Portal Vein Diameter in Patients with Liver Cirrhosis and Hepatic Encephalopathy

Elwir S, Hal H, Veith J, Schreibman I, Kadry Z, Riley T

Abstract P246, Poster Presentation
ACG 2012 Annual Scientific Meeting and Postgraduate Course
Las Vegas, NV
October 21, 2012
Portal Vein Diameter in Patients with Liver Cirrhosis and Hepatic Encephalopathy: Objective

Objective: To assess the correlation between hepatic encephalopathy (HE) with findings detected on radiographic imaging studies and the patient’s clinical profile

Portal Vein Diameter in Patients with Liver Cirrhosis and Hepatic Encephalopathy: Methods

- Retrospective review of patients evaluated in the liver transplant clinic in 2009 and 2010
  - Excluded patients with HCC, ejection fraction <60%, and patients who had a TIPS procedure
  - Patient’s imaging studies were correlated with their baseline demographics, medical history, and clinical presentation
- Variables found to be significant on univariate analysis ($P<0.05$) were analyzed by multivariate logistic regression model

Portal Vein Diameter in Patients with Liver Cirrhosis and Hepatic Encephalopathy: Results

- 117 patients met inclusion criteria; divided into an HE group (n=58) and a control group (n=59) based on whether or not they had clinical evidence of HE
- Mean portal vein diameter:
  - HE group: 12.1 ± 2.9 mm
  - Control group: 14 ± 3.1 mm (P=0.001)
- 1-mm increase in portal vein diameter is associated with a 15% decrease in the odds of encephalopathy (OR 0.85; 95% CI 0.73-0.99)

Portal Vein Diameter in Patients with Liver Cirrhosis and Hepatic Encephalopathy: Results (cont)

• Significant correlation with HE on univariate analysis:
  – Smaller portal vein diameter
  – Smaller liver anteroposterior diameter
  – Diuretic use
  – Use of centrally acting medications
  – Liver nodularity

• Significant correlation with HE on multivariate analysis:
  – Portal vein diameter
  – Use of diuretics
  – Use of centrally acting medications

Portal Vein Diameter in Patients with Liver Cirrhosis and Hepatic Encephalopathy: Conclusion

- A decrease in portal vein diameter was associated with increased risk of HE
- Identifying patients with smaller portal vein diameter may warrant screening for HE by more advanced psychometric testing, protein restriction, and more aggressive control of constipation and other factors that may precipitate encephalopathy

Probiotics in Minimal Hepatic Encephalopathy: A Meta-Analysis

Agrawal M, Homel P, Badalov N, Mayer I, Rahmani R

Abstract P772, Poster Presentation
ACG 2012 Annual Scientific Meeting and Postgraduate Course
Las Vegas, NV
October 22, 2012
Probiotics in Minimal Hepatic Encephalopathy: Objective

- Objective: Meta-analysis of studies conducted to identify the role of probiotics in the management of minimal hepatic encephalopathy (MHE)

Probiotics in Minimal Hepatic Encephalopathy: Methods

- Search on Pubmed and Medview to identify randomized controlled trials (RCT) on probiotics in minimal hepatic encephalopathy (MHE) in last 20 years
- Eligible studies had to include at least 2 randomized groups with a pre/post comparison of mean ± SD of serum ammonia levels
  - 5 studies compared probiotics vs placebo/no treatment
  - 3 studies compared probiotics vs. lactulose
- Analyses done using Comprehensive Met Analysis 2.2

Probiotics in Minimal Hepatic Encephalopathy: Results

- Treatment with probiotics was:
  - Superior to placebo ($P=0.006$)
  - Superior to lactulose ($P=0.02$)

- Standardized difference (95% CI):
  - Probiotics vs. placebo: 0.44 (0.13, 0.75)
  - Probiotics vs. lactulose: 0.32 (0.06, 0.58)

Probiotics in Minimal Hepatic Encephalopathy: Results (cont)

Studies comparing probiotics with placebo/no treatment

<table>
<thead>
<tr>
<th>Study</th>
<th>Std diff in means</th>
<th>SE</th>
<th>Variance</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-Value</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saji et al, 2011</td>
<td>-0.212</td>
<td>0.317</td>
<td>0.101</td>
<td>-0.833</td>
<td>0.410</td>
<td>-0.667</td>
<td>0.505</td>
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<td>Pereg et al, 2011</td>
<td>0.515</td>
<td>0.339</td>
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<td>-0.149</td>
<td>1.179</td>
<td>1.521</td>
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<td>Bajaj et al, 2008</td>
<td>-0.121</td>
<td>0.444</td>
<td>0.197</td>
<td>-0.990</td>
<td>0.749</td>
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<td>Malaguamera et al, 2007</td>
<td>0.551</td>
<td>0.263</td>
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<td>Liu et al, 2004</td>
<td>8.509</td>
<td>1.073</td>
<td>1.151</td>
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<td>10.612</td>
<td>7.931</td>
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<td>0.439</td>
<td>0.160</td>
<td>0.026</td>
<td>0.125</td>
<td>0.752</td>
<td>2.741</td>
<td>0.006</td>
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</tbody>
</table>

Probiotics in Minimal Hepatic Encephalopathy: Results (cont)

Standard differences and 95% CI in studies comparing probiotics with placebo/no treatment

Probiotics in Minimal Hepatic Encephalopathy: Results (cont)

Studies comparing probiotics with lactulose

<table>
<thead>
<tr>
<th>Study</th>
<th>Std diff in means</th>
<th>SE</th>
<th>Variance</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-Value</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maguamera et al, 2009</td>
<td>0.394</td>
<td>0.181</td>
<td>0.033</td>
<td>0.040</td>
<td>0.748</td>
<td>2.181</td>
<td>0.029</td>
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<td>Sharma et al, 2007</td>
<td>0.015</td>
<td>0.247</td>
<td>0.061</td>
<td>-0.469</td>
<td>0.498</td>
<td>0.060</td>
<td>0.953</td>
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<tr>
<td>Loguercio et al, 1994</td>
<td>0.639</td>
<td>0.333</td>
<td>0.111</td>
<td>-0.013</td>
<td>1.291</td>
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<td>0.055</td>
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<tr>
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<td>0.322</td>
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<td>0.018</td>
<td>0.061</td>
<td>0.584</td>
<td>2.415</td>
<td>0.016</td>
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</table>

Probiotics in Minimal Hepatic Encephalopathy: Results (cont)

Standard differences and 95% CI in studies comparing probiotics with lactulose

Malaguamera et al, 2009
Sharma et al, 2007
Loguercio et al, 1994

Probiotics in Minimal Hepatic Encephalopathy: Conclusion

• Results indicate the beneficial role of probiotics in lowering serum ammonia levels in MHE patients
• Results compare favorably with lactulose, with possibly fewer adverse effects such as diarrhea and bloating
• Large randomized controlled trials are warranted to further validate the role of probiotics in MHE

Does Inhibitory Control Test (ICT) Diagnose Minimal Hepatic Encephalopathy (MHE)?

