxants, analgesics and sedatives are all likely to be affected.

Propofol is probably the most commonly used induction agent in this group as it undergoes considerable extra-hepatic metabolism. It should be remembered that sensitivity to the sedative and cardio respiratory effects of propofol are increased in liver failure and so the dose should be reduced.

If thiopentone is to be used, a reduced dose is again needed, as reduction in plasma proteins causes an increased unbound fraction of the drug. The distribution half life and duration of action are also prolonged. Chronic alcohol use may increase IV anaesthetic requirements however all agents should be used with care.

In terms of muscle relaxant choice, suxamethonium may have a prolonged duration of action due to reduced pseudocholinesterase concentrations slowing its metabolism, although in practise this is unlikely to be clinically significant. Vecuronium and rocuronium have a prolonged elimination phase in severe disease. Atracurium and cisatracurium are better options as they are not reliant on hepatic excretion. Monitoring of neuromuscular blockade is advised whatever the choice of agent.

Choice of opioids can be difficult. The elimination of morphine is delayed in cirrhotic patients due to reduced hepatic blood flow and extraction ratio. In patients with associated renal failure, accumulation of the active metabolite morphine-6-glucuronide will occur. Morphine may therefore precipitate encephalopathy and is possibly best avoided in severe liver dysfunction.

Fentanyl in low doses may be a better option as it is renally excreted, however it will accumulate in larger doses. The elimination of alfentanil is reduced whilst its volume of distribution is increased. A deficiency in alpha-1-acid glycoprotein results in reduced protein binding. These changes mean that the dose of alfentanil should be reduced. Remifentanyl is commonly used intra-operatively, its metabolism by tissue and plasma esterases (which are preserved in patients with severe liver disease) means it does not impact on the post-operative period.

Intraoperatively hepatic blood flow and oxygen delivery should be maintained to avoid any further hepatocellular injury and resultant decompensation. In the presence of portal hypertension, hepatic blood flow is dependent on hepatic arterial blood flow. All volatile anaesthetic agents reduce cardiac output and MAP and hence reduce hepatic blood flow, thereby increasing the risk of exacerbating liver dysfunction. Surgical traction, positive pressure ventilation, hypocapnia and pneumoperitoneum can all further reduce hepatic blood flow. Catecholamine responses are blunted in liver disease further impacting on cardiovascular stability.

With regards to the choice of volatile agent, isoflurane, sevoflurane and desflurane all undergo minimal hepatic metabolism. Desflurane has the advantage of being least metabolised and providing the quickest emergence, it also has minimal effect on the hepatic arterial buffer response and so relatively preserves hepatic blood flow.

Post-operative concerns

Anaesthesia and surgical interventions in patients with significant liver dysfunction precipitate decompensation. Patients with decompensated liver disease are at increased risk of postoperative hepatic failure, infection, sepsis, bleeding, poor wound healing and renal dysfunction. Hence post-operative critical care management should be considered for all Childs A, B and C patients. Benefits of critical care include ensuring optimal fluid management, renal and respiratory function monitoring, and swift correction of coagulopathy and metabolic disturbances.

Post operative renal dysfunction is increased in this patient group. Fluid shifts and anaesthesia related reduction in SVR and MAP on a background of haemodynamic dysfunction, all result in renal hypoperfusion. This may lead to the development of acute kidney injury or worsening of pre-existing renal dysfunction and renal replacement therapy may be needed peri-operatively. Close monitoring and the minimisation of exacerbating factors is needed to reduce this risk as far as possible.

Post operative pain relief can be challenging. The role of regional techniques is very much restricted by the high incidence of coagulation defects. Placement of epidural catheters should be undertaken with caution and with careful consideration to timing of catheter removal. Similarly, intra-muscular and subcutaneous injections can lead to haematoma formation and should be avoided.

Non steroidal anti-inflammatory medications and their association with increased risk of GI bleeding, platelet dysfunction and nephrotoxicity means they are often avoided. Paracetamol is sometimes used in this patient group, depending on the origin of their liver dysfunction, but this should be done with caution and appropriate monitoring implemented. Fentanyl PCA is generally well tolerated, but accumulation can occur over time and the patient needs to be nursed in an appropriate facility, morphine PCA can also be used but a lower bolus dose may be needed, again to avoid accumulation.

