ORIGINAL PAPER

Plasma and semen viral loads discordance in HIV-positive patients receiving antiretroviral treatment (ART) in Tehran: an implication for a healthy pregnancy

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Abstract

Introduction: In human immunodeficiency virus (HIV)-positive patients, viral load replication in blood plasma (BP) and genital fluid, such as semen plasma (SP), are different. Several factors, including HIV concentration in semen, virus infectiousness, and susceptibility of host cells determine the risk of transmission from HIV male patients to their sexual partners. Previous studies had controversial results on the correlation of BP viral load and SP viral load and the impact of antiretroviral therapy (ART) on BP and SP viral load. The aim of the study was to evaluate the impact of different ART regimens on BP and SP viral loads.

Material and methods: Nineteen HIV-positive male patients, with a mean age of 35.8 years, were included in the study, each of whom had been receiving various ART regimen for at least six months. Both whole blood and semen samples were collected on the same day and subsequently, HIV-1 RNA copy was measured in both samples for each patient.

Results: Our results indicated that in patients who were at least six months under ART regimen, mean HIV RNA copy number in BP and SP were 1,371 copy/ml and 273 copy/ml, respectively. Our results demonstrated a significantly higher BP viral load level than SP viral load ($p = 0.001$). Moreover, a significant correlation between BP viral load and SP viral load was observed (Pearson correlation = 0.97).

Conclusions: We conclude that SP viral load of HIV-positive patients with undetectable BP viral load was below detection range. This point should be communicated to sero-discordant couples who want to have a safe pregnancy and healthy offspring.

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Introduction

Human immunodeficiency virus (HIV) is mainly transmitted through unprotected sexual intercourse worldwide. HIV-infected genital tract in males has been an important source of transmission [1-4]. The phrase 'sero-discordant couple' refers to a romantic relationship, in which one person is HIV-positive and the other one is not [5, 6]. Sero-discordant couples play an important role in the maintenance of HIV epidemic. HIV transmission between sero-discordant couples worsens the overall disease burden. In sub-Saharan Africa, known as a high prevalence region, about half of HIV-positive individuals have negative partners; however, in areas with low HIV prevalence, this percentage increases to approximately 75% [7, 8]. Of note, 29% (range, 10-52%) of all new infections in 20 countries in sub-Saharan Africa were detected among sero-discordant couples in 2013 [9]. Furthermore, 60.3 to 94.2% of new HIV transmissions among heterosexuals in Zambia were related to sero-discordant couples [10].

In HIV patients, viral load replication in blood plasma (BP) and genital fluid, such as semen plasma (SP), are different. Several factors including HIV concentration in semen, virus infectiousness, and susceptibility of host cells determine the risk of transmission from HIV male patients to their sexual partners. Previous studies had controversial results regarding the correlation of BP viral load and SP viral load and the impact of antiretroviral therapy (ART) on BP and SP viral loads [1, 11-14]. SP viral load is associated with BP viral load, but their amount is not the same; however, BP viral load can, to some extent, predict the infectiousness of genital secretions. It is noteworthy to know that understanding this correlation can help evaluate potential benefits of ART regimens for the reduction of HIV transmission risk [1, 15-17]. This correlation has been robustly recommended in a cohort study by Quinn *et al.* [18]. In this study, there was no report of HIV transmission in 415 heterosexual couples with BP viral load lower than 1,500 copies/ml who were not under the ART regimen. However, these findings may not be extrapolated to patients who are under different ART regimens.

This study was aimed to evaluate the impact of different ART regimens on BP and SP viral loads. Also, the correlation between BP and SP viral loads among male HIV-infected patients of sero-discordant couples in Iran was examined.

Material and methods

Patients

All patients were recruited at a voluntary counselling and testing (VCT) center located at the Imam Khomeini Hospital of Tehran, University of Medical Sciences, Tehran, Iran. Inclusion criteria were age over 18 years, good adherence to ARTs, and not having any signs of urethritis or active liver disease. Moreover, patients with other STDs, especially positive polymerase chain reaction (PCR) test for chlamydial or gonococcal urethritis were excluded.

Methods

A sample of 8 ml whole blood was collected in EDTA tubes. On the same day, semen samples were also received from patients collected by masturbation, following at least five days of sexual abstinence. Subsequently, blood and semen samples were centrifuged for 10 minutes in 20°C at 2,000 g and 3,500 g, respectively. Each plasma was stored at –70°C for further analysis. HIV-1 nucleic acids were isolated using QIAamp-DSP virus kit (QIAamp, Qiagen, Hilden, Germany). Based on manufacturer's instruction, cDNA synthesis was conducted using Artus HI virus-1 kit (QIAamp, Qiagen, Hilden, Germany). qRT-PCR test was done using SYBR green reagents (Qiagen, Germany) with all specific primers using Rotor-Gene Q, real-time PCR system (Qiagen, Germany). BP and SP viral loads were reported in HIV-1 RNA copies/ml. The lowest detection limit was 50 copies/ml.

Ethical considerations

All ethical necessities of the present study were reviewed and approved by the ethic committee of Tehran University of Medical Sciences (IR.TUMS.VCR.REC.1395.1841). Furthermore, informed consent was obtained from each patient included. National standards were considered to respect patients' rights and ensure data confidentiality.

