The Risk of Hepatitis B, Hepatitis C and Human Immunodeficiency Virus in Multitransfused Children with Hematological Diseases

Çok Sayıda Transfüzyon Alan Hematolojik Hastalıklı Çocuklarda Hepatit B, Hepatit C ve İnsan İmmün Yetmezlik Virüs Riski

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Abstract

Objective: Children with hematological diseases, who had received at least three transfusions, were included to estimate the transmission risks of hepatitis B (HBV), hepatitis C (HCV) and human immunodeficiency virus (HIV) infections through blood transfusions at a Pediatric Hematology Clinic in Ankara, Turkey.

Material and Methods: This study was conducted at Dr. Sami Ulus Children's Hospital, Pediatric Hematology Department, through 1 January 2004-1 June 2008. Children with the diagnoses of anemia, coagulation factor deficiency or leukemia and who had no antigen positivity for HBV, HCV or HIV at their first admission, were recruited retrospectively. After receiving three and more transfusions, their serologic results were re-evaluated for HBV, HCV and HIV.

Results: The study included a total of 220 children, of whom 59.1% were boys. The mean age was 9.1±4.25 years. After transfusion of 9402 units of blood products, the seroconversion rates were: HBsAg 5.9% (n=13), antiHCV 1.4% (n=3) and anti HIV 0%.

Conclusion: The estimated risk HBV infection in children with leukemia and aplastic anemia, receiving multiple blood transfusions was surprisingly higher than the other groups. A prospective, multicentre study is required to estimate hepatitis and HIV transmission risks more precisely.
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Key words: Children, hematological diseases, hepatitis, human immunodeficiency virus, transfusion

Özet

Amaç: Ankara'da bir Pediyatrik Hematoloji Kliniği'nde, en az üç defa transfüzyon yapılmış, hematolojik hastalığı olan çocuklarda, kan transfüzyonu ile geçen hepatit B (HBV), hepatit C (HCV) ve insan immün yetmezlik virüsü (HİV) enfeksiyonları riski değerlendirilmesi yapıldı.

Gereç ve Yöntemler: Bu çalışma, Dr. Sami Ulus Çocuk Hastanesi, Pediatrik Hematoloji Bölümü'nde 1 Ocak 2004-1 Haziran 2008 tarihleri arasında yapıldı. Anemi, pıhtılaşma faktörü eksikliği veya lösemi tanıları olan, ve ilk başvurularında HBV, HCV veya HİV saptanmayan çocuk hastalar geriye dönük olarak toplandı. Kan ürünü transfüzyonları öncesinde, ve üç ve daha fazla transfüzyon aldıktan sonra, bunların HBV, HCV ve HİV serolojilerinin sonuçları tekrar incelendi.

Bulgular: Çalışmaya alınan 220 çocuktan %59.1'i (n=130) erkekti. Ortalama yaş 9.1±4.25 olarak bulundu. Toplam 9402 ünite kan ürünü transfüzyonu sonrası serokonversiyon oranları şöyleydi: HBsAg %5.9 (n=13), antiHCV %1.4 (n=3) ve antiHİV %0.

Sonuç: Lösemi ve aplastik anemisi olan ve çok sayıda kan transfüzyonu alan çocuklarda gözlenen HBV riski şaşırtıcı olarak diğer gruplardan yüksek bulunmuştur. İleriye dönük, çok merkezli bir çalışma ile hepatit ve HİV'in kan ürünleriyle geçiş risklerinin daha kesin olarak belirlenmesi gereklidir.
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Anahtar kelimeler: Çocuk, hematolojik hastalıklar, hepatit, insan immün yetmezlik virüsü, transfüzyon

Introduction

Transfusion is the essential supportive treatment for children with hematological disorders. However, it brings many risks; even transfusion complications may cause more severe problems than the primary disease. Hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infections are the most important complications of transfusion (1-5). Sensitive screening tests and efficient virus inactivation methods both decrease the risk of infection due to transfusion substantially; however, it cannot be possible to prevent it entirely (5-7). In spite of the combination of the most sensitive tests, an estimated risk of transfusion transmitted hepatitis still exists in 1 in 200 000-500 000 units transfused for HBV and 1 in 2 000 000 units transfused for HCV and HIV (1, 5).

In Turkey, HBsAg prevalence among blood donors was reported as 4.19% and HCV antibody positivity 0.38% between the years 1989-2004 (8). In a more recent study, seropositivity rates for HBsAg, antiHCV and HIV were determined as 1.76%, 0.07% and 0.008% respectively (9). Decrease in HBV and HCV seroprevalence were related to expansion of HBV vaccination coverage, intense standards of donor screening and more diligent donor questioning upon screening (9).

