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RESEARCH ARTICLE / *ARAŞTIRMA MAKALESİ*

Hepatitis B antibody Response in Patients with Celiac and Inflammatory Bowel Diseases

Çölyak Hastaları ve İnflamatuvar Bağırsak Hastalarında Hepatit B Antikor Yanıtı

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ABSTRACT

Objective: In some patient groups, special vaccination protocols need to be followed for vaccine preventable diseases like Hepatitis B (HB). We aimed to evaluate the antibody response against the HB vaccine in Inflammatory Bowel Disease (IBD) and Celiac Disease (CD) patients, emphasizing the efficiency of the routine vaccine protocol for these patient groups.
Material and Methods: We included 219 patients (CD and IBD) and 125 in the healthy control group (HCG). The patients who had received only 3 doses of HB vaccine were included. The design of the study is retrospective in manner.
Results: The patients age with positive antibody (anti-HBs titers) were lower than in patients with negative anti-HBs titers. In patients having positive anti-HBs titers, both the serum glutamic-oxaloacetic transaminase (SGOT) and serum glutamic-pyruvic transaminase (SGPT) values were found to be significantly higher.
Result: Following periodic control measures and administering an additional dose of the HB vaccine is required because the antibody protection decreases as the illness continues to progress with the increasing age of the patients.

Keywords: Celiac disease (CD), Hepatitis B (HB) vaccine, antibody (Anti-HBs titers), inflammatory bowel disease (IBD), pediatric

ÖZ

Amaç: Bazı hasta gruplarında özellikle Hepatit B virüs enfeksiyonu gibi, aşı ile önlenebilen hastalıklar açısından özel aşılama protokollerine ihtiyaç vardır. Biz çalışmamızda İnflammatuvar Bağırsak Hastalığı (İBH) ve Çölyak Hastalığında (ÇH) Hepatit B aşı cevabını değerlendirerek bu hasta gruplarında kullanılan aşı protokolünün hastaları korumadaki etkinliğini araştırmak istedik.
Gereç ve Yöntem: Çalışmaya toplam 219 kronik hastalığı olan çocuk (ÇH ve İBH) ve 125 sağlıklı (kontrol grubu) çocuk dahil edildi. Tüm gruplarda sadece 3 doz Hepatit B aşısı yapılmış olan hastalar çalışmaya dahil edilerek ek doz yapılmış ya da eksik doz uygulanmış hastalar çalışma dışında bırakıldı. Çalışma retrospektif olarak tasarlanmıştır.
Bulgular: Çalışmaya dahil edilen hastaların anti HBs titreleri değerlendirildiğinde tüm gruplarda Anti HBs titresi pozitif olan hastaların yaş ortalamaları Anti HBs titresi negatif olan hastalara kıyasla daha düşük idi. Hastaların Anti HBs titresi pozitif olanlar değerlendirildiğinde Aspartat aminotransferaz (AST) ve Alanin aminotransferaz (ALT) değerleri daha yüksek bulundu.
Sonuç: Hastalarda antikor koruyuculuğunun zamanla azaldığı gösterilmiştir. Özellikle infeksiyon açısından risk taşıyan, immunsüpresif ilaç kullanmak zorunda olan, ÇH ve İBH, gibi hasta gruplarında aşı titresi hastalık seyri sırasında belirli aralıklar ile takip edilmeli ve gerekirse ek doz aşılama düşünülmelidir.

Anahtar Kelimeler: Çölyak Hastalığı (ÇH), Hepatit B virüs aşısı, Anti HBs antikor titresi, İnflammatuvar bağırsak hastalığı (İBH), çocuk

INTRODUCTION

Hepatitis B virus (HBV) infection is the most important cause of chronic hepatitis in children. The course of the disease may be severe in some patient groups, especially in patients with inflammatory bowel disease (IBD) and Celiac disease (CD). Both CD and IBD are chronic diseases that commonly affect children. Using immunosuppressive agents to treat IBD posses additional risks for patients in addition to infectious diseases. Moreover, patients whose autoimmunity is triggered (e.g., patients suffering from CD) are at risk of infection due to defects in their spleen function (1, 2).

