Published in final edited form as:
AIDS. 2014 June 19; 28(10): 1539–1541. doi:10.1097/QAD.0000000000000268.

Prevention of HIV-1 Transmission with Post-Exposure Prophylaxis after Inadvertent Infected Blood Transfusion

Sami H. Al-Hajjar[1], **Husn H. Frayha**[1], **Mohammad Al-Hazmi**[2], **Reem Batawi**[1], **Kenneth McIntosh**[3,4], **Paul E. Sax**[4,5], **Sahar Al-Thawadi**[1], **Sulaiman Al-Jumaah**[1], **Michael P. Busch**[6,7], **Emily Hanhauser**[5], **Daniel R. Kuritzkes**[4,5], **Jonathan Z. Li**[4,5], and **Timothy J. Henrich**[4,5]

[1]King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia

[2]King Fahad Central Hospital, Jazan, Saudi Arabia

[3]Boston Children's Hospital, USA

[4]Harvard Medical School, Boston, USA

[5]Brigham and Women's Hospital, Boston, MA

[6]Blood Systems Research Institute, San Francisco, CA

[7]University of California, San Francisco

Keywords

HIV-1; Post-exposure prophylaxis; antiretroviral therapy; HIV-1 antibodies; residual viremia; HIV-1 DNA

While post-exposure prophylaxis (PEP) is commonly prescribed in the setting of occupational and non-occupational HIV-1 exposures [1,2], there is limited evidence documenting efficacy in the setting of transfusion with infected blood. Furthermore, there are a paucity of data regarding blood-borne exposures that lead to passive transfer of antibodies against HIV [3,4]. We describe the efficacy of PEP in such a situation using highly-sensitive assays for HIV-1 DNA and low-level residual viremia.

We report the case of a 12 year old girl with sickle-cell disease admitted for management of a vaso-occlusive crisis who inadvertently received HIV-infected packed red blood cells (PRBCs). She required intermittent PRBC transfusions since the age of 2, with the last transfusion 5 years ago. Her white blood cell count was 10,100 per uL, and hemoglobin 9.6 g/dL. Hemoglobin electrophoresis revealed 57% hemoglobin S. During her admission, she was transfused with one PRBC unit that was collected 32 hours prior to administration.

Corresponding Author: Prof. Sami Al Hajjar, Head, Pediatric Infectious Diseases, Department of Pediatrics, King Faisal Specialist Hospital & Research Centre, PO Box 3354, Riyadh 11211 Saudi Arabia, T: +966 1 4647271 F: +9661 4427784, hajjar@kfshrc.edu.sa.

Conflicts of Interest: D.R.K receives consulting fees or honorariums from Gilead; P.E.S. receives consulting fees or honorariums from AbbView, Bristol-Meyers Squibb, Gilead, Glaxo-Smith-Kline, Janssen pharmaceuticals, and Merk, and receives grant support from Gilead, BMS and GSK

Despite the standard practice of pre-screening blood products, the laboratory at the public hospital in the Kingdom of Saudi Arabia became aware that the PRBCs were contaminated with HIV-1 within hours of her transfusion as a result of human error involving mixing an unscreened bag with screened bags. The donor blood was discovered to be HIV-1 antibody positive and subsequently determined to have a viral load of 9740 copies/mL (subtype C); the donor was not receiving antiretroviral therapy (ART). The Ministry of Health conducted an in-depth investigation and halted blood transfusions at the responsible blood blank. Approximately 24 hours after transfusion, the patient was started on tenofovir, emtricitabine, ritonavir-boosted darunavir (subsequently changed to lopinavir) and raltegravir. Blood tests were positive 24 hours after transfusion for HIV antibodies by ELISA and confirmatory western blot (WB), but negative for HIV-1 DNA and plasma HIV-1 RNA by PCR. The pattern of reactive bands on WB was identical for samples obtained from the donor and patient (gp120, gp41, gp31, p24 and p17). Genotyping revealed that she was CCR5 wild-type.

The patient demonstrated no signs or symptoms of acute infection during 13 weeks of ART in a tertiary care center. Testing of donor blood revealed no HIV-1 resistance to the antiretrovirals chosen. Longitudinal testing of the patient's plasma and peripheral blood mononuclear cells (PBMCs) was performed by both clinical laboratories and by sensitive research assays with thresholds of detection down to 0.06 HIV-1 DNA copies/10^6 PBMCs and 0.4 RNA copies/mL of plasma during and after ART. All tests were negative prior to and 8 months after ART interruption. She continued to have declining but detectable HIV-1 antibodies with positive confirmatory line immunoassay up to 5 months after transfusion, but confirmatory testing was negative by month 6. Viral load testing 8 months following exposure remained negative. See Table 1.

