参考資料９

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REVIEW PAPER

Liver Transplantation Using Hepatitis B Core Antibody – Positive Grafts: Review and University of Tokyo Experience

Nobuyuki Takemura · Yasuhiko Sugawara · Sumihito Tamura · Masatoshi Makuuchi

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Abstract Hepatitis B surface antigen – negative and hepatitis B core antibody – positive grafts were considered unsuitable for transplantation. The number of potential recipients for liver transplantation now exceeds that of potential donor organs, which has led us to reevaluate the feasibility of these grafts. Several strategies involving prophylactic administration of hepatitis B immunoglobulin and/or lamivudine to transplant recipients have been proposed. At the University of Tokyo, we have continued to use hepatitis B immunoglobulin monoprophylaxis with zero recurrence.In this article we report our experience with the use of hepatitis B surface antigen – negative/hepatitis B core antibody – positive grafts with hepatitis B immunoglobulin monotherapy. We conducted a review of the literature regarding the feasibility of these grafts to reconfirm optimal prophylactic strategies for preventing *de novo* hepatitis B virus infection in transplant recipients.

Keywords Hepatitis B virus · *De novo* hepatitis · Living donor liver transplantation · Hepatitis B core antibody · Hepatitis B immunoglobulin

Abbreviations
HBV: Hepatitis B virus
LDLT: Living donor liver transplantation
HBcAb: Hepatitis B core antibody
HBsAb: Hepatitis B surface antibody
HBsAg: Hepatitis B surface antigen
HBIG: Hepatitis B immunoglobulin

N. Takemura · Y. Sugawara (✉) · S. Tamura · M. Makuuchi
Artificial Organ and Transplantation Division,
Department of Surgery,
Graduate School of Medicine,
University of Tokyo, 7-3-1 Hongo,
Bunkyo-ku,
Tokyo 113-8655, Japan
e-mail: yasusuga-tky@umin.ac.jp

Introduction

Hepatitis B surface antigen (HBsAg) – negative and hepatitis B core antibody (HBcAb) – positive grafts are sources of *de novo* hepatitis B virus (HBV) infections. Therefore, they were considered unsuitable for transplantation during the early 1990s [1–3]. As shown in Table 1, the occurrence of *de novo* HBV hepatitis in recipients that received the grafts might be influenced by the pre-existing HBV immunity of the recipient [4–10].

The number of potential recipients for liver transplantation now exceeds that of potential donor organs, leading us to reevaluate the feasibility of using these grafts. Several strategies involving the prophylactic administration of hepatitis B immunoglobulin (HBIG) and/or lamivudine to the recipients have been proposed [7, 10–20]. Liver transplantation from live donors (LDLT) is currently the most effective alternative to overcome the organ shortage. Live donors are often restricted to the relatives of the recipient. In regions where HBV is prevalent, there is no choice other than a graft from a live donor who is HBsAg-negative/HBcAb-positive.

HBsAg-negative/HBcAb-positive grafts are now important topics in LDLT. The optimal prophylactic strategy remains a matter of debate. We conducted a review of the literature regarding the feasibility of HBsAg-negative/HBcAb-positive grafts to reconfirm optimal prophylactic strategies for preventing *de novo* HBV infection in recipients.

Table 1 Recipient's viral status and *de novo* HBV infection rates after transplant of HBcAb-positive grafts without prophylaxis

Author, year	Recipient viral status (HBsAb/HBcAb) +/+	+/−	−/+	−/−	Total (%)
Douglas, 1992 [1]	ND	ND	ND	ND	3/7 (43)
Chazouilleres, 1994 [2]				7/8	7/8 (88)
Wachs, 1995 [3]				3/6	3/6 (50)
Dickson, 1997 [5]	0/1	1/2	0/1	14/16	18/23 (78)
Dodson, 1997 [6]		0/7	2/15	18/25	20/47 (43)
Uemoto, 1998 [7]		1/1		14/15	15/16 (94)
Prieto, 2001 [8]	0/2	0/2	0/3	15/23	15/30 (50)
Manzarbeitia, 2002 [9]	0/13	1/1	2/11	2/2	3/27 (11)
Donataccio, 2006 [21]		0/1		3/4	3/5 (60)
Barcena, 2006 [40]	0/6		0/3		0/9 (0)

Note. HBsAb, hepatitis B surface antibody; HBcAb, hepatitis B core antibody; ND, not described.

