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Poster for you

CHRONIC DELTA HEPATITIS WITHOUT EFFICIENT TREATMENT POSES A GREATER RISK FOR HEPATOCELLULAR CANCER DEVELOPMENT THAN CHRONIC HEPATITIS B WITH EFFICIENT TREATMENT

ONUR KESKIN[1,2], ÇAĞDAŞ KALKAN[1], MESUT GÜMÜŞSOY[1], ESRA YURDCU[3], ZEYNEP MELEKOĞLU ELLIK[2], YUSUFCAN YILMAZ[2], HASAN SAHIN[1], YAVUZ EMRE PARLAR[1], BENGI OZTURK[1], RAMAZAN IDILMAN[2,3], A MITHAT BOZDAYI[3], CIHAN YURDAYDIN[2,3,4]
[1]Department of Gastroenterology, University of Hacettepe Medical School, Ankara
[2]Department of Gastroenterology, University of Ankara Medical School, Ankara
[3]Hepatology Institute, University of Ankara, Ankara, Turkey
[4]Department of Gastroenterology and Hepatology, Koç University, Istanbul, Turkey

Introduction/Summary

- The risk of hepatocellular carcinoma (HCC) in patients with chronic hepatitis B (CHB), treated with entecavir (ETV) or tenofovir (TDF) has been explored in large cohort studies.
- However, data in chronic hepatitis D (CHD) patients are limited.
- This study aimed to compare in well-defined CHD and CHB cohorts the effect of treatment with respect to HCC development. We analyzed the effect of maintained viral suppression on development of HCC in CHD and yearly incidence rates of HCC in CHB and CHD patients within the first 60 months and beyond the first 60 months of therapy.

Study Design and Methods

- We searched our CHB and CHD databases for patients who had received treatment for CHB and CHD. 124 CHD patients (88M/36F; mean age: 40.3±10.3 years, 28 cirrhotic/96 non-cirrhotic at baseline) had received at least 6 months and up to a cumulative duration of 10 years of IFN (**Figure 1**). In the CHB group, 238 chronic CHB patients (164M/74F; mean age: 48.5±12.7, 63 cirrhotic/175 non-cirrhotic at baseline) were included.
- All CHB patients were receiving TDF (n:163) or ETV (n:75) and 94% of patients had a virological response. Of 238 patients in CHB cohort, 65 patients had a history of IFN and/or lamivudine and/or adefovir treatments. Of the 124 CHD patients, 40 had a maintained virological response (MVR) which was defined as durable negative HDV RNA for at least 2 years of post-treatment follow-up.

Results-1

- Median follow up time after start of therapy was 111 (10-144) months for CHB patients and 115 (11-144) months for CHD (p:0.5).
- HCC developed in 21 (8.8%) of CHB and in 21 (16.9%) of CHD patients. Univariate analysis shows that CHB and CHD patients who developed HCC were older (59.3±8.2 vs 47.5±12.6¸p<0.01 and 47.4±7.5 vs 38.9±10.1; p<0.01, respectively). In both groups, the platelet count in patients who developed HCC was found to be lower than in those who did not develop HCC.
- By multivariate analysis, age [95% CI OR: 1.09 (1.05-1.14);p<0.01], presence of CHD [95% CI OR: 5.29 (2.11-13.3);p<0.01] and GGT levels [95% CI OR: 1.010 (1.006-1.014);p<0.001] and to have a cirrhosis [95% CI OR: 2.77 (1.28-6.06);p:0.01] were independent predictors of HCC development (**Table 1**).
- When the analysis was performed only among MVR (-) CHD patients and CHB patient groups, the presence of delta hepatitis was found to be a stronger predictor of HCC development [95% CI OR: 9.09 (2.99-23.8); p<0.001].
- While the HCC development rate was 21% (18/84) in CHD patients in whom MVR could not be achieved, this rate was 8.8% (21/238) in the CHB group (p:0.003). In CHD patients in whom MVR was achieved, HCC developed in 3 patients (7.5%). This rate was found to be similar to the CHB patient group (p:0.53).
- Cumulative probability of HCC development was 0.4%, 3.8%; 7.2%, 8.2%, 10.0% and 10.0% and 0.8%, 4.9%, 9.3%, 11.2%, 18% and 23.2% at 12, 36, 60, 84,120 and 144 months of follow-up for CHB and CHD patients, respectively (**Figure 2**).
- While the HCC incidence rate in patients with CHB monoinfection was 1.04% per 100 patients per year, the incidence rate in CHD patients was calculated as 1.95% (p:0.04). The HCC incidence rate was found to be 0.78% in CHD patients in whom MVR was achieved, and 2.59% in CHD patients in which MVR could not be achieved.

