Care of the Hospitalized Patient with Advanced Liver Disease

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Associate Professor of Internal Medicine and Pediatrics
I have no conflict of interest to disclose
Objectives

• By the end of this session participants will:
  – Recognize the HIGH risk of mortality in these patients
  – Remember at least 3 tips for managing the common complications of cirrhosis encountered by hospitalists
  – Consider early referral for transplant evaluation in patients with decompensated cirrhosis
Clinical Case

- 56 yr old male with a history of Hepatitis C presents with confusion and dyspnea and is admitted to the Hospital Medicine Service. Family reports he’s “just not himself” but has left by the time he arrives on the floor.

- Medications: lactulose, omeprazole, furosemide, spironolactone, simvastatin
Physical Exam

• Vitals: T 99.6, BP 87/45, HR 98, RR 20, O2 sats 91% on RA
• Jaundiced, confused, somnolent but responds to loud or noxious stimuli
• OP with poor dentition, dry mucous membranes; scleral icterus
• No adenopathy
• Cor RRR, NI S1, S2, 2/6 SEM without radiation
• Lungs clear anteriorly, dullness to percussion half way up on right
• No obvious trauma, Moves all extremities but has asterixis
• Abdomen distended with bulging flanks, fluid wave present, no rebound or guarding, caput medusae
• Extremities with 3+ pitting edema bilaterally, palmar erythema
• Skin with some petechia where BP cuff compresses arm and spider angiomata on chest
Labs / Images

- BMP remarkable for Na 126, HCO3 18 with anion gap of 6, Cr 2.2 (0.9)
- CBC remarkable for Hgb 9 (11.8), WBC 12, Plts 64k
- ALT/AST normal, Alk Phos nl, T. Bili 9
- INR 2.4
- NH3 64
- UA- SG 1.031, LE/nitrite/protein -, 1 WBC, 1 RBC
- CXR- Right pleural effusion, no other acute cardiopulmonary pathology
- Abdominal U/S- large ascites with thickened and distended gallbladder, shrunken nodular liver c/w cirrhosis, reversal of flow in portal vein with collateralization.
Pathophysiology of Cirrhosis

Progression of fibrosis

Normal → Inflamed → Fibrotic → Cirrhotic

Healing → Repetitive injury

Adapted from Hepatitis C Education Society: http://hepcbc.ca/stages-of-liver-disease/
The splanchnic circulation. (Redrawn with permission from Gelman S, Mushlin PS: Catecholamine induced changes in the splanchnic circulation affecting systemic hemodynamics. Anesthesiology 100:434–439, 2004.)

**Complications of Portal HTN**

- Variceal Bleeding
- Jaundice
- Hepatic Encephalopathy
- Ascites / SBP / HH
- Hepatorenal Syndrome
- Hepatopulmonary Syndrome
- Portal Vein Thrombosis
- Portopulmonary HTN
- Hepatocellular Carcinoma
Natural History and Prognosis

- **Portal HTN**
- **Clinically Significant Portal HTN**
  - HVPG >5 mm Hg
  - HVPG >10 mm Hg
  - HVPG >12 mm Hg
- **Compensated Cirrhosis**
  - 75% progress within 10 years
- **Decompensated Cirrhosis**
  - Median Survival 2 years
- **7% new varices/yr**
- **12% variceal bleed/yr**
Baveno IV International Consensus Workshop Staging System for Cirrhosis: 1-Year Outcome Probabilities


1. NO VARICES NO ASCITES
   - Compensated: 1%
   - 7% to NO VARICES NO ASCITES
   - 4.4% to VARICES NO ASCITES

2. VARICES NO ASCITES
   - 3.4% to DEATH
   - 6.6% to ASCITES ± VARICES
   - 4% from DEATH

3. ASCITES ± VARICES
   - 20% to DEATH
   - 7.6% from DEATH

4. BLEEDING ± ASCITES
   - 57% to DEATH
   - 7.6% from DEATH
### Classification of Cirrhosis Severity Determinants for Child-Turcotte-Pugh (CTP)

