Liver transplantation in HBV

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Indications for liver transplantation Include

- Acute liver failure,
- Cirrhosis with complications,
- Some liver neoplasms,
- Liver-based metabolic conditions with systemic manifestations

Acute liver failure

- Is defined by the development of severe acute liver injury with encephalopathy and impaired synthetic function (INR of ≥1.5) in a patient without cirrhosis or preexisting liver disease.
- While the time course that differentiates acute liver failure from chronic liver failure varies between reports, a commonly used cutoff is an illness duration of <26 weeks.

King's College Hospital criteria for liver transplantation in acute liver failure

- *Acetaminophen-induced disease :*
- Arterial pH <7.3 (irrespective of the grade of encephalopathy)

OR

- Grade III or IV encephalopathy AND
- Prothrombin time >100 seconds AND
- Serum creatinine >3.4mg/dL (301 µmol/L)

King's College Hospital criteria for liver transplantation in acute liver failure

- All other causes of acute liver failure prothrombin time >100 seconds (irrespective of the grade of encephalopathy)

OR

*Any **three** of the following variables (irrespective of the grade of encephalopathy)*

- 1.Age <10 years or >40 years
- 2. Etiology: non-A, non-B hepatitis, halothane hepatitis, idiosyncratic drug reactions
- 3. Duration of jaundice before onset of encephalopathy >7 days
- 4. Prothrombin time >50 seconds
- 5. Serum bilirubin >18 mg/dL (308 µmol/L)

Cirrhosis

- The presence of cirrhosis alone is not sufficient to warrant transplantation.
- Transplantation is generally considered when a patient has suffered either a complication of portal hypertension or a manifestation of compromised hepatic function.

Patient selection in pretransplantation

- Patients with cirrhosis are typically candidates for liver transplantation once:
- Model for End-stage Liver Disease (MELD) score is ≥15 . (The transplantation evaluation is typically started once a patient has a MELD score >10. This permits the patient to meet the transplantation team prior to developing end-stage liver disease.)
- MELD exception: HCC, hepatopulmonary syndrome, portopulmonary hypertension, Familial amyloid polyneuropathy, Primary hyperoxaluria, Cystic fibrosis, Hilar cholangiocarcinoma
- Patients with cirrhosis may be considered for liver transplantation if they have other complications related to cirrhosis such as refractory ascites, Recurrent cholangitis, Refractory hepatic encephalopathy, Refractory variceal hemorrhage, Portal hypertensive gastropathy leading to chronic blood loss, Intractable pruritus in a patient with PBC

Contraindications to liver transplantation include

- Cardiopulmonary disease that cannot be corrected and is a prohibitive risk for surgery
- Malignancy outside of the liver not meeting oncologic criteria for cure
- Metastatic HCC
- Hemangiosarcoma
- Anatomic abnormalities
- Uncontrolled sepsis
- Acquired immunodeficiency syndrome (AIDS)
- Intrahepatic cholangiocarcinoma
- Acute liver failure with a sustained intracranial pressure >50 mmHg or a cerebral perfusion pressure <40 mmHg
- Persistent nonadherence with medical care
- Lack of adequate social support

HBV reinfection after LT

- High risk patients: HBV DNA levels greater than 10(5) copies/mL , Anti drug resistance prior LT
- Low risk patients: HBV DNA levels lesser than 10(5) copies/mL ,Fulminant HBV ,Coinfection with HDV

Diagnosis and clinical course

- HBV reinfection has traditionally been diagnosed by the reappearance of HBsAg in the serum. Most reinfected patients are also HBeAg positive and have high levels of circulating HBV DNA.
- Studies using PCR assays have demonstrated that HBV DNA can be detected in serum prior to the reappearance of HBsAg or elevation of aminotransferases

Diagnosis and clinical course

- Reinfection is almost always accompanied by recurrent liver disease, which is often severe and rapidly progressive .If untreated, cirrhosis occurs within one to two years of reinfection.
- An unusual form of liver disease with severe cholestasis and rapidly progressive liver failure ,termed fibrosing cholestatic hepatitis, characterized by prominent cholestasis and extensive fibrosis

Prevention of HBV reinfection after LT

- Use of antiviral therapy pre- LT and continuation of antiviral therapy with or without HBIG post LT.

Goal in pre - LT

- The ideal goal of antiviral therapy in patients awaiting liver transplantation is to reverse cirrhosis complications and the need for liver transplant.
- In patients who present late, the goal is to achieve viral suppression, thereby stabilizing liver disease, allowing the patient to receive a liver transplant, and (in those who proceed to transplant) decreasing the risk of HBV reinfection.

Choice and timing of therapy

- Antiviral therapy should be started as soon as possible in patients with HBV-related decompensated and compensated cirrhosis detectable serum HBV DNA, regardless of HBV DNA and alanine aminotransferase levels.

Choice and timing of therapy

- Entecavir is preferred for patients who are nucleoside naïve or who had prior treatment with adefovir, while tenofovir is preferred for patients who had prior treatment with lamivudine or telbivudine.

