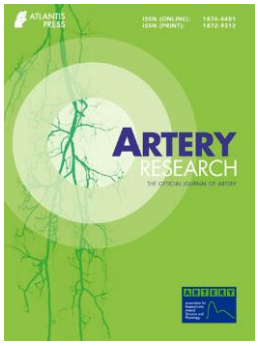

Artery Research

ISSN (Online): 1876-4401 **ISSN (Print): 1872-9312**
Journal Home Page: https://www.atlantis-press.com/journals/artres

P3.01: A COMPARISON OF ARTERIAL FUNCTION OF HIV INFECTED (TREATED AND NEVER-TREATED) AND UNINFECTED BLACK SOUTH AFRICANS AFTER FIVE YEARS: PURE STUDY

C.M.T. Fourie, J.M. van Rooyen, A. Kruger, R. Schutte, H.W. Huisman, N.T. Malan, L. Malan, A.E. Schutte

To cite this article: C.M.T. Fourie, J.M. van Rooyen, A. Kruger, R. Schutte, H.W. Huisman, N.T. Malan, L. Malan, A.E. Schutte (2011) P3.01: A COMPARISON OF ARTERIAL FUNCTION OF HIV INFECTED (TREATED AND NEVER-TREATED) AND UNINFECTED BLACK SOUTH AFRICANS AFTER FIVE YEARS: PURE STUDY, Artery Research 5:4, 156–157, DOI: https://doi.org/10.1016/j.artres.2011.10.036

To link to this article: https://doi.org/10.1016/j.artres.2011.10.036

Published online: 14 December 2019

[1]*1st Dept of Cardiology, Hippokration Hospital, Athens Medical School, Athens, Greece*
[2]*2nd Dept of Internal Medicine and Infectious Diseases, Hippokration Hospital, Athens Medical School, Athens, Greece*

Purpose: HIV infection is linked to heightened cardiovascular risk; this is partly mediated through endothelial dysfunction. We investigated the interplay of endothelial function with markers of inflammatory and oxidation in two groups of HIV infected patients: on ART and naïve to ART.
Methods: We recruited 47 HIV infected patients (46 male, mean age 35±10 years, mean CD4 count: 579±271). All were free from overt cardiovascular disease. 31 patients were naïve to ART; 17 were on ART. FMD of the brachial artery was used as an index of endothelial function. Markers of inflammatory (CRP, IL6), oxidative (ADMA) and functional (CD4, viral load) status were measured. Between groups comparisons (ART vs naïve patients) were performed using the Mann-Whitney U test.
Results: Endothelial function and inflammatory markers did not differ across groups. ART group had higher ADMA levels, lower viral load and higher CD4 count, thereby a favorable oxidative/functional status compared to naïves.

	Naïve (n=31)	ART (n=17)	P value
FMD (%)	4.2 (2.3, 7.5)	5.2 (3.1, 8.2)	0.740
CRP (mg/dL)	1.37 (0.98, 2.79)	1.05 (0.28, 3.32)	0.249
IL6 (pg/mL)	1.65 (0.83, 3.39)	1.00 (0.77, 1.65)	0.258
ADMA (μmol/L)	0.63 (0.25, 0.79)	0.84 (0.78, 1.06)	0.006
Viral load	19419 (8144, 54025)	50 (50, 50)	0.001
CD4 count	450 (378, 627)	635 (510, 779)	0.011

Conclusion: In HIV infection, ART does not change endothelial function; nevertheless it is linked to a favorable oxidative and functional status.

P2.13
ALTERED MICROVASCULAR RESPONSES TO ANGIOTENSIN II INFUSION INDICATING ENDOTHELIAL DYSFUNCTION IN SUBJECTS WITH FAMILIAL HYPERCHOLESTEROLEMIA

