Predictors of Serum qHBsAg Decline in Chronic Hepatitis B Patients Undergoing Entecavir Therapy

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INTRODUCTION

- Genotype A, high HBV DNA, high ALT, high qHBsAg, and older age were significantly associated with more HBsAg decline in HBeAg-positive CHB patients receiving Entecavir or Tenofovir therapy (JID 2011;204:415-418).

- Patients who cleared HBsAg had a greater median change from baseline in plasma qHBsAg levels at week 24 compared to patients who did not clear HBsAg (2.41 $\log_{10}$ IU/mL vs 0.20 $\log_{10}$ IU/mL) during Tenofovir therapy (GASTROENTEROLOGY 2011: 140:132–143).

- The decline in qHBsAg level and its predictors in CHB patients undergoing long-term ETV therapy remain unclear.

AIM

- To examine the predictors of serum qHBsAg decline in CHB patients undergoing ETV therapy

PATIENTS AND METHODS

- 361 CHB patients (321 compensated and 40 acutely decompensated) receiving ETV therapy for at least 1 year were recruited from the China Medical University Hospital from JUN 2006 to MAY 2013.

- Baseline clinical data included age, gender, cirrhosis, inflammatory activity, fibrosis stage, platelet, alanine aminotransferase (ALT), albumin, total bilirubin, PT, AFP, Cr, genotype, HBV DNA, and qHBsAg. Serum ALT and HBeAg/anti-HBe (for HBeAg-positive CHB) were measured at least every 3 months during therapy. Acute decompensation was defined as total bilirubin >2 mg/dL and PT>3 seconds prolonged over control. Serum qHBsAg levels were quantified using the Abbott Architect HBsAg QT assay (dynamic range, 0.05-250 IU/mL) at baseline (BL), 12, 24 and 52 weeks, and yearly thereafter during therapy. Serum HBV DNA levels were measured with the Cobas Amplicor HBV Monitor Test (Roche Diagnostics, lower limit of detection, 312 copies/mL) at baseline, 12, 24 and 52 weeks, and every 6 months thereafter during therapy.

- Multivariable logistic regression was used to identify factors associated with the decline of serum qHBsAg. Statistical analyses were performed using the SAS 9.3 software.

RESULTS

Table 1 Baseline characteristics of CHB patients (N=361)

Variable Median±IQR or N (%)	Total (N=361)	HBeAg(-) (N=224)	HBeAg(+) (N=137)	P value
Age: year	49.0±17.0	53.0±15.0	42±16.5	<0.0001
Gender				0.8452
Female	89(24.7)	56(25.0)	33(24.1)	
Male	272(75.3)	168(75.0)	104(75.9)	
Genotype				0.0160
B	206(59.2)	138(64.2)	68(51.1)	
C	142(40.8)	77(35.8)	65(48.9)	
Cirrhosis				0.0032
No	246(68.1)	140(62.5)	106(77.4)	
Yes	115(31.9)	84(37.5)	31(22.6)	
Platelet: x10³/μL	154.0±72.5	146.0±69.0	169.0±69.0	0.0008
ALT: IU/L	87.0±219.0	72±151	116±449	0.0001
METAVIR A				0.1406
0-1	141(62.4)	95(66.0)	46(56.1)	
2-3	85(37.6)	49(34.0)	36(43.9)	
METAVIR F				0.4113
0-2	121(52.4)	74(50.3)	47(56.0)	
3-4	110(47.6)	73(49.7)	37(44.0)	
Albumin: g/dL	4.10±0.60	4.00±0.70	4.10±0.50	0.0467
Total bilirubin: mg/dL	1.06±0.72	1.06±0.60	1.09±0.84	0.5082
PT: seconds prolonged	1.20±2.01	1.20±2.04	1.20±1.97	0.9734
AFP: ng/mL	5.76±12.6	5.09±12.5	7.10±13.0	0.0361
Cr: mg/dL	0.88±0.27	0.90±0.27	0.86±0.25	0.0233
HBVDNA: $\log_{10}$ copies/mL	6.56±2.86	6.03±2.23	8.02±2.26	<0.0001
qHBsAg: $\log_{10}$ IU/mL	3.30±0.82	3.13±0.77	3.60±0.90	<0.0001