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Chronic HBV infection is one of the diseases that can be prevented by vaccination. In some patient groups (e.g., patients with CD and IBD), special vaccination protocols need to be followed for vaccine preventable diseases. Several studies are being conducted in this area (3,4). We aimed to evaluate the immune response against the HB vaccine in IBD and CD, and emphasize the efficiency of the routine vaccine protocol for these patient groups. We want to analyze the need for another dose of vaccine for these patient groups.

MATERIAL AND METHODS

We included 219 patients (39 patients diagnosed with IBD and 180 patients CD) and 125 HCG. All the patients were seen in the Pediatric Gastroenterology Outpatient Clinic in the Adana City Training & Research Hospital. The ethics committee approval was received from the same hospital, approval number: 74/1216. Upon clinical supervision, the patients diagnosed with laboratory support and colonoscopic biopsy were included in the IBD group. The diagnoses of CD were performed in accordance with the items determined by the European Society for Pediatric Gastroenterology, Hepatology and Nutrition Committee in 2012 (5). All the anti-HBs titers of IBD and CD were routinely detected prior to the diagnosis. We analyzed the anti-HBs titers of all the patients retrospectively from the patients file. Totally, we included 125 HCG who were examined for anti-HBs titers in the same clinic for a different reason. Only the patients who were in the Ministry of Health's vaccination scheme were analyzed in the study (who completed only/all three doses of HB vaccine) and we excluded the patients with additional vaccination doses. HBs antigen values of the patients were measured to exclude the HB carriers/infections. The examination of anti-HBs titers was conducted in two groups: one group was anti-HBs titers >10 IU/L and second group was anti HBs titers <10 IU/L. Based on the classification by the World Health Organization, patients having anti-HBs titer >10 IU/L were considered positive (i.e., the protective antibodies against the disease were considered sufficient) and anti-HBs titer <10 IU/L (did not possess sufficient levels of protective antibodies) were considered negative (6).

We used the SPSS 23.0 for the statistical analysis of the study. For categorical measurements, we used numbers and percentages. Continuous measurements were summarized as mean (minimum–maximum), median and standard deviation (SD). The Pearson's chi-squared test and Fisher's exact tests were used to compare categorical parameters. The Shapiro–Wilk test was used to determine the parameters in normal distribution. The Mann–Whitney U test was employed in binary variables for the parameters that did not reveal normal distribution. The statistical significance level was considered as 0.05.

RESULTS

We included 219 patients (39 patients diagnosed with IBD and 180 patients CD) and 125 HCG in the study. The incidence of female patients with CD was higher than the other groups (p <0.001). The mean age (p=0.003), and the anti-HBs titer (p=0,11) in the CD group were found to be lower compared to the other two groups. And in CD patients, the SGOT (p<0.001), and SGPT (p<0.001) levels were higher than in the other groups (p<0.05) (Table 1).

In the control group, a weak correlation was found between the SGOT levels and the anti-HBs titers (p<0.05). In CD patients, a weak positive correlation was observed between the SGOT

Table 1: General distribution of the patients' gender, and laboratory data

	Control (n=125)	Coeliac Disease (CD) (n=180)	Inflammatory Bowel Disease (IBD) (n=39)	p
	n (%)	n (%)	n (%)	
Ethnicity				
Turkish	118 (94,4)	169 (93,9)	32 (82,1)	0,024
Others	7 (5,6)	11 (6,1)	7 (17,9)	
Gender				
Male	74 (59,2)	64 (35,6)	22 (56,4)	<0,001
Female	51 (40,8)	116 (64,4)	17 (43,6)	
AntiHbs >10				
Negative	54 (43,2)	91 (50,6)	13 (33,3)	0,110
Positive	71 (56,8)	89 (49,4)	26 (66,7)	
	Control (n=125)	**CD (n=180)**	**IBD (n=39)**	**p**
	Med (Min-Maks)	**Med (Min-Maks)**	**Med (Min-Maks)**	
Age	12,35 (2,39-20,94)	11,11 (2,56-20,32)	15,10 (2,37-20,95)	0,003
SGOT	24,5 (13-150,2)	32 (6,7-133)	21 (4,3-55)	<0,001
SGPT	14 (4-99)	20 (5-147)	14,8 (6-144)	<0,001
AntiHb titer	21,21 (0-4938,2)	10 (0-8138)	39,57 (0,37-1000)	<0,001

SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamic-pyruvic transaminase

(r=0.251) and SGPT (r=0.229) levels and the anti-HBs titers (Table 2). The age of the patients with positive anti-HBs values were lower than in the negative patients (p<0.001). However, in patients with positive anti-HBs titers, the SGOT (p=0.001) and SGPT (p=0.021) levels were significantly higher (p<0.05).

The CD group comprised 57.6% of the patients who had negative anti-HBs titer. When the CD group was evaluated within itself, the anti-HBs titer values were negative in 50% of the patients (i.e., the values were <10). In the control group, 43.2% of the patients had negative anti-HBs titers. In the IBD group, 33.3% of the patients had negative anti-HBs titers (Figure 1).

In HCG, the mean age of the patients with positive anti-HBs titers was low (p=0.001), and their SGOT levels were high (p=0.004). It was also noticed that 57% of the HCG had positive anti-HBs titers.

In the CD group, while the age (p<0.001), Hb (p=0.004), and mean corpuscular volume (MCV) (p=0.034) values of patients having positive anti-HBS titers were low, the SGOT (p=0.001) and the SGPT (p=0.001) levels were significantly higher in anti-HBS titers positive patients than in the negative ones (p<0.05). The classification of the groups according to the level of anti-HBs titers are classified (Table 3).

In the IBD group, the age, Hb, and the MCV values of patients having positive anti-HBs titers were lower than in patients with negative anti-HBS titers. In IBD patients, both the SGOT and SGPT levels were significantly higher (p<0.05).

In patients who had negative anti-HBs titer values, the diagnosis of CD was higher in females (p=0.003). The number of female patients was higher in the group diagnosed with CD than in the HCG and IBD groups (p<0.05). The age of the IBD patients were higher than the HCG and CD patient groups. The SGOT and SGPT values were significantly higher in the CD group than in the HCG and IBD patients.

Table 2: Distribution of the patients according to their anti-HBs titer values as positive and negative

Anti Hb titer	Negative (n=158)	Positive (n=186)	Total (n=344)	p
	n (%)	n (%)	n (%)	
Ethnicity				
Turkish	147 (93,0)	172 (92,5)	319 (92,7)	0,841
Others	11 (7,0)	14 (7,5)	25 (7,3)	
Patient groups				
Control	54 (34,2)	71 (38,2)	125 (36,3)	
CD	91 (57,6)	89 (47,8)	180 (52,3)	0,110
IBD	13 (8,2)	26 (14,0)	39 (11,3)	
Gender				
Male	68 (43,0)	92 (49,5)	160 (46,5)	0,234
Female	90 (57,0)	94 (50,5)	184 (53,5)	
	Negative (n=158)	**Positive (n=186)**	**Total (n=344)**	**p**
	Med (Min-Maks)	**Med (Min-Maks)**	**Med (Min-Maks)**	
Age	13,4 (2,98-20,82)	10,52 (2,37-20,95)	11,81 (2,37-20,95)	<0,001
SGOT	26 (11-133)	29 (4,3-150,2)	27,9 (4,3-150,2)	0,001
SGPT	16 (4,1-121)	18 (4-147)	16,5 (4-147)	0,021

CD: Celiac Disease, IBD: Inflammatory Bowel disease, SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamic-pyruvic transaminase