M. Ekholm [1], G. Jörneskog [2], H. Wallén [3], J. Brinck [4], T. Kahan [5]
[1]*Karolinska Institutet, Dept of Clinical Sciences, Danderyd Hospital, Division of Cardiovascular Medicine, Stocholm, Sweden*
[2]*Karolinska Institutet, Dept of Clinical Sciences, Danderyd Hospital, Division of Medicine, Stockholm, Sweden*
[3]*Karolinska Institutet, Dept of Clinical Sciences, Danderyd Hospital, Division of Cardiovascular Medicine, Stockholm, Sweden*
[4]*Dept of Medicine, Karolinska University Hospital, Huddinge, Stockholm, Sweden*
[5]*Karolinska Institutet, Dept of Clinical Sciences, Danderyd Hospital, Division of Cardiovascular Medicine, Stockholm, Sweden*

Purpose: Angiotensin II (ANG) is implicated in the development of cardiovascular disease. We examined vascular responses to ANG in subjects with familial hypercholesterolemia (FH), a group at high cardiovascular risk.
Methods: The effects of ANG (3h iv infusion, 10 g/kg/min) on brachial blood pressure and forearm skin microvascular function were studied in 8 female and 8 male FH (mean age 43±8 ys) and in 16 matched healthy controls. Skin microcirculation was studied by laser Doppler fluxmetry during rest and local heating of the skin to 44°C (microvascular hyperaemia). Microvascular resistance was assessed by mean arterial pressure/microvascular hyperaemia, and macrovascular reactivity by blood pressure changes. Measurements were performed before, at 1 and 3h of ANG, and 1h after stopping infusion. Mean values ±SD.
Results: Baseline systolic blood pressure was higher in FH (127±14 vs 115±12 mm Hg; p=0.02), while pressure responses to ANG were similar in both groups (eg +24±10 vs +21±7 mm Hg, ANG 3 h). There were no baseline differences in microvascular hyperaemia or resistance between the groups. However, during and after ANG microvascular hyperaemia was impaired (p=0.01; eg 126±95 vs 184±102 units, ANG 3 h), and microvascular resistance higher (p=0.01; eg 1.9±0.9 vs 0.9±0.8 mm Hg/units; ANG, 3 h) in FH. Saline infusion verified stability of the experimental design (n=8).
Conclusions: Despite similar blood pressure responses to ANG in FH and controls, microvascular dilatation capacity was impaired in FH, indicating endothelial dysfunction. These findings and increased microvascular resistance may lead to hypertension and cardiovascular complications in FH.

P2.14
RELATION OF HEART RATE VARIABILITY TO ENDOTHELIAL FUNCTION IN HEALTHY SUBJECTS – DEPENDENCE UPON CARDIAC CYCLE LENGTH

A. Pinter, T. Horvath, M. Kollai
Institute of Human Physiology and Clinical Experimental Research, Semmelweis University, Budapest, Hungary

In various diseased states reduced cardiac vagal modulation (CVM) is accompanied by impaired endothelial function. It is unclear whether CVM and endothelial function undergo dysregulation independently, or these systems affect each other negatively as a consequence of the disease process. Since the respective physiology is unclear, we aimed to investigate if such relationship between CVM and endothelial function exists in healthy subjects.
46 young males were studied. From 10 minute long ECG recordings mean RR interval (RRI) and time and frequency domain vagal heart rate variability (HRV) indices (SDNN; RMSSD; pNN50 and HF, respectively) were determined. HRV indices were used to define CVM. Endothelial function was assessed by measuring brachial artery flow mediated dilation (FMD). Hyperemic, diastolic shear rate was used to normalize FMD (nFMD).
RRI was related to most HRV indices, but not to FMD. On the other hand, all HRV indices correlated significantly and positively with FMD across subjects ($r = 0.49$, $p<0.01$ for HF–nFMD). After adjusting for potential confounders, RMSSD and HF remained significantly associated with nFMD. When subjects were dichotomized according to median RRI, the HRV–nFMD relations lost significance at higher (RRI<910 ms), and gained further significance at lower (RRI>910 ms) heart rates ($r = 0.57$, $p<0.01$ for HF–nFMD).
Our data demonstrate that vagal HRV indices are related to FMD across healthy male subjects. Although RRI is not related to FMD, the HRV-FMD relation is dependent upon RRI. The underlying mechanism may involve centrally released endothelial mediators, which enhance CVM through vasculo-neural communication.

