Immune Response to Recombinant Hepatitis B Vaccine in Persons With Isolated Serum Antibody to Hepatitis B Core Antigen

İZOLE ANTİ-HBc POZİTİFLİĞİ TESPİT EDİLEN BİREYLERİN REKOMBİNAN HEPATİT B AŞISINA İMMUN CEVAPLARI

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SUMMARY

Twenty people (10 males, 10 famelas, mean age: 46.30+15.34 years), referred to our hepatology clinic between October 1991 and April 1992 because of their isolated anti-HBc seropositivity, were evaluated for their immune response to recombinant HBV vaccine (GENHEVAC B Pasteur). The vaccine was injected intramuscularly in the deltoid muscle. The immunisation regimen consisted of 3 injections of 0.5 ml given one month apart. Satisfactory anti-HBs response was observed 13 of 20 patients (65%) after the first dose (mean serum anti-HBs titers: 47.16+24.92 IU/liter); this rate was 75% after the third dose (mean anti-HBs: 48.40+26.69 IU/liter).

We conclude that persons with isolated anti-HBc seropositivity may develop an appreciable anti-HBs response to HBV vaccination and investigation of this response may be useful in differing chronic HBV carriers with undetectable levels of HBsAg in their sera from people with isolated anti-Hbc seropositivity related to other clinical conditions.

Key Words: Isolated anti-HBc seropositivity, HBV vaccination

Turk J Gastroenterohepatol 1992, 3:226-228

ÖZET

izole anti-HBc pozitifliği sebebi ile, Ekim 1991-Nisan 1992 arasında hepatoloji polikliğinimize gönderilen 20 kişinin (10 erkek, 10 kadın, ortalama yaş: 46.30+15.34 yıl) rekombinan HBV aşısına (GENHEVAC B Pasteur) immun cevapları araştırıldı. Aşı intramuskuler olarak deltoid adeleye uygulandı (Bir ay ara ile toplam 3 kez 0.5 ml). ilk dozdan sonra 20 bireyin 13'ünde (%65) yeterli anti-HBs cevabı (ortalama serum anti-HBs fitresi: 47.16±24.92 IU/L) gelişti. Üçüncü dozdan sonra ise bu oran % 75 idi (ortalama anti-HBs: 48.40±26.69 IU/L).

Bu çalışmanın sonucunda izole anti-HBc pozitifliği saptanan hastaların önemli bir kısmının HBV aşısına cevap verebildiği ve bu cevabın araştırılmasının, serumlarında HBsAg tespit edilemeyen ancak kronik HBV taşıyıcısı olanlar ile diğer sebeplere bağlı izole anti-HBc pozitifliği olanlar arasında ayırıcı tanıda kullanılabileceğ sonucuna varılmıştır.

Anahtar Kelimeler: izole anti-HBc seropozitifliği, HBV aşısı

T Klin Gastroenterohepatoloji 1992; 3:226-228

Isolated anti-HBc seropositivity is still a diagnostic dilemma for most physicians. This finding may suggest a number of clinical situations including low-level HBV viremia with undetectable serum HBsAg which should be differentiated from other related conditions, especially in countries with intermediate or high HBV endemicity like Turkey. The suitability of the detection of the anti-HBs response to HBV vaccination for this purpose was suggested by a number investigators (1,2). We have assesed the usability of this method for this intent and evaluated the associated liver pathology and clinical conditions.

Submitted: 3.7.1992 **Accepted: 3.8.1992**

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MATERIALS AND METHOD

The study population consisted of 20 persons (10 males, 10 females, mean age: 46.30 + 15.34 years) referred to our Hepatology clinic because of their isolated anti-HBc seropositivity. They were evaluated for anti-HBs response to recombinant HBV vaccine (GENHEVAC B Pasteur), given one month apart. Prior to each injections and after the last dose, all individuals

were tested for serum HBsAg (EIA), anti-HBs (EIA), HBV-DNA (hybridization), anti-HCV (EIA) and transmaninase activities. Titers of anti-HBs were expressed in IU/liter by dilution method. A value of 10 III/liter was considered to be positive. In addition, people with clinical and/or with biochemical signs suggestive of hepatic disease or anti-HCV seropositvity sustained liver biopsy.

