Background
Although favorable outcome after liver transplantation for HBV-related liver disease was possible with high-dose HBIG immunoprophylaxis, overall recurrence rates were reported from 15% to 35%. Combination of lamivudine and HBIG showed recurrence rates between 0% and 18% in a few studies. In patients receiving HBIG, HBV reinfection may be the consequence of the followings: HBV overproduction coming from extrahepatic sites, an insufficient protective titer of HBIG or the emergence of escape mutants. We performed this retrospective study to assess recurrence rate of B viral hepatitis and its mechanism after HBIG monotherapy or HBIG + entecavir combined therapy after liver transplantation in our clinic.

Methods
157 patients underwent liver transplantation for hepatitis B-related liver disease (From January 2005 through June 2010)

- 120 patients high-dose HBIG monotherapy
- 37 patients high-dose HBIG + entecavir

Indefinite immunoprophylaxis: HBIG
- 10,000 U during anhepatic phase
- 10,000 U daily during the 6 postoperative days
- 10,000 U weekly for 1 month
- 10,000 U monthly for 1 year

After that, 10,000 U: every 6-8 weeks to maintain the anti-HBs titer of > 250 IU/L.

Entecavir: Daily 0.5 mg per oral

Results
Over all recurrence rate of HBV was 10.1% (17/157), and recurrence rates of monotherapy group and combination group were 14.2% (17/120) and 0% (0/37), respectively. All of recurrent patients were controlled with entecavir therapy (0.5mg, daily). Gene sequencing of 3 patients showed multiple mutations in all 3 cases. G145R mutation was commonly found, and other mutations were the followings: I126T and P142T in case I, I126T and F134I/V in case 2 and D144E in case 3.

Figure 1. Timing and HBIG titer in patients with hepatitis B recurrence after LT

Case No. 0 6 12 18 24 30 36 42 48 54 60 (months)

1 X 1: ALT > 228
2 1: ALT > 367
3 1: ALT > 325
4 1: ALT > 180
5 1: ALT > 407
6 1: ALT > 253
7 1: ALT > 370
8 1: ALT > 587
9 1: ALT > 587
10 1: ALT > 587
11 1: ALT > 209
12 1: ALT > 360
13 1: ALT > 153
14 1: ALT > 111
15 1: ALT > 191
16 1: ALT > 343
17 1: ALT > 151

D: HCC
X A

Potential mechanisms of HBV recurrence we got from the analysis of the 17 recurrent cases.
1. Recurrent timing: mainly around 2 years after liver transplantation;
2. Lower HBIG titer group (5): an insufficient protective titer of HBIG after HCC recurrence;

Figure 2. Treatment and outcomes of HBV recurrent cases

![Graph showing treatment and outcomes of HBV recurrent cases](image)

Figure 3. Summary of sequencing results for α determinant

![Sequence results for α determinant](image)

Conclusion
As HBV recurrence rate despite high-dose HBIG monotherapy was 14.2% after liver transplantation, we think that the Entecavir+HBIG combination protocol could be considered as alternative protocol against HBV recurrence after liver transplantation for HBV-related liver disease.