

High Prevalence of Parvovirus B19 IgG Antibody among Hemophilia Patients in Center for Special Diseases, Shiraz, Iran

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Abstract

Human parvovirus B19, the causative agent of fifth disease in childhood, is non-enveloped DNA virus and resistant to many physicochemical agents. B19 is a potential risk to hemophiliac patients receiving blood products. To determine the prevalence of the corresponding antibody in patients with hemophilia A or B or Von Will brand's disease (VWBD), we tested 180 hemophilia patients aged 1-45 years for anti B19 IgG. This work was descriptive, cross-sectional study. The results were compared with those of 400 age-matched controls, male blood donors and male children (18-45 and 3-17 years of age, respectively). The overall prevalence of B19 IgG in the hemophilia patients was 74% (133/180), and in the controls 56.5% (226/400, $P<0.001$). The significant difference in prevalence of B19 IgG between hemophiliacs and healthy persons demonstrated that there was a high risk of transmission of parvovirus B19 through plasma-derived clotting products. These observations demonstrate that parvovirus B19 is frequently transmitted in blood products. Existing virus-inactivating methods do not prevent transmission.

Keywords: *Parvovirus B19, Hemophilia, Viral inactivation of plasma products, Iran*

Introduction

Human parvovirus B19 is a single-stranded, non-enveloped DNA virus and a member of the family parvoviridae (1). Human parvovirus B19 causes a number of clinical illnesses including erythema infection (fifth disease), hydrops fetalis, transient aplastic crisis, arthropathy and congenital aplasia (2). Persistent infection with human parvovirus B19 is an important treatable cause of anemia in HIV-infected patients (3). B19 virus is resistant to many physicochemical agents (4, 5), and is mostly transmitted via the respiratory tract (6). In the production of blood products, current virus-inactivating steps seem to be ineffective to prevent transmission of parvovirus B19 (7, 8). In particular, hemophilia patients receiving blood products on a regular basis are at risk of acquiring B19 infection (8,9).

A higher prevalence of anti-B19 was found in French children previously treated with solvent/detergent high-purity non-immunopurified and non-Nan filtered FVIII or IX concentrates than in children treated with albumin-stabilized recombinant FVIII only, independently of the other factors studied (10). In this study, the prevalence of the corresponding antibody in patients with hemophilia A or B or Von Will brand's disease was determined. The results were compared with those of age-matched controls.

Materials and Methods

This work was a descriptive, cross-sectional study. To determine the prevalence of the corresponding antibody in patients with hemophilia A or B or Von Will brand's disease, we tested a

group of hemophilia patients (n=180) aged 1-45 years who attended in Center for Special Diseases, Shiraz, Iran. Two ml blood was taken from each patient and then centrifuged at 3500 g at room temperature. Sera were separated and transferred into fresh tubes. Serum samples were kept at -20 C° until the day of examination. Serum samples of 180 patients with hemophilia A (n=120), hemophilia B (n=50) and Von Will brand's disease (n=10) were tested during Sep 2001 to Sep 2002.

Age, severity and type of hemophilia, number of cumulative days of exposure to factor VIII or IX, previous history of red blood cells or plasma transfusion, were considered as potential confounding variables. The results were compared with an age-matched control group consisting of 400 male blood donors and male children (18-45 and 3-17 years of age, respectively). Patients or their parents approved testing for B19 IgG. Parvovirus B19- specific IgG (B19 IgG) was determined using an ELISA test, IBL, Hamburg, Germany. All samples were analyzed at the viral diagnostic laboratory of the blood transfusion organization, Shiraz, Iran. We used the χ^2 test to determine the difference in prevalence of B19 IgG among the different patient populations and the control groups.

After 1992, hemophilia A patients and Von Will brand's disease were treated with a F.VIII concentrate from different sources (Kate-DVI, Bayers USA-Biotest Pharma GmbH, Germany-Octonative M, Pharmacia, Sweden) or a cryoprecipitate or fresh frozen plasma (FFP). Before that time, hemophilia A patients and Von Will brands were mainly treated with a cryo-precipitate or fresh frozen plasma (FFP). Hemophilia B patients were mainly treated with a factor IX from different sources (F.IX Nano-tive, Pharmacia, Sweden-F.IX Alma Forma, Biagin, Italy) or a cryoprecipitate or fresh frozen plasma.