<table>
<thead>
<tr>
<th></th>
<th>Points</th>
<th>1</th>
<th>2</th>
<th>3</th>
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<tbody>
<tr>
<td></td>
<td>Encephalopathy</td>
<td>None</td>
<td>Grade 1 - 2 (or precipitant-induced)</td>
<td>Grade 3 - 4 (or chronic)</td>
</tr>
<tr>
<td></td>
<td>Ascites</td>
<td>None</td>
<td>Mild/Moderate (diuretic-responsive)</td>
<td>Severe (diuretic-refractory)</td>
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<tr>
<td></td>
<td>Bilirubin (mg/dL)</td>
<td>&lt;2</td>
<td>2-3</td>
<td>&gt;3</td>
</tr>
<tr>
<td></td>
<td>Albumin (g/dL)</td>
<td>&gt;3.5</td>
<td>2.8 - 3.5</td>
<td>&lt;2.8</td>
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<tr>
<td></td>
<td>Prothrombin Time (seconds prolonged)</td>
<td>&lt;4</td>
<td>4-6</td>
<td>&gt;6</td>
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</table>

<table>
<thead>
<tr>
<th>Total Numerical Score</th>
<th>Child-Pugh Class</th>
<th>Patients in Class A are considered “compensated”</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 - 6</td>
<td>A</td>
<td>Patients in Classes B and C are considered “decompensated”</td>
</tr>
<tr>
<td>7 - 9</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>10 - 15</td>
<td>C</td>
<td></td>
</tr>
</tbody>
</table>

Classification of Cirrhosis Severity
Model for End Stage Liver Disease score

- MELD - determines the severity of liver disease based on:
  - serum bilirubin,
  - serum creatinine
  - international normalized ration (INR)
    - developed in 2002 by UNOS

- Calculation:
  - \[0.957 \times (\text{Serum creatinine mg/dL}) + 0.378 \log_e (\text{Total bilirubin mg/dL}) + 1.12 \log_e (\text{INR}) + 0.64] \times 10

- Range: 6 – 40
  - equates to estimated 3-month survival rates from 90% to 7% respectively
Most Common Causes of Death

Hepatorenal Syndrome
- Renal failure increases mortality 7X
- 50% mortality within one month

Sepsis
- Infections common- SBP, UTI, CAP, Skin
- 30% mortality at 1 month, 60% at 1 year

Variceal Hemorrhage
- 12% incidence of bleed per year, then
- 57% mortality at one year

Hepatocellular Carcinoma
- 4-30% incidence over 5 years depending on etiology of cirrhosis and origin of patient

**Assessment: Decompensated cirrhosis with MELD 32 complicated by**

1) Overt hepatic encephalopathy  
2) Ascites  
3) Right pleural effusion  
4) Acute kidney injury  
5) Anemia  
6) Coagulopathy  
7) Hyponatremia  
8) Hypotension  
9) Hypoxia  
6) Distended gallbladder
Overt Hepatic Encephalopathy (OHE)

- Associated with a poor prognosis

- Retrospective review of 111 cirrhotic patients for 12±17 months following first episode of acute OHE:
  - 82 (74%) died during follow-up period
  - Survival probability
    - 42% at 1 year
    - 23% at 3 years

Treatment Goals for OHE

- Provision for supportive care
- Identification and removal of precipitating factors
  - Infection, GI bleed, dehydration
- Reduction of nitrogenous load from gut
- Correction of electrolyte abnormalities
- Long-term therapy assessment
  - Control of potential precipitating factors
  - Higher likelihood of recurrent encephalopathy
  - Assessment of need for liver transplantation

Lactulose

- Currently the mainstay of therapy of HE; ~70% to 80% of patients with acute and chronic HE improve with lactulose treatment

- Mechanism of action:
  - A non-absorbable dissacharide that is fermented in the colon
  - Metabolism by the bacterial flora in the colon to lactic acid lowers the colonic pH
  - Cathartic effect can increase fecal nitrogen excretion with up to a 4-fold increase in stool volume

Ferenci P. Semin Liver Dis. 2007;27(suppl 2):10-17.
Bajaj JS. Aliment Pharmacol Ther 2010;31:537-547.
Rifaximin

- Minimally absorbed (<0.4%) oral antibiotic
- Broad-spectrum in vitro activity against aerobic and anaerobic enteric bacteria
- No clinical drug interactions reported
- No dosing adjustment required in patients with liver disease or renal insufficiency
- Approved for overt recurrent HE risk reduction in patients ≥18 years of age
Rifaximin Trial: Time to First Breakthrough HE Episode
Primary End Point

Proportion of Patients Without Breakthrough HE (%)