Table 2 Factors associated with serum qHBsAg decline from baseline of ≥ 50% at 3M of therapy in HBeAg-positive CHB patients(N=137)

Variables	Univariable analysis Odds Ratio(95% CI)	P value	Multivariable analysis Odds Ratio(95% CI)	P value
Age: year	0.950(0.917-0.984)	0.0045		
Gender (male vs female)	1.180(0.507-2.745)	0.7004		
Genotype (B vs C)	3.244(1.490-7.065)	0.0030	2.572(1.017-6.504)	0.0460
Cirrhosis(no vs yes)		NA		
Platelet: x10³/μL	1.003(0.996-1.010)	0.3449		
ALT: IU/L(≥120 vs <120)	10.833(4.505-26.050)	<0.0001	9.295(3.610-23.932)	<0.0001
METAVIR A (2-3 vs 0-1)	3.579(1.294-9.901)	0.0141		
METAVIR F(0-2 vs 3-4)	5.383(1.623-17.852)	0.0059		
Albumin: g/dL	0.812(0.390-1.692)	0.5779		
Total bilirubin: mg/dL	1.219(1.001-1.484)	0.0483		
PT: seconds prolonged	1.119(0.940-1.330)	0.2058		
AFP: ng/mL (≥8 vs <8)	2.704(1.275-5.734)	0.0095		
Cr: mg/dL	0.792(0.241-2.608)	0.7014		
HBVDNA: $\log_{10}$ copies/mL	1.781(1.290-2.458)	0.0004		
qHBsAg: IU/mL (≥5000 vs <5000)	4.315(1.995-9.336)	0.0002	3.795(1.513-6.504)	0.0045

NA: odds ratio cannot be estimated because of empty cell (qHBsAg declines from baseline in all cirrhosis patients <50% at 3M of therapy

Table 3 Factors associated with serum qHBsAg decline from baseline at 12 months of therapy in HBeAg-negative CHB patients(N=224)