P3 – Interventional studies 1

P3.01
A COMPARISON OF ARTERIAL FUNCTION OF HIV INFECTED (TREATED AND NEVER-TREATED) AND UNINFECTED BLACK SOUTH AFRICANS AFTER FIVE YEARS: PURE STUDY

C. M. T. Fourie [1], J. M. van Rooyen [1], A. Kruger [2], R. Schutte [1], H. W. Huisman [1], N. T. Malan [1], L. Malan [1], A. E. Schutte [1]
[1]*Hypertension in Africa Research Team (HART), School of Physiology, Nutrition and Consumer Sciences North-West University, Potchefstroom, South Africa*
[2]*Africa Unit for Transdisciplinary Health Research (AUTHeR), North-West University, Potchefstroom, South Africa*

The prevention and treatment of hypertension is marginalized in South Africa by the overwhelming prevalence of HIV. HIV-1 infection and the treatment thereof paradoxically affect cardiovascular risk factors and may add to the cardiovascular risk of these individuals.
We aimed to compare the 5 year cardiovascular changes of black South Africans who were (a) HIV-1 infected without treatment, (b) HIV-1 infected with antiretroviral therapy and (c), uninfected. In this study 164 uninfected and 145 HIV-1 infected (77 never-treated and 68 treated) participants were followed-up after a 5 year period. Two hundred and ninety one participants were lost to follow-up, 11 were newly HIV infected, 39 died and 241 did not partake. The cardiovascular and anthropometric variables were assessed and the percentage change determined. Follow-up analysis (cross-sectional) showed a lower IMT ($p<0.01$), central systolic blood pressure ($p<0.01$) and augmentation index ($p=0.03$) in the HIV infected compared to the HIV uninfected participants. After 5 years (2005-2010) the treated HIV-1 infected participants showed an increase in pulse pressure ($p=0.03$) and no change in pulse wave velocity, whilst a decrease ($p=0.02$) was encountered in the never-treated HIV infected participants. No difference in the % change was seen between the treated and uninfected participants.
In conclusion, the cardiovascular profile of the treated HIV-1 infected Africans show signs of an early development of arterial dysfunction over 5 years which is not seen in the never-treated participants. How the

antiretroviral therapy is going to influence the HIV-1 infected South Africans' long-term risk for cardiovascular disease remains to be seen.

P3.02
ROSUVASTATIN IMPROVES ARTERIAL WAVE REFLECTION AND PULSE PRESSURE AMPLIFICATION BY RESTORING ENDOTHELIAL FUNCTION

C. Ott, U. Raff, M. P. Schneider, R. E. Schmieder
Department of Nephrology and Hypertension, University of Erlangen-Nuremberg, Erlangen, Germany

Objective: One of the major indicators of intact endothelial function is basal nitric oxide (NO) activity. Further, is seems to be likely that statin therapy exerts beneficial effects on vascular function, at least in part via an improvement of NO bioavailability.
Design and Methods: In a double-blind crossover study twenty-nine hypercholesterolemic patients were randomly assigned to receive rosuvastatin and placebo for 42 days. Pulse wave analysis was assessed after 30 minutes of rest (baseline) and after infusion of L-NMMA. The magnitude of the increase in central augmentation index (cAIx) in response to inhibition of NO synthase (NOS) by L-NMMA is indicative of basal NO activity.
Results: CAIx was significantly lower (18.3±10 versus 21.9±12%, p=0.027) with rosuvastatin compared to placebo. There was no increment of cAIx in response to L-NMMA in placebo group. In contrast, cAIx increased significantly in response to L-NMMA (20.5±11 versus 25.7±10mmHg, p=0.001) in rosuvastatin group. The percentage of increase of cAIx tended to be more pronounced after treatment with rosuvastatin compared to placebo (53.7±92 versus 14.1±36%, p=0.087), indicating increased basal NOS activity with rosuvastatin treatment. Pulse pressure amplification (PPA) improved (1.31±0.2 versus 1.26±0.2 %, p=0.016) after rosuvastatin compared to placebo. Regression analyses revealed that both LDL-cholesterol and CRP-levels are independent determinants of basal NO activity improvement, which itself is an independent determinant of vascular function, expressed by an improvement of arterial wave reflection and PPA.
Conclusion: Rosuvastatin improves vascular function by restoring endothelial function expressed by improved NO production in patients with hypercholesterolemia, thereby exerting anti-atherosclerotic effects on the vascular wall.