Patients with hematological diseases receiving frequent blood products are the high risk group for transfusion transmitted infections. The aim of this study is to evaluate seroconversion rates of hepatitis B, hepatitis C and human immunodeficiency virus in multitransfused children with hematological diseases.

Material and Methods

In this retrospective study, children followed at Dr. Sami Ulus Children's Hospital, Pediatric Hematology Department from 1 January 2004 to 1 June 2008 were enrolled. Patients who had negative hepatitis B, hepatitis C or HIV antigens serologically before their first transfusions and subsequently received at least three transfusions, were included in the study. Those who had HBV antibody levels below 10 mIU/mL at their first admission or during follow-up were routinely vaccinated for HBV according to the national immunization schedule. Children with acute leukemia were vaccinated with 40 µgr per dose, which is double the standard dose.

Patients who received less than three transfusions or had positive tests for HBV, HCV and HIV before receiving transfusion or patients undergoing surgical or dental procedures during the study period, were excluded from the study.

Two hundred and twenty two patients were compatible with the study criteria. Viral serology of all patients were studied routinely at their first admission and then bi-yearly in terms of HBsAg, HBeAg, antiHBc total, anti-HBc IgM, antiHBe, antiHCV and antiHIV antibodies by Vitros (Orthodiagnostic, Johnson and Johnson Company) with original kits with the strengthened chemiluminescent method. Results were recorded as positive and negative.

Patients were divided into five disease groups such as acute leukemia, thalassemia major, congenital or acquired aplastic anemia, coagulation factor deficiency (factor II, VII, VIII, IX, X, XI and vonWillebrand factor deficiencies) and other anemias (such as hereditary spherocytosis, sickle cell anemia). The number and type of blood products transfused to each patient during the study period were recorded.

Study data was analyzed by Statistical Package for Social Science (SPSS) 11.5 Windows Version. Descriptive statistics was used for describing continuous variables as mean±standard deviation, median (minimum-maximum), and for categorical variables as number of patients and %. The Kruskal Wallis test was used to compare the disease groups according to the amount of blood products used. The Chi-square and Fisher's exact test was used for categorical comparisons. In HBsAg/ AntiHCV negative and positive patients, mean age was compared with Student's t test. The amount of blood products and laboratory measures were compared with the Mann-Whitney U test. Statistical significance was set at $p<0.05$.

Results

Two hundred and twenty two patients were recruited to the study. Mean age was 9.1±4.25 years and 59.1% were boys. They received a total number of 9402 units of blood transfusions during the study period. Among these, 6662 units were erythrocyte suspensions, 1663 units were platelet suspensions and 1077 units were fresh frozen plasma (FFP). Ninety five patients had only received erythrocyte suspensions, 17 had only received FFP and 108 had received more than one type of blood product. When groups were compared according to the median number of blood products transfused, children with thalassemia major received the highest number of erythrocyte suspensions (median: 60 units, min-max: 13-119) ($p<0.001$) (Table 1). On the other hand, the median number of platelet suspensions transfused to children in the acute leukemia (median: 5 units, min-max: 0-40) and aplastic anemia (median: 40 units, min-max: 0-81) groups were higher than other groups ($p<0.001$ for each). As expected, FFP were mostly transfused to children with factor deficiencies ($p<0.001$) (Table 1).

Incidence of HBsAg positivity was determined as 5.9%. Incidences of HBeAg, antiHBc total, antiHBc IgM, antiHBe, antiHBs were 5.9%, 7.7%, 1.1%, 5.4%, and 75.5%, respectively. AntiHCV and antiHIV positivity was

Table 1. Median number of blood products transfused according to disease groups

Disease groups (n)	Erythrocyte suspension Median (min-max)	Platelet suspension Median (min-max)	Fresh frozen plasma Median (min-max)
Acute leukemia (69)	7 (1-39)	*5 (0-40)	1 (0-21)
Thalassemia major (64)	*60 (13-119)	0 (0-0)	0 (0-0)
Aplastic anemia (33)	60 (1-79)	*40 (0-81)	0 (0-3)
Factor deficiency (33)	0 (0-16)	0 (0-2)	*17 (3-73)
Other anemia (21)	16 (0-119)	0 (0-0)	0 (0-0)
Total (220)	15 (0-119)	0 (0-81)	0 (0-73)

*The p values were detected <0.001 for all comparisons
Median number of erythrocyte suspensions transfused to children with thalassemia major was higher than other groups (p<0.001). However, children with acute leukemia and aplastic anemia received more platelet suspensions than other groups (p<0.001 for each group), and as expected, children with factor deficiencies were transfused more FFPs than other groups (p<0.001)

Table 2. Hepatitis B and hepatitis C serology according to disease groups in multiple blood transfused pediatric hematologic patients

