The risk of HBV reactivation among HBV/HCV co-infected patients treated with direct-acting antiviral agents : A single center experience

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1 INTRODUCTION

- As the number of reports of hepatitis B virus (HBV) reactivation increases in patients with HBV/HCV co-infection with direct-acting antiviral (DAA) agents, the US Food and Drug Administration has issued warnings about the potential risk of HBV reactivation in these patients.
- So far, there are very limited clinical data.

2 AIM

- To report the efficacy of anti-HCV treatment in CHC patients co-infected with HBV
- To report the HBV reactivation rate in CHC patients co-infected with HBV during and afer anti-HCV treatment
- To elucidate the factors affecting HBV reactivation in CHC patients co-infected with HBV during and after anti-HCV treatment

3 METHOD

- Retrospective observational study
- **62 patients** with HBV/HCV co-infection between January 2005 and April 2018 at the Pusan National University Hospital
- Definition of HBV reactivation
  - ≥1 $\log_{10}$ increase in HBV replication from baseline levels

  or
  - new appearance of HBV DNA in patient with previously undetectable levels

4 RESULTS

Table 1. Clinical characteristics

Characteristics	Value
Age, yr, mean ± SD	63 ± 11
Sex, Male/Female, n (%)	37 /25 (59.7) / (40.3)
Genotype of HCV, n (%)	
1b	33 (53.2)
2	21 (33.9)
3	1 (1.6)
4	1 (1.6)
Not detected	3 (4.8)
Unknown	3 (4.8)
Presence of cirrhosis, n (%)	23 (37.1)
Treatment experience, n (%)	
No treatment	13 (21.0)
IFN only	25 (33.9)
DAA only	15 (24.2)
DAA after treatment failure of IFN	9 (14.5)
Regimen of DAA, n (%)	
Daclatasvir + Asunaprevir	10 (41.7)
Sofosbuvir + Ribavirin	8 (33.3)
Daclatasvir + Sofosbuvir	1 (4.2)
Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir	5 (20.8)
ALT level before treatment, mean ± SD	50.3 ± 44.3
HCV RNA level before treatment, mean ± SD	$2.96*10^6 \pm 4.64*10^6$

Table 2. Comparison of the efficacy

	Treatment group		
		DAA	
	IFN only (n = 25)	DAA after treatment failure of IFN (n = 9)	DAA only (n = 15)
SVR, n (%)	20/34 (61.8)	19/24 (79.2)	
		7/9 (77.8)	12/15 (80.0)

Table 3. Comparison of the HBV reactivation rates

	Treatment group		
		DAA	
	IFN only (n = 25)	DAA after treatment failure of IFN (n = 9)	DAA only (n = 15)
HBV reactivation, n (%)	2 (8.0)	9/24 (37.5)	
		5/9 (55.6)	4/15 (26.7)

Table 4. Predictive factors affecting HBV reactivation

Characteristics	No HBV reactivation N = 38	HBV reactivation N = 11	*P* value
Sex, n (%)			0.037
Male	25 (65.8)	3 (27.3)	
Female	13 (34.2)	8 (72.7)	
Age, mean ± SD	64.2 ± 8.5	61.6 ±12.8	0.147
HCV genotype, n (%)			0.039
1b	18 (47.4)	9 (81.8)	
2	18 (47.4)	1 (9.1)	
3	0 (0.0)	1 (9.1)	
4	1 (2.6)	0 (0.0)	
Not detected	1 (2.6)	0 (0.0)	
ALT level before treatment, mean ± SD	56.4 ± 48.8	49.5± 47.8	0.679
HCV RNA level before treatment, mean ± SD	$3.31*10^6 \pm 5.54*10^6$	$2.16*10^6 \pm 1.93*10^6$	0.294

Characteristics	No HBV reactivation N = 38	HBV reactivation N = 11	*P* value
Treatment group, n (%)			0.010
IFN only	23 (60.5)	2 (18.2)	
DAA only	11 (28.9)	4 (36.4)	
DAA after treatment failure of IFN	4 (10.5)	5 (45.5)	
Experience of DAA treatment, n (%)			0.013
No	23 (60.5)	2 (18.2)	
Yes	15 (39.5)	9 (81.8)	
Presence of cirrhosis, n (%)			0.492
No	22 (57.9)	8 (72.7)	
Yes	16 (42.1)	3 (27.3)	

✓ On multivariate analyses, the experience of DAA (odds ratio [OR] 19.306, 95% confidence interval [CI] 1.600–107.825, *P* = 0.016) and female (OR 13.193, 95% CI 1.614-107.825, *P* = 0.020) were significant factors associated with HBV reactivation after HCV treatment.

Table 5. Virological characteristics of patients experience HBV reactivation during or after anti viral therapy for CHC

	Sex	Age	HCV GT	HCV treatment	SVR	Initial HCV RNA (IU/mL)	Initial HBV DNA (IU/mL)	HBV reactivation						NUC therapy	F/U (days)
								Time	HBV DNA (IU/mL)	ALT	Peak HBV DNA (IU/mL)	Peak ALT	Recovery	HBV DNA (IU/mL)	
1	M	39	3	IFN	Yes	1320000	129	149 wks after Tx. termination	1510	13	2360	35	561 wks after Tx. termination	<20	No	4188
2	F	56	1b	IFN	Yes	3140000	Not detected	113 wks after Tx. discontinuation	28	26	778	26	279 wks after Tx. discontinuation	335	No	2135
3	F	80	1b	D+A, 24wks	Yes	62000	42	4 wks after Tx. initiation	7480	17	7480	35	12 wks after Tx. initiation	<20	No	295
4	F	69	2	S+R, 16wks	Yes	1890000	Not detected	38 wks after Tx. termination	35	14	35	14	51 wks after Tx. termination	<20	No	456
5	F	76	1b	OBV/PTV/r+DSV, 12wks	Yes	502000	Not detected	12 wks after Tx. initiation	835	23	835	23	12 wks after Tx. termination	<20	No	85
6	F	63	1b	D+A, 24wks	Yes	1390000	Not detected	12 wks after Tx. initiation	42	26	42	113	16 wks after Tx. initiation	<20	No	270
7	F	66	1b	IFN → D+A, 10wks	No	6700000	Not detected	52 wks after Tx. discontinuation	114	76	114	76	Transfer		No	367
8	M	48	1b	IFN → D+A, 24wks	Yes	1300000	Not detected	48 wks after Tx. termination	9180	47	9180	47	Ongoing follow up		No	337
9	F	74	1b	IFN → D+S, 12wks	Yes	3410000	102	4 wks after Tx. initiation	22900	11	22900	11	12 wks after Tx. initiation	<20	No	437
10	M	52	1b	IFN → OBV/PTV/r+DSV, 12wks	Yes	452000	Not detected	4 wks after Tx. initiation	46	14	197	16	12 wks after Tx. initiation	Not detected	No	169
11	F	55	1b	IFN → D+A, 24wks	Yes	3580000	<20	16 wks after Tx. initiation	693	24	1010	42	24 wks after Tx. termination	<20	No	253

5 CONCLUSIONS

- HBV reactivation occurs more frequently in HBV/HCV co-infected patients who were treated with DAAs compared with IFN-based therapy.
- However, biochemical breakthrough was not occurred.

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