P3.03
BIOACTIVES OF WILD BERRIES: POTENTIAL ALTERNATIVES TO VASODILATOR DRUGS

K. S. Bhullar, H. P. V. Rupasinghe
Nova Scotia Agricultural College, Truro, Canada

Hypertension is described as one of the risk factors in arterial and cardiovascular health. With increasing hypertension risk in all age groups and side-effects of vasodilator drugs, need for an effective natural cure is crucial. Wild berries provide valuable biologically active phytochemicals which can also neutralize reactive oxygen species (ROS) that are pathological mediators in many chronic diseases including hypertension. Present research was carried out to study the total bioactive content and antioxidant capacity of ethanol extracts of wild berries and their ability to inhibit angiotensin converting enzyme (ACE) which is principal blood pressure regulating enzyme. Among the investigated five species of cloudberry (*Rubus chamaemorus* L.), crowberry (*Empetrum nigrum*), blueberry (*Vaccinium corymbosum)*, cranberry (*V. macrocarpon)*, partridgeberry (*V. vitis-idaea*), the highest anthocyanin content was found in early harvested crowberry while late harvested fruit of lingonberry exhibited the highest antioxidant capacity and phenolic content ($p \leq 0.05$). The ACE inhibition by berry extracts was measured by using a florescence based assay at presence of histidine −L-hippuryl-L-histidine-chloride substrate. All the berry extracts showed a concentration responsive enzyme inhibition *in vitro* indicating effective ACE inhibition. However, partridgeberry and cranberry were among the most effective ($p=0.05$). This study has demonstrated potential cardiovascular health benefits of berries and further studies are warranted to confirm the results using cell lines, animal and clinical studies.
Keywords: cardiovascular disease, hypertension, natural health products, wild berries

P3.04
EFFECTS OF ANTIHYPERTENSIVE DRUGS ON CENTRAL BLOOD PRESSURE

D. Agnoletti [1], Y. Zhang [2], C. Borghi [3], J. Blacher [1], M. E. Safar [1]
[1]*Paris Descartes University; AP-HP; Diagnosis and Therapeutic Center, Hôtel-Dieu, Paris, France*
[2]*Centre for Epidemiological Studies and Clinical Trials, Ruijin Hospital, Shanghai, Shanghai, China*
[3]*Department of Internal Medicine, University of Bologna, Bologna, Italy*
Background: Central blood pressure (BP) is considered a better predictor of cardiovascular events than brachial BP, and mechanisms influencing central BP are mostly related to reduction of arterial stiffness and/or reflected waves. Comparison between drugs on their effect in central hemodynamics has poorly been studied.
Objective: To assess the role of 3 antihypertensive drugs on central BP, in comparison with placebo, and their associated mechanisms.
Methods: Multicenter, multinational, randomized, double blind, placebo-controlled clinical trial analyzing the effects of a 12-week treatment with amlodipine, candesartan, indapamide sustained release, or placebo in 145 outpatients with essential hypertension and no cardiovascular complications, enrolled in the X-CELLENT (NatriliX SR versus CandEsartan and amLodipine in the reduction of systoLic blood prEssure in hyperteNsive patienTs) study. Post-hoc analysis focusing on central hemodynamics.
Results: Each active drug reduced brachial and mostly central BP. Amlodipine and indapamide produced a greater reduction of central than brachial pulse pressures, while candesartan had a similar but lesser effect. Augmented pressure, a well established wave reflection index, was reduced by all active drugs. Within duration of the trial, no effect was achieved on pulse wave velocity. Pulse pressure amplification was similarly increased by all active treatments.
Conclusions: Amlodipine and indapamide, more than candesartan, have an effect on both static and pulsatile central BP, causing a reduction of central systolic, diastolic and pulse pressures. Within the limits of the investigation, central BP reduction was not due to changes in arterial stiffness, but rather in wave reflections and pulse pressure amplification.

