Missed treatment in an Italian HBV infected patients cohort: HBV RER

P1410

G Cuomo[1]; V. Borghi[1], P. Andreone[2], M. Massari[3], E. Villa[4], A. Pietrangelo[5], G. Verucchi[6], C. Ferrari[7], HBV-RER Study Group

BACKGROUND AND AIMS

Chronic Hepatitis B virus (HBV) infection is a worldwide spread disease with different clinical patterns. National and international guidelines suggest the use in first line treatment of both pegylated interferon (PE-IFN) or nucleot(s)ide analogues (entecavir or tenofovir). Very little is known about the access to treatment for CHB in the real clinical practice and mainly to the epidemiologic and clinic characteristics of the patients that not receive an antiviral therapy. In this paper we analyze exactly the clinic and epidemiologic features of the "missing treatments" derived from a multicenter observational study conducted on a HBsAg positive cohort of patients.

METHODS

HBV-RER is an observational multicenter Italian network that collects clinic and virologic data of patients with CHB coming from 33 different medical units (infectious diseases, gastroenterology, hepatology, internal medicine) of the Emilia-Romagna region. All patients with HBsAg positivity, that underwent to almost one medical visit in one of the centers involved to the study from 1st January 2009 to 31st December 2012 were considered to be eligible for the enrolment in the study Other data achieved from each patients were: demographic, haematologic and virologic parameters (transaminase, HBV viral load at baseline and during follow-up). An ALT level > 40 UI/ml was considered to be upper del normal level. The FIB4 score, a non-invasive scoring system, was used; a value <1.6 was considered as null fibrosis, between 1.6 and 3.6 as mild fibrosis, and > 3.6 as cirrhosis. We defined as missing treatments patients that underwent at least to 3 visits during the observational period.

RESULTS

Among a total of 2527 HBsAg positive patients enrolled, 1099 were never treated (NT); As showed in FIG. 1 only 698 were considered for the analysis. General characteristics of NTpatients are reported in TABLE 1. We divided patients according to transaminase and HBV DNA level, following national and international guidelines: normal (NALT) or upper level ALT (>ALT), and HBV DNA level > or < 2000 IU/ml for HbeAg negative patients and > or < 20000 IU for HbeAg positive patients and only 280 patients result to be eligible to treatment (TABLE2); a minority of these was HBeAg-positive. The median age was 42. Liver biopsy (performed in 25.9% of patients), showed that most patients had Metavir score of F0-F1. Univariate analysis (TABLE 3) between NT patients and the 290 patients receiving therapy for the first time (naive) showed that NT patients were mostly female (P=0.002), not Italian (P= 0.044), younger (P<0.001). Metavir score was lower in NT group (P0.002), such as the Fib4 score (P<0.001). HBV DNA level was significantly higher in naive patients. Al logistic regression analysis (TABLE 4) independent variables associated with the no-treatment were younger age, female gender, Metavir score F0-F1, Fib4 value lower to 1.6 and lower blood level of HBV-DNA.

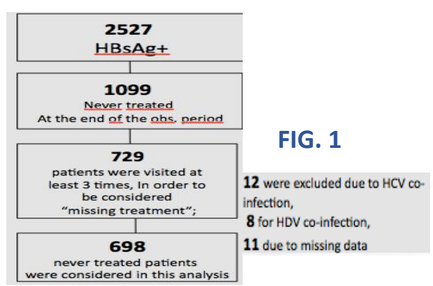

FIG. 1

Characteristics	Never Treated Num.: 698
Gender Male	431 (61.7%)
Strangers	326 (46.7%)
Ethnicity	
Caucasian	556 (79.7%)
Asian	67 (9.6%)
Black	71 810.2%)
Ispanic	4 (0.6%)
Age (median)	42 (18-83)
HBeAg	
Positive	92 (13.2%)
Negative	606 (86.8%)
HBV DNA IU/ml (median)	2165 (0 – 10000000)
Biopsy	
Performed	181 (25.9%)
Not Performed	517 (74.1%)
Fibrosis	
F0-F1	141 (77.9%)
F2	15 (8.3%)
F3-F4	9 (5%)
NC	16 (8.8%)
FIB4	
<1.6	545 (78.1%)
≥1.6 - <3.6	81 (11.6%)
≥3.6	16 (2.3%)
NC	56 (8%)

