Secrets to Caring for the Hospitalized Cirrhotic Patient

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Outline

- Ascites
- Albumin Replacement
- Paracentesis Complications
- Malnourished Cirrhotic Patients
- Hepatic Encephalopathy
- Pain Medications in Cirrhosis

The International Ascites Club was founded in Florence, Italy on November 30, 1990 during an international liver meeting organized by Professor Paolo Gentilini. The reason to found a club of experts in this complication of portal hypertension originated from the peculiarity of the expertise doctors who treat patients with ascites must have.

Case #1 – How much albumin??

- 56M with alcoholic cirrhosis
- Abdominal distention, known history of ascites
- Wt – 70kg, Afebrile, non toxic appearing
- Paracentesis completed – 6 liters removed
- WBC – 1000 (Seg – 60%)
- SBP with more than 250 PMNs in fluid
- How much albumin does this patient need?
  - **A. 25 grams**
  - **B. 50 grams**
  - **C. 100 grams**

Ascites: AASLD practice guidelines

Table 3. Ascitic Fluid Laboratory Data*

Routine	Optional	Unusual	Unhelpful
Cell count and differential	Culture in blood culture bottles	AFB smear and culture	pH
Albumin	Glucose	Cytology	Lactate
Total protein	Lactate dehydrogenase	Triglyceride	Cholesterol
	Amylase	Bilirubin	Fibronectin
	Gram's stain		Glycosaminoglycans

Abbreviation: AFB, acid-fast bacteria. *Adapted from Runyon.[17] Reprinted with permission from W.B. Saunders.

- Ascites not always liver related
- Useful tests
  - Initial Presentation - albumin & protein
  - Every Presentation - cell count
- SAAG > 1.1, Protein < 2.5
- Cell count - PMNs > 250

Albumin Replacement

- Large Volume Paracentesis
  - 8g of albumin for every Liter removed
  - Usually necessary when LVP > 5 Liters
- Spontaneous Bacterial Peritonitis
  - Day 1 - 1.5g/kg replacement
  - Day 3 - 1g/kg replacement
  - Reduce renal failure and mortality
    - NNT (renal failure) = 4
    - NNT (mortality) = 5

Case #1

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- Wt – 70kg
- How much albumin does this patient need?
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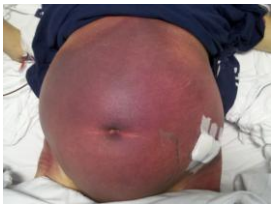
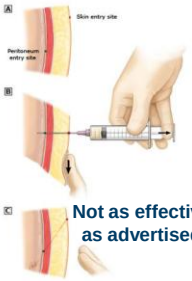
Complications of Paracentesis

- Rare short term complications
  - Hemorrhage
  - Intestinal Perforation



Z tracking and Paracentesis Location



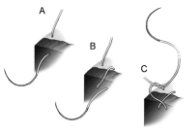
Prospective Study on Complications

- 2005 - 2007 - France and Switzerland
- 515 paracentesis in 171 patients
- Ultrasound available for all - only used 11.7%
- 461 NO complications (89.5%)
- 54 complications (10.5%)
  - Minor - self-limited - 46 cases (8.9%)
  - Major - medical intervention - 8 cases (1.6%)

De Gottardi, et al., Clinical Gastro Hepatology, 2009 (7), 906-909

Post Procedure Leakage

- Ostomy bag - can lead to secondary infection
- Lay patient on opposite flank
- Dry completely
- Use skin adhesive to bond site
- If refractory, consider figure of 8 stitch



Prospective Study on Complications

- Higher risk in those patients:
  - Undergoing therapeutic tap
  - Child-Pugh Class C
  - Platelet count < 50,000/L
  - Underlying alcoholic liver disease
- INR elevation did not increase risk

De Gottardi, et al., Clinical Gastro Hepatology, 2009 (7), 906-909

Case #2 – Appropriate Diet

- 45F with HCV cirrhosis with asterixis
- Admitted to the hospital for fever work up
- History of severe encephalopathy and SBP
- What diet is appropriate for this admission?
  - **A. Low fat diet**
  - **B. Low sodium diet**
  - **C. Low protein diet**
  - **D. Low taste diet**

Malnutrition in Cirrhosis

- 20% of compensated cirrhotics
- 60% of decompensated cirrhotics
- Affects clinical outcomes
- Higher mortality in those patients:
  - Older age
  - More severe liver failure
  - Lower caloric intake
  - Lower protein intake
  - Lower transthretin levels
  - Higher Cr levels
  - Higher CRP levels

Campillo, et al., Nutrition, 2003 (19), 515-521

Malnutrition in Cirrhotics

- Highest nutritional deficits had tense ascites
  - Increased expenditure
  - Depleted body protein
  - Decreased dietary intake
- May have role for enteral tube feeding
- Often patient discomfort precludes nasal feeding tube

