Safety of Transjugular Liver Biopsy in Children with Acute Liver Failure: The Role of Cryoprecipitate, rFVIIa, and FFP

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Introduction: Acute liver failure is the onset of liver dysfunction, encephalopathy, and coagulopathy within 26 weeks of symptom onset in patients without prior liver dysfunction. It is associated with platelet dysfunction, decreased synthesis of clotting factors, accelerated fibrinolysis, DIC, and coagulopathy.


Case Report #1: 14 yo previously healthy F presented with fatigue, pruritus, abdominal pain, and scleral icterus. No recent illness, travel, sick contacts, Tylenol, iron ingestion or URI symptoms. Transjugular liver biopsy on Day 2 under GA with pre-op transfusion of 1 unit of PRBCs and 2 units of FFP for H/H 7.7/23, Coags 2.3/24.1/38.3, fibrinogen 188. Despite atraumatic intubation, pt with frank blood in ETT during case. Upper endoscopy performed by ENT negative. Transfused one unit PRBC then sent to ICU intubated. Pt developed significant GI bleeding and hepatic encephalopathy. CVHV instituted, along with intermittent Profilnine, Novoseven, FFP infusions (50ml/hr), Amikar drip (18mg/kg/hr), cryoprecipitate boluses and vasopressor support. Pt succumbed to her illness on Day 8 while awaiting a liver transplant for biopsy proven autoimmune hepatitis.

Case Report #2: 12yo previously healthy F who presented w/emesis, abdominal pain and scleral icterus. Vitals 36.7, 73, 20, 103/64, 99% on RA. Coags of 2.1/24.1/38.3, bilii 13.7, dbili 6.9, AST 1642, and ALT 1131. Presented to the OR for transjugular liver biopsy. Pre-surgical INR of 2.5 treated with cryoprecipitate and Profilnine. Repeat labs prior to procedure revealed an INR of 4, so liver biopsy was postponed. Patient rapidly worsened overnight, developing encephalopathy and worsening coagulation profile. She was listed for transplant, but suffered cardiac arrest and expired less than 24 hours from presentation. Autopsy was non-diagnostic.

Liver Biopsy: Percutaneous biopsy risks pain, hypotension, subcapsular hematoma, intraportal hemorrhage, pneumothorax, hemobilia, and puncture of visscera. The risk is elevated in patients with coagulopathy, with up to 23% of patients having subcapsular hematomas detectable by ultrasound. Mortality ranges from 0.13-0.33% Transjugular liver biopsy obtains tissue without traversing the liver capsule and confines the bleeding to within the SVC and hepatic veins, which can be beneficial in a coagulopathic patient. The complication rate ranges from 1-20% and the mortality rate is 0.1 to 0.5%.

Management: Spontaneous, significant bleeding only occurs in 5-10% of acute liver failure patients. PT/INR poorly reflect bleeding risk in liver failure patients since levels of anticoagulants like proteins C and S and anti-thrombin are decreased. Despite supporting evidence, liver failure patients are typically given FFP prior to procedures.

FPP: FFP contains all coagulation factors and inhibitors present in circulating blood. 1ml of FFP/kg increases the activity of clotting factor by 1-2% and typically 12-15ml/kg of FFP corrects the PT 20% of the time. The duration of effect is 8-12 hours. Transfusion risks infection, fluid overload, & TRALI.

Cryoprecipitate and rFactor VII: Cryoprecipitate only contains factor VIII, fibrinogen, vWF, and factor XIII. It is not useful in the global coagulation factor deficiency of ALF. Recombinant activated factor VII (rFVIIa) has been considered when FFP failed to correct PT/INR or to avoid volume overload before invasive procedures. rFVIIa (40–90mcg/kg) lasts ~2 hours. Risk of thrombotic complications, especially in higher doses (90 mcg/kg) or after repetitive dosing.

Discussion: What is the optimal approach for such high risk patients? Correction of the coagulopathy of ALF is difficult due to the short half-life of clotting factors and the large volumes required. The risk for volume overload, infection and TRALI are significant. Patients with liver failure are not necessarily at an elevated intra-operative bleeding risk during minor procedures like transjugular liver biopsy. Furthermore, the risk of bleeding cannot be accurately predicted by mild to moderate elevation of coagulation times.

References:

Clinical Significance: Acute liver failure is associated with a mortality rate of 65-85%. Early diagnosis is paramount in predicting prognosis, management, and suitability for liver transplantation. Liver biopsy can rapidly elucidate the cause of failure, hastening treatment. A study found 16.7% of patients had a different diagnosis after liver biopsy and in 20% a new diagnosis.

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