TABLE 1: *General Characteristics of NT pts*

Characteristics	Never Treated Num.: 280	Naive Num.: 290	P value
Gender			
Male	164 (58.6%)	206 (71%)	0.002
Strangers	148 (52.9%)	128 (44.1%)	0.044
Ethnicity			0.393
Caucasian	205 (73.2%)	223 (76.9%)	
Asian	39 (13.9%)	38 (13.1%)	
Black	34 (12.1%)	29 (10%)	
Ispanic	2 (0.7%)	0 (0%)	
Age (median)	39 (18-77)	47 (18-91)	<0.001
HBeAg +	55 (19.6%)	69 (23.8%)	0.264
Biopsy Performed	94 (33.6%)	95 (32.8%)	0.859
HBV DNA UI/ml	22647 (2080 - 1000000000)	1525176 (2026 - 2000000000)	0.001
Fibrosis			0.002
F0-F1	80 (85.1%)	56 (59%)	
F2	8 (8.5%)	16 (16.8%)	
F3-F4	4 (4.3%)	17 (17.9%)	
NC	2 (2.1%)	6 (6.3)	
FIB4			<0.001
<1.6	227 (81.1%)	142 (49%)	
≥1.6 - <3.6	32 (11.4%)	100 (34.5%)	
≥3.6	4 (1.4%)	44 (15.2%)	
NC	17 (6.1%)	4 (1.4%	

TABLE 3: *Univariate analysis*

TABLE 2: *Eligible pts to treatment*

HbeAg +	
>ALT<20000	23 (3.4%)
>ALT>20000	55 (7.9%)
NALT<20000	11 (1.6%)
NALT>20000	3 (0.4)
HbeAg -	
>ALT<2000	233 (33.4%)
>ALT>2000	225 (32.2%)
NALT>2000	57 (8.2%)
NALT<2000	91 (13%)

TABLE 4: *Logistic regression analysis*

Factors	OR	95% CI	P=
Age	0.968	0.953-0.984	<0.001
Gender M vs F	1.712	1.177-2.491	0.005
Strangers vs Italians	1.296	0.848-1.981	0.230
HBV-DNA (IU/ml)	1.000	1.000-1.000	0.001
Metavir F3-F4 vs others	3.321	1.051-10.495	0.041
Fib4 ≥ 3.6 vs others	8.764	3.034-25.322	<0.001

DISCUSSION AND CONLUSIONS

- A more advanced liver disease (Fib4 < 3.6, Metavir F3-F4 at the biopsy) was associated to the choice of treatment, this according to most guidelines. We have to put attention to the fact that 4 patients presented a severe liver disease (fib4 >3.6) and were not treated.
- HBV DNA level was independently associated to the choice to treat or not. (probably related to many studies that have demonstrated the relationship between elevated HBV DNA level and the risk of deteriorate liver function and the advancement of cirrhosis from a compensatory to a decompensated stage and HCC?).
- The availability of potent antiviral agent that ensure a durable viral suppression and a consequent control on the disease progression, that on the other hand must be used long life, can explain the choice of defer treatment in patients with mild HBV disease.

[1]Infectious Disease, Azienda Ospedaliero Universitaria di Modena, Modena, [2]Internal Medicine, Azienda Ospedaliero Universitaria di Bologna, Bologna, [3]Infectious Disease, IRCCS – ASMN Reggio Emilia, Reggio Emilia, [4]Gastroenterology, Azienda Ospedaliero Universitaria di Modena, [5]Internal Medicine, Azienda Ospedaliero Universitaria Modena, Modena, [6]Infectious Disease, Azienda Ospedaliero Universitaria di Bologna, Bologna, [7]Infectious Disease and Hepatology, Azienda Ospedaliero Universitaria di Parma, Parma,

26th ECCMID Amsterdam, Netherlands 9 – 12 April 2016 ESCMID