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TOPIC HIGHLIGHT

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Management of portal hypertension in children

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Abstract

Portal hypertension can be caused by a wide variety of conditions. It frequently presents with bleeding from esophageal varices. The approach to acute variceal hemorrhage in children is a stepwise progression from least invasive to most invasive. Management of acute variceal bleeding is straightforward. But data on primary prophylaxis and long term management prevention of recurrent variceal bleeding in children is scarce, therefore prospective multicenter trials are needed to establish best practices.

Key words: Portal hypertension; Variceal hemorrhage; Children

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INTRODUCTION

Normal portal pressure is between 5 and 10 mmHg. Once portal pressure rises to 12 mmHg or greater, complications such as varices and ascites may occur.

The portal system drains the capillaries of the mesenteric and splenic veins and ends in the hepatic capillaries. The portal vein supplies partially oxygenated blood to the liver, supplementing the highly oxygenated blood of the hepatic artery to the liver. Blood flow to the liver is finely tuned; any disturbance of the flow in one of these vessels can be offset to a certain degree by increased flow through the other vessel. This is known as the arterial buffer response. Blood from both the portal venous system and the hepatic arterial systems combine within the sinusoids.

Portal hypertension occurs when there is increased portal resistance and/or increased portal blood flow. Generally, the portal venous system has a low baseline portal pressure of 7-10 mmHg and the hepatic venous pressure gradient (HVPG) ranges from 1 to 4 mmHg. Portal hypertension is defined as a portal pressure greater than 10 mmHg or gradient greater than 4 mmHg. Pressure gradients above 10 mmHg have been associated with esophageal varices formation, and those above 12 mmHg are associated with ascites and variceal bleeding in adults[1]. To measure the portal pressure gradient, a catheter can be wedged into the hepatic vein *via* the femoral or transjugular approach and a wedged hepatic venous pressure (WHVP) measurement obtained. If the catheter is then retracted into a free flowing hepatic vein, a free hepatic venous pressure (FHVP) can be measured. The HVPG is the difference between the WHVP and the FHVP. The cause of portal hypertension can be suggested by the

HVPG value. In pre-sinusoidal obstruction, the HVPG is normal but the WHVP is raised, whereas in cirrhosis both HVPG and WHVP are increased.

HEMODYNAMIC CHANGES

Clinically, portal hypertension causes splenomegaly with resulting hypersplenism and the formation of a collateral circulation. Despite formation of a significant collateral network, portal hypertension persists. This is a result of an increase in cardiac output (result from increased venous return and diminished afterload); and a decrease in splanchnic arteriolar tone (mediated by several factors including glucagon and nitric oxide). Retention of sodium and water *via* a hepato-renal reflex increases the circulating blood volume. There is also production of vasodilatory factors that cause arterial vasodilation of the splanchnic circulation. Increases in the intrahepatic resistance are due to hepatocyte swelling, fibrosis and inflammation within the portal tracts. Clinical studies and animal models have demonstrated the hemodynamic events that occur; however, most of these investigations have not been performed in children or in pediatric models. The hyperdynamic circulatory state has not been well characterized in any cohorts of children.

GASTROINTESTINAL BLEEDING

The clinical presentation of portal hypertension can be dramatic because it may be the first symptom of long-standing silent liver disease. In several large series of children with portal hypertension, approximately two thirds presented with hematemesis or melena, usually from rupture of an esophageal varix[2]. Gastrointestinal hemorrhage also may be associated with bleeding from portal hypertensive gastropathy, gastric antral vascular ectasia, or gastric, duodenal, peristomal, or rectal varices. Variceal hemorrhage is the result of increased pressure within the varix, which leads to changes in the diameter of the varix and increased wall tension. When the wall tension exceeds the variceal wall strength, physical rupture of the varix occurs. The majority of patients reported in the series had splenomegaly at the time of hemorrhage; thus, the combination of gastrointestinal bleeding and splenomegaly suggests portal hypertension until proven otherwise. The sentinel bleeding episode in children may occur in a wide range of ages, starting as early as 2 mo of age[3]. The risk of first-time bleeding from studies in children with cirrhosis is 22%, but rises to 38% in children with known varices over a 5 year period[4]. Bleeding occurs in 15%-25% of patients with biliary atresia in long term follow up[5,6]. The age of bleeding is dependent on the underlying etiology of cirrhosis. Patients who have surgically corrected but progressive biliary atresia bleed for the first time at a mean age of 3 years while children with cirrhosis due to cystic fibrosis bleed at a mean age of 11.5 years[7].

