

#U-130 : Effect of Plasma Preparation Tubes (PPT) vs. Standard EDTA Tubes on Viral “Blips” in Patients with Optimally Suppressed Plasma HIV-1 RNA

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ABSTRACT

Background: Patients with optimally suppressed plasma HIV-1 RNA concentrations occasionally experience transient increases in HIV-1 RNA, commonly referred to as “blips”. This may be the result of factors such as short treatment interruption, development of drug resistance, intermittent illness or recent immunization. It has been reported that falsely elevated HIV-1 RNA levels are associated with the use of Plasma Preparation Tubes™ (PPT). We observed that patients at Northwestern Memorial Hospital (NMH) experienced blips during a period of time (January to August 2003) when the HIV-1 RNA specimen collection procedure changed from using standard ethylenediaminetetraacetic acid (EDTA) tubes to PPT tubes. Prior to and after this period, specimens were collected in EDTA tubes. We investigated whether transient HIV-1 RNA elevations were related to the type of tube used for plasma collection.

Methods: The CDC NMH HIV Out-Patient Study (HOPS) database was surveyed to determine the frequency of blips during periods of PPT or EDTA tube use for plasma HIV-1 RNA collection. Patients with ≥ 3 undetectable HIV-1 RNA levels (<50 copies/mL, Roche Ultrasensitive Amplicor® v1.0 or 1.5) during the initial period of EDTA use and ≥ 1 HIV-1 RNA measurement during the periods of PPT and resumed EDTA use were evaluated.

Results: Of 595 NMH HOPS patients, 68 had optimally suppressed HIV-1 RNA prior to the switch to PPT tubes and ≥ 1 measurement during PPT and resumed EDTA tube use. HIV-1 RNA blips (range, 50-1779, mean 267 copies/mL) occurred in 53% (n=36) of patients during the period of PPT use, 7% (n=9) during both EDTA and PPT periods, and in only 8% (n=4) during EDTA tube use (p=0.002). 25% of patients maintained suppressed HIV-1 RNA levels without blips. Viral blips resulted in 43% (19/45) of patients with ≥ 1 unplanned repeat blood draws for HIV-1 RNA measurement. At least one patient had an antiretroviral regimen change because of the blip.

Conclusion: The use of PPT tubes for plasma HIV-1 RNA measurement resulted in a viral “blip” in more than 50% of patients. This prompted early and not clinically indicated repeat blood draws for HIV-1 RNA testing and additional clinic visits, as well as a medication change in at least one patient. Although processing of PPT tubes is considered safer, the increased costs related to blips indicate that PPT tubes should not be used for HIV-1 RNA monitoring in maximally suppressed HIV-1 infected patients or in clinical trials where HIV-1 RNA is a clinical endpoint.

BACKGROUND

Quantitative plasma HIV-1 RNA measurements are an essential element of optimal clinical practice for HIV-infected patients on HAART and an important endpoint in HIV clinical trials.

Transient low level viremia (blips) in patients receiving HAART have been attributed to a variety of factors including medications, nonadherence, intercurrent infections, and immunizations.

A recent study presented by Squires et al, demonstrated the detection of low level viremia in plasma that was collected and prepared in Plasma Preparation Tubes (PPT). When compared to plasma collected in standard EDTA tubes, low level viremia was significantly more common in the PPT tubes.

Laboratory studies have shown equivalent plasma HIV-1 RNA measurements in specimens obtained in PPT and EDTA tubes, however only specimens with higher levels of viremia were studied.

From January through August 2003, the clinical laboratory at Northwestern Memorial Hospital instituted the routine use of PPT tubes for the testing of plasma HIV-1 RNA.

OBJECTIVES

- Determine whether viral blips were related to the type of collection tube used for measurement of plasma HIV-1 RNA
- Describe the clinical characteristics of the patients who experienced a blip during PPT tube use
- Determine the clinical consequence of the blip, such as resource utilization (resistance testing) or antiretroviral regimen changes



Plasma Preparation Tube™ (PPT)
Safe, convenient one-tube system for whole blood collection and plasma separation

Plastic tube contains EDTA K2 with polyester gel barrier that separates most of RBCs and WBCs

Plasma prepared in PPT contains more platelets than plasma prepared from standard EDTA tubes