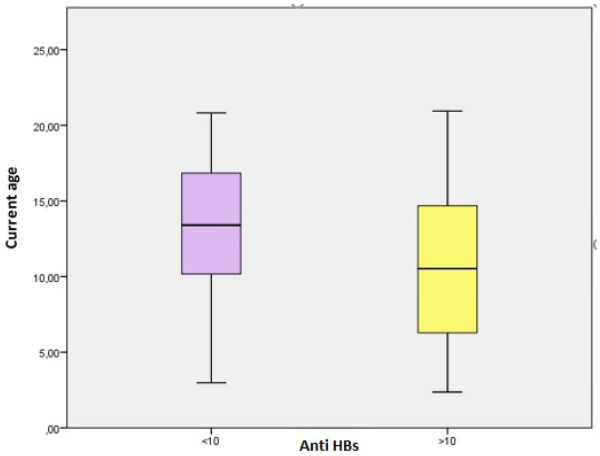

Figure 1: Relationship of anti-HBs titer values with age

DISCUSSION

The age values of all the patient groups (CD and the IBD patients both) and the HCG with positive anti-HBs titer values (p<0.001) were lower than the patients with negative anti-HBs

Table 3: Classification of the groups according to the level of anti-HBs titer values

Anti Hb titer	<10 (n=158)	10-100 (n=118)	>100 (n=68)	p
	n(%)	n(%)	n(%)	
Patient group				
Control	54 (34,2)	47 (39,8)	24 (35,3)	0,203
CD	91 (57,6)	57 (48,3)	32 (47,1)	
IBD	13 (8,2)	14 (11,9)	12 (17,6)	
Ethnicity				
Turkish	147 (93,0)	111 (94,1)	61 (89,7)	0,533
Others	11 (7,0)	7 (5,9)	7 (10,3)	
Gender				
Male	68 (43,0)	58 (49,2)	34 (50,0)	0,489
Female	90 (57,0)	60 (50,8)	34 (50,0)	

CD: Celiac Disease, IBD: Inflammatory Bowel Disease

titers ($p<0.05$). In a retrospective study conducted with CD patients, the most important element associated with the anti-HBs titer levels was the age at which anti-HBs titer values were measured (7). The findings of the study in which an inverse relationship was noticed between the anti-HBs titer values and age support the literature.

Similarly, in a cohort study, it was revealed that anti-HBs titer values were inversely related to the age of the participants at which the measurements were taken. This can be explained by the fact that, over time, as age progresses, the B-type memory cells formed against the vaccine begin to decrease and lose their protective properties (7). As was the case in the CD patient group, the results were not found to be very different from those obtained in the IBD patient group.

In the IBD patient group, the average anti-HBs titer value decreases as a patient's age increases. Anti-HBs titer values were found to decrease over time (8). In the literature (9), it has been revealed that, following vaccination, the protective anti-HBs titer value decreases by a range of 75–87% in the fifth year, and by 50–70% after 10–12 years. The most important finding was the anti-HBs titers of >100 IU/L were higher in the HCG than in the IBD group. In the patient group, unlike what is found in the literature with different ethnic groups, the anti-HBs titer values were positive in only 57% of the patients in the control group, which suggests that environmental factors play a role in the formation of anti-HBs titers (10).

In our study, in the patients who had negative anti-HBs titer values, 57.6% of them were in the CD group, 43.2% were in HCG and 33.3% were IBD patients. As indicated in the literature, the anti-HBs titers of CD were significantly lower than HCG(11). However, as shown by more recent studies, the hepatitis B vaccine unresponsiveness, which was at the rate of around 70%, was not present in the patient group (12). From this study, it can be concluded that following periodic control measures and administering an additional dose of the vaccine, the fourth dose is required because the antibody protection in CD and IBD patients decreases as the illness continues to progress with the patients getting older. This evaluation is mandatory, especially in newly CD diagnosed patients and IBD patients planning to start immunosuppressive therapy. In IBD, it is recommended that the anti-HBs titer values of patients be checked before starting immunosuppressive therapy (4) and that three new doses of the vaccine be administered to patients whose antibody titer is insufficient (13,14). In some studies, it has been recommended that CD patients also follow re-vaccination protocols (15).