Variceal bleeding in children often follows an acute upper respiratory infection, fever, or aspirin ingestion[8]. The combination of factors including increased abdominal pressure from coughing or sneezing, increased cardiac output from fever, and ulceration from medications such as nonsteroidal antiinflammatory drugs or aspirin contribute to the rupture of varices. Prolonged gastroesophageal reflux can contribute to erosions over the varices that could result in bleeding.

Triger *et al*[9] followed 44 children aged 12 years for a mean follow-up of 8 years. At the time of portal venous obstruction diagnosis, no child had either abnormal liver enzymes or abnormal liver function. The actuarial probability of bleeding was 49% at age 16 years and 76% at 24 years of age. If the child bled before 12 years of age, the probability of bleeding was higher than in those who had not bled before aged 12. Further, there was no evidence of variceal regression over time. Instead, progression of varices occurred in the majority of children suggesting that the previous hypothesis that variceal bleeding decreased in adolescence due to development of spontaneous porto-systemic collaterals was incorrect.

SPLENOMEGALY

Splenomegaly is the second most common finding in children with portal hypertension after gastrointestinal bleeding. In many instances, an enlarged spleen is first discovered on routine physical examination. Many children will admit to a vague fullness in the left upper quadrant for many years prior to the diagnosis. Occasionally, manifestations of hypersplenism including thrombocytopenia, leukopenia, petechiae, or ecchymoses will prompt evaluation, leading to the discovery of portal hypertension. Hematologists should consider a biochemical liver profile and a Doppler ultrasonographic examination in the evaluation of any child with thrombocytopenia, especially if leukopenia is also present. Rarely will associated cytopenias lead to clinically relevant disease. Although splenomegaly is a common finding in patients with portal hypertension, splenic size does not correlate well with portal pressure[10,11]. Hypersplenism rarely requires surgical intervention. Exceptions include symptoms of symptomatic anemia and severe physical discomfort[12].

ABDOMINAL VENOUS PATTERNING

Specific cutaneous vascular patterns are observed with portal hypertension. Prominent vascular markings on the abdomen are the result of porto-collateral shunting through subcutaneous vessels. The direction of flow through these veins may be indicative of the site of obstruction. When the inferior vena cava is occluded, drainage is usually cephalad, but caudad below the umbilicus if the inferior vena cava is patent. Portal hypertension decompression through the umbilical vein results in prominent periumbilical collaterals, referred to as caput medusae. An audible venous hum (Cruveilhier-Baumgarten murmur) may occasionally be heard. Caput

Table 1 Initial manifestation of portal hypertension

Reference	Mitra *et al*[60] (1978)	Pinkerton *et al*[62] (1972)	Spence *et al*[33] (1984)	Howard *et al*[61] (1988)
Patients	70	33	27	152
% Presenting with				
Hemorrhage	80	97	85	46
Splenomegaly	99	24	100	94
Ascites	17	21	8	7

medusae are rare in children, partly because of the high prevalence of portal vein obstruction associated with umbilical vein obliteration. Rectal varices are more common in children[13]. In children with short bowel syndrome, stomal varices which are a site of low resistance, are often present and a common site for hemorrhage[14].

ASCITES

Ascites arises when the hydrostatic and osmotic pressures within the hepatic and mesenteric capillaries result in a net transfer from blood vessels to lymphatics at a rate that overcomes the drainage capacity of the lymphatics. It is the presenting sign of portal hypertension in 7%-21 % of children (Table 1).

