ESOPHAGEAL VARICES

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A 57-year-old man with HBV-induced cirrhosis, was admitted for a chief complaint of hematemesis. (92/8/5)
He has a history of 2 times ESOPHAGEAL VARICES bleeding and EVL.

**Drug history:**
Tab Propranolol : 20 mg TDS
Tab Pantoprazole 20 mg QD
Management of variceal bleeding:
Introduction:

✓ Approximately half of patients with cirrhosis have esophageal varices, and one-third of all patients with varices will develop variceal hemorrhage.

✓ New varices develop at a rate of 5% to 10% per year in cirrhotic patients. Once varices develop, they enlarge by 4% to 10% each year.

✓ A major cause of morbidity and mortality in patients with cirrhosis.
Increase in resistance to flow within the liver is in part due to intrahepatic vasoconstriction secondary to impaired nitric oxide production within the liver.

About 30 percent of the intrahepatic resistance may be reversible and is not due to fixed changes in the vasculature.
Revising consensus in portal hypertension: Report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension

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AASLD PRACTICE GUIDELINES

Prevention and Management of Gastroesophageal Varices and Variceal Hemorrhage in Cirrhosis

Guadalupe Garcia-Tsao,1 Arun J. Sanyal,2 Norman D. Grace,3 William Carey,4 and the Practice Guidelines Committee of the American Association for the Study of Liver Diseases, the Practice Parameters Committee of the American College of Gastroenterology
Treatment:
Introduction:

There are four major issues related to the prevention and treatment of variceal hemorrhage:

1- Prediction of patients at risk.
2- Prophylaxis against a first bleeding.
3- Treatment of an active bleeding.
4- Prevention of rebleeding.
**Definition:**

**Time zero:** the time of admission to a medical care facility.

**Clinically significant bleeding:**
  Transfusion requirement of two units of blood or more within 24 hours of time zero together with:
  - a systolic BP $< 100$ mmHg.
  - a postural systolic change of more than 20 mmHg.
  and/or a pulse rate above 100 beats/min at time zero.

**Acute bleeding episode:** represents the events in the interval of 120 hours (5 days) from time zero. Bleeding during this time is considered to represent failure of therapy.
Failure of therapy:

is defined by any of the following criteria:

1) Fresh hematemesis or >100 mL of blood in the nasogastric aspirate more than two hours after the start of a specific drug or endoscopic treatment.

2) Development of hypovolemic shock.

3) Drop in hemoglobin of ≥3 gm within a 24 hour period.

✔ Early rebleeding: Any bleeding occurring after initial hemostasis and more than 120 hours from time zero but less than six weeks is considered to represent early rebleeding.
GENERAL PRINCIPLES OF MANAGEMENT:

✓ 3 primary goals of management during the active bleeding episode:

1) hemodynamic resuscitation.
2) prevention and treatment of complications.
3) treatment of bleeding.
**Hemodynamic resuscitation:**

- **Restoration of the intravascular volume** should be aggressively managed with large bore peripheral intravenous lines or a central line.

- **Blood loss** should be replaced by packed cells and clotting factors should be replaced as needed.

- **Platelet counts** often drop within the first 48 hours after a bleed and may necessitate platelet transfusions if values below 50,000/mm$^3$ occur in an actively bleeding patient.

- **In extreme settings**, correction of the coagulopathy is necessary but cannot be adequately with FFP, particularly in patients who are severely volume overloaded.
Coagulopathy in severely volume overloaded → FFPs inadequate.

At least 2 RCTs – no clear benefit of recombinant factor VII.

Awaits further clarification.
<table>
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<tr>
<th>Therapy</th>
<th>Therapy Mechanism</th>
<th>Side Effects and Risks</th>
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<tr>
<td>Octreotide</td>
<td>Selective and potent vasoconstrictor that reduces portal and collateral blood flow by constricting splanchnic vessels.</td>
<td>Diarrhea, hyperglycemia, hypoglycemia, constipation, rectal spasms, abnormal stools, headache, dizziness, fat malabsorption</td>
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<tr>
<td>Vasopressin</td>
<td>Nonspecific vasoconstrictor of all parts of the vascular bed.</td>
<td>Abdominal cramping, nausea, tremor, skin blanching, phlebitis, hematoma at the site of the infusion, worsening of hypertension, angina, arrhythmias, myocardial infarction, bowel necrosis, gangrene, dilutional hyponatremia</td>
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<tr>
<td>Endoscopic band ligation (EBL) or endoscopic variceal ligation (EVL)</td>
<td>An elastic band is placed around the mucosa and submucosa of the esophageal area</td>
<td>Moderate bleeding, hypotension, gastrointestinal discomfort, esophageal ulceration, perforation</td>
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Terilpressin