Allampati S, Prakash R, Perzynski A, Theethira T, Mullen K

Abstract P804, Poster Presentation
ACG 2012 Annual Scientific Meeting and Postgraduate Course
Las Vegas, NV
October 22, 2012
Inhibitory Control Test for Diagnosis of Minimal Hepatic Encephalopathy: Objective

- Objective: To study the reliability and validity of the Inhibitory Control Test (ITC) for the diagnosis of minimal hepatic encephalopathy (MHE)

Inhibitory Control Test for Diagnosis of Minimal Hepatic Encephalopathy: Methods

- 68 outpatient cirrhotics included in study
- Inclusion criterion: Presence of cirrhosis proven by biopsy or ultrasound regardless of cause
- Exclusion criteria: Presence of overt hepatic encephalopathy (OHE) on presentation to the clinic or history of OHE ≤30 days prior
- Full batteries of the Psychometric Hepatic Encephalopathy Score (PHES) and the Inhibitory Control Test (ICT) were administered
- Controls for PHES were generated by testing >100 healthy volunteers

Inhibitory Control Test for Diagnosis of Minimal Hepatic Encephalopathy: Results (cont)

- Patients with cirrhosis had lower scores on all PHES domains than the healthy control group
  - Patients with cirrhosis were categorized as MHE+ if they exhibited a score ≥2 SD below the healthy controls in ≥1 tests
  - Using this criteria, 36/68 (52.9%) of the cirrhosis patients were diagnosed as MHE+ and 32/68 (47.1%) were MHE-
- MHE+ patients performed significantly worse on ICT than MHE- patients
- Mean ICT values for MHE+ and MHE- cirrhotics were higher than seen in prior studies

### Inhibitory Control Test for Diagnosis of Minimal Hepatic Encephalopathy: Results (cont)

Comparison of PHES results between controls and cirrhotics

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=104)</th>
<th>Cirrhotics (n=68)</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>48.9</td>
<td>55.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Education (years)</td>
<td>14.4</td>
<td>12.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>NCT-A (seconds)</td>
<td>29.6</td>
<td>44.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>NCT-B (seconds)</td>
<td>72.3</td>
<td>123.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>DST (raw score)</td>
<td>50.4</td>
<td>37.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>SDT (seconds)</td>
<td>64.3</td>
<td>99.4</td>
<td>&lt;.001</td>
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</tbody>
</table>
Inhibitory Control Test for Diagnosis of Minimal Hepatic Encephalopathy: Results (cont)

Comparison of PHES and ITC results in cirrhotics with and without MHE

<table>
<thead>
<tr>
<th></th>
<th>With MHE (n=36)</th>
<th>Without MHE (n=32)</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57.9</td>
<td>53.6</td>
<td>.039</td>
</tr>
<tr>
<td>Education (years)</td>
<td>11.9</td>
<td>12.5</td>
<td>.304</td>
</tr>
<tr>
<td>NCT-A (seconds)</td>
<td>59.4</td>
<td>29.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>NCT-B (seconds)</td>
<td>165.5</td>
<td>78.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>DST (raw score)</td>
<td>29.3</td>
<td>45.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>SDT (seconds)</td>
<td>121.7</td>
<td>75.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Response to ICT lures (number out of 40)</td>
<td>17.8</td>
<td>11.3</td>
<td>.006</td>
</tr>
<tr>
<td>Response to ICT targets (percentage score)</td>
<td>81.1%</td>
<td>96.1%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Weighted lures</td>
<td>26.1</td>
<td>8.7</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Inhibitory Control Test for Diagnosis of Minimal Hepatic Encephalopathy: Conclusions

- Prior work has supported ICT as a reliable and valid test for the diagnosis of MHE
- Current study raises question regarding the threshold for the diagnosis of MHE with ICT since mean ICT values for MHE+ and MHE- cirrhotics were higher than seen in prior studies
Effect of Computer Literacy on Psychometric Test Performance in the Diagnosis of Minimal Hepatic Encephalopathy

Karanth P, Chikkanna R, Allampati S, Prakash R, Anna K, Mullen K, Perzynski A

Abstract P807, Poster Presentation
ACG 2012 Annual Scientific Meeting and Postgraduate Course
Las Vegas, NV
October 22, 2012
Effect of Computer Literacy on Psychometric Test Performance: Objective

• Objective: To study the effect of computer literacy on performance in a psychometric test (CNS Vital Signs) used in the diagnosis of minimal hepatic encephalopathy (MHE)

Effect of Computer Literacy on Psychometric Test Performance: Methods

- Cirrhotic patients between ages of 18 - 70 years were recruited prospectively from outpatient liver clinic
  - Received thorough clinical examination and mini mental status examination to rule out low grade overt hepatic encephalopathy
  - Patients asked about educational status, computer literacy, and handedness (left or right predominant)
  - Computer literacy assessed by asking patients whether they were frequent users, infrequent users, or non-users

- Patients subjected to paper and pencil psychometric test battery (Psychometric Hepatic Encephalopathy Score, PHES) and computerized psychometric test battery called CNS Vital Signs (CNSVS; available online at cnsvs.com)

Effect of Computer Literacy on Psychometric Test Performance: Results

- 57 patients recruited
  - 12 (21.1%) diagnosed as MHE+ with PHES
  - 11 (19.3%) diagnosed as MHE+ with CNSVS testing

- Level of education was not associated with performance on either PHES or CNSVS tests

Effect of Computer Literacy on Psychometric Test Performance: Results (cont)

• Patient self-reported computer usage was frequent (22.8%), infrequent (57.9%), and non-user (19.3%)
  – Computer usage was not associated with education level
  – Computer use had a small to moderate significant positive association (r=0.28 to r=0.48) on nearly all domains of the computerized and the paper and pencil tests
  – Mean time to complete number connection task was lower among frequent computer users (31.7 seconds) than among non-computer users (60.4 seconds, $P = 0.003$)
  – Frequent computer users were on average 18.1 seconds faster on the computerized processing speed test ($P = 0.001$)

Effect of Computer Literacy on Psychometric Test Performance: Conclusion

• Higher levels of computer usage are associated with better performance on cognitive tests in this sample of patients with liver disease
• Magnitude of the association is similar for both paper and pencil and computerized tests suggesting differences in cognitive performance rather than bias based upon testing medium
• Further research is necessary to determine how computer use (independently of education) influences performance in cognitive tests

Outcomes in Length of Hospital Stay in Cirrhotics Admitted for Overt Hepatic Encephalopathy