In patients with portal hypertension, increased sodium retention and raised portal pressure may cause accumulation of fluid within the abdomen. Impaired lymphatic drainage compounds the situation. Treatment includes salt and fluid restriction and the use of diuretics. Albumin infusions can be used to increase intravascular osmotic pressure, followed by diuretic dosing to facilitate urination. Paracentesis has been used safely in children and is reserved for use when the ascites is difficult to control resulting in respiratory compromise or if peritonitis is suspected for cell count and culture[15,16].

PULMONARY COMPLICATIONS

Hepatopulmonary syndrome (HPS) and portopulmonary hypertension are undoubtedly underdiagnosed in children. Barbé *et al*[17] reported on the presence of HPS in 29 pediatric patients of which 26 had cirrhosis and 3 had an extrahepatic cause of portal hypertension. HPS progresses more rapidly in patients with biliary atresia associated with polysplenia[18]. Patients with HPS have a higher incidence of dyspnea, cyanosis, clubbing and spider nevi[19-21]. There are two forms of HPS. In type I , the vessels enlarge such that the red blood cells traveling through the center of the vessel do not have significant contact time with the oxygen-rich alveoli. In type Ⅱ HPS, the diffusion-perfusion mismatch is presumed to be due to arteriovenous communications completely bypassing alveoli[22,23]. HPS is thought to occur as a result of shunting of vasodilatory mediators from the mesentery away from the liver in portal hypertension. Liver transplantation reverses HPS in greater than 80% of patients. If large shunts are present and the arterial partial pressure of oxygen is less than 50 mmHg on 100% oxygen, a poorer outcome may be expected.

Portopulmonary syndrome eventually leads to right-sided heart failure. Histologically there is pulmonary arteriopathy with concentric laminar intimal fibrosis consistent with a vasoconstrictive etiology. Pediatric cases have been reported[24,25]. The condition is defined by a pulmonary arterial pressure greater than 25 mmHg at rest and above 30 mmHg with exercise, raised pulmonary vascular resistance with pulmonary arterial occlusion pressure, or a left-ventricular end-diastolic pressure of less than 15 mmHg[26]. The most common symptom of pulmonary hypertension is exertional dyspnea. Other symptoms include fatigue, palpitations, and syncope or chest pains.

THERAPY

Therapy of portal hypertension is primarily directed at the management of its most dramatic manifestation, variceal hemorrhage. Variceal bleeding is a life threatening medical emergency, and patients with chronic liver disease should be instructed to seek immediate medical attention for any signs or symptoms of bleeding. The management can be divided into preprimary prophylaxis, prophylaxis (primary) of the first episode of bleeding, emergency therapy, and prophylaxis (secondary) of subsequent bleeding episodes. As with many other aspects of portal hypertension, almost all the modes of therapy are based on adult trials (Figure 1). Many of the trials are well-controlled randomized double-blinded studies, and comprehensive meta-analysis of these trials have been performed[27-30]. The literature on the management of variceal hemorrhage in children is predominantly descriptive and anecdotal. There have been few randomized trials of therapy for portal hypertension in children[31,32].

Preprimary prophylaxis

The concept is that early treatment of portal hypertension has the potential to delay or prevent the development of esophageal varices or other manifestations of portal hypertension. In a *S. mansoni* mouse model of portal hypertension, the administration of propranolol 5 wk into the infection resulted in a significant reduction in the development of portal hypertension, portosystemic shunting, and portal venous inflow[34]. A randomized controlled trial of timolol, a non-selective beta blocker, on the development of varices in adults did not show a significant benefit[35]. Currently, preprimary prophylaxis remains an interesting concept that is not applicable in clinical practice.

Primary prophylaxis

The issue of prophylaxis of the first episode of variceal bleeding in children is controversial and is predicated on experience with adults who primarily have alcoholic cirrhosis. Surveillance endoscopy in children with liver disease and stigmata of portal hypertension is justified if the clinician anticipates recommending a prophylactic

