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Seroprevalence of Hepatitis B, Hepatitis C, and HIV in children with cancer at diagnosis and following therapy in Turkey: progress within the last 25 years

Çocukluk çağı kanserlerinde tanıda ve tedavi sonrası Hepatit B, Hepatit C ve HIV seroprevelansı: 25 yılda gelişmeler

Rejin Kebudi[1,2], Tarkan Agasoy[3], Hande Kizilocak[1], Gül Nihal Ozdemir[1]

[1]Department of Pediatric Hematology-Oncology, İstanbul University Cerrahpaşa Faculty of Medicine, İstanbul, Turkey
[2]Oncology Institute, İstanbul University, İstanbul, Turkey
[3]Department of Pediatrics, İstanbul University Cerrahpaşa Faculty of Medicine, İstanbul, Turkey

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Abstract

Aim: Children with cancer receiving intensive chemotherapy require multiple transfusions and are at increased risk for blood transmittable diseases such as hepatitis B virus (HBV), hepatitis C virus (HBC), and HIV infections. The aim of this study was to investigate the seroprevalence of HBV, HCV, and HIV in children with cancer and to compare the results with findings in our previous cancer studies conducted before the national free HBV vaccination and the HCV screening program in blood banks were established.

Material and Methods: Sera from 100 children (51 females, 49 males) with cancer treated between January 2010 and January 2012 who received multiple transfusions were investigated for hepatitis B surface antigen (HBsAg), anti-HBs, anti-HCV, anti-HIV at diagnosis and at the end of treatment. Patients were born after 1998 when the national free hepatitis B vaccination program began.

Results: HBsAg, anti-HCV, and anti-HIV seropositivities were 0% at diagnosis and at the end of treatment. Anti-HBs seropositivity was 58% at diagnosis and 42% at the end of treatment. HBsAg seropositivity, which was 0% at the end of treatment, was lower than 10% during 1994–95, and 40% from 1986 to 1989. Anti-HCV was 0% in contrast to 14% between 1994 and 1995. Seventeen patients with anti-HBs seropositivity at diagnosis were found to be seronegative after intensive chemotherapy.

Conclusion: The nil seroprevalence of anti-HBsAg, anti-HCV, and anti-HIV in this cohort of children with cancer is encouraging. This progress is due to advances in donor screening techniques in blood banks, good hygenic practices, and the national free hepatitis B vaccination program in Turkey.

Keywords: HBsAg, HCV, HIV, pediatric oncology, transfusion

Öz

Amaç: Çocukluk çağı kanserlerinde yoğun kemoterapi sonrası kan transfüzyonu gerekliliği artmakta ve buna bağlı olarak hepatit B, hepatit C ve HIV gibi enfektif hastalıkların bulaşma olasılığı oluşmaktadır. Bu çalışmanın amacı çocukluk çağı kanserlerinde hepatit B, hepatit C ve HIV seroprevalansını incelemek ve bu sonuçları ulusal Hepatit B aşılaması başlamadan önceki ve kan bankalarında rutin hepatit C virüs (HCV) tarama programları olmadığı dönemki çalışmalarla karşılaştırmaktır.

Gereç ve Yöntemler: Ocak 2010–Ocak 2012 arası kanser tedavisi gören ve çoklu kereler kan transfüzyonu alan 100 olguda (51 kız, 49 erkek) tanıda ve tedavi sonrası HBsAg, anti-HBs, anti-HCV ve anti-HIV çalışıldı. Hastalarımız 1998 ve sonrası doğumlu olup, aynı yıl başlatılan ulusal hepatit B aşı programına dahil idiler.

Bulgular: HBsAg, anti-HCV ve anti-HIV seropozitifitesi tanıda ve tedavi sonu %0 saptandı. Anti-HbS seropozitivitesi tanı anında %58 iken, tedavi sonunda %42 idi. HBsAg seropozitifitesi tedavi sonunda 1986–89'da %40, 1994–95'te %10 iken son çalışmamızda %0 olarak bulunarak anlamlı fark gösterdi. Anti-HCV ise 1994–95'te saptanan %14'e oranla %0 bulundu. Tanıda Anti-HBs'si pozitif olan 17 hastanın kemoterapi sonrası Anti-HBs'leri negatifleşmesine rağmen hiçbirinde HBV enfeksiyonu gelişmedi.

Çıkarımlar: Bu sonucun elde edilmesinde en önemli etkenler kan bankalarındaki donör tarama tekniklerinde gelişme, hijyen koşullarının iyileşmesi ve ulusal ücretsiz hepatit B aşı programı olarak düşünülebilir. Bu sonuç, gelişmekte olan ülkeler için yol gösterici olacaktır.