Management protocols for prevention of *de novo* HBV infection (Table 2)

HBIG monoprophylaxis

Uemoto et al. [7] first reported the successful prevention of *de novo* HBV infection using HBIG in recipients who received HBcAb-positive grafts from live donors. Although some authors followed their prophylaxis, the risk of reactivation remained high [4, 9, 11, 15, 21]. Decreased hepatitis B surface antibody (HBsAb) titer seems to be a significant risk factor for *de novo* infection [15]. More recent reports with satisfactory results targeted higher HBsAb levels for an indefinite period [19].

Lamivudine and HBIG

Dodson et al. [11] reported therapy using a combination of prophylactics: HBIG doses ranged from 10,000 IU only during the anhepatic phase [13] to 10,000 IU for seven days after transplantation [11, 14]. The minimum amount of HBIG required to prevent *de novo* infection is unclear. In either case, lamivudine was started after the initial HBIG administration or simultaneously. Suehiro et al. [22] reported that HBIG

Table 2 Prophylaxis for HBcAb-positive graft and infection rate

Author, year	*N*	Followup (months)	Protocols	Rate (%)
HBIG monotherapy				
Radomski, 1996 [4]	1	8	2000 IU/month	1/1 (100%)
Uemoto, 1998 [7]	3	13–24	100 IU/kg for 7 days and 1000 IU/m thereafter	0/3 (0%)
Dodson, 1999 [11]	1	11	10,000 IU for 7 days and monthly for 6 months, 1000 IU biweekly for 18 month	1/1 (100%)
Roque-Afonso, 2002 [15]	12	6–36	5000 IU for 7 days and subsequently to keep HbsAb > 100 IU/L	1/12 (8%)
Lee, 2004 [19]	18	13–80	10,000 IU for 7 days and subsequently to keep HbsAb > 200 IU/L	0/18 (0%)
Donataccio, 2006 [21]	6	18–62	10,000 IU for 7–10 days and stopped	4/6 (67%)
Donataccio, 2006 [21]	4	11–34	10,000 IU for 7–10 days and subsequently continued indefinitely	0/4 (0%)
Takemura, 2006	17	3–96	10,000 IU in anhepatic phase and subsequently to keep HbsAb > 200 IU/L for a year, then > 100 IU/L indefinitely	0/17 (0%)
HBIG + Lam				
Dodson, 1999 [11]	15	6–25	HBIG; 10,000 IU for 7 days and monthly for 6 months, 1000 IU biweekly for 18 months. LAM; 150 mg/day	0/15 (0%)
Holt, 2002 [14]	12	2–38	HBIG; 10,000 IU for 7 days, LAM; 300 mg/day	0/12 (0%)
Jain, 2005 [20]	28	36 ± 19[a]	HBIG; 10,000 IU for 4 days, LAM; 100 mg/day	3/28 (11%)
Suehiro, 2005 [22]	22	25–86	HBIG; 10,000 IU in anhepatic phase, 2000 IU for 7 days and subsequently to keep HbsAb > 100 IU/L, LAM; 100 mg/day	0/22 (0%)
Lam				
Yu, 2001 [12]	9	2–36	LAM; 100 or 150 mg/day	0/9 (0%)
Prakoso, 2006 [24]	10	2–69	LAM; 100 mg/day	0/10 (0%)

Note. HBIG, hepatitis B immunoglobulin; LAM, lamivudine.

[a] Mean ± standard error.

