58 Year-old Male with Alcoholic Cirrhosis Presents with Hyponatremia

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11/8/12
HPI

• Fluid leaking from umbilical hernia secondary to his ascites
• Went to OR for drain placement which was complicated by hepatorenal syndrome
• Kidney function improved after 10 days and he was discharged home with follow-up with transplant clinic for eval for liver transplant
2 weeks later

• Admitted from clinic for acute on chronic kidney injury
• He has had a history of hyponatremia with Na ranging from 128-132
• Morning of discharge, underwent cosyntropin stim which was abnormal, endocrinology consulted
Symptoms

- No orthostasis, weakness,
- No anorexia, lethargy
- No nausea or vomiting
- No hyperpigmentation, salt craving
- No palpitations, no pre-syncope
- No AMS per family
- Occasional shortness of breath depending on his ascites. Feels much better after paracentesis.
PMH
  Alcoholic cirrhosis
  CKD (GFR 40-50)

PSH
  Lower back surgery
  Umbilical hernia

Meds: Lasix 40 mg daily,
     Ativan 1 mg daily,
     Nadolol 40 mg daily,
     Aldactone 25 mg daily

FH
  Father: HTN, CKD
  Mother: DM2

SH
  Abstinent of EtOH since admission
  No Tobacco
Physical exam

Vitals: 36.2 121/53, 69, BMI 26, 96% RA
HEENT: mild scleral icterus
CV: RRR, no murmurs
Pulm: CTA bilaterally
GI: soft, +ascites, no rebound or guarding
MSK: 1+ LE edema
Neuro: A+Ox3, no asterixis
Skin: no hyperpigmentation but mild icterus
Psych: normal mood
Initial Labs HD #1

INR 1.9

U\textsubscript{Na} 15

8AM Cortisol 5.2 \rightarrow 12.8 \rightarrow 18.3

MELD score: 22
Child score: 10, class C
Post Discharge Day #1 Labs

8AM Cortisol 5.9 mcg/dL, ACTH 29.2
8AM Fr Cortisol 1.07 mcg/dL (RR 0.07-0.93)
TSH 3.07 (RR 0.3-4.0)
FT4 1.08 (RR 0.9-1.7)

Seen in endo clinic 2 weeks after discharge. Hemodynamically stable, no symptoms of adrenal insufficiency. Not started on steroids.
Clinical Questions

- Assessment of adrenal insufficiency in cirrhosis?
- Effect of corticosteroid therapy in critically ill patients with cirrhosis?
- Etiology of hyponatremia in cirrhosis?
Total Cortisol in Cirrhosis

• 90% serum cortisol is bound to albumin (20%) and CBG (70%)

• Reduction in these proteins are associated with a reduction in the bound-cortisol fraction.

• Serum total cortisol could be lower without having a low free biologically active hormone.
Adrenocortical Dysfuncn in Cirrhosis

- AI reportedly found in 40-48% patients with variceal bleeding and 26-64% w/ascites
- Hepatoadrenal syndrome: inadequate glucocorticoid activity w/respect to the severity of illness
  - Glucocorticoid resistance in inflammation
  - Decreased HDL levels → decreased steroidogenesis
Adrenocortical Dysfn in Cirrhosis

- 250 mcg Cosyntropin is recommended to diagnose AI in critically ill
- Serum total and plasma free cortisol were used to study 43 clinically stable cirrhotics.
  - Prevalence of AI
    - 39% w/standard criteria (peak total < 18mcg/dL)
    - 47% w/CIRCI criteria (∆ cortisol < 9mcg/dL)
    - 12% w/free cortisol (peak plasma < 1.2mcg/dL)
- Free cortisol index: total cortisol/CBG
- LDSST
- Salivary Cortisol
# Corticosteroid Use in Cirrhosis + Critical Illness