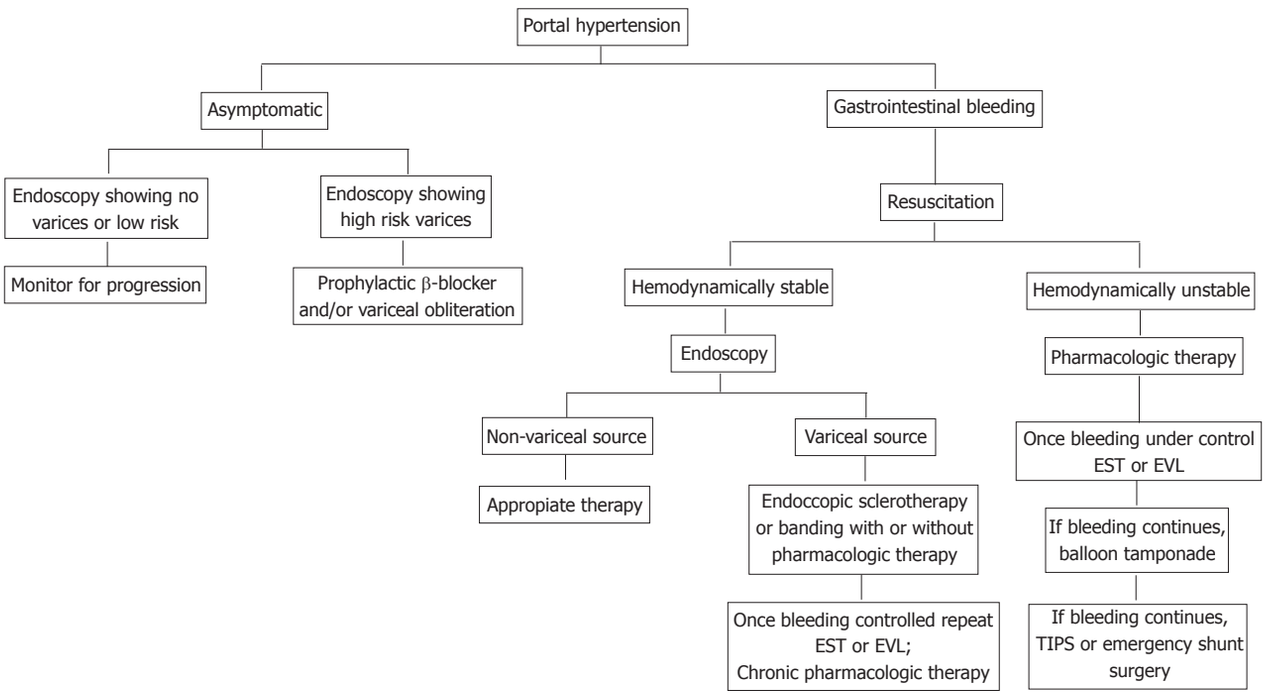

Figure 1 Portal hypertension. EST: Endoscopic sclerotherapy; EVL: Endoscopic variceal band ligation; TIPS: Transjugular intrahepatic portosystemic shunt.

regimen. Prophylaxis may also be valuable in patients who live in remote areas far from emergency medical care. Given the unpredictable timing of the first episode of variceal bleeding, primary prophylaxis regimens need to be associated with relatively low morbidity and mortality. As such, beta blockade has been more extensively used in this setting. The improved risk-benefit ratio of endoscopic ligation therapy relative to sclerotherapy has led to reassessment of its role in primary prophylaxis[36,37]. Uncontrolled preliminary pediatric experience of variceal hemorrhage using beta blockade has recently been reported[38-40]. Beta blocker use in children has reduced the frequency of bleeding episodes, and in some trials has improved long-term survival in patients with esophageal varices. Initial randomized trials demonstrated efficacy in patients who had a previous bleeding episode[41]. Subsequently, propranolol was shown to be effective in patients with varices who had never bled. In a study of 230 subjects randomized to propranolol or placebo, the incidence of bleeding and mortality over a 14 mo period was reduced by almost 50%[42]. Several meta-analyses have demonstrated the success of propranolol[43-50]. It is clear that a goal of at least 25% reduction in resting heart rate needs to be achieved to realize these effects. In patients in whom HVPG drops below 12 mmHg, subsequent variceal bleeding is unlikely. Achieving such a large reduction in resting heart rate and achieving a HVPG below 12 mmHg may be problematic in children in whom baseline measurements may be difficult. A wide range of dosing (0.6-0.8 mg/kg per day) divided into two to four doses of propranolol has been required in children in order to observe a "therapeutic effect".