We report the successful use of combination ART PEP following large-volume transfusion of HIV-infected blood from a viremic donor with passive transfer of antibodies to HIV-1. The observation that no HIV was detected in her blood after stopping ART and that antibody levels disappeared over time, strongly suggests that PEP successfully prevented HIV acquisition. The overall transmission rate from HIV-1 antibody positive blood transfusions was 89% in one study with non-transmission attributed to lower viral load and prolonged blood-product storage [5]. HIV-1 transmission from transfusion of PRBCs stored for <48 hours is essentially 100% regardless of viral load [5]. Furthermore, experiments of simian immunodeficiency virus primary infection in primate models suggest that infectivity of plasma virus from acute infection is higher compared to set-point virus, but the correlation between cell-associated HIV-1 DNA levels and transmissibility is poorly understood [6,7]. Our patient received effective prophylaxis despite transfusion with PRBCs stored for <36 hours, but was from a donor with relatively low viral load.

Passive transfer of HIV-1 antibodies after occupational exposure has been documented but is rare [3, 4]. For example, one individual became infected with resistant virus despite the use of zidovudine two hours after a deep laceration with contaminated blood, whereas another individual was not infected after transfusion with a contaminated unit of PRBCs from a donor with a low viral load (2000 copies/mL); she was started on zidovudine, lamivudine and indinavir 19 days after exposure. These cases illustrate the sensitivity of

current antibody testing platforms and cautions against presuming that individuals have pre-existing HIV-1 infection, and not initiating or stopping PEP due to the presence of antibody reactivity immediately following contaminated blood exposure. Highly sensitive laboratory assays may also help guide the duration of PEP to guarantee the prevention of infection.

Acknowledgments

Sources of Funding: This work was supported by the Foundation for AIDS Research (amfAR) ARCHE grant, NIH grant UM1 AI068636, NIH/NIAID U19 AI096109 (DARE Collaboratory)

We would like to acknowledge Sheila Keating for help with antibody testing.

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Table 1

HIV-1 DNA, plasma RNA and antibody tests results before and after infected blood transfusion

Day Post- Transfusion	Clinical Course	Clinical Laboratory Testing					Research Laboratory Testing		
		HIV ab ELISA/WB[a]	Architect HIV-1/2 Ag/Ab Combo[b]	Line Immunoassay Confirmation[c]	HIV-1 DNA (Blood)[d]	Quantitative HIV-1 RNA PCR[e]	HIV-1 DNA (copies/ 10^6 PBMC)	HIV-1 plasma RNA by SCA (copies/ mL)	HIV Ab by VITROS assay
Donor									
−1		Positive				9,740 copies/mL			
Patient									
−1		Negative							
0	Transfusion								
1	Start ART	Positive			ND	ND			
4			463.44	Pos	ND	ND			
34					ND	ND			
50			132.74	Pos	ND	ND			
78					ND	ND			
82			33.89	Pos	ND	ND		<0.4[g]	1.7[h]
91	Stop ART								
98					ND	ND			
105					ND	ND			
112			8.43	Pos	ND	ND	<0.07[f]	<0.4	0.35
119					ND	ND			
126			4.5	Pos	ND	ND			
133					ND	ND			
140			2.73	Pos	ND	ND	<0.06	<0.4	0.1
154			1.62	Pos	ND	ND			
175			0.69	Neg	ND	ND			
240			0.19	Neg	ND	ND			

ND = not detected; WB = western blot; ART = antiretroviral therapy; SCA = single copy HIV-1 RNA assay; Ab = antibody, Ag = antigen

[a] screening HIV-1 enzyme linked-immunoassay with western blot confirmation at transfusing health care facility

[b] Abbot Architect HIV antibody/antigen combination chemiluminescent microparticle immunoassay (the presence of antigen and antibody are not differentiated); value = relative light units (RLU; positive assay cutoff value = mean calibrator RLU value x 0.40)

[c] INNO-Lia HIV I/II Line Immuno Assay (LIA) used to confirm the presence of antibodies against the HIV-1/2

[d] HIV-1 proviral DNA qualitative detection by PCR performed at Mayo Laboratories (lower limit of detection = 66 copies/mL whole blood)

[e] measured by quantitative real-time PCR (detection threshold = 40 RNA copies/mL of plasma)

[f] threshold of detection in DNA copies/10^6 PBMCs (no DNA detected at all time-points tested)

[g] threshold of detection in RNA copies/mL of plasma (no RNA detected at all time-points tested)

[h] signal/cutoff value from VITROS Anti-HIV-1 + 2 assay