Intensive care aspects of the post-operative liver transplant patient

Nicholas Slamon M.D.
duPont Hospital for Children
Early post-operative complications

- Temperature is a major issue
  - Liver is chilled pre implantation
  - Abdominal cavity is open for several hours
  - Bleeding from liver and bowel dissection is ongoing
- All attempts are made to maintain patient normothermia with conscientious replacement of blood and FFP
Early post-operative complications

- Hyperkalemia – K+ is elevated in the post-operative period secondary to albumin washout of the preservative fluid.
- Fluid overload – attempts should be made to run the patient dry (q6 lasix and 80% maintenance) to avoid cerebral edema and graft engorgement which can worsen portal HTN.
Early post-operative complications

- Primary graft dysfunction – marked by dramatic (>2x q6hr increase) in ALT/AST/GGT levels, bilirubin and ongoing coagulopathy and bleeding. No change in neurologic status seen even with weaning of sedation due to rising NH3.
Early post-operative complications

- Attempts to extubate should occur if possible at 24-36hr to perform a full neurologic evaluation. The transplant service prefers rocuronium if needed and fentanyl.

- If a benzodiazepine is needed Versed is preferred rather than Ativan which is primarily metabolized by the liver and due to its longer half life can continue to obscure mental status.
Neurologic complications

- Hepatic encephalopathy should resolve within the first 2 days following transplantation.
- If however there is primary graft dysfunction or acute rejection the development of cerebral edema and increased ICP can occur.
- Seizure in transplant patients is usually electrolyte related and due to side effects of immunosuppressive agents. Note that use of Pb or phenytoin can decrease FK levels.
Hepatic Encephalopathy

Cerebral edema secondary to acute hepatic failure
Hepatic Encephalopathy
Pulmonary complications

- Sometimes graft is so large that it becomes difficult to ventilate against the distended, tense abdomen
- Rules for conventional mechanical ventilation and pulmonary toileting still apply
- Bottom line is that early extubation when possible improves neurologic examination and prevents ongoing damage to the pulmonary system from shear forces, volutrauma etc.
Early post-operative complications

- Hepatic Artery Thrombosis – paramount concern in the post operative patient. Transplanted liver dependent on hepatic flow solely as well as the biliary system which will stricture if flow is compromised.
- Avoidance of graft engorgement and delaying platelet transfusion until <20K and bleeding can help prevent this complication.
Early post-operative complications

- Hepatic artery thrombosis is often due to small end to end anastomosis with low flow that leads to clotting.
- However hypercoagulability is also a concern. The transplanted liver makes procoagulant factors 2, 7, 9, 10 initially faster than the anticoagulant protein C & S and antithrombin III. FFP transfusions BID for the first 5 days post transplant can supply these anticoagulant factors and restore the balance.
Early post-operative complications

* Due to the high concern surrounding hepatic artery thrombosis an ultrasound is performed first thing on post operative day #1.

Patent hepatic flow

Absent hepatic flow
Hepatic artery thrombosis

Hepatic infarcts secondary to thrombosis

Hepatic artery thrombosis at the hilum

Collateralization around a hepatic thrombosis
Early postoperative management issues

- Ampicillin and gentamicin are used in the early post op period as prophylaxis and continue until the 3 JP drains are removed.
- Mycelex 10mg troches are dissolved in the mouth to prophylax against oral candidiasis. Fluconazole is avoided if possible due to its metabolism by cytochrome P450 enzymes and subsequent ability to increase FK levels.
Early postoperative management issues

- Hypertension is a post operative issue for several reasons including high steroid dosing, tacrolimus use as well as early relative fluid overload.
- The management sequence usually follows hydralazine (vasodilator) as a first line, followed by B blockade, followed by calcium channel blockade which takes several days to work unless using nicardipine in a continuous infusion.
Early postoperative management issues

- Early immunosuppression consists of the following...
  - Simulect
  - Steroid
  - Tacrolimus (FK506)
Interleukin-2 Receptor antibodies

- Simulect (Basiliximab)
- Mouse/Human chimer monoclonal antibody directed at the alpha chain of IL-2 receptor.
- Dose 2 hours pre-op and post-op day #4 provided IL-2 saturation for 42 days +/-16 days.
- Side effect profile similar to placebo except...
  - Severe hypersensitivity seen in 1^{st} and subsequent doses.
**Maintenance Immunosuppression**

