



The Association Between Increasing Blood Pressure and Use of NNRTIs and Lopinavir/Ritonavir



Heidi M. Crane, MD, MPH¹, Stephen Van Rompaey, PhD¹, and Mari M. Kitahata, MD, MPH^{1,2}.

From the ¹Department of Medicine and ²School of Public Health and Community Medicine, University of Washington, Seattle, WA

Background

- The dramatic decline in HIV-related mortality resulting from advances in antiretroviral therapy has been accompanied by an increase in metabolic complications
- Hypertension (HTN) has been increasingly noted among HIV-infected patients during the HAART era
- Prior studies have focused predominantly on the impact of HAART versus no HAART and have not been able to examine antiretroviral medications individually. The potential role of particular antiretroviral medications and classes of medications is therefore unknown
- The purpose of this study was to explore the effect of antiretroviral medications on the development of elevated blood pressure (BP) and HTN among HIV-infected patients

Methods

- **STUDY SETTING:** University of Washington Harborview Medical Center's HIV specialty clinic, the single largest provider of HIV care in the northwestern United States
- **STUDY SUBJECTS:** A cohort of 414 HIV-infected patients aged 18 or older who initiated routine clinical care at the clinic on or after 1/1/1998. Patients were PI and NNRTI naive at first visit and subsequently were started on HAART
- **DATA SOURCE:** The University of Washington HIV Information System (UWHIS) captures comprehensive clinical data for the HIV infected population receiving care from 1995 to the present
 - BP values measured by the nursing staff at the start of all clinic visits
 - Laboratory test results
 - Pharmacy dispensing data (96% of patients receive their medications from a UW pharmacy)
 - Clinical encounter and billing data capturing all inpatient and outpatient diagnoses
 - Historical clinical information collected at time of initial visit by standardized intake process including antiretroviral treatment history
- **INCLUSION CRITERIA:**
 - First primary care visit on or after 1/1/1998 and 2nd visit within 12 months
 - ≥3 or more visits prior to starting HAART and while on initial HAART regimen
- **EXCLUSION CRITERIA:**
 - Diagnosis of HTN prior to initiating HAART
 - PI or NNRTI use prior to first clinic visit

Methods cont.

- **ELEVATED BP DEFINITION:** mean BP measures before and during initial HAART regimen used to examine change in BP for individual patients. Elevated SBP and DBP were defined as an increase in mean SBP or DBP ≥10 mmHg while on initial HAART regimen compared to the same patient's mean BP prior to starting HAART
- **NEW DIAGNOSIS OF HTN DEFINITION:** diagnosis of HTN made by clinician as reason for visit and confirmed by patient receiving BP lowering medication
- **ANTIRETROVIRAL THERAPY:** examined as PI class and NNRTI class, and as individual medications
- **STATISTICAL ANALYSES:** Logistic regression was used to examine the odds of a patient experiencing an increase in SBP or DBP or a new diagnosis of HTN, and antiretroviral medications, patient demographics, risk factors for HIV transmission, BMI, CD4 cell count, and HIV-1 RNA level after initiation of first HAART regimen
- Final models (see Table 2 and Figure 1) are adjusted for age, race, and gender. Reference group contains patients whose initial HAART regimen contained a PI excluding Lopinavir/Ritonavir

Results

- In analyses adjusted for age, race, and sex, patients receiving first HAART regimens containing Lopinavir/Ritonavir, Efavirenz, or Nevirapine were more likely to develop increased BP and/or a new diagnosis of HTN compared with patients on a PI based regimen that did not include Lopinavir/Ritonavir
- Median duration on initial HAART regimen 51 weeks
- Smoking status, change in BMI, risk factor for HIV infection, baseline CD4, and HIV-1 RNA level were not associated with BP increases

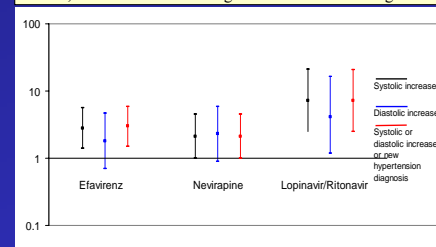
Table 1: Demographic characteristics of cohort

Characteristic	Patients without change in BP (N=355)	Patients with increased SBP, DBP, or new diagnosis of HTN (N=59)	p value
Sex	N (%)	N (%)	
Male	305 (86)	54 (92)	
Female	50 (14)	5 (8)	>0.1
Age			
<30	86 (24)	10 (17)	
30-39	184 (52)	32 (54)	
40-49	65 (18)	13 (22)	
≥ 50	20 (6)	4 (7)	>0.1
Race/Ethnicity			
White	221 (62)	33 (56)	
Black	112 (32)	24 (41)	
Other	22 (6)	2 (3)	>0.1
Risk Factor for HIV Transmission			
MSM	191 (54)	34 (58)	
Injection drug users	89 (25)	13 (22)	
Heterosexual	64 (18)	9 (15)	
Other	11 (3)	3 (5)	>0.1

Table 2: Odds of developing BP increases and/or new diagnosis of HTN adjusted for age, race, and sex

Variable	SBP increase or new diagnosis of HTN	DBP increase or new diagnosis of HTN	SBP or DBP increase or new diagnosis HTN
	OR (95% CI; p)		
Lopinavir/Ritonavir	7.2 (2.5-20.8; p<0.001)	4.2 (1.1-16.4; p=0.04)	7.2 (2.5-20.9; p<0.001)
Nevirapine	2.1 (1.0-4.5; p=0.05)	2.3 (0.9-5.9; p=0.08)	2.1 (1.0-4.5; p=0.05)
Efavirenz	2.8 (1.4-5.6; p=0.049)	1.8 (0.7-4.7; p=0.2)	3.0 (1.5-5.9; p=0.002)

Figure 1: Adjusted odds for developing an increase in SBP, DBP, and/or a new HTN diagnosis on 1st HAART regimen



Limitations

- Observational study design can not provide evidence for causal relationship
- Larger sample size with increased power may be needed observe effects of other drugs that may be smaller

Conclusions/Future Directions

- This study suggests patients receiving 1st HAART regimens containing Lopinavir/Ritonavir, Efavirenz, and Nevirapine are at higher risk of developing elevated BP or HTN than patients on HAART regimens not containing these medications
- The role of recently approved antiretroviral medications such as Atazanavir and Amprenavir could not be assessed due to insufficient numbers of patients taking these medications. With longer follow-up over the next few years, these additional analyses may be undertaken
- Future analyses will examine the role of NRTIs, time-to-event analyses will be conducted to examine impact of duration of medications
- A strength of UWHIS is complete capture of pharmacy data and BP values facilitating evaluation of the impact of antiretroviral medications on BP
- Additional larger cohort studies are needed to to examine the effect of clinical and treatment factors in greater detail and better understand the effect of HTN and other metabolic complications on long-term outcomes to optimize antiretroviral treatment strategies