Table 3 Tailored approach based on graft HBVDNA and recipient HBV immunity

Author, Year	N	HBVDNA in donor		Recipient HBsAb	Protocols
		Graft	Serum		
Loss, 2001 [13][a]	1	–	–	ND	10,000 IU of HBIG in anhepatic phase + LAM 150 mg/day → discontinued after confirming the HBVDNA status (graft and donor serum)
	0	+	+	ND	HBIG + LAM → continued
	5	+	NA	ND	HBIG + LAM → LAM; 150 mg/day
Fabrega, 2003 [16][a]	7	–	–	ND	10,000 IU of HBIG for 7 days + Lam; 100 mg/day → discontinued after confirming the HBVDNA status (graft and donor serum)
	0	+	+	ND	HBIG + LAM → LAM; 100 mg/day
Nery, 2003 [17][a]	10	+	+	ND	10,000 IU HBIG for 7 days, weekly for 1 month, and monthly for 6 months + LAM; 100 mg/day
	13	–	–	–	LAM; 100 mg/day
	13	–	–	+	None
	2	NA	ND	–	LAM; 100 mg/day
	5	NA	ND	+	None

Note. HBVDNA, hepatitis B virus deoxyribonucleic acid; HBIG, hepatitis B immunoglobulin; NA, not available; ND, not described; LAM, lamivudine.

[a]No reinfection was seen in all the patients with these protocols.

use with lamivudine over an indefinite period of time might have prevented *de novo* infection in 22 patients receiving HBsAg-negative/HBcAb-positive grafts.

Long-term use of lamivudine is associated with the risk of mutated HBV infection. Jain et al. [20] reported 3 of 28 patients with *de novo* mutated HBV infection who used a protocol of short-term treatment with HBIG (10,000 IU HBIG for 4 days) and indefinite use of lamivudine (100 mg/day). Among these three infected patients, two had a YMDD mutation. Yen et al. [23] experienced a case complicated with a lamivudine-resistant mutation while using a similar protocol.

Lamivudine monoprophylaxis

Yu et al. [12] advocated lamivudine monoprophylaxis. HBV infection was prevented in nine patients who received HBsAg-negative/HBcAb-positive allografts. Six of the nine patients died of recurrent hepatocellular carcinoma (HCC) and sepsis, however, and the followup periods were limited (3–36 months). Prakoso et al. [24] reported that they successfully prevented HBV infection in ten HBsAg-negative patients with lamivudine monotherapy.

Tailored approach (Table 3)

Loss et al. [13] and Nery et al. [25] advocated that prophylaxis should be selected according to the serum and liver HBVDNA status of the donor or the recipient's preoperative serology. Loss et al. administered HBIG during the anhepatic phase and started lamivudine on postoperative day 1. If HBVDNA was detected in neither the donor liver nor serum, lamivudine was stopped. If HBVDNA was detected in the donor liver and serum, HBIG was continued with lamivudine. Fabrega et al. [16] started prophylaxis with a combination of HBIG and lamivudine on the first operative day until they obtained HBVDNA results from the donor samples. They stopped the prophylaxis when the donor's HBVDNA in serum and liver tissue was negative, even in a naïve recipient. None of their seven patients developed *de novo* hepatitis B with a mean followup period of 23 months.

The protocol of Nery et al. [17] was more complicated because the strategy was changed by not only the results of the donor HBV profile but also the recipient's HBV serology. The recipients of HBVDNA-positive grafts received HBIG and lamivudine combination therapy. If the donor serum and liver graft HBVDNA were both negative and the recipient was HbsAb-negative, lamivudine monotherapy was selected. If the recipient was HbsAb-positive, no therapy was administered. Their selective protocol successfully prevented 43 patients from reactivation of HBV, including 18 patients without prophylaxis. Two patients were excluded from their study because of low compliance; both recipients developed *de novo* hepatitis. Their allografts were HBVDNA-negative but they were infected with hepatitis. One was naïve and the other was only HBcAb-positive preoperatively.

A tailored approach is based on the results of testing for HBVDNA in the allografts. The sensitivity for HBVDNA detection, however, depends on the methodology [26]. Van Thiel et al. [27] reported that HBVDNA was detected in 11 (8%) of 133 livers from HBsAg-negative/HBcAb-positive donors. Marusawa et al. [28] reported that HBVDNA was detected in 14 of 17 grafts (82%) from HBcAb-positive donors.