LIVER TRANSPLANTATION

Liver transplantation is the most effective treatment for many patients with both acute and chronic liver disease from a variety of causes. Transplantation can have a profound impact on patient care and quality of life. First performed in 1963, between 2000 and 2010, 6599 liver transplants took place in the UK in seven specialist units. Currently approximately 600-700 transplants per year take place in the UK.

Alcohol related liver disease is the commonest indication for a liver transplant, accounting for 112 patients in 2008-09. The second highest is hepatitis C with 107 transplants and primary biliary cirrhosis third highest with 58 transplants. The average survival at one year post transplant is around 88%.

Determining the need for liver transplantation must take into account the natural history of the patient's disease and carefully compare it to the anticipated survival after liver transplantation. Listing a patient for transplant was previously based on relatively subjective criteria relating to expected survival without transplant, quality of life and the Child-Pugh score, which can arguably be manipulated.

In chronic liver disease this criteria has been superseded by a new scoring system for patients, the United Kingdom Meld (UKELD) Score which is derived from the patient's serum sodium, creatinine,

bilirubin and INR. The minimum criteria required for liver transplant listing are a projected 1-year liver disease mortality without transplantation of more than 9%, predicted by a UKELD score of 49 or greater.

In acute liver failure the Kings College Criteria is used, it differs depending on the presence or absence of paracetamol overdose as demonstrated below.

Kings College criteria for liver transplantation

With paracetamol overdose

- pH < 7.3
- PT > 100
- Creatinine > 300
- Grade 3-4 encephalopathy

Without paracetamol overdose

- PT > 100 or 3 of following:
- Age < 10 or > 40
- Cause – halothane hepatitis, idiosyncratic drug reaction, not hepatitis A or B
- Duration of jaundice before encephalopathy > 7 days
- PT > 50
- Bilirubin > 300

Anaesthesia in the post liver transplant patient

Anaesthesia for a post liver transplant patient for an unrelated surgical procedure, requires a standard full pre-operative assessment as well as some additional considerations. The reason for transplantation, timing of surgery and well being post transplant should be sought. Additional attention to immunosuppressive agents and their common side effects needs to be made in pre-operative assessment.

Commonly used immunosuppressive agents and their side effects are listed below:

- Corticosteroids – hypertension, hypokalaemia, Cushing's syndrome, adrenal suppression, hyperglycaemia with insulin resistance and osteoporosis all may be present.
- Tacrolimus- has similar immunosuppressive properties as cyclosporine, but is more potent. It has been shown to have better outcomes post liver transplant and so has now superseded cyclosporine in many centres. Common side effects include increased risk of infection, hypertension, renal dysfunction, electrolyte abnormalities and hyperglycaemia.
- Azathioprine – bone marrow suppression with anaemia, thrombocytopenia, granulocytopenia, and an increased risk of infection along with hepatic fibrosis and pulmonary infiltrates have all been described.
- Cyclosporin – nephrotoxicity with hyperkalaemia, hepatotoxicity, neurotoxicity, hirsutism, hypertension, skin rashes and an increased vulnerability to fungal and viral infections need to be considered.

Pre-operative investigations are guided by patient history and co-morbidities. Intra-operative management is guided by the individual patient characteristics and the surgical procedure. The anaesthetic management of the post transplant patient is similar to that of a patient with liver impairment.

CONCLUSION

Due to the complex role the liver plays in metabolism, hepatic dysfunction provides many anaesthetic challenges. The multi-system impact of liver failure means assessment and management of these patients often requires multi-disciplinary discussion and critical care admission to optimise outcome.

ANSWERS TO QUESTIONS

1. Temperature monitoring is standard in abdominal surgery.
Arterial line and CVP monitoring is commonly used.
Cardiac output monitoring is also commonly used but the presence of oesophageal varices may preclude the use of an Oesophageal Doppler.
2. Isoflurane, sevoflurane and desflurane all undergo minimal hepatic metabolism.
Desflurane has the advantage of being least metabolised and providing rapid emergence.
Desflurane also has minimal effect on the hepatic arterial buffer response and so relatively preserves hepatic blood flow.
3. For acute liver disease, the King's College criteria is used to assess transplant suitability. The United Kingdom MELD score (UKELD) is used to assess transplant suitability in chronic liver failure.

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