

# B

1

## Abstract

### The Effect of Long-term Lamivudine Therapy for Chronic Liver Disease due to Hepatitis B Virus

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**Background/Aims :** We studied to evaluate the virological and biochemical responses to lamivudine and to detect YMDD mutants in patients who received long-term lamivudine therapy. **Methods :** We conducted a one-year trial of lamivudine in 45 Korean patients with chronic liver disease due to hepatitis B virus. The patients were treated with a single oral average dose of 100 mg of lamivudine every day for 12 months. **Results :** The suppression of serum HBV DNA was sustained in 77.8% of the patients and the normalization of serum ALT in 80%. The proportions of patients with HBeAg seroconversion were 25%. YMDD mutants were detected in 4 of 8 patients who showed sustained HBV DNA and serum ALT response (n=31) and in 3 of 8 patients who showed HBV DNA or serum ALT breakthrough (n=9). The response to lamivudine therapy in HBeAg-negative patients was excellent. **Conclusion :** Lamivudine therapy resulted in a significant virological and biochemical improvements and were well tolerated. But, YMDD mutants were detected during lamivudine therapy. (Korean J Hepatol 1999;5:97 - 104)

**Key Words :** Lamivudine, HBV DNA breakthrough, ALT breakthrough, HBeAg seroconversion, YMDD mutant

134

가

73%

B (HBV) 77% B

.14

B

56 HBeAg YMDD motif

B

30% HBeAg

5

가 78 , 1.

B B 3

(immune tolerance) .9-12 HBV DNA 5 pg/mL

ALT 40 IU/L 39

가 B 6 . 45

41 , 4

(lamivudine) (pyrimidine 35.6 (14- 72) . 18

analogue) HBV DNA (polymerase) 가 27

HIV (human immunodeficiency virus) . HBV DNA

B 718.1 ± 967.1 pg/mL (116.6- 3940),

B ALT 242.7 ± 196.9 IU/L (53- 957)

.13 2 (phase HBeAg 32 (71.1%) .

clinical trial) anti-HCV 가

HBV DNA가 3.5 g/dL ,

2.0 mg/dL ,

70% ,

100 mg 가

가 가

.14-16 B 2.

1 3 (phase 100 mg

study) (necro- 12

inflammation) , HBV DNA, ALT, HBeAg anti-

ALT (alanine aminotransferase) HBe

HBV DNA HBeAg

(seroconversion) 가 anti-HBe monoclonal (Dade Behring, Malburg, Germany) , HBV DNA hybridization (Digene Diagnostic Inc, Bestivelle, MD, USA) .

.17-19 (predominant) , HBV DNA가

(wild type) ALT 40 IU/L

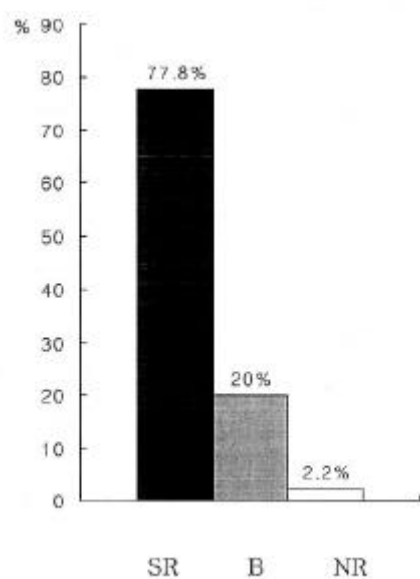
.17, 21, 21

B 1

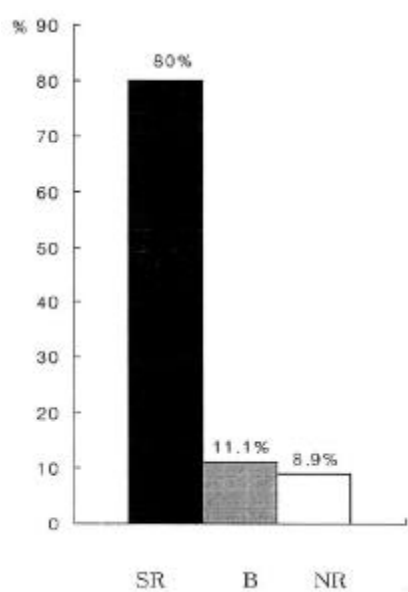
가

B HBV DNA가 가

5 pg/mL 가



**Figure 1.** Response of serum HBV DNA to lamivudine. SR, sustained response; B, breakthrough; NR, non-response.



**Figure 2.** Response of serum ALT to lamivudine. SR, sustained response; B, breakthrough; NR, non-response.

ALT 40 IU/L 가  
 40 IU/L  
 HBV DNA ALT brea-  
 kthrough  
 가 (sustained response),  
 breakthrough (non-response)  
 .  
 1  
 , breakthrough  
 ,  
 1  
 Chayama 21 nested PCR (polymerase  
 chain reaction) YMDD motif

3.  
 Exact test HBeAg  
 95% Fisher's  
 ,

1. B  
 45 1  
 44 (97.8%) HBV DNA가  
 44 9  
 HBV DNA가  
 breakthrough가 45  
 HBV DNA가  
 35 (77.8%), HBV DNA breakthrough가  
 9 (20%), HBV DNA가  
 1 (2.2%) (Figure 1).  
 ALT 45 41 (91.1%)  
 41 5  
 ALT가  
 45 ALT가  
 36 (80%), ALT breakthrough  
 가 5 (11.1%),  
 ALT가 4 (8.9%)  
 (Figure 2). 32 12

**Table 1.** YMDD Mutants during Lamivudine Therapy

	Group *	Group #	Group +
No. of patients			
(Selected/Total)	8/31	8/9	2/5
No. of YMDD mutants			
YIDD + wild type	3	0	
YVDD + wild type	1	0	0
Wild type	4	5	2

Group \*, sustained undetectable HBV DNA and sustained normalization of serum ALT; Group # serum HBV DNA breakthrough or serum ALT breakthrough; Group +, persistently detectable serum HBV DNA or elevated serum ALT.