Suchiro et al. [22] detected HBVDNA in 20 of 20 grafts. HBVDNA in all grafts was detected by polymerase chain reaction (PCR) methods, but the details of the methods differed. Van Thiel used primers targeting surface antigen sequences with a sensitivity of an approximately 600 HBV copies per milliliter serum sample. Marusawa used primers targeting the surface and pre-C/C region. The first PCR products were subjected to either Southern blotting analysis or to a second PCR amplification (seminested PCR for pre-C/C region and nested PCR for the surface region). The sensitivity of their assay was 10 copies per 20 μg DNA. Suchiro selected real-time PCR with a sensitivity of 10 copies per gram DNA.

Vaccination

The response rates to recombinant hepatitis B vaccine in liver transplantation candidates (with HBV unrelated liver failure) varied from 16% to 62% [29–38]. It is difficult to explain the variations in hepatitis B vaccine response rates. HBsAb titers rapidly decline and become undetectable in a significant proportion of patients after transplantation. HBsAb titers become undetectable in 37%–73% of the responders within one year after transplantation [33, 35, 38]. Dominguez et al. [30] reported a 62% response rate with 40-μg hepatitis B vaccinations three times preoperatively with a one-month interval and an additional three doses for nonresponders. Conventionally, patients with HBsAb titers of more than 10 IU/L are considered immunized [39].

Kaohsiung's group performed preoperative vaccination in all patients awaiting transplantation because approximately 80% of adults are HBcAb-positive in Taiwan [10]. They reported *de novo* HBV infection in three of eight preoperatively immunized patients who received an HBcAb-positive graft. They made a policy change [18] and began to use lamivudine after surgery with preoperative vaccination. Thereafter, none of 44 patients developed *de novo* hepatitis. Barcena et al. [40] vaccinated only those who were HBsAb- or HBcAb-negative and receiving an HBcAb-positive allograft. No postoperative prophylaxis against HBV was performed in their protocol. They immunized 14 recipients with 40-μg hepatitis B vaccinations three times with a 15-day interval, although the vaccine response rate was not described. One of the 14 recipients developed *de novo* HBV infection after receiving an HBcAb-positive liver; this might have occurred because of an immune escaped HBV mutant with a structural variation in the epitope of the surface antigen recognized by the HBsAb [41, 42].

University of Tokyo experience

From January 1996 to December 2005, 351 LDLT were performed at the University of Tokyo. All donors were HBsAg-negative and 34 (10%) were HBcAb-positive. Of the recipients of HBsAg-negative/HBcAb-positive grafts, 19 were HBV-unrelated recipients and the others had HBV-related cirrhosis. The 19 liver grafts were the subjects of the study. The serum HBV status included HbcAb- and HBsAb-negative ($n = 9$), HbcAb- and HBsAb-positive ($n = 5$), HBcAb-positive ($n = 2$), or HBsAb-positive ($n = 3$). There were 14 men and 5 women with a median age of 51 years [21–64]. The immunosuppression regimen for all recipients consisted of tacrolimus and corticosteroids.

Postoperative prophylaxis consisted of HBIG monotherapy. A total of 10,000 IU HBIG was administrated intravenously during the anhepatic-phase. HBIG was administered once a month to maintain the HBsAb level above 200 IU/L during the first year and above 100 IU/L thereafter. We do not use nucleotide analogs for prophylactics to those who received HBcAb-positive graft to avoid the emergence of multidrug resistance.

Our strategy of anhepatic and low-dose HBIG monoprophylaxis prevented perioperative *de novo* HBV infection in all 19 patients that were preoperatively HBsAg-negative and received HBcAb-positive livers. Among the 19 patients, 3 patients died of HBV-unrelated causes between 2 and 13 months after transplantation without any evidence of HBV infection. Two patients were dropped from the prophylaxis protocol because of poor compliance. They skipped the monthly HBIG administration and as a result developed *de novo* HBV infection. Preoperatively, one was naïve and the other was HBsAb- and HBcAb-positive. HBsAb titers at the onset decreased to 10 and 15 IU/L. *De novo* hepatitis was defined as the development of positive serum HBsAg. Their HBsAg were detected 51 and 35 months after the operation. Hepatitis B e antigen became positive and serum HBVDNA was detected. They received antiviral therapy using lamivudine and their hepatitis B e antigen and HBVDNA became negative thereafter. The remaining 14 patients showed no evidence of HBV infection with followup periods of 3–86 months (median = 31 months).