Abstract P926, Poster Presentation
ACG 2012 Annual Scientific Meeting and Postgraduate Course
Las Vegas, NV
October 22, 2012
Assessing Hospital Stays in Patients with Overt Hepatic Encephalopathy: Objective

Objective: To retrospectively investigate treatment regimens and their impact upon length of hospital stay in cirrhotics admitted for overt hepatic encephalopathy (OHE)

Assessing Hospital Stays in Patients with Overt Hepatic Encephalopathy: Methods

• Medical charts of hospitalized patients admitted with OHE (Conn Score grade 3 or 4) from December 2010 to May 2012 were evaluated

• Patients were grouped according to medication received prior to admission and medication received during hospitalization

• MELD score, HE management protocol, length of stay, time to starting a full diet, HE hospitalization number (frequency) and days to readmission were analyzed

### Assessing Hospital Stays in Patients with Overt Hepatic Encephalopathy: Results

<table>
<thead>
<tr>
<th>Group (outpatient therapy→hospital therapy)</th>
<th>n</th>
<th>MELD score (mean)</th>
<th>Length of Stay (days)</th>
<th>Time to start of full diet (days)</th>
<th>HCUP (7,500/d)</th>
<th>Insured/MC/MD costs (8,382/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Lac→Lac</td>
<td>18</td>
<td>11.5</td>
<td>5.75</td>
<td>4.1</td>
<td>43,125</td>
<td>48,147</td>
</tr>
<tr>
<td>(2) RFX→Lac</td>
<td>19</td>
<td>12.5</td>
<td>3.4</td>
<td>2.25</td>
<td>25,500</td>
<td>28,329</td>
</tr>
<tr>
<td>(3) Lac→RFX</td>
<td>20</td>
<td>10.5</td>
<td>4.25</td>
<td>3.5</td>
<td>31,875</td>
<td>35,624</td>
</tr>
<tr>
<td>(4) NT→Lac/RFX</td>
<td>14</td>
<td>11.5</td>
<td>5.25</td>
<td>3.8</td>
<td>39,375</td>
<td>44,006</td>
</tr>
<tr>
<td>(5) NT→Lac</td>
<td>28</td>
<td>13</td>
<td>6.5</td>
<td>4.5</td>
<td>48,750</td>
<td>54,483</td>
</tr>
</tbody>
</table>

MELD, Model for End-Stage Liver Disease; HCUP, Healthcare Cost & Utilization Project; Lac, Lactulose monotherapy; RFX, rifaximin monotherapy; Lac/RFX, lactulose + rifaximin combination therapy; NT, no treatment

Assessing Hospital Stays in Patients with Overt Hepatic Encephalopathy: Results (cont)

- Readmission: Groups discharged with Lac monotherapy performed worse amongst all groups
- Financial comparison: All Lac monotherapy groups approached $125-150,000 US within a six-month period
  - Escalated cost was based upon frequent repeat hospitalizations

Assessing Hospital Stays in Patients with Overt Hepatic Encephalopathy: Conclusion

- Patients maintained on RFX monotherapy outperformed all groups and utilized less healthcare dollars when compared to all LAC groups

Long Term Survival Following Overt Hepatic Encephalopathy


Abstract P927, Poster Presentation
ACG 2012 Annual Scientific Meeting and Postgraduate Course
Las Vegas, NV
October 22, 2012
Objective: To compare the long-term survival of overt hepatic encephalopathy (OHE) patients according to post discharge HE therapy.

Long Term Survival Following Overt Hepatic Encephalopathy: Methods

• Medical charts of outpatient and hospitalized patients admitted for OHE from December 2000 to May 2012 were examined

• Information collected included post discharge HE management protocol, HE hospitalization number (frequency), and time (days) to transplant or death

Four groups were identified: 1) Lactulose (Lac) monotherapy, 2) Lac combined with rifaximin (RFX), 3) RFX monotherapy, and, 4) No therapy.

RFX dose: Initially 1,200 mg/day dosing; later changed to 1,100 mg/day (550 mg twice/day).

Lac dose: 30 - 120 mL/day, adjusted to acquire 2 to 3 loose to soft bowel movements.

Long Term Survival Following OHE Depends on Post-Hospital Discharge Therapy


Lac vs. Lac/RFX, \( P=0.057 \); Lac vs. RFX, \( P=0.049 \)

Long Term Survival Following OHE Depends on Post-Hospital Discharge Therapy


Lac vs. Lac/RFX, $P=0.057$; Lac vs. RFX, $P=0.049$
Long Term Survival Following Overt Hepatic Encephalopathy: Conclusion

- The results reveal improvement in short and long-term survival with the addition of rifaximin to post-discharge management of patients following hospitalization for OHE compared to lactulose monotherapy or no therapy.
Readmission Rates and Maintenance of Overt Hepatic Encephalopathy


Abstract P1349, Poster Presentation
ACG 2012 Annual Scientific Meeting and Postgraduate Course
Las Vegas, NV
October 23, 2012
Readmission Rates and Maintenance of Overt Hepatic Encephalopathy: Objective

Objective: To evaluate the economic differences (primarily hospitalizations) associated with the various medical therapies for overt hepatic encephalopathy (OHE)

Readmission Rates and Maintenance of Overt Hepatic Encephalopathy: Methods

- Medical charts of outpatient and hospitalized patients admitted for OHE between December 2010 and May 2012 were examined.
- Information retrieved included MELD score, post-discharge HE management protocol, HE hospitalization number (frequency) and time to readmission (days, range), and health insurance coverage.
- Discharge therapies analyzed:
  - Group 1: Lactulose (Lac) monotherapy
  - Group 2: Rifaximin (RFX) monotherapy
  - Group 3: Lac/RFX combination therapy

Readmission Rates and Maintenance of Overt Hepatic Encephalopathy: Methods

- RFX dose was 1,100 mg/day (550 mg twice daily); Lac dose was 30 to 120 mL/day adjusted to acquire 2 to 3 loose of soft bowel movements
- Time from discharge to readmission and adherence to follow-up visits, maintenance of family support, and employment were measured
- Patients were divided according to compliance or noncompliance with outpatient follow-up

