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Update article

Infection with human T-lymphotropic virus types-1 and -2 (HTLV-1 and -2): Implications for blood transfusion safety

L'infection par le virus human T-lymphotropic types-1 et -2 (HTLV-1 et -2) : implications pour la sécurité de la transfusion sanguine

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Abstract

Many countries currently perform antibody screening for HTLV-1 infection in blood donors, and this intervention is likely cost-effective in preventing HTLV-1 related diseases in high prevalence countries. However, a number of high-income countries with low prevalence of HTLV-1 infection also perform universal HTLV-1 screening and debate has arisen regarding the cost-effectiveness of these strategies. Filter-based leukoreduction is likely to substantially reduce HTLV-1 transmission by removing infected lymphocytes, but actual laboratory data on its efficacy is currently lacking. Similarly, cost-effectiveness research on HTLV-1 prevention strategies is limited by poor data on prevalence, transmission efficacy and the cost of treating HTLV1 diseases.

Keywords: HTLV-1; Blood transfusion; Immunoassay; Prevention and control

Résumé

De nombreux pays effectuent actuellement le dépistage des anticorps anti-HTLV-1 chez les donneurs de sang. Cette mesure a un bon rapport coût-efficacité dans la prévention des pathologies liées à ce virus dans les pays à forte prévalence. Cependant, un certain nombre de pays à revenu élevé et à faible prévalence de l'infection réalisent aussi un dépistage universel des anti-HTLV-1. Cette politique sécuritaire soulève la question du bénéfice de cette stratégie en termes de coût-efficacité au regard de l'existence parallèle et systématique de mesures de déleucocytation susceptible de réduire la transmission virale par la suppression des lymphocytes infectés. Toutefois, les données de l'efficacité de cette procédure de filtration des produits sanguins obtenues en laboratoire font actuellement défaut. De même, la recherche de la rentabilité des stratégies de prévention HTLV-1 est limitée par les données sur la prévalence, l'efficacité de la transmission et le coût de traitement des maladies du HTLV-1.

Mots clés : HTLV-1 ; Transfusion sanguine ; Dépistage immunologique ; Prévention et contrôle

1. Introduction

Human T lymphotropic virus types-1 and -2 (HTLV-1 and -2) were discovered in the early 1980s and cause chronic infection of humans. Soon after their discovery, it was realized that blood transfusion was associated with high rates of transmission due to the infusion of infected lymphocytes. Transfusion-transmitted HTLV-1 was also associated with the accelerated onset of HTLV associated myelopathy (HAM), a debilitating spinal cord condition and with case reports of adult T-cell leukemia/lymphoma (ATL). Antibody screening for HTLVs was therefore introduced in many countries and remains in place today. In addition to its primary purpose of preventing transfusion transmission, such screening also provides a public health resource in allowing estimation of population prevalence of HTLV infection.

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Paradoxically, most countries performing HTLV screening of blood donors have very low prevalence and incidence, while certain countries in Africa with probable high HTLV-1 prevalence in their donors do not currently perform antibody screening due to cost concerns. By analogy to cytomegalovirus, it is likely that filter leukoreduction of blood products reduces the transfusion risk of HTLV, although there are only suggestive data to support this hypothesis and leukoreduction is similarly impractical in many high prevalence countries.

My late colleague Jean Jacques Lefrere was an avid scholar of all threats to transfusion safety. Unbeknownst to me until I researched this article, he had published several articles on HTLV-1 infection, including an early comparison of donor prevalence between endemic Guadeloupe and the non-endemic Paris region and a comprehensive review of HTLV-1 and transfusion safety [1,2]. Our community of scientists will be diminished by the absence of his keen intellect and energy, but we shall also miss him as a faithful and cultivated friend.

2. Early epidemiologic studies of transfusion transmission

Soon after HTLV-1 was discovered and prior to the introduction of HTLV antibody screening, several studies were able to quantify the risk of transfusion-transmitted HTLV-1 infection. In Japan, Okochi et al. were the first to demonstrate transfusion transmission of HTLV-1 [3]. Of the 41 patients who received cellular blood products from HTLV-1 positive donors, 26 (63%) seroconverted to HTLV-1. None of 14 recipients of HTLV-1 positive plasma transfusions seroconverted. Blood products stored less than four days led to seroconversion in 13 of 15 patients while those stored longer did so in 12 of 25 patients ($P = 0.015$). Patients under 30 years of old were more likely to seroconvert than those aged greater than 30. IgG antibodies to HTLV1 were detected from 21 to 47 days after transfusion.