Days Since Randomization

*Rifaximin 550 mg or placebo twice daily
Hazard ratio with rifaximin, 0.42 (95% CI, 0.28–0.64) P<0.001
Key Points

- **Always** look for and correct inciting factors: infection, bleeding, dehydration, constipation, portal vein clot, porto-systemic shunt, medications
- 1st Line Rx: Lactulose 45-90 gm/d (NNT 4)
  - Nurse driven protocol (oral, NG, or PR)
- If on lactulose, add Rifaximin 550 mg bid
- **DO NOT** check Ammonia levels daily
Ascites

- Most common complication of cirrhosis
- ~60% of patients with compensated cirrhosis develop ascites within 10 years
- 50% mortality rate within 3 years
- Hepatic hydrothorax may be seen with minimal abdominal ascites
- SBP a risk in patients with high SAAG (serum albumin – ascites albumin = > 1.1) PPIs increase risk > 4X
- Patients should generally be considered for liver transplantation referral

Management of Ascites

**First-Line Therapy**

- Tense ascites
  - Paracentesis
  - Sodium restriction (<2 Gm/24 Hrs) and diuretics*
    - Diuretics: Spironolactone 100 mg/day, furosemide 40 mg/day or bumetanide 1 mg/day; uptitrate stepwise to spironolactone 400 mg/day, furosemide 160 mg/day or bumetanide 4 mg/day as tolerated

- Non-tense ascites

**Second-Line Therapy**

- Repeated large volume paracentesis (LVP)†
- TIPS
- Liver Transplantation

†Albumin infusion of 8-12 gm/liter of fluid removed is a consideration for repeated LVP; post-paracentesis albumin infusion may not be necessary for < 5 liters removed

Systematic Review of Safety of Paracentesis

Nine cases of severe bleeding were identified among 4729 procedures. The occurrence of severe haemorrhage represented 0.19% of all procedures with a death rate of 0.016%. Bleeding was not related to operator experience, elevated international normalized ratio or low platelets. It occurred in patients with high model for end-stage liver disease and Child-Pugh scores. Furthermore, some degree of renal failure was present in all but one patient.

Needle Entry Points
# AASLD Practice Guidelines: Ascitic Fluid Analysis

<table>
<thead>
<tr>
<th>Routine</th>
<th>Optional</th>
<th>Unusual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell count and differential</td>
<td>Culture in blood culture bottles</td>
<td>Acid-fast bacteria smear and culture</td>
</tr>
<tr>
<td>Albumin</td>
<td>Glucose</td>
<td>Cytology</td>
</tr>
<tr>
<td>Total protein</td>
<td>Lactose dehydrogenase</td>
<td>Triglyceride</td>
</tr>
<tr>
<td></td>
<td>Amylase</td>
<td>Bilirubin</td>
</tr>
<tr>
<td></td>
<td>Gram’s stain</td>
<td></td>
</tr>
</tbody>
</table>
Spontaneous Bacterial Peritonitis: Diagnosis

- Diagnosis of SBP:
  - Positive ascitic fluid bacterial culture
  - Elevated ascitic fluid absolute PMN count (ie, ≥250 cells/mm³ [0.25 x 10⁹/L])
  - No evident intra-abdominal source of infection

Prevention of SBP – Prophylaxis

<table>
<thead>
<tr>
<th>Drug Therapy</th>
<th>Dose /Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norfloxacin</td>
<td>400 mg/day orally</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>1g/day IV for 7 days</td>
</tr>
<tr>
<td>Double-strength trimethoprim/sulfamethoxazole</td>
<td>5 doses/week</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>750 mg as single oral dose/week</td>
</tr>
<tr>
<td>High ascitic fluid protein</td>
<td>&gt;1 gram/dL</td>
</tr>
<tr>
<td>Low ascitic fluid protein</td>
<td>≤1 gram/dL</td>
</tr>
</tbody>
</table>

Intermittent dosing of prophylactic antibiotics may select resistant flora; daily dosing preferred.
Key Points

• **Always** perform a diagnostic paracentesis
• **Always** give 8 gm/l albumin when taking over 5 liters of ascites
• **Always** give 1.5 gm/kg albumin on Day 1 and 1.0 gm/kg albumin on Day 3 for SBP
• **Always** start SBP prophylaxis after first episode
• **Avoid** chest tubes in a hepatic hydrothorax
• **Avoid** PPI’s in patients with ascites without PUD
Renal Injury in Cirrhosis