In Turkey, a different vaccination program recommended for certain patient groups, such as the CD and IBD patient groups, has not been established yet. We wanted to emphasize the importance of this issue and the possible need for additional doses in these particular patient groups. Blasco V, Colavolpe JC, Antonini F, Zieleskiewicz L, Nafati C, Albanèse J, et al. Long-term outcome in kidney recipients from donors treated with hydroxyethylstarch 130/0.4 and hydroxyethylstarch 200/0.6. Br J Anaesth 2015;115(5):797-8.

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REFERENCES

1. Di Sabatino A, Brunetti L, Carnevale MG, Giuffrida P, Corazza GR. Is it worth investigating splenic function in patients with celiac disease? World J Gastroenterol 2013;19:2313-18.
2. Di Sabatino A, Rosado MM, Ciccocioppo R, Cazzola P, Morera R, Corazza GR, et al. Depletion of immunoglobulin M memory B cells is associated with splenic hypofunction in inflammatory bowel disease. Am J Gastroenterol 2005;100:1788-95.
3. Gisbert JP, Chaparro M, Esteve M. Review article: prevention and management of hepatitis B and C infection in patients with inflammatory bowel disease. Aliment Pharmacol Ther. 2011; 33:619-33.
4. Carrera E, Manzano R, Garrido E. Efficacy of the vaccination in inflammatory bowel disease. World J Gastroenterol 2013;19:1349-53.
5. Husby S, Koletzko S, Korponay-Szabó IR, Mearin ML, Phillips A, Shamir R, et al. European society for pediatric gastroenterology, hepatology, and nutrition guidelines for the diagnosis of coeliac disease. J Pediatr Gastroenterol Nutr. 2012:54:136-60.
6. Hepatitis B vaccines: WHO position paper—recommendations. Vaccine.2009;28:589-90.
7. Zifman E, Zevit N, Heshin-Bekenstein M. Turner D, Shamir R, Silbermintz A. Efect of a Gluten Free Diet on Hepatitis B Surface Antibody Concentration in Previously Immunized Pediatric Celiac Patients. Pediatr. Gastroenterol. Hepatol. Nutr. 2020;23:132-6.
8. Verso MG, Costantino C, Marrella A, Immordino P, Vitale F, Amodio E. Kinetics of Anti-Hepatitis B Surface Antigen Titers in Nurse Students after a Two-Year Follow-Up. Vaccines 2020;8:467-77.
9. John TJ, Cooksley G. Hepatitis B vaccine boosters: is there a clinical need in high endemicity populations? J Gastroenterol Hepatol. 2005;20:5-10.
10. Anania C, Olivero F, Spagnolo A, Chiesa C, Pacifco L. Immune response to vaccines in children with celiac disease. World J Gastroenterol. 2017;23:3205
11. Ertekin V, Tosun MS, Selimoglu MA. Is there need for a new hepatitıs B vaccine schedule for children with celiac disease? Hepat Mon 2011;11:634-7.
12. Sparks B, Salman S, Shull M, Trout A, Kiel A, Hill I, et al. A Celiac Care Index Improves Care of Pediatric Patients Newly Diagnosed with Celiac Disease. J Pediatr 2020;216:32-6.
13. Dipasquale V, Romano C. Vaccination strategies in pediatric inflammatory bowel disease. Vaccine 2017;35:6070-75.
14. Rahier JF, Ben-Horin S, Chowers Y, C Conlon, P De Munter, G D'Haens, et al. European evidence-based consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease. J Crohn Colitis 2009;3:47-91.
15. Passanisi S, Dipasquale V, Romano C. Vaccinations and Immune Response in Celiac Disease. Vaccines 2020;8:273-78.