The median amount of HBIG that was used during the first month of transplantation was 12,000 IU (10,000–18,000 IU) and that during the following 11 months was 14,000 IU (12,000–31,000 IU). After the first postoperative year, 10,000 IU HBIG (8000–22,000 IU) was required each year to keep HBsAb levels over 100 IU/L.

Future possible alternatives

Lamivudine is often used to treat a patient with chronic hepatitis B but antiviral drug-resistant mutation frequently develops. Resistance to adefovir dipivoxil is less common than for lamivudine [43]. Adefovir dipivoxil shows favorable outcome in patients with *de novo* hepatitis B after liver

transplantation [44] and in the patients with lamivudine-resistant hepatitis B [45, 46]. Recently, alternative nucleoside analogs adefovir dipivoxil, entecavir [47], telbivudine [48], and tenofovir [49] were administered efficiently in treating wild-type and/or mutated HBV. All of them also have the potential to be used for prophylaxis against *de novo* HBV infection from HBcAb-positive allograft. However, some reports revealed the emergence of mutated HBV which showed resistance not only to lamivudine but also to adefovir dipivoxil [43], entecavir [50], and telbivudine [48].

Conclusions

De novo HBV infection can be prevented with HBcAb-positive grafts when an adequate strategy is applied. HBIG monotherapy can prevent HBV infection from HBcAb-positive liver grafts. Lamivudine use can be reserved for *de novo* HBV infection. Lamivudine or preoperative vaccination monotherapy are still controversial therapies. Vaccination with lamivudine prophylaxis, however, is promising. A tailored approach might reduce the unnecessary administration of antiviral prophylaxis to a recipient. Further studies are needed to elucidate the optimal prophylactic treatment.

