The Management of Ascites & Hepatorenal Syndrome

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Management of Ascites

**Sodium Restriction**

- Mandatory at all stages of ascites in order to reduce the rate of accumulation of ascites
Management of Ascites

**Diuretic Therapy**

- Blocks Na reabsorption at various nephron sites
- Increases renal Na excretion
- Potential for over-diuresis, dehydration, electrolyte abnormalities, renal dysfunction & hepatic encephalopathy
Management of Ascites

**Vasoconstrictor - Midodrine**

- 7.5mg t.i.d. for 7 days
- Delayed improvement in systemic and renal hemodynamics
- Delayed improvement in renal sodium excretion
- Reduction in vasoconstrictor levels
- Significant correlation between change in systemic hemodynamics & increase in GFR and increase in UNaV

*(Kalambokis et al, J Hepatol 2007)*
Management of Ascites

**Vasoconstrictor - Terlipressin**

✓ Placebo controlled study

✓ Patients with ascites

✓ Diuretic responsive or refractory

✓ Single I.V. dose of 2mg

✓ Improvement in GFR & Na clearance

✓ Suppression of renal vasoconstrictor systems

*(Krag et al, Hepatol 2007)*
Management of Ascites

**V₂ Receptor Antagonist-Satavaptan**

- Reduction in number of paracenteses versus placebo
- Relative risk of paracentesis was 0.69, 0.66, 0.63 for the 5 mg, 12.5 mg and 25 mg groups respectively
- Corresponding adjusted p-values are 0.026, 0.018, 0.017 for the three treated groups
**Management of Ascites**

**Albumin**
- Can improve effective arterial blood volume in cirrhosis
- Improves survival in patients with diuretic responsive ascites
- Cost (albumin & medical manpower) is prohibitive in some country
- Await definitive studies to establish albumin as treatment for refractory ascites

*(Gentilini et al, J Hepatology 1999)*
Refractory Ascites

- Weight loss ≤1.5kg/week while on 400mg of spironolactone or 30mg of amiloride plus 160mg of furosemide daily ≥ one week.

- Dietary sodium restriction ≤ 50mmol per day.

(Int Ascites Club, Hepatol 2003)
Transjugular Intrahepatic Porto-systemic stent Shunt (TIPS)

**TIPS**

- Effective in reducing sinusoidal portal pressure which is one of the pathogenetic mechanisms of ascites formation in cirrhosis

- Gradually eliminates ascites even in the absence of diuretic therapy
TIPS for Refractory Ascites

Serum Creatinine

UNaV

# p<0.01, *p<0.05
TIPS for Refractory Ascites

Ascites Control

Better TIPS Better paracentesis

(D’Amico et al, Gastroenterology 2005)
TIPS for Refractory Ascites

Survival

**Mortality**

<table>
<thead>
<tr>
<th>Study</th>
<th>Better TIPS</th>
<th>Better Paracentesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lebrec (1996)</td>
<td></td>
<td>4.50 (0.84, 24.18)</td>
</tr>
<tr>
<td>Rossle (2000)</td>
<td>0.37 (0.13, 1.10)</td>
<td></td>
</tr>
<tr>
<td>Gines (2003)</td>
<td>1.26 (0.49, 3.23)</td>
<td></td>
</tr>
<tr>
<td>Sanyal (2003)</td>
<td>1.16 (0.54, 2.51)</td>
<td></td>
</tr>
<tr>
<td>Salerno (2004)</td>
<td>0.42 (0.16, 1.13)</td>
<td></td>
</tr>
<tr>
<td>Overall (95% CI)</td>
<td>0.90 (0.44, 1.81)</td>
<td></td>
</tr>
<tr>
<td>Excluding Lebrec</td>
<td>0.74 (0.40, 1.37)</td>
<td></td>
</tr>
</tbody>
</table>

*(D’Amico G et al, Gastroenterology 2005)*
Survival

(Salerno, Wong et al, Gastroenterology 2007)
TIPS for Refractory Ascites

Survival

(Salerno, Wong et al, Gastroenterology 2007)
Hepatorenal Syndrome

Definition

A potentially reversible syndrome that occurs in patients with cirrhosis, ascites and liver failure, consisting of impaired renal function, marked abnormalities in cardiovascular function, and intense over-activity of the endogenous vasoactive systems