Disease groups (n)	HBsAg n (%)	HBeAg n (%)	Anti-HBe n (%)	Anti-HBs n (%)	Anti-HCV n (%)
Acute leukemia (69)	8 (11.6)	7 (10.1)	2 (2.9)	37 (*53.6)	0 (0.0)
Thalassemia major (64)	2 (3.1)	2 (3.1)	4 (6.25)	56 (*87.5)	1 (1.6)
Aplastic anemia (33)	2 (6.1)	2 (6.1)	3 (9.1)	24 (72.7)	0 (0.0)
Factor deficiency (33)	0 (0.0)	0 (0.0)	2 (6.1)	31 (*93.9)	1 (3.0)
Other anemias (21)	1 (4.8)	2 (9.5)	1 (4.8)	18 (*85.7)	1 (4.8)
Total (220)	13 (5.9)	13 (5.9)	12 (5.4)	166 (75.5)	3 (1.4)

*AntiHBs positivity rate was lower in the acute leukemia group compared to thalassemia major (p<0.001), factor deficiency (p<0.001) and other anemias (p=0.008) groups

1.4% and 0%. The distribution of HBV, HCV and HIV serology according to disease groups are demonstrated in Table 2. There was no statistical significance between HBsAg, antiHCV and HIV serology according to disease groups. However, children in the acute leukemia group had lower antiHBs positivity rates than the thalassemia major (p<0.001), factor deficiency (p<0.001) and other anemias (p=0.008) groups (Table 2).

The median number of total blood products transfused to HBsAg positive patients was 31 (4-120) units. The total number of blood products transfused to HBsAg positive patients compared to negative patients were not different (p=0.4).

Anti-HCV prevalence was 1.4%. The median number of blood products transfused to antiHCV positive patients was 47 (10-79) units. There was no statistical difference in comparison of the median number of total or specific blood products transfused to anti-HCV positive and negative patients (p=1.0).

HIV positivity was not found in any child.

Discussion

Turkey is an intermediately endemic region for HBV with the incidence being 8.18/100 000 population and 5849 new cases by the year 2008 (10). Seroprevalence in children receiving multiple transfusions, such as hematological malignancies and thalassemia major, was reported between 1.8-66% in previous studies from Turkey (11, 12).

In our study group, overall HBsAg positivity was 5.9%; being 11.6% in acute leukemia and 6.1% in aplastic anemia group. Immune suppression evolving during chemotherapy and radiotherapy causes inadequate virus scavenge and higher carriage rates. During exertion of intensive chemotherapy, anti HBs antibody levels may substantially decrease and hepatitis B may reactivate (13-15), as we have seen in two of our patients with acute leukemia. Acute B hepatitis infection then complicates the disease of these children and cause delay in leukemia therapy, and subsequent relapse leukemia. Immunization is offered to patients receiving chemotherapy with double dose of standard and a rappel dose is advised if the level is below10 mIU/mL (13). However, we think that a higher level of hepatitis B antibody level should be ensured to protect from HBV infection, in such patients Control of antibody levels at frequent intervals and repeat immunization is recommended if it is under the protective level (16). In our centre, every six months, we monitor the HBV, HCV and HIV serology of children receiving multiple transfusions.

Hepatitis C infection is one of the main causes of chronic liver disease and deaths. Its frequency is approximately 1-3% in the world (10). In Turkey, HCV frequency is 1-2.1% in the general population, and 0.07-1.8% in blood donors (17, 18). In a study, including a population of our hospital, antiHCV positivity was determined as 1.5% in blood donors (unpublished report). In our study, anti HCV positivity was determined as 1.4%. In Turkey, HCV seroprevalence was reported as 4.5% in patients with thalassemia and sickle cell anemia who were receiving multiple transfusions, 5.8% in children with cancer-including acute leukemia and 24.4% in children with hemophilia (19-21).

In our country HIV prevalence was detected as 0-0.9% in patients with benign or malignant hematological diseases (19). In the Turkish Red Crescent Blood Centre, anti-HIV positivity rate was determined as 0.008% among 72695 blood donors (9). We have detected no anti-HIV positivity in any of the patients receiving multiple transfusions, which is compatible.

Conclusion

Transfusion transmitted HBV, HCV and HIV is one of the complications of transfusion therapy which may cause considerable morbidity and mortality and is a global health problem. Children with hematological diseases who are receiving multiple transfusions, especially immunocompromised patients, should be closely followed up with frequent intervals for HBV, HCV and HIV serology positivity. Hepatitis B vaccination during childhood decreases the prevalence of hepatitis B in children. Children with acute leukemia and aplastic anemia carry the highest risk of developing hepatitis B infection, so it is essential to implement a vaccination program resulting in more augmented and persistent immunity

Conflict of Interest

No conflicts of interest were declared by the authors.

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