Unfortunately, propranolol often does not reduce HVPG below 12 mmHg, therefore a combination of beta blockade and vasodilatation therapies are now under investigation. Isosorbide-5-mononitrate, a long-acting vasodilator, may potentiate the effects of propranolol on the HVPG[51]. Combination pharmacologic agents, such as carvedilol, may have enhanced efficacy[52]. Unfortunately, there is little if any prospective data in children on the safety and effectiveness of beta blockade with or without vasodilators in patients with portal hypertension.

Endoscopic band ligation therapy has been used with greater frequency in adults with high risk varices[53,54]. As with beta blockade, endoscopic band ligation therapy cannot be recommended for routine use in children with varices. In fact, a small randomized trial of prophylactic endoscopic sclerotherapy in children showed no survival benefit[55].

Emergency therapy of variceal bleeding

The initial management of variceal bleeding is stabilization of the patient. Vital signs, particularly tachycardia or hypotension, can be especially helpful in assessing blood loss. Patients on beta blocker therapy may not manifest the usual compensatory tachycardia and are at higher risk of developing significant hypotension. Fluid resuscitation in the form of crystalloid initially, followed by red blood cell transfusion, is critical. One needs to administer these carefully to avoid overfilling the intravascular space and increasing portal pressure. Optimal hemoglobin levels in adults with variceal hemorrhage are between 7 and 9 g/dL[56]. Nasogastric tube placement is safe and may be an essential part of the management of these patients. It allows documentation of the rate of ongoing bleeding and removal of blood, a protein source that

may precipitate encephalopathy. In addition, blood in the stomach increases splanchnic blood flow and could aggravate portal hypertension and ongoing bleeding. Platelets should be administered for levels less than 50×10^9/L, and coagulopathy corrected with vitamin K and fresh frozen plasma. There may be a value to the use of recombinant factor VIIa in severe coagulopathy as the fluid requirements may be diminished[57]. Intravenous antibiotic therapy should be considered for all patients with variceal bleeding in light of the high risk of potentially fatal infectious complications[58,59]. Once the patient is stabilized, endoscopy should be performed to document that hemorrhage is indeed from variceal rupture. Continued bleeding at the time of endoscopy is a finding that portends poor prognosis. A significant percentage of both adults and children with chronic liver disease will have a source of bleeding other that varices, including duodenal or gastric ulceration[58]. Pharmacotherapy of acute hemorrhage should not be withheld until endoscopy can be performed. In fact, it may facilitate the procedure. At the time of initial endoscopy, management can begin in the form of sclerotherapy or band ligation. Bleeding that lasts more than 6 h or requires more than one red blood cell transfusion necessitates further investigation. A wide variety of therapeutic options exist in adults. Documentation of their efficacy in adults is fairly convincing, but data in children is scarce

Pharmacology

The pharmacologic therapy of variceal bleeding usually consists of vasopressin or somatostatin (or their analogs) infusions. Vasopressin has the longest history of usage and acts by increasing splanchnic vascular tone and thus decreasing portal blood flow. Its use is often limited by the side effects of vasoconstriction, which include left ventricular failure,, bowel ischemia, angina, and chest/abdominal pain[53]. In a study of 215 children with acute variceal hemorrhage, 184 had bleeding arrested by the combined use of fluid support and vasopressin. Vasopressin has a half-life of 30 min and is usually given as a bolus followed by continuous infusion. The recommended dose for children is 0.33 U/kg as a bolus over 20 min, followed by an infusion of 0.2 U/1.73 m^2 per minute (may be increased up to 3 times the initial rate). These recommendations are empiric, based on clinical practice, and derived from extrapolation of adult dosages. Terlipressin, a long-acting synthetic analogue of vasopressin, has shown similar effects and does not require continuous infusion[57]. Side effects appear to be reduced compared to vasopressin, but prospective data in children are lacking.