- Steroids
- Broad effects on cell mediated immunity while sparing humoral response.
- Multiple side effects including osteopenia, poor linear growth, hypertension, ulcer disease, glucose intolerance, cataracts, psychosis, polyphagia, weight gain, cushinoid features etc.
Calcineurin Inhibitors

- FK506 – (Tacrolimus, Prograf) product of the fungus Streptomyces tsukubaenis
  - macrolide structure similar to cyclosporine but different binding site.
- Binds to the FK binding protein and inhibits T cell production of IL-2, 3, 4, interferon gamma and inhibits the clonal expansion of Th and Tc cells.
Calcineurin Inhibitors

- Serum level goal of tacrolimus is transplant center dependent and at AIDI is usually in the mid teens.
- Side effects include nephrotoxicity, neurotoxicity, increased infection risk and the 4H’s
  - HTN, Hyperglycemia, Hyperkalemia and Hypomagnesemia
- There is also an increased risk of lymphoproliferative disorder when compared to cyclosporine. However the level of HTN is less and the cosmetic altering effects are also substantially less than cyclosporine.
Calcineurin Inhibition

- Cyclosporine (Sandimmune, Neoral)—peptide of fungal origin that binds cyclophilins and prevents transcription factor movement into the nucleus, therefore blocking IL-2 production, Tcell proliferation and differentiation.

- Side effects are HTN, liver toxicity, gum hyperplasia, hirsuitism, hyperK, infection, and malignancy risk.
Calcineurin Inhibition

- Measurement and stable reference ranges are difficult to achieve in all laboratories and facilities thus affecting the # of programs using cyclosporine.
- Interactions with the cytochrome P450 system makes its metabolism and that of other drugs using this system challenging to predict.
Early postoperative management issues

- Nutrition is usually poor preoperatively and preoperatively had been longstanding. Fat malabsorption in addition to caloric malnutrition is common.
- TPN is usually begun 24 hours after surgery and an attempt at enteral nutrition should begin on post-op day 3, 4, or 5.
Complications seen in the first week after transplant

- Infection – lines, foley catheters, JP drains are all cultured daily and antibiotic prophylaxis is continued until they are removed.
- However 5-6 days post-op is the time at which the patient is at greatest risk of bowel perforation and/or biliary leak.
- These complications are usually marked by fever, increased WBC count, signs of peritonitis and frank JP drainage resembling bile or increased serum bilirubin levels secondary to reabsorption.
Infectious complications

- PCP prophylaxis is needed in the post operative period
- Incidence of viral infections usually increases 1-2 months post transplant.
- CMV #1, EBV, HSV, RSV and Adenovirus also common. Gancyclovir use fairly standard as well as prophylaxis with Cytogam (monoclonal Ab directed against CMV)
- Fungal infections most common in subsequent months and risk increased with the use of broad spectrum antibiotics.
- Note that use of fluconazole can increase FK levels
Complications seen in the first week after transplant

- The other significant complication seen in the 1\textsuperscript{st} week post-op involves massive GI bleeding from the Roux-en-Y site when the healing scab sloughs off.
- This is usually managed with massive transfusion, NPO, but sometimes patient will need to return to the OR for revision.
Sites of potential roux-en-Y bleeding
Late Complications

- Biliary strictures more common in LRLT than cadaveric and is marked by elevations in bilirubin, GGT.
- Diagnosis options include ultrasound and intraoperative cholangiogram. MRI cholangiogram may gain importance in the future.
- Management options include stenting if the stricture is caught early enough, otherwise retransplantation will eventually be needed.
Biliary stricture from hepatic artery thrombosis
Stent insertion opens the right and left tracts
Sludge and debris clogs stents and common bile duct is strictured
Now common bile duct stented as well
Late Complications

- Other late complications include continued HTN with development of concentric hypertrophy in children less than 1yo. Therapy of choice is beta blockade.
- Pseudotumor cerebri is also a possible complication in children <1yo and is typically seen when steroids are rapidly weaned. Situation maybe confused with chronic headaches caused by FK506.
Concentric hypertrophic heart disease