LIVER TRANSPLANTATION AND VIRAL HEPATITIS

Eduardo Barroso
Hepato-Bílio-Pancreatic and Transplantation Center
Hospital Curry Cabral, Lisbon

Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010
Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010
Comparison between our center and other center’s results

Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010
João Rodrigues Pena

Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010
Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010
Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010
Our Experience as of October 2010

- 929 Kidney Transplants
- 1191 Liver Transplants

Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010
Transplant Etiology

CIR (39,9%)  DHM (21,1%)  PAF (32,0%)

FHF (6,5%)  DIV (0,5%)

Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010
## HCV Cirrhosis (n=193)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV cirrhosis alone</td>
<td>55</td>
</tr>
<tr>
<td>HCV + Alcoholic cirrhosis</td>
<td>50</td>
</tr>
<tr>
<td>HCV cirrhosis + HIV</td>
<td>4</td>
</tr>
<tr>
<td>HCV cirrhosis + CHC</td>
<td>83</td>
</tr>
<tr>
<td>NASH</td>
<td>1</td>
</tr>
<tr>
<td>Condition</td>
<td>Count</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>HBV cirrhosis alone</td>
<td>13</td>
</tr>
<tr>
<td>HBV + Alcoholic cirrhosis</td>
<td>6</td>
</tr>
<tr>
<td>FAP + HBV</td>
<td>5</td>
</tr>
<tr>
<td>FHF + HBV</td>
<td>13</td>
</tr>
<tr>
<td>HBV + cirrhosis + CHC</td>
<td>24</td>
</tr>
</tbody>
</table>

Viral Hepatitis Prevention Board Meeting  
Lisbon, November 2010
In the United States, about 40% of all liver transplants are performed due to HCV infection.

In our center:
- About 25% of all transplants have viral etiology (HBV + HCV)
- About 40% of all cirrhotic patients have viral etiology
FACT!

- Graft and patient survival in HCV Cirrhosis are inferior to other indications.

WHY?
Hepatic Cirrhosis and C Virus

- Infection occurs during reperfusion of the graft
  - Day 4: Viral Load matches the values before the transplantation
  - Day 10: C Virus Ag with hepatocitary expression in 25% of the patients
  - After 1 year: Viral load is 10 to 100 times higher than before the transplantation
- Hepatic lesion is established after three weeks

Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010
HCV Virus Graft Recurrence

- Dynamic process, within a highly variable disease progression pattern

  - Fibrosis
    - After Liver Transplantation: 0.3 to 0.8 stages/year
    - Non Liver Transplant: 0.1 to 0.2 stages/year

Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010
Dynamic process, within a highly variable disease progression pattern

- Cirrhosis development
  - After Liver Transplantion: 10 years
  - Non Liver Transplant: 20 to 40 years
Dynamic process, within a highly variable disease progression pattern

- Hepatic Disfuncion Risk
  - After Liver Transplantation:
    - 42% in the first year
    - 62% within 5 years
  - Non Liver Transplant:
    - Less than 5% in the first year
    - Less than 20% within 5 years

Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010
20-30% of patients with hepatic chronic disease will not develop clinical or biochemical hepatitis.

In the early post-transplantation period, histological alterations are dubious:
- Rejection?
- Preservation and reperfusion lesions?
By the third post-operative month
- HCV-RNA positive in all hosts
- 90% of liver biopsies have HCV Ag
## HCV Graft Recurrence

<table>
<thead>
<tr>
<th>Acute</th>
<th>Chronic</th>
<th>Cholestatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>70% (2-5 months)</td>
<td>Bridging Fibrosis</td>
<td>5% (1-6 months)</td>
</tr>
<tr>
<td>Bilirubin &lt; 6 mg/dL</td>
<td></td>
<td>Fibrosing Cholestatic Hepatitis</td>
</tr>
<tr>
<td>AST/ALT 2x normal</td>
<td></td>
<td>AST/ALT 2-5x normal</td>
</tr>
<tr>
<td>↑↑ VHC-RNA</td>
<td></td>
<td>Alkaline phosphatase &gt; 500 U/L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>GGT &gt; 1000 U/L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cytopathic lesion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HCV – RNA +</td>
</tr>
</tbody>
</table>

Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010
Risk factors associated with the severity of the recurrence

- Donor related
- Host related
- Viral
- Clinical
Therapeutic Strategies in HCV Graft recurrence

- Objectives
  - Viral Clearance
  - Sustained Viral Load

- Different timing approaches
  - Pre-Liver Transplantation
  - Peri-operative period
  - Post-Transplantation

Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010
Very polemic!

Risk factors associated with worse prognosis

- Total Bilirubin > 10mg/dL
- Creatinine > 2mg/dL
- Creatinine Clearance < 40ml/mn
- Patient Age > 55 yo
- Donor Age > 40 yo
- Early recurrence with Cirrhosis
The main purpose is to suppress viral replication before the transplant!
### Our protocol for HBV patients

<table>
<thead>
<tr>
<th>Status</th>
<th>Ag HBs +</th>
<th>Ag HBs +</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA HBV -</td>
<td>DNA HBV +</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pre-Transplant</th>
<th>No antiviral therapy</th>
<th>Agressive antiviral therapy</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Anhepatic period</th>
<th>10000 IU Hyper Imune gamaglobuline IV bolus</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>First week Post-transplant</th>
<th>1000 IU Hyper Imune gamaglobuline IM / day</th>
</tr>
</thead>
</table>

| Follow-up | 1000 IU Hyper Imune gamaglobuline IM / month + antiviral therapy |

---

Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010
Our results

Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010
Survival in HCV patients

- 81.0% at 1 year
- 76.4% at 5 years
- 74.6% at 10 years
- 57.0% at 10 years

Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010
Only chronic patients (fulminant hepatitis not contemplated)

Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010
Thanks to Dr. Ana Morbey for helping me in the preparation of this presentation!
Dear friend:

Wish you were here

António Costa Freire
1951-2009

Viral Hepatitis Prevention Board Meeting
Lisbon, November 2010