Alternatives to vasopressin have been investigated because of its poor side effect profile. Somatostatin and its synthetic homologue octreotide also have been shown to decrease splanchnic blood flow. Their effects on acute variceal hemorrhage appear to be similar to those of vasopressin, with fewer side effects[58,59]. Continuous infusion of 1-5 μg/kg per hour of octreotide appears to be effective but may need to be initiated by the administration of a bolus. New longer-acting somatostatin analogues are currently under investigation[59].

Endoscopy

Approximately 15% of children will have persistent hemorrhage despite conservative management plus some form of splanchnic vasoconstriction. The most common secondary approach is endoscopic sclerotherapy or endoscopic band ligation. Endoscopic therapy is very effective in controlling bleeding, although it may be technically challenging. An extensive experience with emergency sclerotherapy exists in children, and it's rare for additional therapy to be required. A variety of agents have been used (sclerosants, chemically irritating compounds such as ethanolamine/tetradecyl sulfate). These sclerosants are injected either intra-or para-variceal, until bleeding has stopped. In the setting of emergency sclerotherapy it is important to be aware of the significant incidence of associated bacteremia and to consider antibiotic prophylaxis in most patients.

Endoscopic band ligation of varices may be a preferable approach because it is easier and safer. A randomized trial of band ligation versus sclerotherapy in adults demonstrated similar control of active bleeding and recurrence of hemorrhage with significantly lower overall complications and mortality). A potential concern of this technique in children (whose esophageal wall is thinner than adults), is entrapment of the full thickness of the esophageal wall by the rubber band with subsequent ischemic necrosis and perforation.

Mechanical

The Sengstaken-Blackmore tube (SSBT) was designed to stop hemorrhage by mechanically compressing esophageal and gastric varices. The device consists of a rubber tube with at least two balloons. It is passed into the stomach, where the first balloon is inflated and pulled up snug against the gastroesophageal junction. Once the tube is secured in place, the second balloon is inflated in the esophagus at a pressure (60-70 mmHg) that compresses the varices without necrosing the esophagus. A channel in the rubber tube allows gastric contents to be sampled for evidence of bleeding. This therapy is very effective in controlling acute bleeding. Unfortunately, it is associated with significant number of complications and high incidence of re-bleeding when the tube is removed. Most patients find the treatment uncomfortable, and its use in children requires significant sedation. Use of the SSBT increases the risk of aspiration pneumonia, which can be a life threatening complication in a patient with liver failure. Re-bleeding has been reported in 33%-60% of patients. Given these problems it is reserved for severe uncontrollable hemorrhage and generally serves as a temporizing measure until a more definite procedure can be performed.

Surgical and interventional radiology

Surgical therapy is usually a last resort approach to acute

Table 2 Major complications of endoscopic sclerotherapy in children[61] (%)

Bleeding before treatment	39
Esophageal ulceration	29
Stricture formation	16
Recurrent varices	8

variceal hemorrhage. The reluctance to perform emergency surgery partly stems from its associated high mortality but also from concerns of an increased incidence of encephalopathy and greater difficulty for subsequent liver transplantation. The surgical procedures available can be divided into transection, devascularization, and portosystemic shunting. The first two techniques are rarely used and work by interrupting blood flow through the esophagus. Liver transplantation may be an effective means of treating esophageal variceal bleeding if an acceptable organ can be procured quickly enough. Variceal embolization *via* a percutaneous transhepatic or transsplenic approach has been advocated by some hepatologists as another method of controlling acute hemorrhage. Transjugular intrahepatic portosystemic shunt (TIPS) placement may be the optimal approach for intractable bleeding since it does not require surgery or puncture of an organ that is predisposed to hemorrhage. A catheter is inserted into the jugular vein and is advanced into the hepatic vein where a needle is used to form a tract between the portal vein and the hepatic vein. This tract is expanded with a balloon angioplasty catheter, and a stent is then placed forming a permanent portosystemic shunt. The experience in children is limited. Size limitations and local expertise may be limiting factors in some cases, but given the high risk associated with emergency surgery or the use of SSBT, TIPS may be the treatment of choice in the emergent setting, especially when liver transplantation is imminent.