Economic Differences According to Treatment: Patients Compliant with Follow-Up

<table>
<thead>
<tr>
<th>Treatment</th>
<th>n</th>
<th>Events</th>
<th>MELD Score (mean)</th>
<th>Length of Time to Admission</th>
<th>Medicaid Time to Admission</th>
<th>Medicare Time to Admission</th>
<th>Insured Time to Admission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lac</td>
<td>21</td>
<td>44</td>
<td>12.2</td>
<td>55</td>
<td>25</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>RFX</td>
<td>10</td>
<td>15</td>
<td>13.5</td>
<td>65</td>
<td>33</td>
<td>48</td>
<td>55</td>
</tr>
<tr>
<td>Lac + RFX</td>
<td>18</td>
<td>30</td>
<td>13.0</td>
<td>56</td>
<td>32</td>
<td>50</td>
<td>45</td>
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</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Medication (Lac 720/yr; RFX 13,200/yr)</th>
<th>HCUP 38,500/6 days</th>
<th>Combined Total Cost</th>
<th>Total Mean Cost Per Patient</th>
<th>Cost Range Per Patient</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lac</td>
<td>73,440</td>
<td>3,927,000</td>
<td>4,000,440</td>
<td>61,545</td>
<td>39,220 - 122,545</td>
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<td>RFX</td>
<td>422,400</td>
<td>847,000</td>
<td>1,269,400</td>
<td>39,669</td>
<td>14,609 - 90,450</td>
<td>0.055</td>
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<tr>
<td>Lac + RFX</td>
<td>570,720</td>
<td>1,501,500</td>
<td>2,072,220</td>
<td>50,542</td>
<td>26,339 - 105,666</td>
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</table>

Economic Differences According to Treatment: Patients Non-Compliant with Follow-Up

<table>
<thead>
<tr>
<th>Treatment</th>
<th>n</th>
<th>Events</th>
<th>MELD Score (mean)</th>
<th>Length of Time to Admission</th>
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<td>13.5</td>
<td>65</td>
<td>33</td>
<td>48</td>
<td>55</td>
</tr>
<tr>
<td>Lac + RFX</td>
<td>18</td>
<td>30</td>
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<td>32</td>
<td>50</td>
<td>45</td>
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<th>HCUP 38,500/6 days</th>
<th>Combined Total Cost</th>
<th>Total Mean Cost Per Patient</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lac</td>
<td>15,120</td>
<td>1,694,000</td>
<td>1,709,120</td>
<td>81,387</td>
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<tr>
<td>RFX</td>
<td>132,000</td>
<td>577,500</td>
<td>709,500</td>
<td>70,950</td>
<td>0.035</td>
</tr>
<tr>
<td>Lac + RFX</td>
<td>252,680</td>
<td>693,000</td>
<td>945,680</td>
<td>52,538</td>
<td>0.065</td>
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HE Readmissions According to Treatment: Patients Non-Compliant with Follow-Up

<table>
<thead>
<tr>
<th>Treatment</th>
<th>n</th>
<th>Events</th>
<th>Frequency of 2nd Admission (%)</th>
<th>Time to 2nd Admission (Days)</th>
<th>Frequency of 3rd Admission (%)</th>
<th>Time to 3rd Admission (Days)</th>
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</thead>
<tbody>
<tr>
<td>Lac</td>
<td>21</td>
<td>44</td>
<td>66%</td>
<td>55</td>
<td>40%</td>
<td>59</td>
</tr>
<tr>
<td>RFX</td>
<td>10</td>
<td>15</td>
<td>40%</td>
<td>110</td>
<td>10%</td>
<td>145</td>
</tr>
<tr>
<td>Lac + RFX</td>
<td>18</td>
<td>30</td>
<td>48%</td>
<td>54</td>
<td>15%</td>
<td>58</td>
</tr>
</tbody>
</table>

Readmission Rates and Maintenance of Overt Hepatic Encephalopathy: Conclusion

• Choice of maintenance therapy following an OHE episode has a significant effect on overall costs associated with overt hepatic encephalopathy

• Rifaximin is nearly 50% more cost efficient than lactulose monotherapy or lactulose/rifaximin combination therapy
  – Rifaximin therapy results in less frequent hospitalizations and longer intervals between readmissions

The Liver Meeting®
The 63rd Annual Meeting of the American Association for the Study of Liver Diseases
NOVEMBER 9-13
HYNES CONVENTION CENTER • BOSTON, MASSACHUSETTS, USA
Randomized, Controlled, Double Blind Study of Glycerol Phenylbutyrate in Patients with Cirrhosis and Episodic Hepatic Encephalopathy


Abstract 112, Oral Presentation
The Liver Meeting® 2012
The 63rd Annual Meeting of the American Association for the Study of Liver Diseases
Boston, MA
November 12, 2012
Glycerol Phenylbutyrate in Patients with Cirrhosis and Episodic Hepatic Encephalopathy: Objective

- Objective: To evaluate the efficacy and safety of glycercyl tri(4phenylbutyrate) [GPB] in patients with episodic hepatic encephalopathy (HE)
  - GPB is an investigational drug which lowers ammonia (NH₃) through metabolism to phenylacetylglutamine, a urea surrogate excreted in urine

Glycerol Phenylbutyrate in Patients with Cirrhosis and Episodic Hepatic Encephalopathy: Methods

- Randomized, placebo-controlled, double-blind study
- Enrolled patients with $\geq 2$ West Haven Grade $\geq 2$ HE episodes in the prior 6 months while on standard of care (SOC, lactulose and/or rifaximin)
  - Enrollment stratified for rifaximin use
- Patients could remain on study and SOC could be changed after their first HE event

Glycerol Phenylbutyrate in Patients with Cirrhosis and Episodic Hepatic Encephalopathy: Methods (cont)

• Primary endpoint: Proportion of patients with at least one HE event
• Secondary endpoints: Total HE events, hospitalizations, symptomatic days as assessed using Clinical Hepatic Encephalopathy Staging Scale (CHESS), and venous NH$_3$

# Glycerol Phenylbutyrate in Patients with Cirrhosis and Episodic Hepatic Encephalopathy: Results


<table>
<thead>
<tr>
<th>All Patients</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GPB</td>
<td>Placebo</td>
<td>P value</td>
</tr>
<tr>
<td>Number of patients</td>
<td>90</td>
<td>88</td>
<td>--</td>
</tr>
<tr>
<td>Patients with at least one HE event (ITT; 1° analysis)</td>
<td>21%</td>
<td>36%</td>
<td>0.021</td>
</tr>
<tr>
<td>Total HE events</td>
<td>35</td>
<td>57</td>
<td>0.035</td>
</tr>
<tr>
<td>Days with CHESS score ≥3</td>
<td>13</td>
<td>27</td>
<td>0.015</td>
</tr>
<tr>
<td>HE hospitalizations</td>
<td>13</td>
<td>25</td>
<td>0.064</td>
</tr>
<tr>
<td>HE hospital days</td>
<td>66</td>
<td>134</td>
<td>NA</td>
</tr>
<tr>
<td>NH₃–time-normalized AUC (µmol/L)</td>
<td>45</td>
<td>58</td>
<td>0.037</td>
</tr>
</tbody>
</table>

Glycerol Phenylbutyrate in Patients with Cirrhosis and Episodic Hepatic Encephalopathy: Results (cont)