P3.05
EFFECTS OF ACETAZOLAMIDE ON BLOOD PRESSURE AND PULSE WAVEFORM CHANGES INDUCED BY HIGH ALTITUDE EXPOSURE

M. Revera [1], P. Salvi [2], A. Giuliano [3], G. Bilo [1], A. Faini [1], F. Gregorini [1], C. Lombardi [1], G. Mancia [4], G. Parati [3]
[1]*Dept. Cardiology, San Luca Hospital, Istituto Auxologico Italiano, Milan, Italy*
[2]*Dept. Internal Medicine, University of Bologna, Bologna, Italy*
[3]*Dept. Cardiology, Ospedale San Luca, Istituto Auxologico Italiano and University of Milano-Bicocca, Milan, Italy*
[4]*Dept. of Clinical Medicine and Prevention Univ. Milano-Bicocca, Milan, Italy*

Background: Exposure to high altitude (HA) may induce mountain sickness and increase blood pressure (BP) but little is known on the effects on arterial properties. Acetazolamide (AC) has been proposed to prevent and treat mountain sickness, but no information is available on its effects on cardiovascular parameters at HA. Our aim was to assess these issues in healthy volunteers acutely exposed to very HA.
Methods: 42 subjects (age 36.8±8.9, 21 Male) were randomized to double blind AC 250 mg bid or placebo (PL). Arterial tonometry (PulsePen, DiaTecne, Milan) including carotid-femoral and carotid-radial PWV (CF-PWV,CR-PWV) and pulse wave analysis (augmentation index, AIx and subendocardial viability ratio, SEVR) was performed: at baseline (BAS), after 2 days of treatment at sea level (SLpost); within 6 hours from arrival at Capanna Margherita(Mount Rosa, 4559 m,HA1); and on 3rd full day of exposure to HA(HA2). Systolic (S) and diastolic (D)BP were measured with validated oscillometric device (AND UA 767-PC). Heart rate (HR) was derived from the ECG signal. Data are shown as means±SD.
Results. (See table, p=peripheral, c= central, M=mean). At HA, AIx (adjusted for HR) increased but was significantly lower in AC group, moreover AC treatment partially counteracted the decrease in SEVR.
Conclusions: Acute exposure to HA induced both a BP rise and changes in vascular function, partly counteracted by treatment with AC. These haemodynamic effects may contribute to the beneficial role of AC at HA and may have implications for the possible clinical usefulness of AC in patients with hypoxemia.

	BAS		SLpost		HA1		HA2	
	PL	AC	PL	AC	PL	AC	PL	AC
pSBP	114,8±12,2	115,4±13,4	114,5±12,2	110,1±12,8	115,7±9,8	108,3±9,6 #	120,7±8,4 **	114,2±11,7
cSBP	109,5±11,1	110,1±14,4	109,3±11,7	107,5±12,8	110,3±9	104,6±9,6	115,4±7,8 *	109,6±12,3
MBP	89,2±8,3	88,0±9,1	87,8±8,3	84,9±8,5	92,7±6,8 *	85,3±6,0 #	96,8±6,8 **	91,2±8,3 #
DBP	72,1±6,7	69,8±7,3	70,1±6,9	68,1±6,3	77,4±6,8 *	70,1±5,3 #	89,9±7,5 **	74,1±7,3 *#
HR	59,5±6,4	64,1±9,4	57,6±5,5	58,2±6,6 *	83,5±10,4 **	76,4±8,8 **#	68,7±10,9 **§	63,3±9,8 *§
AIx75	-8,4±12,5	-11,7±10,9	-7,3±11,3	-15,5±10 #	1,54±12,6 **	-7,5±12,6 *#	2,1±11,8 **	-8,1±10,9 *#
SEVR	0,88±0,14	0,78±0,23	0,89±0,19	0,87±0,2	0,58±0,14 **	0,67±0,13 *	0,74±0,17 **§	0,87±0,15 §#
cf-PWV	6,3±1,1	6,4±1,3	6,7±2,3	6,0±1,1	6,6±1,2	5,9±0,9	6,3±1,1	6,0±0,8
cr-PWV	7,7±1,1	7,7±1,2	8,1±1,7	7,9±1,3			6,7±1,5	8,3±1,6

*-p<0,05 Vs SIpre; *-p<0,05 Vs SIpost; §-p<0,05 Vs HA1; #-p<0,05 Vs PL at same step