Short Communication

HIV Infection Associate with Prophylactic Highly Active Antiretroviral Therapy does not Affect Placental Invasion and Endothelial Function in the First Half of Pregnancy

Evilane do Carmo Patrício1, Regina Amélia Lopes Pessoa de Aguiar2, Henrique Vitor Leite2, Victor Hugo de Melo2, Antônio Carlos Vieira Cabral3 and Augusto Henriques Fulgêncio Brandão4*

1Physician at the Maternity of Hospital das Clínicas - Universidade Federal de Minas Gerais (UFMG), Brazil
2Gynecology and Obstetrics, School of Medicine - Universidade Federal de Minas Gerais (UFMG), Brazil
3Center of Fetal Medicine, Hospital das Clínicas - Universidade Federal de Minas Gerais (UFMG), Brazil
4*Corresponding author

Abstract

Background: Highly Active Antiretroviral Therapy (HAART) represented a breakthrough towards vertical transmission of HIV. Despite several reports of important collateral effects, the use of HAART quickly widespread due to its incontestable benefit to the fetus regarding the risk of infection. Endothelial dysfunction and abnormal placentation have been pointed out as one of the consequences of HAART and also as pathophysiological events of many disorders in pregnancy, such as Preeclampsia (PE). The association between PE, HIV and HAART presented conflicted data in literature.

Objectives: to evaluate possible differences in endothelial function and placental invasion between HIV-positive pregnant women receiving prophylactic HAART and HIV-negative healthy pregnant women from 16+0 to 19+6 weeks of pregnancy.

Patients and Methods: in this cross-sectional study, a total of 20 HIV-positive pregnant women and 40 HIV-negative pregnant women were submitted to Flow-mediated dilation (FMD) of brachial artery and dopplerfluxometry of uterine arteries, in order obtain its pulsatility index (UtA-PI).

Results: there were no statistical differences between the results of FMD (6,53 ± 3,61 X 4,98 ± 3,17, p=0,13) and UtA-PI (1,08 ± 0,29 X 1,06 ± 0,23, p=0,91) between HIV-positive group an HIV-negative group.

Conclusions: our findings suggest adequate placentation and absence of endothelial dysfunction in the first half of pregnancy in HIV positive women using prophylactic HAART.

ABBREVIATIONS

HAART: Highly Active Antiretroviral Therapy; PE: Preeclampsia; FMD: Flow-mediated dilation, UtA-PI: uterine arteries pulsatility index; 3TC: Lamivudine; AZT: Zidovudine; LPV/r: Lopinavir/Ritonavir; TDF: Tenofovir

INTRODUCTION

Highly active antiretroviral therapy (HAART) represents a breakthrough in vertical transmission of HIV, once it reduced its levels from 25% to less than 1% [1,2]. Prophylactic HAART is defined by the use of 3 antiretroviral drugs in a patient with no previous indication of these drugs, except pregnancy itself and the intention to reduce vertical transmission of the virus.

Due to its incontestable benefit to the fetus, lowing by near zero, the chance of HIV infection by the mother, not much consideration towards the risks and collateral effects of HAART in the mother or her fetus. It is, for instance, well known that antiretroviral drugs, particularly protease inhibitors (IP), can promote dyslipidemia and endothelial dysfunction [3], including damage in the blood-brain barrier4. HIV infection, by itself, can also cause endothelial dysfunction5.
In pregnancy, any loss in the capacity of vascular endothelium to promote vasodilation can lead to a hemodynamic status that leads to end organ acute failure, such as in Preeclampsia (PE) [6,7,8]. Therefore, it is possible to hypothesize that HAART or HIV infection might increase the risk of PE, what is not confirmed in most studies.

Savvidou et al. 2011 demonstrated that HIV infection and HAART therapy did not affect placental invasion in the first trimester of pregnancy in women that were using antiretroviral drugs since before pregnancy [9]. The short-term effects towards placental invasion and endothelial function in HIV pregnant women using prophylactic HAART had, to our knowledge, not been yet reported.

Therefore, our objective is to compare placental invasion, evaluated by dopplerfluxometry of uterine arteries and endothelial function, evaluated by Flow-mediated dilation (FMD), between HIV patients using prophylactic HAART and non-infected pregnant women from 16 to 20 weeks of pregnancy.