According to the amount of clotting factor product used, patients were placed into three treatment groups. 1) No treatment patients who received no treatment at all or less than 5 infu-

sions, 2) little treatment patients, who were treated on demand and received less than 10 infusions per year, and 3) heavily treated-patients, who were treated on a prophylactic basis or who received more than 10 infusions per year.

Results

Table 1 shows the sero prevalence of B19 IgG antibody in patients with hemophilia and control groups. In our study, we did not observe significant differences between patients with hemophilia A, B or Von Will brand's disease. The significant difference in prevalence of B19 IgG between hemophiliacs and healthy persons demonstrates that there is a high risk of transmission of parvovirus B19 through plasma-derived clotting products.

Table 2 shows the prevalence of B19 IgG in the various treatment groups. Patients who had received little treatment had a significantly lower risk as compared to the heavily treated group ($P<0.002$). It was striking that most children with severe hemophilia A who had been treated on a prophylactic basis with clotting factor concentrates were positive.

Table 1: Seroprevalence of B19 IgG antibody in patients with hemophilia and in control groups ($P<0.001$)

	Positive / Total	Positive (%)
Hemophilia A	89/120	74
Hemophilia B	37/50	74
Von Will brand	7/10	70
Total	133/180	74
Control group	226 / 400	56.5

Table 2: Relation between the amount of clotting factor product used and B19 IgG prevalence ($P<0.002$)

	Negative	Positive n%
No treatment	3	0
Little treatment	8	55
Heavily treatment	36	77
Total	47	74

Discussion

The prevalence of parvovirus B19 IgG was less than that was found in Dutch, or Spanish hemophilia patients (11, 12), perhaps it is due to the lower number of participants involved in our study, selected only from one geographic area. The overall prevalence of B19 IgG in Dutch hemophilia patients (11) was 302/326 (93%) and in the controls 123/203 (61%). In Spanish report (12), 84% of the patients (93.3% of those previously transfused) and 60.3% of the controls showed IgG antibodies against parvovirus B19. Also, a higher prevalence of anti-B19 was found in French children previously treated with solvent/detergent high-purity non-immunopurified and non-nanofiltered FVIII or IX concentrates than in children treated with albumin-stabilized recombinant FVIII only, independently of the other factors studied (10). In another report, IgG antibodies to B19 were present in 29 of the 39 patients (74%), 18/26 (69%) with Hemophilia A and 12 of the 13 (85%) with Hemophilia B in South Africa (13).

McOrnish et al, (14) studied the prevalence of parvovirus B19 viremia in blood donors. They found that 1:3300 donors were B19 DNA PCR positive, whereas during the seasonal outbreaks, 1:260 was viremic. The presence of parvovirus B19 DNA in 2,440 blood donations from the United Kingdom and sub-Saharan Africa (Ghana, Malawi, and South Africa) was screened (15). Sensitive qualitative and real-time quantitative PCR assays revealed a higher prevalence of persistent infection with the simultaneous presence of immunoglobulin G (IgG) and viral DNA (0.55 to 1.3%) than previously reported (15).

Zakrzewska et al, (6) showed 9 of 25 clotting products to be B19 DNA positive by PCR. They found B19 DNA in low-purity non-inactivated product as well as in solvent-detergent, steam-and dry-heat-treated products and also in monoclonally purified clotting factor concentrates. They did not detect B19 DNA in seven

concentrates inactivated by pasteurization techniques.

The significant difference in prevalence of B19 IgG between hemophiliacs and healthy persons demonstrates that there is a high risk of transmission of parvovirus B19 through plasma-derived clotting products. These observations together with other results from other researchers, demonstrate that parvovirus B19 is frequently transmitted in blood products. Therefore, measures should be taken to reduce the risk of transmission of B19 virus in clotting products. Elimination of B19 virus by nanofiltration of factor IX concentrates looks promising (16).

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