Hospitalized patients with cirrhosis

Chronic renal failure
  1%

AKI
  19%

Pre-renal
  68%

- Volume-responsive
  66%
  - Infection
  - Hypovolemia
  - Vasodilators
  - Other

Intra-renal (ATN, GMN)
  32%

Post-renal (obstructive)
  <1%

Not volume-responsive

HRS type 1
  25%

HRS type 2
  9%

Survival Is Decreased With Renal Dysfunction

Survival in Cirrhosis Based on Level of Renal Dysfunction

Survival Among Patients With Cirrhosis and Hepatorenal Syndrome

Prevention of Acute Renal Injury in Cirrhotics

• Prevent/treat volume depletion or vasodilatation
  – Careful use of diuretics
  – Avoidance of diarrhea with use of lactulose
  – Use of albumin after large-volume paracentesis

• Avoid use of aminoglycosides and NSAIDs

• Aggressively treat hypovolemia/hypotension occurrence

Volume Challenge

- 1 gm/kg body weight up to 100 gm albumin infusion for at least 2 days

- Withdrawal of antibiotics

- Failure of improvement in renal function is concerning for hepatorenal syndrome (part of diagnostic criteria)
Hepatorenal Syndrome: Risk Factors

- Development of bacterial infections, particularly SBP, is the most important risk factor
  - Hepatorenal syndrome develops in ~30% of patients with spontaneous bacterial peritonitis
  - Treatment with albumin infusion/antibiotics reduces the risk of developing hepatorenal syndrome and improves survival

Hepatorenal Syndrome: Prognosis

- The prognosis of hepatorenal syndrome is poor
  - Average median survival ~ 3 months
  - High MELD score and type 1 hepatorenal syndrome are associated with very poor prognosis
- Median survival of patients with untreated type 1 hepatorenal syndrome is ~ 1 month

Key Points

- **Always** closely monitor renal function in hospitalized cirrhotic patients
- **Always** correct volume depletion in the setting of a rising creatinine
Gastroesophageal Varices

- Gastroesophageal varices present in ≈50% of patients with cirrhosis
  - Presence correlates with severity of liver disease
  - 40% of Child A patients have varices
  - 85% of Child C patients have varices

- Cirrhotic patients without varices develop them at a rate of 7-8% per year
  - Patients with small varices develop large varices at a rate of 8% per year

Gastroesophageal Variceal Hemorrhage

• Occurs at a yearly rate of 5% to 15%

• Most important predictor of hemorrhage is size of varices

• Other predictors of hemorrhage are:
  – Decompensated cirrhosis (Child B/C)
  – Endoscopic presence of red wale marks

• Associated with a mortality of ≥20% at 6 weeks

• Bleeding ceases spontaneously in ≤40% of patients
Cirrhosis Screening and Surveillance Management

Esophagogastrroduodenoscopy

- No varices
  - Repeat endoscopy in 3 years (well compensated); in 1 year if decompensated
  - No beta-blocker prophylaxis

- Small varices (<5 mm), Child B/C, red wales
  - Beta-blocker prophylaxis

- Medium or large varices
  - Child Class A, no red wales: Beta blockers
  - Child class B/C, red wales: Beta blockers, or endoscopic band ligation

Management of Acute Hemorrhage

• Patients with suspected acute variceal hemorrhage require intensive-care unit setting for resuscitation and management

• Acute GI hemorrhage requires:
  – Intravascular volume support
  – Blood transfusions
  – Maintaining hemoglobin of ~7-9 g/dL

• Institute short-term (5-7 day) antibiotic prophylaxis

• Initiate therapy with somatostatin (or its analogs)

• Perform esophagogastroduodenoscopy within 12 hours; treat with endoscopic band ligation or sclerotherapy

Acute Hemorrhage: Role of Early TIPS

Figure 2. Actuarial Probability of the Primary Composite End Point and of Survival, According to Treatment Group.

The probability of remaining free from uncontrolled variceal bleeding or variceal rebleeding is shown in Panel A, and the probability of survival is shown in Panel B. EBL denotes endoscopic band ligation, and TIPS transjugular intrahepatic portosystemic shunt.