- Synthetic analog of vasopressin.
- Effectively controls acute bleeding from esophageal varices in 80% of patients.
- Fewer cardiovascular side effects have been associated with terlipressin than with vasopressin.
- Terlipressin is the only medication for the acute treatment of variceal hemorrhage that has been shown to improve patient survival.
Sengstaken tube
The principal complications that cause death:

1) Aspiration pneumonia
2) Sepsis
3) acute-on-chronic liver failure
4) hepatic encephalopathy
5) renal failure
Aspiration:

- Massive bleeding – Endotracheal intubation to protect airway → use unclear

- NG tube – unclear
  - Can decompress stomach for subsequent endoscopy
Sepsis:

• Bacterial infections – 20% of cirrhotics hospitalized with GI bleed

• Additional 50% develop infection in hospital

• Most common
  • UTI (12 – 29%)
  • SBP (7 – 23%)
  • respiratory (6 – 10%)
  • primary bacteraemia (4 – 11%)
Antibiotics :

- overall ↓ in infectious complications
- possibly ↓ mortality
- ↓ risk of recurrent bleeding

- IV Ciprofloxacin x 7 days or Oral Norfloxacin (400mg bd)
- Advanced cirrhosis, IV Ceftriaxone (1G od)
Hepatic encephalopathy:

- aggressive search for potentially reversible factors
  - GI bleed
  - hypokalemia
  - metabolic alkalosis
- Lactulose or L-Ornithine
Renal failure:

- acute tubular necrosis or hepatorenal syndrome

- minimized by
  - appropriate volume replacement
  - avoid aminoglycosides
  - avoid mismatched transfusions
BP: 110/70  
BUN: 30
AST: 30  
WBC: 38000
ALT: 24  
Hb: 7
ALP: 176
Bili T/D: 1.2/0.3
CRP: 2
Amylase: 24
INR: 1.5
PTT: 23
Cr: 1.2

Amp Pantoprazole initial IV bolus 80 mg followed by a continuous IV infusion of 8 mg/hour
Amp Octreotide 100 µg IV TDS
Serum 1/3 2/3 1000 ml IV
AST: 26  BUN: 27
ALT: 19  WBC: 23000
ALP: 141  Hb: 6.9
Bili T/D: 1.1 / 0.3
CRP: 1
Amylase: 19
INR: 1.6
PTT: 27

1) Amp Octreotide 50 µg/hr infusion
2) AMP Pantoprazole 8mg/h infusion
3) Tab Domperidone 10 mg PO TDS
4) AMP Ceftriaxone 1g QD IV
5) Transfusion of 1 unit Packed cell.
1) AMP Pantoprazole  DC
2) Tab  Pantoprazole 20mg  BD

1) Amp  Octreotide  DC

1) AMP Ceftriaxone  DC
2) Tab  Ciprofloxacin 500mg  BD

92/8/7
92/8/8
92/8/10
Prophylaxis
PRE-PRIMARY PROPHYLAXIS:

✓ Aims to prevent the development of varices in patients with portal hypertension who have not yet developed varices.

✓ Treatment of the **underlying liver disease** may help to prevent variceal development.

✓ Treatment with **nonselective beta blockers** is not recommended because studies have failed to show a benefit.
✓ prevention of a first variceal hemorrhage in a patient with varices.

⚠️ Approaches:

1) Pharmacologic prophylaxis using a nonselective beta blocker.

2) Endoscopic prophylaxis using endoscopic variceal ligation (EVL).
Both beta blockers and EVL are superior to no treatment for the prevention of a first variceal hemorrhage.

- **nonselective beta blocker:**
  - low risk of serious side effects.
  - decrease the risk of developing ascites or SBP, by ↓ portal pressure and ↓ bacterial translocation.