Anahtar sözcükler: Çocuk kanserleri, HBsAg, HCV, HIV, transfüzyon

Corresponding Author /Sorumlu Yazar: Rejin Kebudi E-mail /E-posta: rejinkebudi@yahoo.com
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Introduction

The survival of children with cancer has increased dramatically in parallel with the advances in therapy protocols including intensive chemotherapy. These children require multiple transfusions during intensive chemotherapy and are at increased risk for blood-transmittable infections such as hepatitis B virus (HBV), hepatitis C virus (HCV), and HIV infections (1–5). The risks of these infections vary among countries depending on the frequency of the infections in the donor population and screening technology for blood and blood products used in different countries (1–6). The aim of this study was to investigate the seroprevalence of hepatitis B surface antigen (HBsAg), HCV, and HIV in children with cancer and to compare the results with findings in our previous cancer studies conducted before the national free HBV vaccination in Turkey and the HCV screening program in blood banks were established.

Material and Methods

One hundred children (51 females, 49 males) who were diagnosed as having cancer and received multiple transfusions during treatment in the Division of Pediatric Hematology-Oncology, Cerrahpasa Faculty of Medicine, University of Istanbul between January 2010 and January 2012 were enrolled in the study. All participants received multiple transfusions of blood or blood products. All patients were born in Turkey after September 1st, 1998, when the national free hepatitis B vaccination program for neonates and infants began. All patients received blood products screened for HBsAg, anti-HCV, anti-HIV1/2 using an enzyme-linked immunosorbent assay (ELISA) performed in the local blood bank. The diagnoses of patients were as follows; 70 leukemia (69 acute lymphoblastic leukemia, 1 acute myeloid leukemia), 30 solid tumors (7 neuroblastoma, 6 brain tumors, 7 lymphomas, 4 sarcomas, 3 Wilms tumors, 2 retinoblastomas, 1 germ cell tumor).

Blood samples of children were collected at diagnosis and at least 3 months (3–6 months) after cessation of therapy. The patients' sera were tested for HBsAg, anti-HBs, anti-HBsAg, anti-HCV, and anti-HIV using an ELISA. All blood and blood products have been routinely tested for HBsAg since 1975, for anti-HIV since 1987, and for anti-HCV since September 1995 in the blood banks that supplied these products to the patients in this study. Disposable and sterile materials were used in all invasive procedures. This study was approved by the Istanbul University Ethics Committee (B-24/03.05.2011). This study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

Table 1. Distribution of the anti-HBs serology before and after treatment of the patients

	Anti-HBs Negative	After treatment Positive	Total
Anti-HBs			
Negative	42	0	42
Before treatment			
Positive	17	41	58
Total	59	41	100
	Value	Exact significance value	
McNemar test	100	<0.001	

Table 2. Seroconversion of anti-HBs at the end of treatment

	Leukemia	Solid tumor		
	n	n	Total	P[a]
Negative	14 (14/41)	3 (3/17)	17 (17/58)	0.209
Positive	0 (0/0)	0 (0/0)	0 (0/0)	

[a]Pearson Chi-square test

Statistical analysis

Data were entered into the Statistical Package for the Social Sciences (SPSS) version 15 database for analysis. Pearson Chi-square tests or McNemar tests were used to compare proportions.

Results

One hundred children (51 females, 49 males) with a mean age of 4.09±2.45 (range, 4 months – 11) years were enrolled in the study. None of the patients were seropositive for HBsAg, anti-HCV, and anti-HIV, either at diagnosis or at the end of treatment (Table 1).

All patients were vaccinated for hepatitis as infants. Fifty-eight percent of the patients were seropositive for anti-HBsAg at diagnosis; however, only 41% were positive for anti-HBsAg at the end of therapy, thus 17 of the 58 patients who were positive for anti-HBsAg were seronegative for anti-HBsAg at the end of therapy (p<0.001) (Table 1).

There was no significant difference between the leukemia (14/41) and solid tumor (3/17) groups in terms of anti-HBsAg seroconversion from positive to negative (p=0.209) (Table 2). None of the patients developed HBV infection during treatment.

Discussion

The survival rates of children with cancer have increased dramatically in correlation with advances in treatment, including chemotherapy. These children require multiple transfusions during chemotherapy and are at increased

risk for blood-transmittable infections such as HBV, HCV, and HIV infections (1–6).

We have conducted three previous studies on the seroprevalence of hepatitis B, hepatitis C, and HIV in multitransfused children with cancer and benign hematologic disorders at various time points in our center and observed improvement in parallel to advances in screening methods used in blood banks, hygienic measures, and free national vaccination programs (1–3).