Campillo, et al., Nutrition, 2003 (19), 515-521

Nutritional Management

Table 2 Results of a questionnaire sent through the website of the Italian Society of Gastroenterology and Hepatology in 2005

Proposed questions	Proposed answers	Percentages of physicians preferences
"How many proteins do you prescribe in the hospital diet when a cirrhotic patient admitted *for severe hepatic encephalopathy* improves and is able of eating?"	>50 g/protein/day	6%
	30–50 g/protein/day	42%
	<30 g/protein/day	52%
"How many proteins do you prescribe in the hospital diet when a cirrhotic patient is admitted *for mild hepatic encephalopathy*?"	>50 g/protein/day	25%
	30–50 g/protein/day	72%
	<30 g/protein/day	3%

Merli & Riggio, Metabolic Brain Disease, Dec 2008.

Nutritional Management

- Cirrhosis depletes body mass
- Liver unable to derive glucose
- Decreased ability for gluconeogenesis
- Glucose thus derived from muscle and adipose catabolism
- <u>Increased protein requirements</u>

Case #2

- 45F with HCV cirrhosis with asterixis, Hx of SBP
- What diet is appropriate for this admission?
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PEG tubes in Cirrhosis

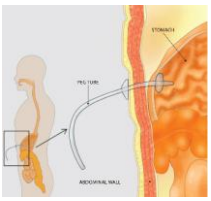
- Series of 26 patients, 17 with ascites (65%)
- 10 patients died within 30 days (38.5%)
- 9 of these patients had ascites

- High rate of complications in cirrhotic patients
- Those without ascites may be less risky

Baltz, Argo, Al-Osaimi, Northup, GI Endoscopy, 2010 (72), 1072-5

PEG tubes in Cirrhosis

Difficulties of PEG Placement with Ascites
Apposition of the stomach and abdominal wall more challenging
Impaired tract formation and healing
Reaccumulation and catheter dislodgement
Leakage of ascites
Increased risk of infection
Increased risk of bleeding

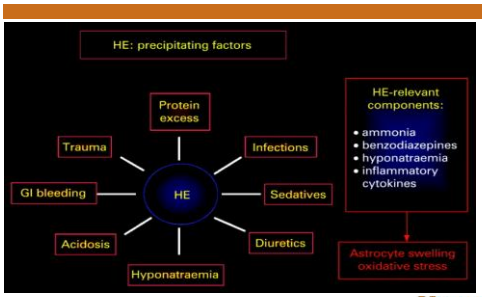


Vance, Shah, Practical Gastroenterology, 36 (5), May 2012.

Case #3 – Cirrhosis & Confusion

- 46F NASH cirrhosis
- Attended family reunion picnic
- Spent previous day outside in the sun
- Now with confusion and asterixis
- What caused her confusion?
  - **A. Medication non-compliance**
  - **B. Dehydrated**
  - **C. Toxin Ingestion**
  - **D. Infection**

Hepatic Encephalopathy - Causes



Haussinger, D et al. Gut 2008;57:1156-1165

Hepatic Encephalopathy - Stages

- Stage I
  - **Mild confusion, day night reversal, altered mood, no asterixis**
- Stage II
  - **Drowsy, inappropriate behavior, + asterixis**
- Stage III
  - **Extremely drowsy, barely able to speak and obey simple commands**
- Stage IV
  - **Coma, sometimes able to respond to painful stimuli**

Ammonia Level in PSE

- Nicolao et al., 2003
  - 17 patients followed with PSE resolved
  - Ammonia levels did NOT decrease
  - Some levels increased with PSE resolution

- Conclusion
  - Ammonia levels limited use for diagnosis or clinical management

Nicolao et al., Journal of Hepatology, 2003, 38, 441-446.

Ammonia Level in PSE

- Kundra et al., 2005
  - Evaluated 20 patients with CLD
  - Stage II mean ammonia level - 72.3
  - Stage III mean ammonia level - 58.7
  - Stage IV mean ammonia level - 42.0
- Conclusion
  - Ammonia levels, no utility in diagnosis of PSE

Kundra et al.,Clinical Biochemistry, 2005, 38, 696-699.

Ammonia Level - Utility?