In 1987–1988, Manns et al. performed a similar study in Jamaica with retrospective antibody testing of samples from blood donors and tracing of the recipients [4]. A total of 66 patients had received blood products donated from donors later found to be HTLV-1 infected. Seroconversion occurred in 24 of 54 (44%) recipients of cellular blood products (packed RBC, platelets or whole blood), none of 12 recipients of acellular blood products and 0 of 52 recipients of blood products from HTLV negative blood donors. Significant risk factors for transmission included storage of the blood product for less than one week, male sex and immunosuppression in the transfusion recipient. The median time to HTLV-1 seroconversion in transfusion recipients was 51 days but there was a significant difference between recipients of blood stored for less than one week, almost all of whom seroconverted rapidly and those who received blood stored for more than one week who had seroconversion intervals as long as one year. It should be noted that the tests used at the time of that study were relatively insensitive compared to antibody assays available today, so the contemporary time to seroconversion should be shorter.

Finally, in the United States, Donegan et al. studied sera that were banked just prior to the introduction of HIV screening of US donors in 1984–1985 [5]. That repository was tested for HTLV-1 and -2 when commercial HTLV assays became available in the late 1980s and recipients of blood products from the HTLV positives were retrospectively traced in the early 1990s. A total of 26 of 95 (27%) recipients of blood products from HTLV infected donors were themselves found to be HTLV infected by serology and polymerase chain reaction (PCR). Estimated rates of transmission were similar for HTLV-1 (9 of 25 or 36%) and HTLV-2 (17 of 70 or 24%; $P = 0.30$) infection. However, the duration of refrigerated blood storage played a major role with 74% transmission after 0 to 5 days storage, 44% transmission for 6 to 10 days storage and 0% transmission for 11 to 14 days storage. None of 17 recipients of acellular plasma and cryoprecipitate blood products became infected.

These three studies show rather similar findings, with the exception that the overall transmission rates in the Japanese and Jamaican study were higher than in the USA, probably due to shorter duration of refrigerator storage, the inclusion of a few whole blood units in the Japanese study or differences in the degree of buffy-coat leukoreduction during production of packed red blood cells. Although not a formal retrospective study, a look back study by Kleinman et al. in the same era showed that 16 of 54 (30%) evaluable recipients of blood products from HTLV-1 or HTLV-2 infected donors themselves became infected [6]. In a Canadian lookback study, of 109 HTLV-positive donors, 508 components were transfused, of whom 147 recipients were tested and 18 (12%) were positive [7].

3. Case reports of transfusion-transmitted HTLV-1 infection

Since HTLV infection is often asymptomatic, clinically recognized reports of patients infected via blood transfusion are rare. However, several case reports document the potential for adverse consequences of infection. A French patient who received a heart transplant and required large volumes of transfused red cells, platelets and plasma developed symptoms and signs of HAM within 4 to 5 months and was found to have seroconverted for HTLV-1 in a blood sample drawn at 14 weeks post transfusion [8]. The report also highlights the danger of HTLV infection in patients receiving immunosuppression. Chen et al. in Taiwan reported two cases of HTLV-1 infection and ATL occurring in patients with pre-existing malignancy (Hodgkin's disease and promyelocytic leukemia) who had received multiple transfusions [9]. The intervals from blood transfusion to ATL diagnosis were six months and 11 years. Although this retrospective report does not definitively implicate the blood transfusions as the source of HTLV-1 infection, it provides suggestive evidence that transfusion-transmitted HTLV-1 carries a risk of ATL. More recently, Hakre et al. report a recent case of transfusion-transmitted HTLV-1 occurring in American soldier in Afghanistan [10]. The US military utilizes "walking blood banks" consisting of fellow soldiers who are called to donate for the wounded colleague. The index patient developed fevers and leukocytosis 1 to 2 years after his initial severe injuries and was found to be HTLV-1 positive; there was no evidence of HAM or ATL by the time of the report. Evaluation of his blood donors