Secondary prophylaxis: The long term management of portal hypertension in children with a previous episode of variceal bleeding is complex. One must take into consideration several factors; first the natural history; as discussed earlier, there are significant differences in the setting of minimal and inactive versus active and progressive hepatic disease. As a result, certain individuals may have the possibility of outgrowing their portal hypertension through the development of spontaneous portosystemic shunts, whereas other might be expected to develop end-stage liver disease and ultimately be candidates for liver transplantation. The second issue stems from the great diversity in therapeutic modalities. The physiologic goal of pharmacologic therapy varies from program to program (i.e, change in heart rate, hepatic portal venous gradient pressures, *etc*). Sclerotherapy may be administered with a wide variety of agents and by two different techniques (i.e, intra or para variceal). Endoscopic band ligation offers an important and generally safer alternative. Finally, at least six different portosystemic shunting procedures have been described, all with their own advantages and disadvantages.

Sclerotherapy and ligation therapy: Sclerotherapy and band ligation therapy work by physical obliteration of esophageal varices. Bleeding may occur during the several weeks required to complete the obliteration. Most importantly the principal problem of portal hypertension is not addressed. Despite these problems, endoscopic therapy has been a mainstay of the treatment of esophageal varices, and there is significant amount of clinical experience with these therapies in children.

The effectiveness of sclerotherapy has been studied for both prevention of initial and subsequent bleeding episodes. Scleroptherapy, which has in general been supplanted by band ligation, with the exception of very young or small children in which band ligation may not be feasible. Intravariceal, paravariceal, and some combination injection protocols have been used. A wide variety of sclerosing agents have been used without a clear cut difference in their efficacy or adverse side effects. A meta analysis of seven studies and 748 patients revealed mortality rates of 47% in the sclerotherapy group and 61% in the conservatively managed group. A variety of complications have been reported (Table 2).

Retrosternal pain, bacteremia, and fever post treatment are common. Esophageal ulceration may occur after sclerotherapy, and the associated symptoms may be ameliorated with sucralfate slurry therapy.

The range of complications associated with sclerotherapy has prompted the development of alternative endoscopic methods such as band ligation. This technique involves suctioning of a varix into the end of an endoscope so that a rubber band can be placed around the varix leading to thrombosis. Direct comparisons of endoscopic sclerotherapy and variceal ligation in adult patients have yielded results in favor of ligation. Similar results have been reported in children by Zargar *et al*. The major advantage of variceal ligation is avoidance of needle injection of varices, which appears to reduce the rate of complications. In addition, variceal ligation appears to lead to obliteration in fewer sessions and is associated with lower rate of rebleeding.

Portosystemic Shunting: A variety of procedures have been used to divert portal blood flow and decrease portal blood pressure: (1) Mesocaval Shunts: formed with the insertion of a graft between the superior mesenteric vein and the inferior vena cava; (2) Portacaval Shunts: formed by side-to-side anastomosis of the portal vein and the inferior vena cava; and (3) Distal Splenorenal Shunt: formed by end-to-side anastomosis of the splenic vein and the left renal vein.

The portacaval shunt diverts nearly all the portal blood flow into the subhepatic inferior vena cava. This is very effective decompressing the portal system, but also diverts a significant amount of blood from its normal hepatic metabolism, predisposing to the development

Table 3 Results of portosystemic shunting in children[63,64]

Type of portal hypertension	No. of patients	Rebleeding	Mortality
Extrahepatic	292	45%	5%
Intrahepatic	76	50%	53%

of hepatic encephalopathy. Decreased hepatic blood flow theoretically also may lead to worsening of underlying liver disease. An intermediate shunt can be made by placing a graft between the mesenteric or portal vein and the vena cava. This decompresses the portal system while allowing a greater amount of portal blood flow into the liver. The use of grafts unfortunately is associated with increased risk of thrombosis and many times with worsening retrograde flow.

Another approach involves diversion of splenic blood flow into the left renal vein, which can be done nonselectively (central) or semiselectively (distal splenorenal shunt).