- "The only confusion an ammonia level measures is the confusion of the provider ordering that test for encephalopathy."
- UVA Hepatic Encephalopathy Protocol
- Lactulose enemas in Stage III-IV
- Addition of Rifaximin therapy

Case #3

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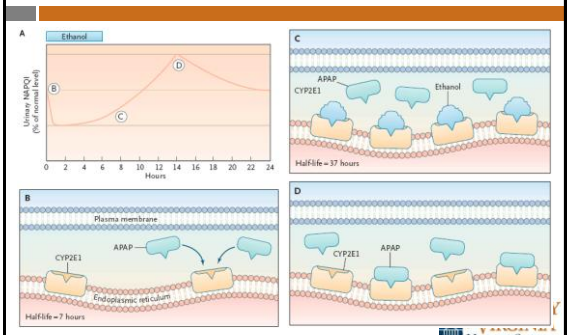
Case #4 – Groin Pain

- 56M significant alcohol use – cirrhosis
- 3rd and 4th degree burns in groin and scrotum
- Burning off frayed edges of jean shorts "jhorts"
- Admitted for 3-4 days at time of consult
- Pain medications for dressing changes?
  - **Acetaminophen**
  - **Ibuprofen**
  - **Morphine**
  - **Tramadol**

Pain Medication in Cirrhosis

- Issues with clearance
- Altered metabolism
- 3 modes of metabolism, often hindered:
  - P450 Pathway
  - Conjugation
  - Biliary Excretion
- Tylenol - up to 2g per day?

Tylenol Toxicity with Alcohol Use



Lee, W. NEJM Jul 31, 2003

NSAIDs in Cirrhosis

- NSAIDs heavily protein bound
- Elevated levels in cirrhosis
- Renal Impairment - decreased perfusion
- Increased bleeding risk with thrombocytopenia

Opioids in Cirrhosis

TABLE 2. **Opioid Analgesic Metabolism**

Drug	Half-life (h)	Protein binding (%)	Hepatic metabolism	Special note
Codeine	4-6	7	CYP2D6	Metabolized to morphine in liver; ceiling effect; serum levels unpredictable
Morphine	3-12	35	Glucuronidation	Metabolite increases toxicity in patients with renal failure; adjust dose in these patients
Meperidine	2-4	70	CYP2B6, 3A4	Avoid in patients with renal failure; increased bioavailability of CNS active metabolite (t½ = 15-30 h) in patients with renal/liver disease; avoid in patients with liver impairment
Hydromorphone	1-3	15	Glucuronidation	Consider dose reduction in patients with liver impairment; safe to use in those with renal failure
Hydrocodone	3-4	7	CYP2D6	Active metabolite is hydromorphone
Fentanyl IV, patch	1-3 17	80	CYP3A4	Lipid soluble; stores in fat and muscle; continuous infusion = prolonged sedation; less histamine release, less hemodynamic disturbance
Oxycodone	2-12	45	CYP3A4, 2D6	Multiple metabolite levels unpredictable; reduce dose and frequency in patients with liver impairment
Tramadol	7	20	CYP3A4, 2D6, and glucuronidation	Reduce dose and frequency in patients with renal and liver impairment
Methadone	8-24	80	CYP3A4, 2D6, several others	Consider dose reduction; equivalence ratios to methadone are dose-dependent (may range from 1:1 to 20:1)—cautious dose titration

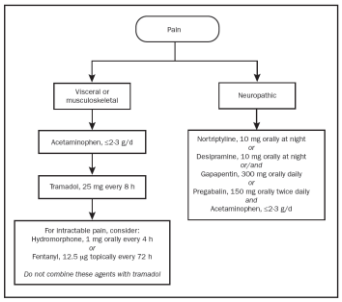
CNS = central nervous system; CYP = cytochrome P450; IV = intravenous.

Chandock, Watt, Mayo Clinic Proceedings, 2010, 85(5), 451-8.

Preferred Opioids in Cirrhosis?

- Tramadol
  - Works on peripheral pain
  - Low affinity for opiod receptors
  - Less sedation effect
  - Lower potential for tolerance
- Fentanyl or Hydromorphone
  - Least affected by renal function
  - Order in lower doses and longer intervals

Pain Medication Algorithm



Start with Acetaminophen

Try Tramadol

Use opiates for intractable pain

Chandock, Watt, Mayo Clinic Proceedings, 2010, 85(5), 451-8.

Clincal Pearls

- Paracentesis
  - Remember albumin replacement
  - Most complications self-limiting
  - Avoid ostomy bag if leaking
  - Use skin adhesive and lay on opposite flank
- Malnutrition
  - Avoid PEG tubes in cirrhosis
  - Especially with presence of ascites
  - Avoid low protein diets
  - Consider NG tube feeds early

Clinical Pearls

- Hepatic Encephalopathy
  - Diagnosis of underlying cause imperative
  - Ammonia level of limited use
- Pain Medication
  - Attempt Tylenol in limited doses
  - Next would attempt Tramadol
  - Consider Fentanyl or Hydromorphone if opiod needed in lower doses, less frequency
  - Alternatives if neuropathic pain

References

- The management of hospitalized patients with cirrhosis: the Mount Sinai experience and a guide for hospitalists.
- Perumalswami PV, Schiano TD. Dig Dis Sci. 2011 May;56(5):1266-81.

- AASLD practice guidelines
- http://www.aasld.org/practiceguidelines/Pages/default.aspx

Questions?