| Variables	Univariable analysis Odds Ratio(95% CI)	P value	Multivariable analysis Odds Ratio(95% CI)	P value
Age: year	0.972(0.944-1.001)	0.0545		
Gender (male vs female)	2.210(0.965-5.062)	0.0608		
Genotype (B vs C)	2.132(1.010-4.497)	0.0469		
Cirrhosis (no vs yes)	2.011(0.994-4.066)	0.0519		
Platelet: x10³/μL	1.002(0.997-1.007)	0.4846		
ALT: IU/L (≥120 vs <120)	8.922(4.386-18.147)	<0.0001	8.255(3.866-17.631)	<0.0001
METAVIR A (2-3 vs 0-1)	3.889(1.637-9.236)	0.0021		
METAVIR F(0-2 vs 3-4)	2.571(1.076-6.145)	0.0337		
Albumin: g/dL	0.994(0.506-1.952)	0.9859		
Total bilirubin: mg/dL	1.135(0.993-1.298)	0.0627		
PT: seconds prolonged	1.317(1.112-1.558)	0.0014		
AFP: ng/mL (≥8 vs <8)	1.744(0.912-3.332)	0.0925		
Cr: mg/dL	1.523(0.756-3.068)	0.2396		
HBVDNA: $\log_{10}$ copies/mL	2.015(1.568-2.589)	<0.0001		
qHBsAg: IU/mL (≥5000 vs <5000)	7.059(3.361-14.825)	<0.0001	6.311(2.724-14.624)	<0.0001
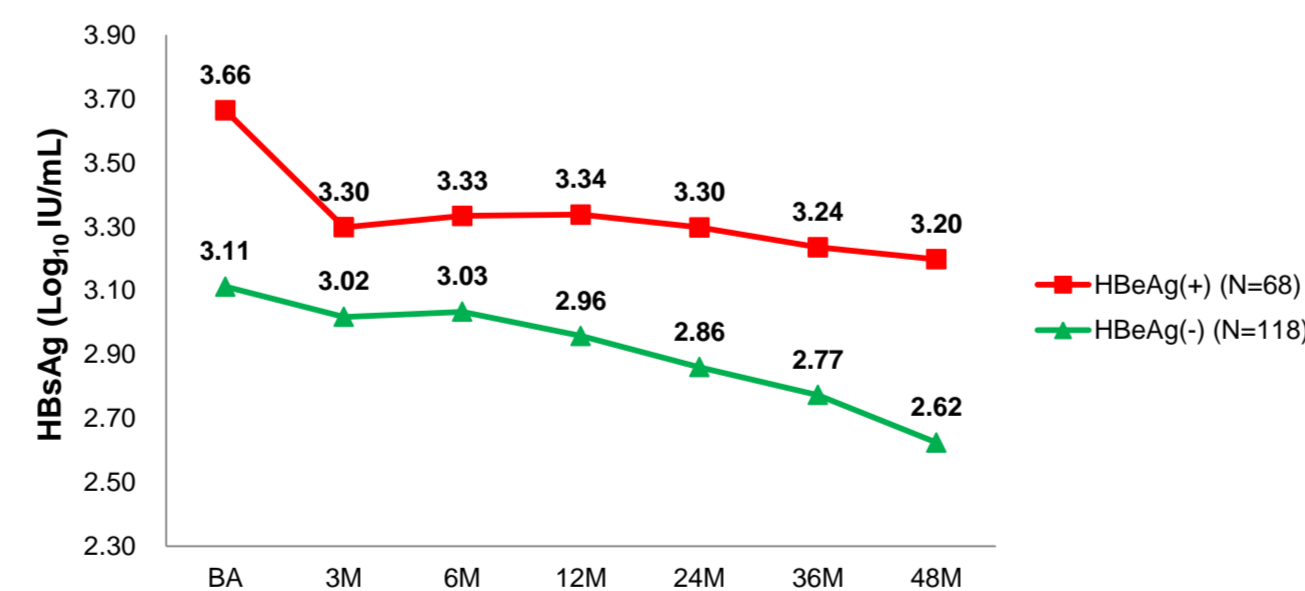
Figure 1. Serial median serum qHBsAg levels during therapy (N=186)

The median serum qHBsAg levels in HBeAg-positive patients were significantly higher than in HBeAg-negative patients at each time point (P value <0.001).

For HBeAg-positive patients, there were significant declines in qHBsAg levels between baseline and 3M, 12 and 24M (P value= 0.0281), 36 and 48M(P value= 0.0116)

For HBeAg-negative patients, there were significant declines in qHBsAg levels between baseline and 3M, 6 and 12M,12 and 24M, 24 and 36M, and 36 and 48M (all P value <0.05).

