Clinical Performance of HBIg in Preventing Recurrent HBV After Liver Transplantation

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Orthotopic liver transplantation (OLT) remains the primary curative modality for end-stage liver disease from chronic hepatitis B (HBV) infection.

Initial attempts at OLT without immunoprophylaxis in this patient population resulted in over 80% re-infection of the allograft followed by accelerated graft failure.
Introduction

- Extra-hepatic reservoirs of HBV, such as peripheral blood mononuclear cells and various organs, likely contributed to the high rate of re-infection.

- These disappointing results caused many centers to abandon transplantation as a treatment option for chronic HBV infection in the late 1980s.
HBIg Immunotherapy

- A review of domestic and international reports on combination therapy with HBIg and a nucleoside analog after OLT reveals consistent results

- Low recurrence rates up to 5 years post-transplant

- Data covers all HBV patients, including patients with high viral loads
## Large Studies and Long-term Follow-up for HBIG Combination Therapy

<table>
<thead>
<tr>
<th>Author</th>
<th>Location</th>
<th># of Patients</th>
<th>Follow-up</th>
<th>Recurrences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roche 2003</td>
<td>France</td>
<td>24</td>
<td>60 months</td>
<td>2 (8.3%)</td>
</tr>
<tr>
<td>Aribizu 2003</td>
<td>Spain</td>
<td>14</td>
<td>58.8 (15-107) months</td>
<td>1 (7%)*</td>
</tr>
<tr>
<td>Honaker 2002</td>
<td>Univ. of Tenn, USA</td>
<td>9</td>
<td>4.2 +/- 1.0 yr</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Dumortier 2003</td>
<td>France</td>
<td>17</td>
<td>30 (12-48) months</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Marzano 2001</td>
<td>Italy</td>
<td>26</td>
<td>29 +/- 9 months</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Engler 2002</td>
<td>Germany</td>
<td>5</td>
<td>26.6 (20-36) months</td>
<td>1 (20%)*</td>
</tr>
<tr>
<td>Rosenau 2001</td>
<td>Germany</td>
<td>21</td>
<td>643 (73-1473) days</td>
<td>4 (19%)</td>
</tr>
<tr>
<td>Angus 2000</td>
<td>Australia-New Zealand</td>
<td>37</td>
<td>18.4 +/- 12.1 (5-45) months</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

*Recurrence occurred after deviation from HBIG protocol*
Alternatives

There are no good alternatives to HBIG for preventing recurrent HBV after OLT

**Lamivudine Monotherapy**

- Not a viable solution for all patients
- Routine development of escape mutants/drug resistance
- Historically 24-67% recurrence rate across all patients undergoing OLT for HBV
The UC Irvine Experience

- Patients with HBV-related end-stage liver failure, followed at our institution

- Transplanted between 1993 and 2001 to ensure long-term follow up

- After OLT, all patients received combination therapy with HBIg and lamivudine
The UC Irvine Experience

**HBIg Protocol**

- During the anhepatic phase, 10,000 IU of HBIg was given intravenously (IV) followed by 10,000 IU of HBIg IV daily for 6 days.
- Administration of HBIg was then changed to the intramuscular (IM) route and the frequency of doses was adjusted to maintain HBsAb titers above 150 IU/L.
- Patients were evaluated on a monthly basis for the presence of HBV DNA and HBsAg until the HBsAb titers stabilized at therapeutic levels.
- Thereafter, serology and HBsAb titers were checked every 2 months.
The UC Irvine Experience

Kaplan-Meier Survival
- 95.0% at 1-month
- 85.0% at 1-year
- 79.7% at 3-years
- 73.1% at 5-years
- 66.4% at 10-years
- mean 87.8 month follow-up
## Overall Results

<table>
<thead>
<tr>
<th># of Patients</th>
<th># DNA + prior to OLT</th>
<th>Continued HBlg</th>
<th>Recurrent HBV</th>
<th>Follow-up months</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>2</td>
<td>Yes</td>
<td>0 (0%)</td>
<td>80.2 (range 34-115)</td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>No</td>
<td>3 (50%)</td>
<td>100.6 (range 36.3-148.7)</td>
</tr>
</tbody>
</table>
The UC Irvine Experience

- 3 patients experienced recurrent HBV after cessation of HBIg and institution of lamivudine monotherapy

- Retrospectively, laboratory data demonstrates a marked increase in viral replication as HBsAb titers were depleted
Conclusions

- Published data strongly supports the use of combination therapy with HB Ig and a nucleoside analog to prevent recurrent HBV after OLT.

- There are no viable alternatives at this time.
References