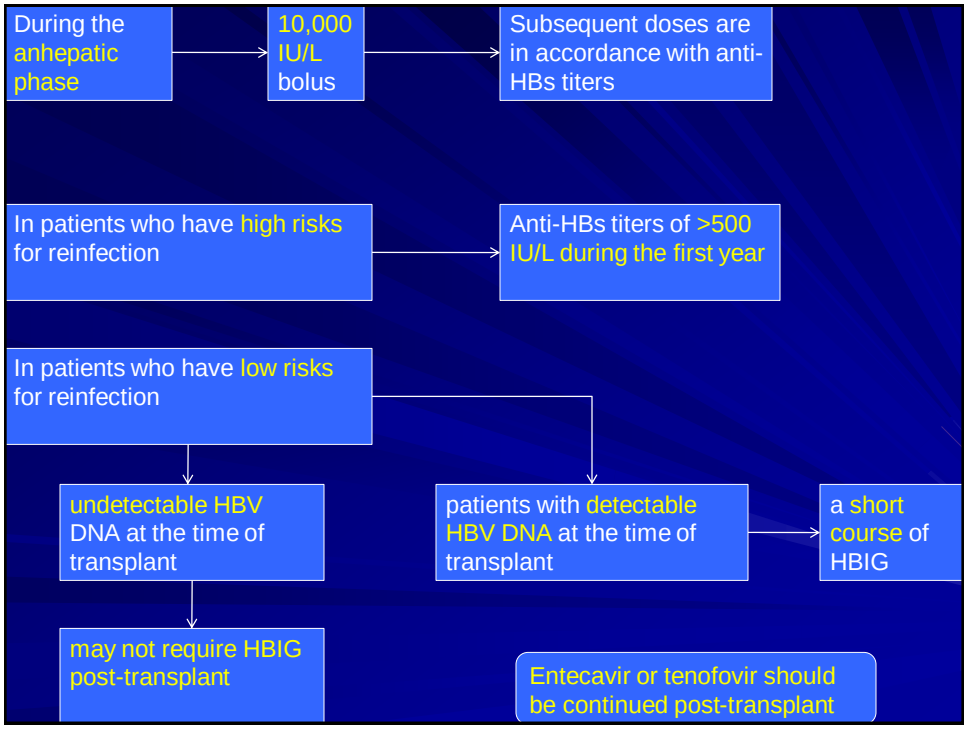
Prophylactic therapies post-transplant

- Antiviral therapy should be initiated in the rare patient who is not on treatment at the time of transplant, and continued indefinitely in all patients post-transplant.
- Antiviral therapy with nucleos(t)ide analogues before transplant decreases the risk of reinfection by decreasing the amount of circulating virus at the time of transplant and by prolonging the half-life of HBIG. (Serum HBV DNA level at the time of transplant is an important predictor of the half-life of HBIG)
- HBIG immunoprophylaxis alone has been less successful in preventing reinfection in patients with detectable HBV DNA .

Hepatitis B immune globulin

- HBIG immunoprophylaxis will bind to and neutralize circulating virions, thereby preventing graft infection.
- Anti-HBs also undergoes endocytosis by hepatocytes, interacting with HBsAg within the cells, and decreasing HBsAg secretion

Dose regimen



Antiviral strategies

- Rare patients who received no prophylaxis or HBIG should be treated with entecavir or tenofovir.
- Entecavir may be preferred because of the lower rate of drug resistance and lack of nephrotoxicity.
- Patients who received nucleos(t)ide analogue prophylaxis should be tested for antiviral drug resistance mutation to guide the choice of rescue therapy.
- In general, combination therapy is recommended, and most patients will need a combination of tenofovir with entecavir.

آمار بیماران پیوند کبد در مرکز پیوند استان خراسان رضوی (بیمارستان منتصریه) از شهریور 92 تا مهر 1397

جمع کل	1397	1396	1395	1394	1393	1392	بر اساس جنسیت
179	33	52	47	31	11	5	مرد
64	9	12	12	13	14	4	زن
							بر اساس سال پیوند
243	42	64	59	44	25	9	

							بر اساس علت بیماری
38	8	7	10	5	6	2	AIH
2	0	0	2	0	0	0	GSD
53	9	9	9	14	8	4	HBV
13	3	4	5	1	0	0	HBV+ HDV+ HCC
3	0	2	1	0	0	0	HCC
18	1	5	1	5	5	1	HCV+
3	1	0	2	0	0	0	HCV+ HCC
2	0	0	2	0	0	0	NASH
3	1	0	0	1	0	1	PBC
13	1	7	3	2	0	0	PSC
5	1	3	0	1	0	0	اگزالوزیس
4	0	1	2	1	0	0	هیداتیدوز مولتی لوکولاریس
1	1	0	0	0	0	0	تیروزینمی + HCC
5	0	0	5	0	0	0	سندرم بودکیاری
2	0	1	0	1	0	0	سیروز الکلیک
1	1	0	0	0	0	0	کریگلر نجار
66	15	20	16	11	3	1	کریپتوژنیك
11	0	5	1	2	3	0	ویلسون
243	جمع کل						

بیماران کبدی فوت شده پس از پیوند (قبل یا پس از ترخیص از بیمارستان) از سال 1392 تا مهر 1397

- کل فوت شده ها : 28 (11.5%)
- فوت قبل از ترخیص: 16 (6/5 %)
- فوت بعد از ترخیص: 12(از 1 تا 4 سال بعد از پیوند غالبا به علت عود بیماری اولیه)