A substantial pediatric experience with surgical portosystemic shunting has been accumulated over the past 20 years. The results are clearly different in patients with extra-or intrahepatic portal hypertension (Table 3).

An alternative shunting procedure for children with extrahepatic portal vein thrombosis is the meso-Rex bypass, this procedure involves the placement of an autologous venous graft from the mesenteric vasculature to the left intrahepatic portal vein. One of the major advantages of this approach is the restoration of normal portal blood flow, which eliminates the risk of hepatic encephalopathy and should preserve hepatic function. The selection of patients for this procedure is not clear both from a clinical indication and surgical feasibility, and some have advocated that this procedure be considered in all children with portal vein thrombosis. Standard diagnostic imaging may not clearly indicate whether there is patency of the intrahepatic portal vein, and the potential in this group of children for hypercoagulable states must be kept in mind.

In stark contrast to the excellent results in portal vein thrombosis, there are generally poor results of portosystemic shunts in children with decompensated liver disease. The incidence of recurrent bleeding and death approaches 50%. Hepatic encephalopathy is a frequent and serious complication of portosystemic shunting in decompensated liver disease, and studies have failed to show improvement in long-term survival in patients with intrahepatic disease.

Overall, surgical portosystemic shunting is an excellent approach to the long-term management of children with intractable variceal bleeding in the setting of compensated cirrhosis. In addition, significant gastric variceal hemorrhage in children may be an indication to consider surgical shunting. TIPS may be an alternative shunting procedure for children with refractory bleeding and serves as an effective bridge to transplantation. The procedure is typically feasible, with published success in children as small as 14 kg, although special procedural modifications must be undertaken in small children. Long term shunt occlusions limit the overall application of this efficacious therapy, although newer data with coated stents may improve long-term patency rates for TIPS.

CONCLUSION

The approach to acute variceal hemorrhage in children is a stepwise progression from least invasive to most invasive. Surveillance endoscopy is predicated on the availability of an efficacious primary prophylactic therapy. Beta-blocker therapy is accepted primary prophylactic therapy in adults, and endoscopic ligation therapy is also gaining acceptance. Preliminary data in children appear to indicate that this approach is feasible, but further studies are needed before a wide-spread recommendation for children can be endorsed. Therefore, surveillance endoscopy and primary prophylaxis are not generally be indicated in children with portal hypertension who have not had a variceal bleed. Special medical and or social circumstances in which an initial bleeding episode may be particularly dangerous could justify this approach.

Management of acute variceal bleeding is more straightforward. Initial interventions should include stabilization of the patient, placement of a nasogastric tube, and institution of antibiotic therapy. Diagnostic and/or therapeutic endoscopy should be scheduled as soon as it is safe and feasible. In the interim, pharmacologic treatment with either a vasodilator or octreotide is indicated and may facilitate endoscopic therapy. Intractable and severe hemorrhage should be treated by TIPS.

The long term approach to prevention of recurrent variceal bleeding in children must be adapted for the etiology of portal hypertension, the needs of the specific patient, and the particular skills of the institution. The approach to extrahepatic portal vein obstruction is evolving. In general, the unpredictability of the timing of the sentinel bleeding episode and the low incidence of mortality associated with that episode make prophylactic therapy inadvisable. Enthusiasm for the utilization of the meso-Rex shunt is increasing because of the physiologic nature of the procedure, and should be considered for children with extrahepatic portal vein thrombosis and cavernous transformation and a normal liver. The long term management of portal hypertension in the child with biliary atresia is more complex. In patients with incomplete bile drainage, liver transplantation appears to be inevitable and should be the major focus of therapeutic intervention. Temporizing measures for these children may include band ligation therapy and TIPS. Biliary atresia patients who have a more successful response to Kasai portoenterostomy, have a more favorable long term outlook. Variceal hemorrhage may be followed by a relatively long term survival with medical intervention. Recurrent bleeding might be amenable to portosystemic shunting as opposed to transplantation.

The approach to patients with more slowly progressive intrahepatic disease is more difficult to generalize.

Well-conceived multicenter trials are required to determine whether the principals that have been developed in adults can be extrapolated to children.

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