Turkey is in an intermediate endemicity region for HBV infection (7). In recent studies, the seroprevalence of HBsAg among blood donors and healthy adults in Turkey was reported as 1.76% and 4%, respectively (8, 9). The HBsAg seropositivity among Turkish children was reported as 5.4% before September 1998, before the national free hepatitis B vaccination program for neonates and infants began (10). After the vaccination program, HBsAg seropositivity decreased dramatically to 0.3% among Turkish children (11).

In the 1980s and early 1990s, HBsAg seropositivity was quite high at about 40–47.4% following treatment in pediatric hematology/oncology patients in Turkey (1–3). Although blood and blood products were screened for HBsAg in those years, less sensitive screening tests such as counter immuno-electrophoresis (CIE) and/or indirect hemagglutination (IHA) were used for screening (1–3). We showed that those who were transfused with blood products screened with IHA had lower HbsAg positivity than CIE, suggesting that IHA was more sensitive than the CIE method for screening. The HBsAg positivity was found to be much higher (40–40.9% vs. 8.5–9.2%) in multitransfused children with cancer compared with multitransfused children with benign hematologic disorders such as thalassemia or hemophilia (1). These results suggest that immunosuppressive therapy may increase the development of the chronic carrier state of hepatitis B in children with cancer (1).

By the late 1990s, the improvement of blood screening procedures such as the use of ELISA in blood banks in Turkey and use of disposable equipment for invasive diagnostic and treatment procedures had decreased the incidence of HBV infection (2). In our previous study conducted betwen 1994 and 1995, HBsAg seropositivity was 0% at diagnosis and 10% at the end of therapy in children with cancer, significantly lower than our results in the 1980s, but they were still quite high (1, 2).

In the present study, in which all children were fully vaccinated for hepatitis B as infants, the seroprevalence of HBsAg at diagnosis was 0%, and anti-HBs seropositivity was 58%. In healthy children, the seropositivity of anti-HBs was found at around 60% in children who were born after the hepatitis B vaccination program and who were fully vaccinated (11). In the present study, none of the patients had HBsAg seropositivity at the end of treatment.

In children recieving chemotherapy, it has been shown that there is a decrease or loss of protective levels of previously administered vaccines (12). In this study, 17 patients out of 58 who were anti-HBsAg seropositive at diagnosis were found to be seronegative at the end of treatment, as expected after intensive chemotherapy, but none of them developed HBV infections, similar to results in other local studies (13, 14). These results suggest the high protective role of the national hepatitis B vaccination program and the effectiveness of high serologic screening technology used in blood banks.

Hepatitis C virus (HCV) was a commonly encountered blood-transmittable hepatitis infection around the world among patients with cancer before the initiation of HCV screening at blood banks (15). The seroprevalence of anti-HCV in Turkish blood donors is about 0.54% (8, 16). It was a serious problem among children with cancer who recieved multiple transfusions before routine screening tests; seroprevalences of anti-HCV were reported as 2% at diagnosis and 14% following therapy in our previous study, which was performed between 1994 and 1995 (2). After screening tests for anti-HCV had begun in our country at blood banks, we reported the seroprevalence of anti-HCV as 0% at the end of therapy in pediatric patients with cancer (3). In the present study, none of patients were seropositive for anti-HCV either at diagnosis or at the end of treatment.

The risk of HIV infection in multitransfused patients is well known (6). In our previous study conducted from 1986 to 1989, seropositivity for anti-HIV was found as 0% in 50 children with cancer, and 0.9% in 109 children with benign hematologic disorders, the only patient who was HIV positive had previously been transfused abroad (1). No patients with hemophilia in those years were found to be HIV positive, which may be due to the fact that they had not recieved factor concentrates when most HIV patients in developed countries had recieved factor concentrates before HIV was demonstrated. None of the patients were seropositive for HIV in the present study. This may also be due to the fact that all patients received transfusions screened for anti-HIV.

In conclusion, the zero seroprevalence rates of HBsAg, anti-HCV, and anti-HIV after therapy is suggested to be the result of advances in donor screening techniques in

blood banks and good hygenic practices, and with regard to HBsAg, the neonatal and infant HBV vaccination program in Turkey. The incidence of HBV in children with cancer is still high in some developing countries (4). The progress leading to lower HBsAg, HCV, and HIV seroprevalance in pediatric patients with cancer in Turkey may be a promising example for other developing countries.

Ethics Committee Approval: This study was approved by the Istanbul University Ethics Committee (B-24/03.05.2011).

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