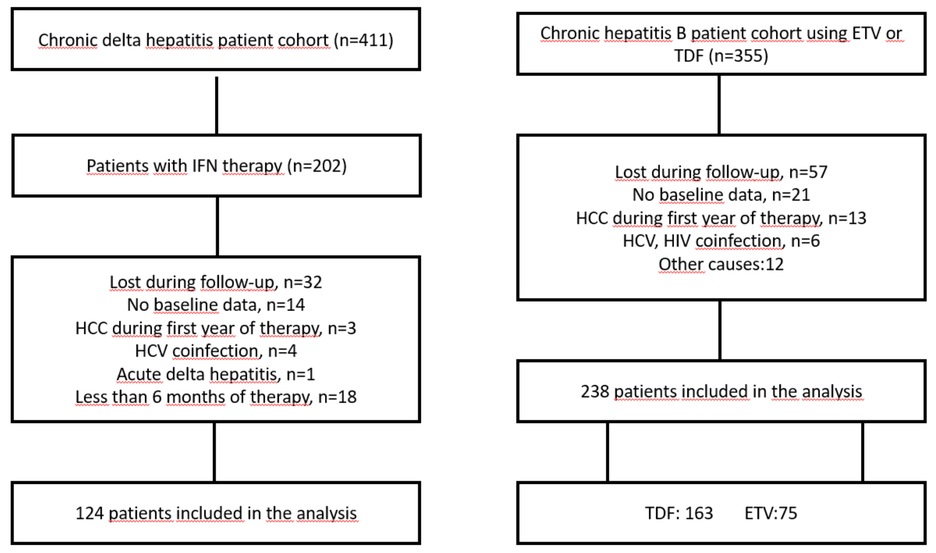

Figure 1. Flow charts of CHB and CHD patient cohorts

Characteristics				Multivariable analysis	
	HCC (n=42)	No HCC (n:320)	p	OR (95% CI)	p
Age	53.02±9.79	44.76±12.49	**<0.001**	1.09 (1.05-1.14)	**<0.01**
Male sex	36M/6F	216M/104F	0.08	0.548 (0,219-1,370)	0.198
Cirrhosis (n/%)	21 (%50)	70 (%21.8)	**0.001**	2.77 (1.28-6.06)	**0.01**
Presence of CDH (n/%)	21 (%47.7)	103 (%32.0)	**0.043**	5.29 (2.11-13.3)	**<0.01**
HbeAg positive n(%)	8 (%18.2)	92 (%28.6)	0.206	0.690 (0.256-1.836)	0.458
ALT	81.27±60.05	89.15±115.26	0.657	0.998 (0.993-1.003)	0.404
Plateletx10^3/µL	144.02±64.47	184.54±70.95	**<0.001**	0.999 (0.991-1.007)	0.751
GGT	124.93±121.68	52.64±56.62	**<0.001**	1.010 (1.006-1.014)	**<0.001**
Bilirubin	1.04±0.46	0.94±0.66	0.353	0.501 (0.238-1.055)	0.069

Table 1. Multivariate analysis showing independent predictors of development of HCC