<table>
<thead>
<tr>
<th>Rifaximin naive</th>
<th>GPB</th>
<th>Placebo</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>60</td>
<td>59</td>
<td>--</td>
</tr>
<tr>
<td>Patients with at least one HE event</td>
<td>10%</td>
<td>32%</td>
<td>0.003</td>
</tr>
<tr>
<td>Patients with an HE event, WH ≥2</td>
<td>5%</td>
<td>28%</td>
<td>0.001</td>
</tr>
<tr>
<td>Total HE events</td>
<td>6</td>
<td>19</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

Rifaximin naive

<table>
<thead>
<tr>
<th>Rifaximin naive</th>
<th>GPB</th>
<th>Placebo</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>60</td>
<td>59</td>
<td>--</td>
</tr>
<tr>
<td>Patients with at least one HE event</td>
<td>10%</td>
<td>32%</td>
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<tr>
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<td>28%</td>
<td>0.001</td>
</tr>
<tr>
<td>Total HE events</td>
<td>6</td>
<td>19</td>
<td>0.0002</td>
</tr>
</tbody>
</table>
Glycerol Phenylbutyrate in Patients with Cirrhosis and Episodic Hepatic Encephalopathy: Results (cont)

Rifaximin at baseline

<table>
<thead>
<tr>
<th></th>
<th>GPB</th>
<th>Placebo</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>30</td>
<td>29</td>
<td>--</td>
</tr>
<tr>
<td>Patients with at least one HE event</td>
<td>13%</td>
<td>13%</td>
<td>0.909</td>
</tr>
<tr>
<td>HE hospitalizations</td>
<td>11</td>
<td>20</td>
<td>0.095</td>
</tr>
<tr>
<td>HE Hospital days</td>
<td>57</td>
<td>90</td>
<td>NA</td>
</tr>
</tbody>
</table>

Rifaximin at baseline or after 1st event

<table>
<thead>
<tr>
<th></th>
<th>GPB</th>
<th>Placebo</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>31</td>
<td>38</td>
<td>--</td>
</tr>
<tr>
<td>Patients with at least one HE event</td>
<td>13%</td>
<td>22%</td>
<td>0.190</td>
</tr>
</tbody>
</table>

Glycerol Phenylbutyrate in Patients with Cirrhosis and Episodic Hepatic Encephalopathy: Results (cont)

- The study met its primary and key secondary endpoints
- GBP significantly reduced NH$_3$
  - Reduction correlated with HE events at baseline ($P=0.0001$) and during the study ($P=0.0109$)
Glycerol Phenylbutyrate in Patients with Cirrhosis and Episodic Hepatic Encephalopathy: Results (cont)

- Adverse events (AEs) were similar on GPB (78.9%) vs. placebo (76.1%)
  - Most common: Nausea, diarrhea, abdominal pain and increased AST
- There were no changes in MELD score, liver or other laboratory tests
- 3 patients died (2 on GPB, 1 on placebo; all unrelated)
- Serious AEs occurred in 20 patients on GPB (1 related) and 12 patients on placebo (4 related)
  - GI bleeding and UTIs were the most common
  - 66% of Child-Pugh C patients experienced SAEs
Conclusion

- GPB reduces HE events in patients with episodic HE
- NH$_3$ is important in HE pathogenesis
- GPB warrants further development for the treatment of HE
The Stroop Smartphone App is a Short and Valid Screening Tool for Minimal Hepatic Encephalopathy


Abstract 123, Oral Presentation
The Liver Meeting® 2012
The 63rd Annual Meeting of the American Association for the Study of Liver Diseases
Boston, MA
November 12, 2012
Stroop Smartphone App as Screening Tool for Minimal Hepatic Encephalopathy: Objective

- Stroop tasks have been used to evaluate psychomotor speed and cognitive flexibility and are now available as a smartphone app
- Objective: To validate the Stroop task iPod app for MHE screening

Stroop Smartphone App as Screening Tool for Minimal Hepatic Encephalopathy: Methods

• Stroop app has 2 settings:
  – Off: Subject identifies colors presented without words
  – On: Subject identifies colors of words written in discordant colors (e.g., “green” is written in blue color)

• Each run has 10 stimuli; a mistake ends the run immediately

• 2 training runs given for both settings

• Actual task run until 3 correct runs achieved

• Output: Time needed to complete the correct runs and number of trials needed to achieve 3 correct runs

Stroop Smartphone App as Screening Tool for Minimal Hepatic Encephalopathy: Methods (cont)

• Cirrhotics with/without overt hepatic encephalopathy (OHE) and age/education-matched healthy controls tested using the psychometric hepatic encephalopathy battery (PHES score ≤ -6 = minimal hepatic encephalopathy [MHE]) and the iPod Stroop app

• Outcomes compared:
  – Cirrhosis with/without MHE and OHE
  – Test/retest reliability (a subgroup was tested twice)
  – External validity (before and after MHE treatment)

### Stroop Smartphone App as Screening Tool for Minimal Hepatic Encephalopathy: Results

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=47)</th>
<th>All cirrhotics (n=86)</th>
<th>Cirrhotics without OHE (n=58)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>MHE (n=38)</td>
<td>no MHE (n=48)</td>
</tr>
<tr>
<td>Stroop off time (sec)</td>
<td>35.5 ± 5.2</td>
<td>57.0 ± 13.1*†</td>
<td>41.3 ± 7.2</td>
</tr>
<tr>
<td>Stroop on time (sec)</td>
<td>43.2 ± 6.5</td>
<td>71.3 ± 20.7*†</td>
<td>50.2 ± 9.3</td>
</tr>
<tr>
<td>No. of trials for 3 correct off (median)</td>
<td>3</td>
<td>3.5*</td>
<td>3.5</td>
</tr>
<tr>
<td>No. of trials for 3 correct on (median)</td>
<td>3</td>
<td>4*†</td>
<td>3</td>
</tr>
</tbody>
</table>

* P<0.05 compared to controls; † P<0.05 compared to no-MHE

• Test-Retest reliability
  – 15 subjects underwent Stroop Test twice 45 ± 15 days apart
  – There was no significant difference
    • Off: Pre 42.5 sec; post 41.2 sec ($P=0.4$)
    • On: Pre 50.2 sec; post 47.8 sec ($P=0.08$)

• External validity
  – MHE treatment significantly reduced time taken on Stroop
    • Off: Pre 48 sec; post 44 sec ($P=0.02$)
    • On: Pre 61 sec; post 55.3 sec ($P=0.009$)
Stroop Smartphone App as Screening Tool for Minimal Hepatic Encephalopathy: Results (cont)

- **ROC/sensitivity**
  - Total time in Stroop off state >45.5 seconds had highest AUC and sensitivity for MHE diagnosis
    - All patients: AUC = 0.89; sensitivity = 90%
    - Patients without OHE: AUC = 0.83; sensitivity = 87%

- **Testing/training time was <6 minutes**
Stroop Smartphone App as Screening Tool for Minimal Hepatic Encephalopathy: Conclusion

• Stroop task, using a smart phone app, is a quick, reliable and valid tool for diagnosing MHE