MATERIALS AND METHODS

Patients

In this cross-sectional study, 20 HIV positive pregnant women using prophylactic HAART, with no other comorbidity, and 40 healthy women, were submitted to dopplerfluxometry of uterine arteries and Flow-mediated dilation (FMD) of brachial artery between 16th and 19th weeks of pregnancy. HAART was always composed by at least 3 drugs: Lamivudine (3TC) was given to all the 20 HIV positive patients, Zidovudine (AZT) to 11 patients (55%), Lopinavir/Ritonavir (LPV/r) to 13 patients (65%) and Tenofovir (TDF) to 3 patients (15%). The most common association was composed by 3TC+AZT+LPV/r, given to 10 patients (50%).

Dopplerfluxometry of uterine arteries

A transabdominal transducer was placed on the lower quadrant of the abdomen, angled medially, and color Doppler was used to identify the uterine artery, at the apparent crossover with the external iliac artery. Measurements were taken approximately 1 cm distal to the crossover point. Care was taken to ensure that the angle of insonation was less than 60°.

Flow-mediated dilation of brachial artery

The assessing of flow-mediated dilatation of the brachial artery was made by using a high-resolution ultrasound with a 5 - 7 MHz linear transducer. The patients rested for 15 minutes before the ultrasound examination in dorsal decubitus. The brachial artery of dominant arm was identified medially in antecebial fossa. A clearest image of the artery was scanned over a longitudinal section, approximately, 5 cm above the elbow, at the end of the diastole. This moment was monitored using the B-mode of the echocardiographic equipment as the moment presenting the lowest distension of the vessel walls (to prevent larger vascular calibers originated from the vascular distension caused by the systole), which can be correctly captured by receding the image using the equipment cine loop of the equipment. Arterial diameter was obtained from frozen screen images, by calculating the mean of three measurements of the caliber of the vessel (D1). After this first procedure, a pneumatic cuff was inflated, placed on the forearm, distal to the ultrasound imaging site, to suprasystolic pressure (250mmHg) for 5 minutes, and after, the cuff was slowly deflated. One minute after the deflation, the mean of three new measurements of the caliber of the vessel was obtained by the same technique previously described (D2).

Based on the previously described standards, a new measurement of the brachial arterial caliber was carried out. The FMD value was obtained from the following calculation: FMD (%) = [(D2 - D1)/D1] × 100, where D1 = basal diameter and D2 = post-occlusion diameter.

Statistical analyses

Normality of continuous data was assessed with Shapiro-Wilk test. Student’s t test was used to compare variables between the two groups. Data was expressed as mean ± SD (limits). The statistical analyses were performed using the Statistical Package for Social Sciences (Version 18) (SPSS, Chicago, IL, USA).

RESULTS AND DISCUSSION

Results

The descriptive characteristics of the patients are shown in table 1, as well as viral load and CD4 count in HIV-positive group. There were no significantly differences between demographic and pregnancy characteristics.

Flow-mediated dilation of brachial artery results were no significantly different between HIV-positive and HIV-negative patients. Mean UtA-PI and lower UtA-PI were also no different between the two groups. These results are expressed in table 2.

Discussion

Pregnancy is a physiological condition with important endothelial adaptations. Many clinical complications are associated with endothelial dysfunction in pregnancies, as preeclampsia, gestational diabetes and intra-uterine growth restriction (IUGR) [6,7,8,10,11].

The mechanism involved in endothelial lesion in HIV infection is probably due to an inflammatory response to viral action [12]. The antiretroviral drugs can affect the endothelium by promoting oxidative stress leading to endothelial cell damage [13,14,15].

The association between HAART and HIV infection could increase the degree of endothelial dysfunction [16,17], but this is a statement not always confirmed by studies 18.

Our results showed absence of endothelial dysfunction with in HIV group, once FMD results were similar to control group. Possible explanations for this fact are the low viral count with high levels of CD4 in HIV patients in this particular group. Only 8 patients (40%) have viral load higher than 1000 copies/mL and only one patient (5%) had a CD4 count lower than 200 cells/mL. The low period that HIV group was taking HAART could also be insufficient to promote any kind of endothelial dysfunction.

Another complication associated with endothelium dysfunction in pregnancy is placental dysfunction [19,20]. Our results showed also, in that aspect, absence of abnormal placental invasion, once UtA-PI had no significantly differences
between the two groups. Our results are similar to another study developed in United Kingdom with 76 HIV-positive pregnant women taking prophylactic or therapeutic HAART [9].

**CONCLUSION**

In conclusion, our findings suggest adequate placentation and absence of endothelial dysfunction in the first half of pregnancy in HIV positive women using prophylactic HAART. These results corroborate studies that show no increase of some pregnancy complications related to these pathophysiological events such as PE and IUGR [21,22].

**ACKNOWLEDGEMENTS**

We would like to thank Jorge Andrade Pinto for all his contribution to this study.

**REFERENCES**