(International Ascites Club, Gut 2007)
Hepatorenal Syndrome

Clinical Presentation

Type 1

Rapid reduction in renal function in < 2W

: Doubling of initial serum creatinine to >2.5mg/dL

Or : 50% reduction of the initial 24 hour creatinine clearance to < 20ml/min

Severely ill patient
Jaundice
Coagulopathy

Type 2

Renal function slowly deteriorates over weeks to months

Occurs in cirrhotic patients with refractory ascites

Mild jaundice
Some degree of coagulopathy
Clinical Presentation - *Precipitation of Type 1 HRS*

Hepatorenal Syndrome

**Clinical Presentation**

**First Hit**
- Sinusoidal portal Hypertension
- Systemic arterial Vasodilatation
- Liver dysfunction

**Second hit**
- Hepatorenal Syndrome
Treatment for Hepatorenal Syndrome

**Albumin for Type 1 HRS**

- 26 patients
- Mean age: 60±3 years
- Male/female: 11/15
- Child-Pugh score: 11.2±0.8
- Serum creatinine: 256±105µmol/L
- Albumin 1gm/kg body weight on day 1, then 20-40gm/day for 2 weeks

*(Neri et al, Dig Dis Sci: 2008)*
Renal Function

Baseline | Discharge

Albumin for Type 1 HRS (Neri et al, Dig Dis Sci: 2008)

Mean Arterial Pressure

Baseline | Discharge

Treatment for Hepatorenal Syndrome

Albumin for Type 1 HRS

 Terlipressin + albumin

Albumin alone

Treatment for Hepatorenal Syndrome

0.5-2.0mg/4 hours terlipressin as i.v. boluses

1gm/kg of body weight of albumin on Day 1, then 20 to 40gm/day thereafter

Treatment for Hepatorenal Syndrome

Terlipressin & Albumin

(Sanyal A et al. Hepatology 2006)
Treatment for Hepatorenal Syndrome

Terlipressin & Albumin

Serum Creatinine

Mean Arterial Pressure

Treatment for Hepatorenal Syndrome

Norepinephrine

(Duvoux C. et al. Hepatology, 2002)
## Treatment for Hepatorenal Syndrome - TIPS

<table>
<thead>
<tr>
<th>Authors</th>
<th>n</th>
<th>year</th>
<th>Type of study</th>
<th>pre-TIPS creatinine</th>
<th>post-TIPS creatinine</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lake</td>
<td>8</td>
<td>1993</td>
<td>R</td>
<td>3.2±0.9mg/dl</td>
<td>↓ by 1.4mg/dl (5)</td>
<td>4/8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>unchanged (3)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3 with Tx</td>
<td></td>
</tr>
<tr>
<td>Spahr</td>
<td>1</td>
<td>1995</td>
<td>case report</td>
<td>6mg/dl</td>
<td>normal</td>
<td>2 M</td>
</tr>
<tr>
<td>Brensing</td>
<td>16</td>
<td>1997</td>
<td>PU (I &amp;II)</td>
<td>226±140µm/l</td>
<td>104±52µm/l</td>
<td>9/16</td>
</tr>
<tr>
<td>Guevara</td>
<td>7</td>
<td>1998</td>
<td>PU (I)</td>
<td>5.0±0.8mg/dl</td>
<td>1.8±0.4mg/dl</td>
<td>140±68D</td>
</tr>
<tr>
<td>Brensing</td>
<td>41</td>
<td>2000</td>
<td>PU (I &amp; II)</td>
<td>2.3±1.7mg/dl</td>
<td>1.5±1.2mg/dl</td>
<td>75±14 W</td>
</tr>
<tr>
<td>Testino</td>
<td>18</td>
<td>2003</td>
<td>PU (II)</td>
<td>1.9±0.5mg/dl</td>
<td>0.9±0.3mg/dl</td>
<td>12/18 Tx</td>
</tr>
</tbody>
</table>

R: retrospective study, PU: Prospective uncontrolled study, I = Type 1 HRS, II = Type II HRS
Treatment for Hepatorenal Syndrome- TIPS & Vasoconstrictors

(Wong F et al, Hepatology 2004)
Treatment for Hepatorenal Syndrome

**Liver Transplantation**

(B: pre-transplant  
A: post-transplant)

Great advances have been made in recent years in the management of ascites and hepatorenal syndrome. Choosing the appropriate therapy for a particular patient is key to successful treatment.

Early recognition of hepatorenal syndrome and early institution of treatment can be life saving.

All patients with difficult-to-manage ascites and with hepatorenal syndrome should be referred for liver transplantation.