Efficacy and Safety of a Probiotic Preparation in the Secondary Prophylaxis of Hepatic Encephalopathy in Cirrhotic Patients: Interim Results of a Double Blind, Randomized, Placebo Controlled Study

Dhiman RK, Rana BS, Garg A, Khattri A, Chopra M, Thumburu KK, Malhotra S, Duseja AK, Chawla YK

Abstract 124, Oral Presentation
The Liver Meeting® 2012
The 63rd Annual Meeting of the American Association for the Study of Liver Diseases
Boston, MA
November 12, 2012
Probiotic Preparation in the Secondary Prophylaxis of Hepatic Encephalopathy: Objective

- Objective: To assess the efficacy of a probiotic preparation for the prevention of HE recurrence, the reduction in hospitalizations, and in improving the severity of liver disease in cirrhotic patients
Probiotic Preparation in the Secondary Prophylaxis of Hepatic Encephalopathy: Methods

- Randomized, double-blind, placebo-controlled trial
- 103 patients with liver cirrhosis who have recovered from an episode of HE during the previous 1 month were randomly assigned to receive for 6 months either:
  - Probiotic preparation (VSL#3, CD Pharma India Pvt. Ltd, New Delhi) at a dose of 900 billion bacteria daily (n=51)
  - Placebo (n=52)
- Primary efficacy end point: Time to first breakthrough episode of HE
- Key secondary end points: Time to hospitalization, improvement in severity of liver disease, and blood ammonia and cytokine levels

Probiotic Preparation in the Secondary Prophylaxis of Hepatic Encephalopathy: Results

<table>
<thead>
<tr>
<th></th>
<th>Probiotic (n=51)</th>
<th>Placebo (n=52)</th>
<th>Hazard Ratio; (95% CI);</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalizations overall (%)</td>
<td>19.6%</td>
<td>42.3%</td>
<td>0.45 (0.21-0.95)</td>
<td>0.036</td>
</tr>
<tr>
<td>Hospitalizations involving HE (%)</td>
<td>15.7%</td>
<td>36.5%</td>
<td>0.42 (0.18-0.95)</td>
<td>0.037</td>
</tr>
</tbody>
</table>

• There was a trend in the reduction in the risk of an HE episode for probiotic, as compared with placebo, over a 6-month period [Hazard ratio 0.66 (95% CI, 0.33-1.34); P=0.258]
Probiotic Preparation in the Secondary Prophylaxis of Hepatic Encephalopathy: Results

<table>
<thead>
<tr>
<th></th>
<th>Probiotic (n=51)</th>
<th>Placebo (n=52)</th>
<th>P value</th>
<th>Probiotic (n=51)</th>
<th>Placebo (n=52)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>After 6 months</td>
<td></td>
<td>Baseline</td>
<td>After 6 months</td>
<td></td>
</tr>
<tr>
<td>CTP score (95% CI)</td>
<td>8.5 (7.6-9.4)</td>
<td>7.2 (6.6-7.8)</td>
<td>0.009</td>
<td>7.9 (7.1-8.5)</td>
<td>6.6 (5.5-7.8)</td>
<td>0.08</td>
</tr>
<tr>
<td>Serum IL-6 (95% CI)</td>
<td>60.3 (35.8-84.7)</td>
<td>33.4 (19.4-47.3)</td>
<td>0.007</td>
<td>82.5 (28-137)</td>
<td>38 (19.9-56)</td>
<td>0.09</td>
</tr>
<tr>
<td>Blood ammonia</td>
<td>No significant change</td>
<td>No significant change</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- The incidence of adverse events reported during the study was similar in the two groups; there was no serious adverse event

Probiotic Preparation in the Secondary Prophylaxis of Hepatic Encephalopathy: Conclusion

- Treatment with probiotic over a 6-month period significantly reduced:
  - The risk of hospitalization involving HE
  - CTP score
  - IL-6 levels

A Randomized Trial of Polyethylene Glycol 3350-Electrolyte Solution (PEG) and Lactulose for Patients Hospitalized with Acute Hepatic Encephalopathy

Rahimi RS, Singal AG, Cuthbert JA, Rockey DC

Abstract 1546, Poster Presentation
The Liver Meeting® 2012
The 63rd Annual Meeting of the American Association for the Study of Liver Diseases
Boston, MA
November 12, 2012
PEG 3350-Electrolyte Solution and Lactulose for Acute Hepatic Encephalopathy: Objective

- Prior animal models suggest that polyethylene glycol may be effective at clearing gut bacteria and reducing bacterial ammoniagenesis
- Objective: To compare polyethylene glycol 3350-electrolyte solution (PEG, Golytely®) and lactulose for the treatment of acute HE in hospitalized patients

PEG 3350-Electrolyte Solution and Lactulose for Acute Hepatic Encephalopathy: Methods

- Study involved patients with cirrhosis of any etiology hospitalized with HE at Parkland Memorial Hospital
  - Patients with causes of altered mental status other than HE were excluded
- Randomized patients 1:1 to receive lactulose per standard of care or PEG
- Severity of HE measured using hepatic encephalopathy scoring algorithm (HESA) at baseline and 24 hours
- Primary outcome: Absolute difference in HESA score at 24 hours
- Secondary outcome: Length of hospitalization

PEG 3350-Electrolyte Solution and Lactulose for Acute Hepatic Encephalopathy: Results

<table>
<thead>
<tr>
<th></th>
<th>Lactulose (n=25)</th>
<th>PEG (n=23)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline MELD score</td>
<td>18</td>
<td>15</td>
<td>0.94</td>
</tr>
<tr>
<td>Baseline Child Pugh score</td>
<td>9</td>
<td>10</td>
<td>0.31</td>
</tr>
<tr>
<td>Baseline ammonia level</td>
<td>141</td>
<td>152</td>
<td>0.95</td>
</tr>
<tr>
<td>Mean HESA score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline 24 hour value</td>
<td>2.3</td>
<td>2.3</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>1.6</td>
<td>0.9</td>
<td>0.002</td>
</tr>
<tr>
<td>Median length of hospitalization (days)</td>
<td>3</td>
<td>2</td>
<td>0.11</td>
</tr>
</tbody>
</table>

PEG 3350-Electrolyte Solution and Lactulose for Acute Hepatic Encephalopathy: Conclusions

- Peg improved HE over the first 24 hours of hospitalization significantly faster than lactulose and may result in shorter lengths of hospitalization.
- Data suggest that PEG may be superior to lactulose for treatment of patients hospitalized for acute HE.