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Hydrocortisone n = 39</th>
<th>Placebo n = 36</th>
<th>Relative risk (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality</strong></td>
<td></td>
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<tr>
<td>28-day mortality, no. (%)</td>
<td>33 (85)</td>
<td>26 (72)</td>
<td>1.17 (0.92 to 1.49)</td>
<td>0.19</td>
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<tr>
<td>ICU mortality, no. (%)</td>
<td>24 (62)</td>
<td>24 (67)</td>
<td>0.92 (0.66 to 1.30)</td>
<td>0.64</td>
</tr>
<tr>
<td>Hospital mortality, no. (%)</td>
<td>34 (87)</td>
<td>32 (89)</td>
<td>0.98 (0.83 to 1.16)</td>
<td>0.82</td>
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<tr>
<td><strong>Hemodynamic response</strong></td>
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<tr>
<td>Change in norepinephrine infusion rate (day 2 – day 1), µg/kg per min</td>
<td>-0.08 (0.22)</td>
<td>0.09 (0.28)</td>
<td>-0.17 (-0.28 to -0.05)*</td>
<td>0.005</td>
</tr>
<tr>
<td>mean (SD)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Change in norepinephrine infusion rate (day 3 – day 1), µg/kg per min</td>
<td>-0.16 (0.29)</td>
<td>0.11 (0.32)</td>
<td>-0.27 (-0.40 to -0.12)*</td>
<td>0.0006</td>
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<tr>
<td>mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Shock reversal, no. (%)</td>
<td>24 (62)</td>
<td>14 (39)</td>
<td>1.58 (0.91 to 2.55)</td>
<td>0.05</td>
</tr>
<tr>
<td>Vasopressor-free days, mean (SD)</td>
<td>6.8 (7.9)</td>
<td>5.6 (8.9)</td>
<td>1.2 (2.7 to 5.1)*</td>
<td>0.54</td>
</tr>
<tr>
<td><strong>Other outcomes</strong></td>
<td></td>
<td></td>
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<tr>
<td>Ventilation-free days, mean (SD)</td>
<td>6.7 (7.7)</td>
<td>8.1 (10.9)</td>
<td>-1.4 (-5.8 to 2.9)*</td>
<td>0.51</td>
</tr>
<tr>
<td>Renal replacement therapy-free days, mean (SD)</td>
<td>6.7 (7.8)</td>
<td>6.4 (10.6)</td>
<td>0.2 (-4.0 to 4.5)*</td>
<td>0.92</td>
</tr>
<tr>
<td>ICU length of stay for ICU survivors, d, mean (SD)</td>
<td>9.2 (6.4)</td>
<td>9.6 (6.0)</td>
<td>-0.4 (-5.4 to 4.5)*</td>
<td>0.86</td>
</tr>
<tr>
<td>Hospital length of stay for hospital survivors, d, mean (SD)</td>
<td>27.2 (12.8)</td>
<td>43.3 (34.0)</td>
<td>-16.1 (-54.5 to 22.4)*</td>
<td>0.90</td>
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<tr>
<td><strong>Complications</strong></td>
<td></td>
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<tr>
<td>Shock relapse, no. (%)</td>
<td>14 (36)</td>
<td>5 (14)</td>
<td>2.46 (0.98 to 6.21)</td>
<td>0.03</td>
</tr>
<tr>
<td>Arrhythmia, no. (%)</td>
<td>10 (26)</td>
<td>6 (17)</td>
<td>1.54 (0.62 to 3.80)</td>
<td>0.34</td>
</tr>
<tr>
<td>Gastrointestinal bleeding, no. (%)</td>
<td>13 (33)</td>
<td>4 (11)</td>
<td>3.00 (1.08 to 8.36)</td>
<td>0.02</td>
</tr>
<tr>
<td>Hyperglycemia &gt; 10 mmol/L, no. (%)</td>
<td>34 (87)</td>
<td>25 (69)</td>
<td>1.26 (0.98 to 1.61)</td>
<td>0.06</td>
</tr>
<tr>
<td>Ventilator-associated pneumonia, no. (%)</td>
<td>8 (21)</td>
<td>3 (8)</td>
<td>2.46 (0.71 to 8.57)</td>
<td>0.14</td>
</tr>
<tr>
<td>ICU-acquired bacteremia, no (%)</td>
<td>14 (36)</td>
<td>15 (42)</td>
<td>0.86 (0.49 to 1.52)</td>
<td>0.61</td>
</tr>
</tbody>
</table>
Causes of death in Cirrhosis + Septic Shock

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 25)</th>
<th>Group 2 (n = 50)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refractory shock (n)</td>
<td>0</td>
<td>20</td>
<td>.001</td>
</tr>
<tr>
<td>Type-1 hepatorenal syndrome (n)</td>
<td>2</td>
<td>3</td>
<td>NS</td>
</tr>
<tr>
<td>Liver failure (n)</td>
<td>4</td>
<td>4</td>
<td>NS</td>
</tr>
<tr>
<td>Variceal bleeding (n)</td>
<td>0</td>
<td>4</td>
<td>NS</td>
</tr>
<tr>
<td>Fungal infection (n)</td>
<td>2</td>
<td>0</td>
<td>NS</td>
</tr>
</tbody>
</table>

Group 1- adrenal function assessed, IV hydrocortisone if AI (17 patients- 68%)

Group 2- no assessment of adrenal function, no IV hydrocortisone
Corticosteroid therapy is controversial.
Hyponatremia in Cirrhosis

- Prevalence is 21.6% with cut-off of 130 (40% if 135)
- Impaired renal capacity to eliminate free water
Water handling in healthy subjects

Water handling in cirrhosis
Hyponatremia in Cirrhosis

- Poor prognostic indicator
  - Risk factor for hepatic encephalopathy
  - Can be associated with renal failure
  - Patients generally have to be free water restricted
  - Worse prognosis after transplant
Take Home Points

• AI is over-estimated in cirrhosis based on total cortisol, more standardization of free cortisol levels is needed in this population
• Effect of steroids in critically ill liver patients is still controversial
• Pathophysiology of hyponatremia in cirrhosis
References