- **EVL:**
  - Risk of variceal hemorrhage may be lower with EVL compared with βB.
  - there is no benefit with regard to mortality, and EVL puts patients at risk for procedure-related complications.
Patients with small varices:

- **With red signs and/or Child B or C cirrhosis:**
  - Treatment with a nonselective $\beta$B rather than EVL (Grade 2C).
  - Data are lacking regarding the use of EVL for primary prophylaxis in patients with small varices. However, treatment with variceal ligation is a reasonable alternative when:
    1) The patient does not tolerate/has a contraindication to therapy with a beta blocker.
    2) in patients with refractory ascites.
    3) if there is variceal enlargement despite treatment with a beta blocker.

- **without red signs / or Child A cirrhosis:**
  - routine upper endoscopy to monitor for the development of red signs or for variceal enlargement (Grade 2C).
Patients with medium varices:

✓ Treatment with either a nonselective beta blocker or EVL (Grade 2B).

✓ Both treatments have been shown to be effective. The choice depends upon whether:

1) the patient can tolerate a nonselective beta blocker.
2) the patient is willing to accept the risks of EVL and undergo the multiple endoscopic procedures.
3) A provider with expertise in EVL is available.
Treatment with **EVL** rather than a nonselective βB (**Grade 2C**).

Some data suggest EVL may be more effective than beta blockers in patients with large varices.

Treatment with a nonselective βB is a reasonable alternative when:

1) patients are unwilling to accept the risks of EVL or undergo multiple endoscopic procedures for treatment.
2) if a provider experienced in EVL is not available.
The hemodynamic goal:

1) ↓HVPG by 20% or to ≤12 mmHg.

2) If the HVPG is not being used → the dose of the βB may instead be titrated to achieve a resting HR of about 55 to 60 beats/minute.

Monitoring for side effects: especially those with decompensated cirrhosis (Child B or C).

βB may need to be stopped if:

1) Refractory ascites to treatment.
2) Worsening hepatic encephalopathy.
1) **Nitrates** (either alone or in combination with beta blockers).
2) **Surgical shunts.**
3) **Endoscopic sclerotherapy.**

✓ Performing EVL in patients already receiving nonselective βB does not appear to improve outcomes.
Carvedilol leads to a significantly greater decrease in HVPG than propranolol. Using carvedilol for primary prophylaxis a substantial proportion of non-responders to propranolol can achieve a haemodynamic response, which is associated with improved outcome with regard to prevention of variceal bleeding, hepatic decompensation and death.
Results indicate that simvastatin has a **clear potential for the treatment of portal hypertension in patients with cirrhosis**, and prompts new studies in larger patient populations with clinical end points.
It was shown that in patients with cirrhosis and portal HTN, simvastatin administration increases the hepatosplanchnic output of NOx and decreases hepatic resistance, without deleterious effects on systemic circulation.
In summary, unlike propranolol, long-term losartan administration does not significantly reduce HVPG in cirrhotic patients treated after a variceal bleeding episode. In addition, losartan causes arterial hypotension and reduces the GFR in patients with moderate liver failure. Therefore, losartan should not be used as an alternative to propranolol in preventing variceal rebleeding.
In conclusion, this randomized, placebo-controlled, double-blind study shows that irbesartan in a dosage of 150 mg/d only moderately reduces HVPG, but induces marked arterial hypotension and renal impairment in patients with advanced cirrhosis with a highly activated renin-angiotensin-aldosterone system. Thus, our data indicate that angiotensin II receptor antagonists should not be used in these patients.
Prevention of rebleed (Secondary Prophylaxis)

- 70% risk within 1 yr of bleed
- 70% of all untreated patients die within 1 yr of initial bleed

**Options**

- endoscopic sclero / band ligation
- beta blockers and/or oral nitrates
- TIPS (Child A or B)
- Surgery (Child A)
Prevention of rebleed (Secondary Prophylaxis)

• **Beta blockers plus band ligation** — Combination therapy, better at preventing rebleed

• **TIPS** — lesser rebleed, more expensive, more encephalopathy, same survival

• **Surgery** — distal splenorenal shunt, better bleeding control but less survival, sclerotherapy better
Orthotopic Liver transplantation

- only treatment which corrects portal hypertension and liver failure

- long wait for an organ

- Survival → 80 to 90% at 1 yr to
  → 60% at 5 yrs
Thank you