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References

1. Douglas DD, Rakela J, Mamish D, et al. (1992) Transmission of hepatitis B virus (HBV) infection from orthotopic donor livers. Hepatology 16:49
2. Chazouilleres O, Mamish D, Kim M, et al. (1994) Occult hepatitis B virus as source of infection in liver transplant recipients. Lancet 343:142–146
3. Wachs ME, Amend WJ, Ascher NL, et al. (1995) The risk of transmission of hepatitis B from HBsAg(−), HBcAb(+), HBIgM(−) organ donors. Transplantation 59:230–234
4. Radomski JS, Moritz MJ, Armenti VT, et al. (1996) Hepatitis B transmission from a liver donor who tested negative for hepatitis B surface antigen and positive for hepatitis B core antibody. Liver Transpl Surg 2:130–131
5. Dickson RC, Everhart JE, Lake JR, et al. (1997) Transmission of hepatitis B by transplantation of livers from donors positive for antibody to hepatitis B core antigen. Gastroenterology 113:1668–1674
6. Dodson SF, Issa S, Araya V, et al. (1997) Infectivity of hepatic allografts with antibodies to hepatitis B virus. Transplantation 64:1582–1584
7. Uemoto S, Sugiyama K, Marusawa H, et al. (1998) Transmission of hepatitis B virus from hepatitis B core antibody-positive donors in living related liver transplants. Transplantation 65:494–499
8. Prieto M, Gomez MD, Berenguer M, et al. (2001) De novo hepatitis B after liver transplantation from hepatitis B core antibody-positive donors in an area with high prevalence of anti-HBc positivity in the donor population. Liver Transpl 7:51–58
9. Manzarbeitia C, Reich DJ, Ortiz JA, et al. (2002) Safe use of livers from donors with positive hepatitis B core antibody. Liver Transpl 8:556–561
10. Chen YS, Wang CC, de Villa VH, et al. (2002) Prevention of *de novo* hepatitis B virus infection in living donor liver transplantation using hepatitis B core antibody positive donors. Clin Transplant 16:405–409
11. Dodson SF, Bonham CA, Geller DA, et al. (1999) Prevention of de novo hepatitis B infection in recipients of hepatic allografts from anti-HBc positive donors. Transplantation 68:1058–1061
12. Yu AS, Vierling JM, Colquhoun SD, et al. (2001) Transmission of hepatitis B infection from hepatitis B core antibody-positive liver allografts is prevented by lamivudine therapy. Liver Transpl 7:513–517
13. Loss GE, Mason AL, Blazek J, et al. (2001) Transplantation of livers from HBc Ab positive donors into HBc Ab negative recipients: a strategy and preliminary results. Clin Transplant 15:55–58
14. Holt D, Thomas R, Van Thiel D, et al. (2002) Use of hepatitis B core antibody-positive donors in orthotopic liver transplantation. Arch Surg 137:572–575
15. Roque-Afonso AM, Feray C, Samuel D, et al. (2002) Antibodies to hepatitis B surface antigen prevent viral reactivation in recipients of liver grafts from anti-HBC positive donors. Gut 50:95–99
16. Fabrega E, Garcia-Suarez C, Guerra A, et al. (2003) Liver transplantation with allografts from hepatitis B core antibody-positive donors: a new approach. Liver Transpl 9:916–920
17. Nery JR, Nery-Avila C, Reddy KR, et al. (2003) Use of liver grafts from donors positive for antihepatitis B-core antibody (anti-HBc) in the era of prophylaxis with hepatitis-B immunoglobulin and lamivudine. Transplantation 75:1179–1186
18. de Villa VH, Chen YS, Chen CL (2003) Hepatitis B core antibody-positive grafts: recipient's risk. Transplantation 75:49–53
19. Lee KW, Lee DS, Lee HH, et al. (2004) Prevention of *de novo* hepatitis B infection from HbcAb-positive donors in living donor liver transplantation. Transplant Proc 36:2311–2312
20. Jain A, Orloff M, Abt P, et al. (2005) Use of hepatitis B core antibody-positive liver allograft in hepatitis C virus-positive and -negative recipients with use of short course of hepatitis B immunoglobulin and lamivudine. Transplant Proc 37:3187–3189
21. Donataccio D, Roggen F, De Reyck C, et al. (2006) Use of anti-HBc positive allografts in adult liver transplantation: toward a safer way to expand the donor pool. Transpl Int 19:38–43
22. Suehiro T, Shimada M, Kishikawa K, et al. (2005) Prevention of hepatitis B virus infection from hepatitis B core antibody-positive donor graft using hepatitis B immune globulin and lamivudine in living donor liver transplantation. Liver Int 25:1169–1174
23. Yen RD, Bonatti H, Mendez J, et al. (2006) Case report of lamivudine-resistant hepatitis B virus infection post liver transplantation from a hepatitis B core antibody donor. Am J Transplant 6:1077–1083
24. Prakoso E, Strasser SI, Koorey DJ, Verran D, McCaughan GW (2006) Long-term lamivudine monotherapy prevents development of hepatitis B virus infection in hepatitis B surface-antigen negative liver transplant recipients from hepatitis B core-antibody-positive donors. Clin Transplant 20:369–373
25. Nery JR, Gedaly R, Vianna R, et al. (2001) Are liver grafts from hepatitis B surface antigen negative/anti-hepatitis B core antibody positive donors suitable for transplantation? Transplant Proc 33:1521–1522