METHODS

Northwestern Memorial Hospital HIV Out-Patient Study (HOPS/CDC) database (N = 595 patients) surveyed for HIV-infected patients with:

- At least 3 sequential undetectable HIV-1 RNA levels (< 50 copies/mL, Roche Ultrasensitive Amplicor®) during the initial period of EDTA tube use (January – December 2002) AND
 - At least 1 HIV-1 RNA measurement during PPT tube use (January – August 2003) AND
 - At least 1 HIV-1 RNA measurement during resumed EDTA tube use (September – December 2003)
- > Frequency of optimally suppressed patients who experienced blips (HIV-1 RNA 50-2000 copies/mL followed by re-suppression) or virologic failure (>2000 copies/mL) during periods of PPT and/or EDTA tube use was determined.

Retrospective clinical chart reviews of patients (N=36) who experienced a blip during PPT tube use.

- Clinical characteristics of patients before (6 months), during, and after (6 months) blip period that could be related to transient viremia
 - Immunizations, infections or acute febrile illness, CD4 count, treatment interruptions for toxicity or poor adherence, type of insurance, participation in clinical trial
- Clinical consequences, including resource utilization before, during, and after blip
 - Duration of blip period, number of clinic visits, number of viral load tests, resistance testing, antiretroviral drug levels, antiretroviral therapy changes, and pharmacy counseling

RESULTS

68 patients had sequential plasma HIV-1 RNA <50 copies/mL prior to the switch to PPT tube use and at least one measurement during PPT and resumed EDTA tube use.

Collection Tube Use and Virologic Outcome

PPT with blip	36 (53%)	p = 0.002
PPT with VF	4 (6%)	
EDTA with blip	4 (6%)	
EDTA with VF	2 (3%)	
PPT and EDTA with blips	5 (7%)	
No Blips	17 (25%)	
TOTAL No. Patients	68	

- 51 (75%) of patients experienced either a transient blip or virologic failure (VF).
- 36 (53%) experienced a transient blip with PPT tube use only (p=0.002)
- Median HIV-1 RNA during blips: 131 copies/mL (range 50-1779)
- 43% of patients had ≥ 1 unplanned repeat blood draws for HIV-1 RNA measurement.

Characteristics of Patients (N = 36) Who Had Blips During PPT Tube Use

Age (median, yrs)	46		
Race	86%		
Sex/Ethnicity	White (54%) Black (26%) Hispanic (11%) Asian (6%)		
HIV-1 RNA (median, copies/ml)	129 (range 50-852)		
Duration of Blip (months)	1 (range 1-6)		
Antiretroviral Regimen	PI (51%) NNRTI (34%) PI+NNRTI (9%) NRTI (3%)		
CD4 Nadir (median, cells/mm ³)	185 (2-824)		
Median CD4 (range)	Before Blip	During Blip	After Blip
Median CD4 %	455(59-1405)	425(53-1369)	432 (47-1760)
	24	24	24

No. Patients with Factors Related to Transient Viremia

Treatment interruptions:	Before Blip	During Blip
Nonadherence	2	2
Toxicity	0	0
Infection/febrile illness	4	4
Immunizations	1	0

> 13 (37%) patients had factors other than PPT tube use that could explain the transient viremia

Clinical Consequences:

	Before Blip(1 yr)	During Blip	After Blip(6 mo)
No. Clinic Visits, mean	5	2	2
No. HIV RNA Tests, mean	4	2	2

> 13 (37%) of patients had at least 1 unplanned repeat clinic visit and HIV RNA test
> 2 patients had resistance testing: genotype (sensitive to all), phenotype (reduced sensitivity)
> 1 patient had pharmacokinetic measurements (adequate PI levels)
> 1 patient's antiretroviral regimen was changed (intensification with NNRTI)

CONCLUSIONS:

- The use of PPT tubes resulted in 53% of optimally suppressed patients experiencing an unexplained transient low level viremia (blip).
- Blips resulted in unnecessary repeat HIV-1 RNA measurements, clinic visits, resistance testing, pharmacokinetic measurements and treatment changes.
- Although processing of PPT tubes is considered safer, the increased costs and inconvenience related to blips indicate that they should not be used for clinical monitoring in optimally suppressed HIV-1-infected patients.
- PPT tubes should not be used in clinical research where plasma HIV-1 RNA is the study endpoint.