Bacterial Infection and Variceal Bleeding

- Variceal bleeding associated with increased risk of bacterial infection
  - SBP (spontaneous bacterial peritonitis), urinary tract infection, pneumonia or bacteremia
- Develops in 20% of patients within 48 hours and in 35% to 66% of patients within 2 weeks
- Compared to patients without infection, presence of infection is associated with
  - Failure to control bleeding (65% vs 15%)
  - Early rebleeding
  - Mortality (40% vs 3%)

Antibiotic Prophylaxis During/After Acute Variceal Bleeding

- Prophylactic ofloxacin vs antibiotics only at diagnosis of infection
- ↓ infections (2/59 vs 16/61)
- Less rebleeding within 7 days
- ↓ blood transfusions for rebleeding
- Prophylactic antibiotics recommended in management of acute variceal hemorrhage

Key Points

- **Always** consider variceal bleeding in the differential for anemia in a cirrhotic
- **Always** give prophylactic antibiotics in setting of a variceal bleed - they save lives
- **Always** manage in the ICU and get an EGD for therapy and risk stratification
- **Always** consider beta blocker prophylaxis on discharge to prevent or delay rebleed
Liver Transplantation Options
Non-cholestatic cirrhosis

Cholestatic liver disease/cirrhosis

Acute hepatic necrosis

Biliary atresia

Metabolic diseases

Malignant neoplasms

Other/unknown

Cirrhosis Was the Most Common Reason for Liver Transplant in 2007

N = 6223 Recipients of Deceased Donor Livers

Contraindications - Absolute

- Extrahepatic malignancy unless tumor free for > 2 years and probability of recurrence ≤ 10%
- Alcoholic hepatitis /untreated alcoholism / chemical dependency
- Extrahepatic sepsis unresponsive to medical therapy
- High dose or multiple pressors
- Severe multiorgan failure
- Severe psychological disease likely to affect compliance
- Extensive portal vein and mesenteric vein thrombosis
- Pulmonary HTN (mean PAP > 35mmHg)
Contraindications - Relative

- General debility
- Portal vein thrombosis
- HIV infection
- Extensive prior abdominal surgery
- Social isolation
Listing for Transplant

- Once evaluation is completed and contraindications excluded must meet minimum listing criteria: CPT=7
- Currently a MELD score of 15
- UNOS: organs allocated locally then nationally
- Organs are matched by blood type and size
- Priority is based on MELD score
Wait List and Transplant Activity for Liver 1999–2008

Number of Patients

Year


On Waiting List Annually
Received Transplants Annually
Died While on Waiting List Annually

Patients Awaiting Transplantation Management

- Close follow-up with primary GI MD
- Preparation/support of family and patient
- Treat promptly complications
- Avoid therapies/interventions that would make transplantation more difficult
  - Nephrotoxins
  - RUQ surgery/shunts
  - Anesthesia
- Consider living donor transplant
Patient survival by era

Cumulative percent survival over years posttransplant for different eras:
- 1968-1970
- 1971-1975
- 1976-1980
- 1981-1985
- 1986-1990
- 1991-1995
- 1996
• Patients on waiting list have highest risk of death in DSA with poor availability of organs

• Where does Minnesota Stand?
LDLT survival 83% at 5 years

INTENTION TO TREAT ANALYSIS:
Risk of Death is 40% lower compared to
• No living donor
• On the wait list for DDLT

• HCC patients MELD>15 risk of death is 29% lower with LDLT

• NO benefit of LDLT in HCC MELD<15 (due to allocation points)
Assessment: Decompensated cirrhosis with MELD 32 complicated by

1) Overt hepatic encephalopathy
   ➢ Treat infection, bleed, correct hyponatremia, give lactulose, rifaximin

2) Ascites
   ➢ Tap regardless of INR/plts, treat SBP, give albumin d1 and d3 and for LVP, home on SBP prophylaxis but NO PPI

3) Right pleural effusion-
   ➢ Hepatic Hydrothorax. No chest tube.

4) Acute kidney injury
   ➢ Likely pre-renal. Hold diuretics. Volume challenge with 100 gm albumin X 2 days

6) Anemia → variceal bleed
   ➢ ICU, EGD, octreotide, ?early TIPS, prophylactic abx NOW, beta blocker on d/c.

7) Coagulopathy
   ➢ Can’t assume auto-anticoagulated, low risk of bleed with paracentesis

8) Hyponatremia
   ➢ SIADH and diuretics- hold diuretics, volume repletion

9) Distended gallbladder
   ➢ VERY HIGH SURGICAL RISK. Percutaneous gallbladder drainage if acute choly is confirmed. Suspect simply related to ascites.
Objectives

• By the end of this session participants will:
  – Recognize the HIGH risk of mortality in these patients
  – Remember at least 3 tips for managing the common complications of cirrhosis encountered by hospitalists
  – Consider early referral for transplant evaluation in patients with decompensated cirrhosis
Special Thanks

- Mohamed Hassan
- Coleman Smith
- Julie Thompson
- Jack Lake
Questions?