A Critical Flicker Frequency Value of 32 Hz Predicts Recurrence of Overt Hepatic Encephalopathy in a Double-Blind, Placebo Controlled Trial of Rifaximin in Patients with Cirrhosis

Butterworth RF, Golden PL, Bortey E, Paterson C, Forbes WP

Abstract 1548, Poster Presentation
The Liver Meeting® 2012
The 63rd Annual Meeting of the American Association for the Study of Liver Diseases
Boston, MA
November 12, 2012
Critical Flicker Frequency Value of 32 Hz Predicts Recurrence of Overt Hepatic Encephalopathy in Rifaximin Trial: Objective

- Objective: To evaluate the association between the Critical Flicker Frequency (CFF) test and hepatic encephalopathy (HE) as assessed by the Conn score (CS) and to determine the time weighted average (TWA) frequency that is predictive of overt HE

Critical Flicker Frequency Value of 32 Hz Predicts Recurrence of Overt Hepatic Encephalopathy in Rifaximin Trial: Methods

- Rifaximin 550 mg BID for 6 months was evaluated in patients with cirrhosis who had ≥2 episodes of HE (CS ≥2) or CS and asterixis grade increase of 1 each if baseline CS=0.
- CFF (average of 8 replicate measurements) was measured at baseline and biweekly.
- Area under the curve for CFF was normalized to time on study to calculate time-weighted average (TWA).
Critical Flicker Frequency Value of 32 Hz Predicts Recurrence of Overt Hepatic Encephalopathy in Rifaximin Trial: Results

- Of 299 patients randomized to rifaximin (n=140) or placebo (n=159), 104 patients experienced HE (31 rifaximin and 73 placebo)
- Mean TWA correlated with overt HE (Spearman correlation coefficient= -0.62; P<0.0001)
- Area under the ROC curve value for CFF was 0.88 (95% CI= 0.84-0.92), reflecting high degree of predictive accuracy

Critical Flicker Frequency Value of 32 Hz Predicts Recurrence of Overt Hepatic Encephalopathy in Rifaximin Trial: Results

• Increasing quartiles of TWA were associated with lower rates of HE events ($P<0.0001$):
  – CFF Q1: $\leq 11$ Hz
  – CFF Q2: $>11$ to $\leq 32$ Hz
  – CFF Q3: $>32$ to $\leq 38$ Hz
  – CFF Q4: $>38$ Hz

• An optimal TWA cut-off of $\leq 32$ Hz was predictive of overt HE (hazard ratio=0.44, 95% CI=0.020-0.097, $p<0.0001$)

Critical Flicker Frequency Value of 32 Hz Predicts Recurrence of Overt Hepatic Encephalopathy in Rifaximin Trial: Conclusion

- The CFF test independently predicted breakthrough HE
- A cut-off of \( \leq 32 \text{ Hz} \) was predictive of overt HE
- Findings establish CFF as a viable alternative or adjunct to CS grading of HE in patients with cirrhosis

Oral Branched-Chain Amino Acids for Hepatic Encephalopathy: Systematic Review of Individual Patient Data from Randomized Clinical Trials

Gluud LL, Dam G, Borre M, Les I, Cordoba J, Marchesini G, Aagaard NK, Risum N, Vilstrup HV

Abstract 1584, Poster Presentation
The Liver Meeting® 2012
The 63rd Annual Meeting of the American Association for the Study of Liver Diseases
Boston, MA
November 12, 2012
Objective

Objective: To systematically review effects of oral branched chain amino acids (BCAAs) vs. control supplements or placebo for patients with recurrent overt or minimal hepatic encephalopathy (HE)

Oral Branched Chain Amino Acids for Hepatic Encephalopathy Review: Methods

- Analyzed data from 8 randomized trials identified via electronic and manual searches
- Analyses included data on 382 patients with cirrhosis and HE
- Data retrieved by corresponding with the authors of the trials or from published reports
  - Individual patient data were available for 4 trials with 255 patients
  - Trial-level data were available for remaining 4 trials

Oral Branched Chain Amino Acids for Hepatic Encephalopathy Review: Results

- Improvements in HE manifestations were registered for 87 of 172 patients in the BCAA group vs. 56 of 210 controls
- Effect of BCAA was different for patients with overt vs. minimal HE ($P=0.05$ for subgroup differences):

<table>
<thead>
<tr>
<th></th>
<th>Risk Difference, BCAA vs. Controls (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>0.21 (0.09 - 0.34)</td>
</tr>
<tr>
<td>Overt HE</td>
<td>0.30 (0.16 - 0.44)</td>
</tr>
<tr>
<td>Minimal HE</td>
<td>0.10 (-0.05 - 0.25)</td>
</tr>
</tbody>
</table>

- No other predictors of intertrial heterogeneity were identified

Oral Branched Chain Amino Acids for Hepatic Encephalopathy Review: Results (cont)

- BCAA supplements:
  - Had no effect on mortality or markers of nutritional status
  - Did not induce adverse events

Oral Branched Chain Amino Acids for Hepatic Encephalopathy Review: Conclusion

- Oral BCAA supplements improve the manifestations of recurrent HE but have no effect on survival
Predictors of Early Hepatic Encephalopathy in Patients Undergoing Transjugular Intrahepatic Portosystemic Shunt (TIPS)

Jow AZ, Chaudhary N, Merola J, Barboza K, Charles H, Sigal S

Abstract 1585, Poster Presentation
The Liver Meeting® 2012
The 63rd Annual Meeting of the American Association for the Study of Liver Diseases
Boston, MA
November 12, 2012
Predictors of Early Hepatic Encephalopathy Following TIPS: Objective

• Objective: To determine predictors of overt hepatic encephalopathy (HE) within 1 week, specifically the effect of hyponatremia (HN), in patients undergoing transjugular intrahepatic portosystemic shunt (TIPS) insertion
Predictors of Early Hepatic Encephalopathy Following TIPS: Methods

- A single-center, retrospective chart review of 114 consecutive adult patients with cirrhosis who underwent non-emergent TIPS insertion between 2005 and 2011 for non-variceal bleeding indications
- Baseline clinical and laboratory patient characteristics were collected
- A composite mean of serum Na levels was derived from the three days prior to TIPS (pre-TIPS Na)
- Wald $\chi^2$ analysis was conducted to identify significant clinical parameters associated with overt HE within 1 week
- Odds ratios were calculated to determine the relative risk of developing HE for each of the predictive variables

Predictors of Early Hepatic Encephalopathy Following TIPS: Results

- 74 patients who underwent 81 TIPS procedures were included
- Factors predictive of overt HE within 1 week:

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Wald χ²</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-tips Na</td>
<td>4.8</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>5.6</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>MELD-Na</td>
<td>6.1</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

- A history of HE and serum creatinine levels were not significantly associated with the development of OHE within 1 week following TIPS insertion

Predictors of Early Hepatic Encephalopathy Following TIPS: Results

• Odds ratio for developing HE:

<table>
<thead>
<tr>
<th>Clinical Parameter</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-tips Na &lt;135 mEq/L</td>
<td>10.3 (1.3 - 83.1)</td>
</tr>
<tr>
<td>Total bilirubin &gt;4.0 mg/dL</td>
<td>3.0 (0.9 - 10.0)</td>
</tr>
<tr>
<td>MELD-Na &gt;25</td>
<td>5.4 (1.6 - 18.7)</td>
</tr>
</tbody>
</table>

• Pre-TIPS Na categories vs. incidence of overt HE within 1 week:

<table>
<thead>
<tr>
<th>Na Categories</th>
<th>Incidence of HE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤124 mEq/L</td>
<td>37.5%</td>
</tr>
<tr>
<td>125 - 130 mEq/L</td>
<td>24%</td>
</tr>
<tr>
<td>131 - 134 mEq/L</td>
<td>26%</td>
</tr>
<tr>
<td>≥135 mEq/L</td>
<td>3.4%</td>
</tr>
</tbody>
</table>

Predictors of Early Hepatic Encephalopathy Following TIPS: Conclusion

• In patients with cirrhosis and portal hypertension undergoing TIPS insertion, lower pre-TIPS Na, higher total bilirubin, and higher MELD-Na values were predictive of the development of overt HE post-TIPS within 1 week.

• Predictive capability of pre-TIPS Na and MELD-Na for the development of HE indicates that TIPS insertion in patients with low Na levels should be undertaken with caution.

Improvement of Liver Function and Prevention of Encephalopathy by Occlusion of Porto-Systemic Shunt in Patients with Child-Turcrott-Pugh Class B Cirrhosis and Recurrent Hepatic Encephalopathy


Abstract 1586, Poster Presentation
The Liver Meeting® 2012
The 63rd Annual Meeting of the American Association for the Study of Liver Diseases
Boston, MA
November 12, 2012
Improvement of Liver Function and Prevention of HE by Occlusion of Porto-Systemic Shunt: Objective

• Objective: To analyze the effect of occlusion of large spontaneous porto-systemic shunts in preventing the recurrence of hepatic encephalopathy (HE)
Improvement of Liver Function and Prevention of HE by Occlusion of Porto-Systemic Shunt: Methods

- Data of 20 patients who underwent occlusion of a portosystemic shunt for recurrent HE between 2006 and 2011 in a single tertiary referral hospital were analyzed.

Improvement of Liver Function and Prevention of HE by Occlusion of Porto-Systemic Shunt: Results

• Patient demographics
  – Median age: 63 years (range, 48-79 years)
  – Males: 55%
  – Child-Turcott-Pugh (CTP) class:
    • Class B: 12
    • Class C: 8
Improvement of Liver Function and Prevention of HE by Occlusion of Porto-Systemic Shunt: Results (cont)

Cumulative overall survival rate after occlusion

- **Child B**: 89% (n=12)
- **Child C**: 20% (n=8)

*P < 0.01

Improvement of Liver Function and Prevention of HE by Occlusion of Porto-Systemic Shunt: Results (cont)

Number of HE episodes and hospitalizations due to HE*

<table>
<thead>
<tr>
<th></th>
<th>Before Occlusion</th>
<th>After Occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>HE episodes</td>
<td>60</td>
<td>10</td>
</tr>
<tr>
<td>Hospitalizations due to HE</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*3 month period before and 3 month period after occlusion

Improvement of Liver Function and Prevention of HE by Occlusion of Porto-Systemic Shunt: Results (cont)

- Shunt occlusion failed technically in 3 patients
- The median survival time for patients with CTP class C was 4 months
- Among patients with CTP class B, comparing 3 months before and after occlusion
  - HE episodes decreased: 4.83 vs. 0.08, P<0.01
  - HE hospitalizations decreased: 1.67 vs. 0.08, P<0.01
  - CTP score improved in 9/12 (75%)
  - MELD score improved in 6/12 (50%)
- Hepatic decompensation and hepatorenal syndrome after occlusion occurred in 3 CTP class 3 patients
Improvement of Liver Function and Prevention of HE by Occlusion of Porto-Systemic Shunt: Conclusions

• Occlusion of spontaneous porto-systemic shunts is effective in preventing HE, especially in patients with CTP class B; improvement in liver function can also be expected in some class B patients

• Shunt occlusion should be cautiously considered in patients with CTP class C
Assessing Treatment Patterns in Patients With Overt Hepatic Encephalopothy

Neff GW, Frederick RT

Abstract 1612, Poster Presentation
The Liver Meeting® 2012
The 63rd Annual Meeting of the American Association for the Study of Liver Diseases
Boston, MA
November 12, 2012
Treatment Patterns in Cirrhotic Patients Following an Overt HE Episode: Objective

• Background:
  – Overt hepatic encephalopathy (OHE) is associated with a substantial medical and financial burden
  – Patients who have had OHE are at increased risk of recurrence and may experience persistent cognitive impairment
  – Treatment after an OHE episode can increase the duration of HE remission, decrease HE-related hospitalizations, and improve quality of life

• Objective: To examine the outpatient treatment rates for patients who had $\geq 1$ episode of OHE from 2009 to 2011

Treatment Patterns in Cirrhotic Patients Following an Overt HE Episode: Methods

• Review of a subset of national claims for medical and hospital activity from January 2009 to December 2011 collected by Source Healthcare Analytics
  – Patient selection based on claims with and ICD-9 code 572.2 (HE) and any filled prescription in each calendar year
  – Claims from eligible patients were examined for any filled prescription for rifaximin (RFX), lactulose (Lac) or RFX + Lac as an indicator of ongoing treatment

## Treatment Patterns in Cirrhotic Patients Following an Overt HE Episode: Results

<table>
<thead>
<tr>
<th>Year</th>
<th>Eligible Patients with OHE</th>
<th>% of Eligible Patients with Inpatient Claims</th>
<th>% of Eligible Patients Receiving Ongoing Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>13,623</td>
<td>89.2%</td>
<td>39.7%</td>
</tr>
<tr>
<td>2010</td>
<td>15,529</td>
<td>87.8%</td>
<td>37.7%</td>
</tr>
<tr>
<td>2011</td>
<td>16,328</td>
<td>86.4%</td>
<td>36.1%</td>
</tr>
</tbody>
</table>

Treatment Patterns in Cirrhotic Patients Following an Overt HE Episode: Results

Change in treatment paradigm, 2009 vs. 2011

Treatment Patterns in Cirrhotic Patients Following an Overt HE Episode: Conclusions

- Despite medical and financial advantages of treatment after an episode of OHE, results suggest that majority of patients remain untreated as outpatients (63.9% in 2011)
- Treatment paradigm appears to have shifted following approval of RFX in 2010
- Whether low treatment rates are result of patients failing to fill prescriptions (lack of insurance, other financial concerns, and/or noncompliance) remains unclear
- Understanding causes of and correcting the apparent undertreatment of HE is essential