Statistical analysis

Results were reported in mean and standard deviation (SD), using SPSS Statistics software package, version 22 (SPSS Inc., Chicago, IL, USA). HIV-1 viral load in BP was compared to those with SP with paired *t*-test. *P*-value < 0.05 was considered as significant statistical level. Moreover, Pearson's correlation coefficient was applied to investigate the relationship between BP and SP viral loads.

Results

A total of 19 HIV-positive male patients, with a mean age of 35.8 years, were included in the present study, each of whom had received various ART regimens for at least 24 months. The details about ART regimens are summarized in Figure 1. In 11 patients, the viral load of both plasma and sperm samples was measured, and in 8 patients, only the viral load of plasma samples was evaluated. Our results indicated that in patients receiving ART for at least six months, the mean HIV RNA copy number in BP and SP was 1,371 copy/ml and 273 copy/ml, respectively. Our results also demonstrated a significantly higher BP viral load level than SP viral load ($p = 0.001$). Moreover, a significant correlation between BP viral load and SP viral load was observed (Pearson correlation = 0.97). Of note, in patients with undetectable BP viral load, the SP viral load was also not detectable. The results are demonstrated in Table 1.

Discussion

The present study was performed to evaluate the discordancy between BP and SP viral loads in men diagnosed with

Table 1. Comparison between blood plasma (BP) and semen plasma (SP) viral loads

Factor	Mean	SD	Minimum	Maximum
Age (year)	35.8	4.0	29.0	42.0
Time since diagnosis (months)	52.4	16.6	24.0	84.0
Time under antiretroviral therapy regimen (months)	49.0	15.8	24.0	72.0
BP viral load (copy/ml)	1,371	3,620.2	0.0	14,600
SP viral load (copy/ml)	272.7	608.4	0.0	2,000

HIV referred to the VCT center of Imam Khomeini Hospital in Tehran, who were being treated with ART for at least six months. Currently, HIV-positive patients are immediately treated with ART after diagnosis. It is expected that, on average, after approximately six months of ART, BP viral load of the virus would dramatically decrease to undetectable level. Due to concerns of sero-discordant couples planning to have a safe pregnancy and healthy childbirth, it is especially important to verify the virus level in the semen of male partners who are under antiviral treatment. These study results showed that in 100% (8 out of 8) of patients who had undetectable BP viral load, their SP viral load was also below detection level. In cases where there was a measurable viral load in BP samples, the mean viral load of BP was higher compared to the mean SP viral load. Therefore, it can be concluded that in patients under ART regimen whose BP viral load is lower than the detection limit, the risk of sexual transmission is insignificant. Hence, in sero-discordant couples, natural pregnancy might be considered as a reasonable option. Our findings are consistent with several studies, which indicated that in HIV-infected men with undetectable BP viral load, the SP viral load is also undetectable [19-23]. In a study by Lorello *et al.* [24], 33 male patients with undetectable BP viral load and under long-term ART regimen were recruited, and only 2 patients (6%) were identified with more than 700 copies/ mL in SP viral load. Furthermore, a Chinese study was conducted among 54 men who were having sex with men (MSM) and were under ART regimen. BP and SP viral loads analysis showed detectable SP viral load in only three patients (5.6%) who had undetectable BP viral load, which indicates underestimation of SP viral load for calculating transmission risk [25]. Moreover, other studies have reported on patients receiving ART regimens with undetectable BP viral load but detectable SP viral load [26-31]. Several factors are contributed to semen viral persistence, including HIV drug resistance [1], coinfection with other STDs, such as urethritis [1, 32], and insufficient potencies, absorption, and penetration of ART drugs [33]. Recently, the Swiss National AIDS Commission announced that HIV-positive patients are not having other STDs, undetectable BP viral load for at least six months, and good adherence to ART regimens are sexually non-infectious [34-40].

Of note, some patients' incomplete demographic information and lack of access to complete their data are mentioned as the current study's limitations.

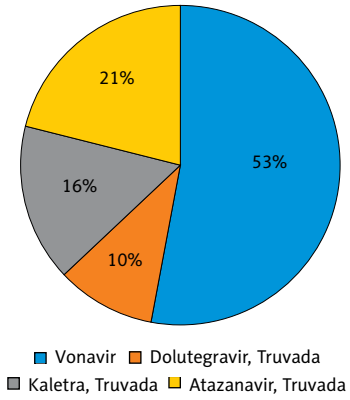

Figure 1. Patients' antiretroviral therapy (ART) regimen. Our patients were under different kinds of ART, including atazanavir, truvada 21% (n = 4), dolutegravir, truvada 10% (n = 2), kaletra, truvada 16% (n = 3), and vonavir 53% (n = 10)

Conclusions

In our study, the BP and SP viral loads of 73% in HIV-positive patients under ART treatment were undetectable. In addition, the SP viral load of the patients whose BP viral load was undetectable was below detection range. This point should be emphasized to sero-discordant couples who want to have a safe pregnancy and healthy offspring. This study concludes that in patients who have been treated with antiretroviral drugs for at least six months, in whom the BP viral load is below detection limit, it is most likely that the SP viral load is also undetectable. Therefore, such couples could be ensured and recommended for having natural impregnation, following all necessary examinations by professional parties.

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Disclosure

The authors declare no conflict of interest.

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