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Surgery in the Liver Patient

30 Day Mortality by MELD Score

Table 3. Relationship Between MELD Score and Postoperative Mortality

<table>
<thead>
<tr>
<th>MELD score</th>
<th>7 Days</th>
<th>30 Days</th>
<th>90 Days</th>
<th>1 Year</th>
<th>5 Years</th>
<th>10 Years</th>
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</thead>
<tbody>
<tr>
<td>0–7 (n = 351)</td>
<td>1.9 (314)</td>
<td>5.7 (301)</td>
<td>9.7 (287)</td>
<td>19.2 (253)</td>
<td>50.7 (123)</td>
<td>72.6 (57)</td>
</tr>
<tr>
<td>8–11 (n = 257)</td>
<td>3.3 (236)</td>
<td>10.3 (219)</td>
<td>17.7 (200)</td>
<td>28.9 (170)</td>
<td>58.5 (83)</td>
<td>78.1 (35)</td>
</tr>
<tr>
<td>12–15 (n = 106)</td>
<td>7.7 (94)</td>
<td>25.4 (78)</td>
<td>32.3 (69)</td>
<td>45.0 (56)</td>
<td>69.5 (24)</td>
<td>87.3 (10)</td>
</tr>
<tr>
<td>16–20 (n = 35)</td>
<td>14.6 (29)</td>
<td>44.0 (19)</td>
<td>55.8 (15)</td>
<td>70.5 (10)</td>
<td>94.1 (2)</td>
<td>94.1 (2)</td>
</tr>
<tr>
<td>21–25 (n = 13)</td>
<td>23.0 (7)</td>
<td>53.8 (4)</td>
<td>66.7 (3)</td>
<td>84.6 (2)</td>
<td>92.3 (1)</td>
<td>100 (0)</td>
</tr>
<tr>
<td>≥26 (n = 10)</td>
<td>30.0 (6)</td>
<td>90.0 (1)</td>
<td>90.0 (1)</td>
<td>100 (0)</td>
<td>100 (0)</td>
<td>100 (0)</td>
</tr>
</tbody>
</table>

Anticoagulation in the Cirrhotic Patient

- Cannot assume auto-anticoagulation
- If bleeding risks are low the balance can shift to pro-thrombotic state.
- Anticoagulation may be safely managed in cirrhosis
- Case by case risk-benefit assessment required
4 am Cross-Cover Call: “Can I get a Tylenol order for Mr. Johnson?”

The Therapeutic Use of Acetaminophen in Patients with Liver Disease.
Benson, Gordon; Koff, Raymond; Tolman, Keith

- Acetaminophen at usual doses (650 mg orally, max 3 gm/d < 1 week) may be used safely in compensated cirrhosis
- May give inpatient at 650 mg dose < 2 gm / 24 hrs for short term use in more severe liver disease
2 am Cross-Cover Call: “Lab called and the Na is 128”

• Common: 50% of hospitalized cirrhotics with Na < 135, 20% < 130

• Associated with worse prognosis: MELD-Na

<table>
<thead>
<tr>
<th>Serum [Na+] mEq/L</th>
<th>≤130</th>
<th>131-135</th>
<th>&gt;135</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatorenal syndrome</td>
<td>3.45</td>
<td>1.75</td>
<td>1 (reference value)</td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td>3.40</td>
<td>1.69</td>
<td>1 (reference value)</td>
</tr>
<tr>
<td>Gastrointestinal bleeding</td>
<td>1.48</td>
<td>0.93</td>
<td>1 (reference value)</td>
</tr>
<tr>
<td>Spontaneous bacterial peritonitis</td>
<td>2.36</td>
<td>1.44</td>
<td>1 (reference value)</td>
</tr>
</tbody>
</table>

Hyponatremia in Cirrhosis

- Renal water retention >> Sodium retention related to SIADH
- Fluid restriction/ low Na diet for most patients
  - Minimally effective
- Reduction or d/c of diuretics often required
- “Aquaresis” with vaptan drugs available and effective but EXPENSIVE