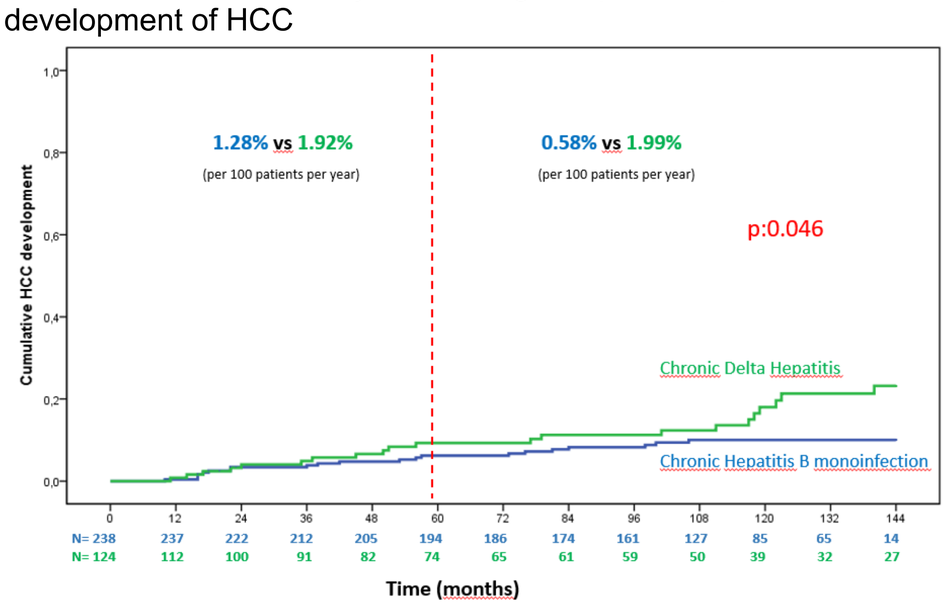

Figure 2. Development of HCC in the CHD cohort than in the CHB cohort

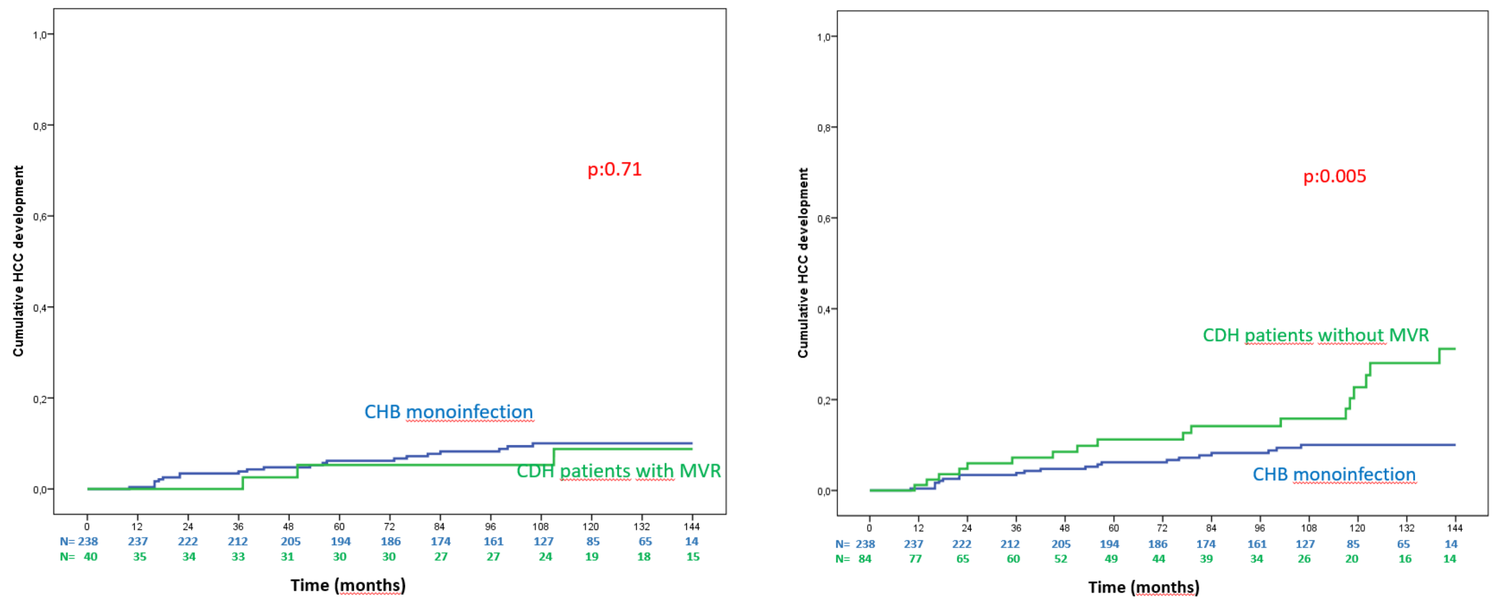

Figure 3. Development of HCC in patients with CHB monoinfection vs. CHD with and without MVR

Results-2

- In CHB monoinfected patients, incidence rate of HCC within the first 60 months was 1.28 per 100 patients per year and decreased to 0.76% after the first 60 months follow up. In CHD patients, the incidence rate was 1.92% in the first 60 months, and 1.99% after the first 60 months of follow-up.
- In CHD, HCC developed in only 3 patients who achieved MVR with a cumulative probability of 8.8% after 144 months of follow up which is similar to the cumulative probability of 10% in the CHB cohort at the same follow-up period interval (**Figure 3**).
- Yearly incidence rate of HCC in successfully treated CHD patients was 1.04% for the first 60 months and 0.52% after first 60 months which again is in accordance with incidence figures of the CHB cohort.
- Contrary, in CHD patients without MVR, HCC developed in 14 patients with a cumulative rate of 29.9% at the end of 144 months of follow up. In this IFN non-responder group, yearly incidence rate of HCC development was 2.87% for the first 5 years and 2.36% after first 5 years (**Figure 3**).
- Both cumulative HCC development and yearly HCC incidence rates in this treatment-non-responder CHD group are in variance with respective data of the CHB cohort.

Conclusion

The data suggest that patients with CHD carry a very high risk for HCC development as with durable IFN virologic response is achieved in only about 15-20% of patients. HCC was more often seen in CHD patients despite CHB being,a known independent risk factor for HCC development. The importance of virologic response is highlighted by the disappearance of the difference of HCC development when comparison to CHB is confined to CHD patients with a MVR. The results underline the urgent need for new drug development in CHD.

References

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