**Table 2.** Response of Serum HBV DNA and Serum ALT According to the Presence of HBeAg

	HBeAg(+) (n=32)	HBeAg(-) (n=13)
<b>HBV DNA</b>		
Sustained response	23	12
Breakthrough	8	1
Non-response	1	0
<b>ALT</b>		
Sustained response	24	12
Breakthrough	5	0
Non-response	3	1

(37.5%) HBeAg anti-HBe 8 (25%), HBeAg

2. YMDD motif

HBV DNA가 ALT가  
31 8  
YMDD , 1 YVDD  
( YVDD ), 3  
YIDD ( YIDD ),  
4  
HBV DNA ALT  
breakthrough가 9 8  
, 3 YIDD ( YIDD

), 5  
HBV DNA가 ALT가  
5 2  
2  
(Table 1).

3. HBeAg  
HBeAg 13  
HBV DNA가 ,  
1 (7.7%) HBV DNA break-  
through가 . 13 12 (92.3%)  
ALT가 12

(Table 2).

4.

18 17 (94.4%)  
HBV DNA가  
17 5 HBV  
DNA breakthrough가 .  
18 HBV DNA가  
12 (66.7%), HBV DNA break-  
through가 5 (27.8%),  
HBV DNA가 1 (5.5%) .  
ALT 18 17 (94.4%)  
17 3  
ALT breakthrough가 . 18

ALT가  
 14 (77.8%), ALT breakthrough가  
 3 (16.7%), ALT가  
 1 (5.5%) (Table 3).  
 18 4 (22.2%) HBeAg  
 HBeAg anti- HBe 3  
 (16.7%)

Lai 17 72%,  
 Dienstag 18 41%, Heathcote 19 40%  
 , 80%  
 . HBeAg  
 anti- HBe가 HBV DNA  
 가 HBeAg  
 , HBeAg  
 16% - 18% ,17-19

**Table 3.** Response of Serum HBV DNA and Serum ALT According to the Previous Interferon Therapy

	INF(+)* (n=18)	INF(-)# (n=27)
<b>HBV DNA</b>		
Sustained response	12	23
Breakthrough	5	4
Non- response	1	0
<b>ALT</b>		
Sustained response	14	22
Breakthrough	3	2
Non- response	1	3

INF(+)\*; previous interferon taken; INF(-)# interferon not taken.

32 12 (37.5%) HBeAg  
 HBeAg 32 8 25%  
 ,  
 가  
 DNA YMDD  
 motif 550 methionine  
 isoleucine (YIDD) valine (YVDD)  
 .22 Lai 17  
 YMDD motif 1  
 14%  
 , Chayama 21  
 nested- PCR YMDD motif  
 HBV DNA breakthrough가  
 1- 4 HBV DNA  
 breakthrough

B RNA  
 (dependent) DNA  
 B 1 3  
 Lai ,17 Dienstag 18 Heathcote 19  
 . Lai 17 B  
 1 , HBV DNA가  
 (median)  
 98% 96%  
 HBV DNA가  
 97.8% HBV  
 DNA가 HBV  
 DNA가 ALT가  
 77.8% HBV DNA가  
 . ALT HBV

3- 4  
 . HBV DNA가  
 ALT가 31  
 8 YMDD  
 , 1 YVDD (  
 YVDD ), 3 YIDD (  
 YIDD ), 4  
 .  
 HBV DNA ALT breakthrough가  
 9 8 , 3  
 YIDD ( YIDD ), 5  
 HBV  
 DNA가 ALT가  
 5 2  
 2 .  
 HBV

DNA가  
가 ALT HBV DNA  
가 .

.17, 22, 23 ,

: B 1

. HBeAg HBV DNA . : B

precore B 39 6

HBeAg B HBeAg 32

가 가 . 100 mg 12

.24 HBeAg 13 .

HBV DNA가 ALT

ALT가 40 IU/L

92.3% , HBV DNA가

HBeAg 32 71.9% 가 5

75% HBeAg HBeAg pg/mL 가 ALT

가 가 40 IU/L

(p>0.05). IU/L HBV

가 18 DNA ALT breakthrough .

HBV DNA가 66.7% , Chayama nested PCR

ALT가 77.8% YMDD motif . :

, 27 1 45 44 (97.8%)

85.2% 81.5% HBV DNA가 9 (20%)

가 (p>0.05). HBV DNA breakthrough가 .

HBeAg HBeAg 32 8 (25%)

16.7% , HBV

18.5% 가 DNA ALT breakthrough가 9

(p>0.05). 8 , YIDD가 3

B 31 8

1 , YVDD가 1 , YIDD가 3

HBV DNA , ALT . HBeAg

HBeAg 가

HBeAg 가 . :

HBV DNA precore B B 1

가

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