26. Burton JR Jr, Shaw-Stiffel TA (2003) Use of hepatitis B core antibody-positive donors in recipients without evidence of hepatitis B infection: a survey of current practice in the United States. Liver Transpl 9:837–842
27. van Thiel DH, De Maria N, Colantoni A, et al. (1999) Can hepatitis B core antibody positive livers be used safely for transplantation: hepatitis B virus detection in the liver of individuals who are hepatitis B core antibody positive. Transplantation 68:519–522
28. Marusawa H, Uemoto S, Hijikata M, et al. (2000) Latent hepatitis B virus infection in healthy individuals with antibodies to hepatitis B core antigen. Hepatology 31:488–495
29. Chalasani N, Smallwood G, Halcomb J, et al. (1998) Is vaccination against hepatitis B infection indicated in patients waiting for or after orthotopic liver transplantation? Liver Transpl Surg 4:128–132
30. Dominguez M, Barcena R, Garcia M, et al. (2000) Vaccination against hepatitis B virus in cirrhotic patients on liver transplant waiting list. Liver Transpl 6:440–442
31. Carey W, Pimentel R, Westveer MK, et al. (1990) Failure of hepatitis B immunization in liver transplant recipients: results of a prospective trial. Am J Gastroenterol 85:1590–1592
32. van Thiel DH, El-Ashmawy L, Love K, et al. (1992) Response to hepatitis B vaccination by liver transplant candidates. Dig Dis Sci 37:1245–1249
33. Loinaz C, de Juanes JR, Gonzalez EM, et al. (1997) Hepatitis B vaccination results in 140 liver transplant recipients. Hepatogastroenterol 44:235–238
34. Chalasani N, Smallwood G, Halcomb J, et al. (1998) Is vaccination against hepatitis B infection indicated in patients waiting for or after orthotopic liver transplantation? Liver Transpl Surg 4:128–132
35. Horlander JC, Boyle N, Manam R, et al. (1999) Vaccination against hepatitis B in patients with chronic liver disease awaiting liver transplantation. Am J Med Sci 318:304–307
36. Dominguez M, Barcena R, Garcia M, et al. (2000) Vaccination against hepatitis B virus in cirrhotic patients on liver transplant waiting list. Liver Transpl 6:440–442
37. Villeneuve E, Vincelette J, Villeneuve JP (2000) Ineffectiveness of hepatitis B vaccination in cirrhotic patients waiting for liver transplantation. Can J Gastroenterol 14:59–62
38. Arslan M, Wiesner RH, Sievers C, et al. (2001) Double-dose accelerated hepatitis B vaccine in patients with end-stage liver disease. Liver Transpl 7:314–320
39. Centers for Disease Control (CDC) (1988) Update: universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus, and other bloodborne pathogens in health-care settings. MMWR Morb Mortal Wkly Rep 37:377–382
40. Barcena R, Moráleda G, Moreno J, et al. (2006) Prevention of de novo HBV infection by the presence of anti-HBs in transplanted patients receiving core antibody-positive livers. World J Gastroenterol 12:2070–2074
41. Moraleda G, Barcena R, Del Campo S, et al. (2006) De novo HBV infection caused by an anti-HBc positive donor in a vaccinated liver transplant recipient in spite of anti-HBs response. Am J Transplant 6:438–440
42. Carman WF, Zanetti AR, Karayiannis P, et al. (1990) Vaccine-induced escape mutant of hepatitis B virus. Lancet 336:325–329
43. Angus P, Vaughan R, Xiong S, et al. (2003) Resistance to adefovir dipivoxil therapy associated with the selection of a novel mutation in the HBV polymerase. Gastroenterology 125:292–297
44. Toniutto P, Fumo E, Caldato M, et al. (2004) Favourable outcome of adefovir-dipivoxil treatment in acute de novo hepatitis B after liver transplantation. Transplantation 77:472–473
45. Schiff ER, Lai CL, Hadziyannis S, Neuhaus P, et al. (2003) Adefovir dipivoxil therapy for lamivudine-resistant hepatitis B in pre- and post-liver transplantation patients. Hepatology 38:1419–1427
46. Lo CM, Liu CL, Lau GK, et al. (2005) Liver transplantation for chronic hepatitis B with lamivudine-resistant YMDD mutant using add-on adefovir dipivoxil plus lamivudine. Liver Transpl 11:807–813
47. Chang TT, Gish RG, de Man R, et al. (2006) A comparison of entecavir and lamivudine for HBeAg-positive chronic hepatitis B. N Engl J Med 354:1001–1010
48. Lai CL, Leung N, Teo EK, et al. (2005) A 1-year trial of telbivudine, lamivudine, and the combination in patients with hepatitis B e antigen-positive chronic hepatitis B. Gastroenterology 129:528–536
49. van Bommel F, Zollner B, Sarrazin C, et al. (2006) Tenofovir for patients with lamivudine-resistant hepatitis B virus (HBV) infection and high HBVDNA level during adefovir therapy. Hepatology 44:318–325
50. Tenney DJ, Levine SM, Rose RE, et al. (2004) Clinical emergence of entecavir-resistant hepatitis B virus requires additional substitutions in virus already resistant to lamivudine. Antimicrob Agents Chemother 48:3498–3507