Pitfalls in Cirrhotic Care

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“I have ascites so I restricted my fluid intake so it would go away”

How does this affect the kidneys?

Portal Hypertension → Splanchnic vasodilation → Decrease in effective arterial blood volume

- Renal sodium and water retention
- Renal vasoconstriction
- Increased CO by heart

Hyperdynamic splanchnic and systemic circulation → Ascites

- Stimulate volume receptors
- Activate sympathetic nervous system
- Renin-angiotensin-aldosterone system
- ADH

Hepatorenal Syndrome
Hormonal Responses are Maximally Activated in HRS

![Graph showing hormonal responses in HRS]

Asbert, M et al. Gastroenterology 1993; 104:1485

Ascites Factors in Cirrhosis

- Sodium
  - Principal osmole essential for maintaining extracellular fluid (ECF) volume and regulation of blood pressure and osmotic equilibrium
  - Principal determinant of the effective circulating volume (ECV)
- In cirrhosis
  - ECV is decreased because of splanchnic vasodilatation
  - Activation of RAA system and ADH release

Ascites Factors in Cirrhosis

- Sodium retention is the main driver of ascites from portal hypertension and treatment involves the initiation of naturesis.
- Fluid restriction does not help eliminate sodium and may lead to intolerance of diuretics from dehydration.
“My sodium level was low, so I was told to take salt tablets”

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Hyponatremia in Cirrhosis

- Increase in ADH relative to aldosterone with more relative free water retention
- As symptomatic hyponatremia is unusual in cirrhosis, the mainstay of therapy is restricting water and salt intake combined with diuretics

Consequences of Salt Tablets

- Salt tablets will worsen sodium load and ascites leading to further decompensation and potential complications

“I was placed on a low protein diet to prevent ammonia and confusion”
**Malnutrition In Cirrhosis**

**Decreased Intake**
- Anorexia
- Early satiety
- Ascites
- Altered mental status
- Frequent Hospitalizations

**Decreased Absorption**
- Inadequate bile flow
- Bacterial overgrowth
- Pancreatic insufficiency

**Metabolic Alterations**
- Increased/decreased metabolic rate
- Increased protein needs
- Insulin resistance
- Reduced glycogen stores
  - Elevated leptin
  - Elevated TNF-αβ
  - Decreased insulin-like growth factor-1

**Iatrogenic Factors**
- Excessive dietary restrictions
- Intolerance of hospital food
- Frequent Paracentesis
- Diuresis (micronutrient losses)
- Lactulose therapy

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**Complications of Cirrhosis**

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**Cirrhotic Nutritional Physiology**

- Early occurrence of the “fasting state” which uses body sources of glycerol and amino acids, the compounds needed for gluconeogenesis from non-carbohydrate sources

- An overnight fast in the cirrhotic ≈ 72 hour fast in the healthy individual

_Amodio et al. Dig Liver Dis 2001;33:492-500._
Cirrhotic Nutritional Physiology

- Constant breakdown of fat and muscle occurs
- Leads to tissue depletion and muscle wasting
- About 80% of visceral protein sources are depleted in malnourished cirrhotic patients
- Malnutrition a major risk factor for mortality!

Amodio et al. Dig Liver Dis 2001;33:492-500
Bajaj J. Aliment Pharmacol Ther. 2010;31(s):1537-547

Nutritional Is Essential!

- Patients with advanced liver disease
  - Decreased intake and absorption of nutrients
  - Increased energy expenditure
  - Altered fuel metabolism with an accelerated starvation metabolism
- Nutritional therapy
  - Improve nutritional status, reduce infection rates, and decrease perioperative morbidity


Protein restriction does not help in acute overt HE

There were no statistical differences between the low-protein diet (white boxes) and the normal protein diet (gray boxes).

Cordoba et al 2004 J Hepatol
Low protein does not prevent Overt Encephalopathy

All subjects received 0.7g protein/kg/day at baseline

Les et al AASLD 2009 #24

Sarcopenia and Survival

Tandon et al. Liver Transplantation 18:1209-1216, 2012

“My ammonia is high so my lactulose was increased to have 8-10 BMs per day” (patient not overtly encephalopathic)
Inter-Orga Trafficking of Ammonia

Normal

Chronic Liver Failure

PERCIPIENTS OF HEPATIC ENCEPHALOPATHY

Azotemia

CNS MEDS
DIET
ELECTROLYTES
HEPATIC NECROSIS
INFECTION
CONSTIPATION
UNKNOWN

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Role of Ammonia Levels

- Unclear if NH4 measurements from peripheral circulation truly reflect NH4 concentrations at the blood-brain barrier
- 2003 study
  - 69% (20/29) of the patients without signs or symptoms of encephalopathy had total arterial ammonia levels greater than that threshold of normal (47 mol/L)


Role of Ammonia Levels

- Accuracy is technique-dependent
  - Efficient venous draw, no fist clenching, rapid transport on ice, quick analysis, pH controlled
- Not specific
  - Elevated in TPN, GI hemorrhage, intense muscular activity, and urosepsis
- Limited reliability
  - Not always accompanied by very high ammonia. Poor correlation.
- Not a Guide to Treatment
  - Not a useful clinical endpoint for HE treatment in practice
Thank you!

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