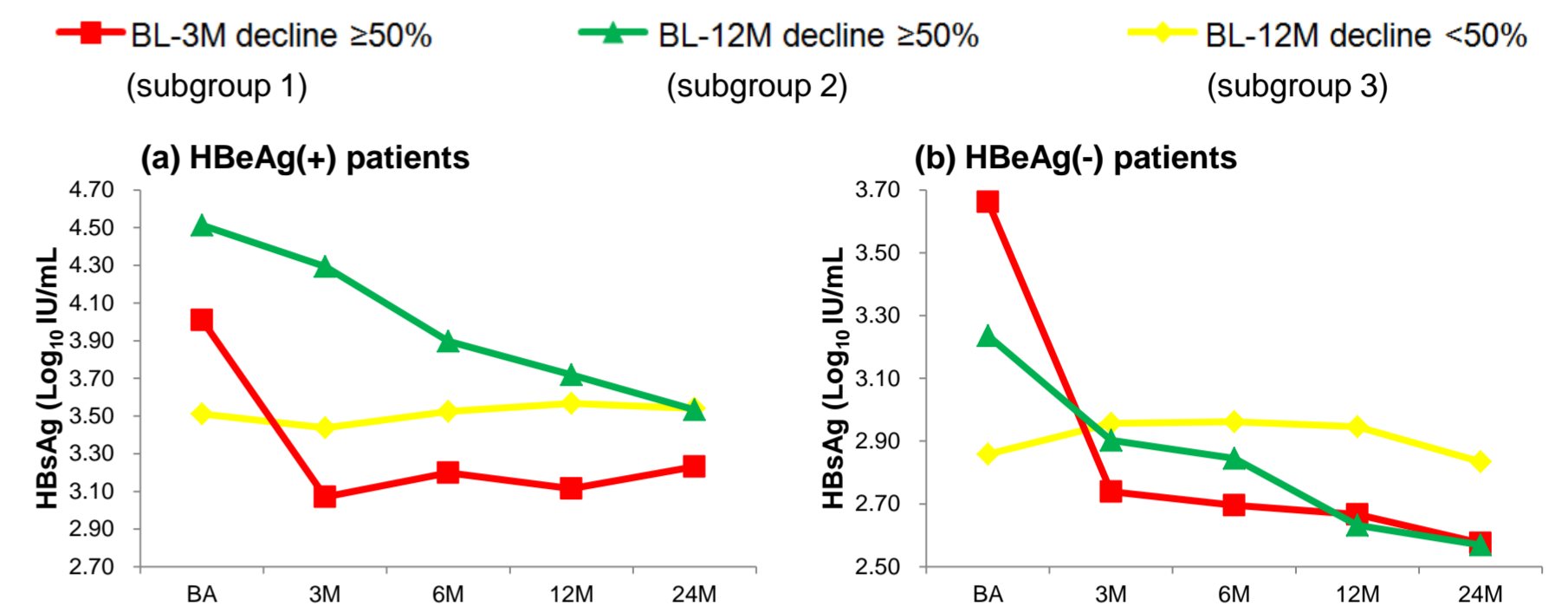This analysis included patients receiving treatment for at least 4 years.

Figure 2. Serial median serum qHBsAg levels during therapy stratified by the qHBsAg decline patterns during the first year

For HBeAg-positive patients, the subgroup 1 had significantly lower qHBsAg levels than the other two subgroups up to 2 years of treatment (All P value <0.05).

For HBeAg-negative patients, the subgroups 1 and 2 were similar except at baseline. The subgroup 1 had significantly lower qHBsAg levels than the subgroup 3 at all on-treatment time points (All P value <0.05)

This analysis included patients receiving treatment for at least 2 years.

DISCUSSION AND CONCLUSIONS

- Patients were categorized in three subgroups according to the pattern of qHBsAg decline from baseline:≧50% at 3M, ≧50% at 12M, and <50% at 12M. Among HBeAg-positive patients, the subgroup with qHBsAg decline from baseline of ≧50% at 3M of therapy had significantly lower qHBsAg levels than the other two subgroups up to 2 years of treatment. Among HBeAg-negative patients, the qHBsAg levels between the subgroups with qHBsAg decline from baseline of ≧50% at 3 or 12M of therapy were similar except at baseline

- For HBeAg-positive patients, genotype B, ALT ≧120 IU/L and baseline qHBsAg ≧5000 IU/mL as predictors of qHBsAg decline from baseline of ≧50% at 3M of therapy

- For HBeAg-negative patients, ALT ≧120 IU/L and baseline qHBsAg ≧5000 IU/mL as predictors of qHBsAg decline from baseline of ≧50% at 12M of therapy

The authors have no financial relationship to disclose relevant to this poster presentation