RESULTS

Adequate anti-HBs response was observed 13 of 20 patients (65%) after the first dose (mean serum anti-HBs titers: 47.16±24.92 IU/liter). This rate was 75% after the third dose (mean anti-HBs: 48.40±26.69 III/liter). One patient who did not respond to vaccination became HBsAg-positive on follow-up. HBV-DNA was negative in all of them.

Participants' anti-HBs response and their clinical characteristics were summarized in Tablo 1.

DISCUSSION

The detection of anti-HBc without other serological markers of HBV infection poses a diagnostic perplexity. In 1-2% of cases, detection of anti-HBc response alone reflects false positive results as a consequence of the limitations of the assay systems (3). True positive results can be explicated by a number of theoretical conditions:

a) Some people who were previously infected with HBV and developed both anti-HBs and anti-HBc may subsequently lose detectable anti-HBs (4,5).

b) In the "core window" period of acute HBV infection, anti-HBc may be the only detectable serological marker when HBsAg, anti-HBs and anti-HBc are measured (6). This condition was excluded in our patients with routine clinical and biochemical follow-up.

c) Chronic HBV Infection with undetectable serum HBsAg levels (3,7). One of the participants in our series became HBsAg positive on follow-up.

d) Genetically determined abnormal response to HBV antigens (8,9).

e) Failure to develop anti-HBs response because of immunosuppressed state (3). In this study, people with diabetes mellitus or renal failure may represent that situation.

f) Passive acquisition of anti-HBc from blood transfusions (3). No participants except two patients with renal failure had blood transfusion prior to this study.

g) Passive transfer of anti-HBc from HBsAg-positive mothers to their newborn infants (10).

h) Infection with non-A, non-B hepatitis agents (including HCV and others) that shares antigenic determinants with HBcAg (11,12). Anti-HCV seropostivity rate among applicants was 20 percent.

Table 1. Anti-HBs titers and clinical features of the subjects

Age/Sex	Anti-HBs at month (IU/liter)			Associated diseas	Liver biopsy
	_L	_2	__4		
53/F	0	0	0	D.mellitus (DM)	Hepatosteatosis
64/F	6	0	0	—	—
70/M	0	0	0	DM+Anti-HCV (+)	Hepatosteatosis
27/MO	0	0	0	—	CPH (")
31/M	12	0	0	tuberculosis (tbc)	normal
68/M	72	100	78	DM	Hepatosteatosis
55/M	70	52	29	cryptogenic cirr.	cirrhosis
36/F	34	66	13	—	—
29/F	50	56	30	—	Septal fibrosis
60/F	80	100	100	DM	Hepatosteatosis
35/F	0	5	70	tbc+Anti-HCV (+)	CAH (***)
57/M	23	30	30	DM	—
61/F	0	100	72	DM	—
64/M	60	0	34	—	Septal fibrosis
48/F	75	48	12	Anti-HCV (+)	CAH (*")
41/F	50	42	32	renal failure	—
35/M	0	34	72	—	—
24/F	34	30	32	—	—
28/M	24	70	52	renal failure	—
40/M	70	36	70	Anti-HCV (+)	CPH (**)

* Became HBsAG-positive on follow-up

** CPH: Chronic persistent hepatitis

*** CAH: Chronic active hepatitis

Despite the presence of multiple causes of isolated anti-HBc seropositivity, it is apparent from this study that most people with anti-HBc alone are immunologically capable to develop adequate anti-HBs response to HBV vaccination. Failing to develop this response may suggest either immunocompromised state or low-level HBV viremia.

Twelve applicants sustained liver biopsy which was revealed hepatosteatosis in four, septal fibrosis in two, chronic persistent hepatitis in two, chronic active hepatitis in two and cirrhosis in one of them. These results mostly reflected associated disease (diabetes mellitus etc.) or underlying etiology (anti-HCV seropositvity etc.).

In summary, isolated anti-HBc seropositvitiy is a heterogenous entitiy that may be detected in a number of clinical conditions. These people may develop an appreciable anti-HBs response to HBV vaccination and investigation of this response may be useful in differing chronic HBV carriers with undetectable levels of HBsAg in their sera from individuals with isolated anti-HBc seropositivity related to other clinical conditions.

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