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Role of Vasoactive Agents in hypertension on HIV positive patients on HAART in Mthatha, South Africa

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Abstract

The progression of cardio vascular disease in patients with obesity and hypertension is attributed to dysfunction of vascular endothelium. The aim of the study was to analyze the relationship between HIV infection, Hypertension and obesity and to link it to the changes in the endothelin and NO levels in patients with treatment on HAART.

Methods

This was a comparative study. The total number of participants participated to the study was 154 and were categorized into the following groups: 57 HIV (-) participants (A), 40 HIV (+) not on treatment participants and 57 HIV (+) on treatment participants. Enzyme immunoassay kit was used for the quantitative determination of ET-1 and Nitrate/nitrite colorimetric assay kit was used for the determination of NO. All anthropometric measurements were also taken into account.

Results

Low mean levels of resting metabolism, waist circumference and hip circumference is shown in HIV positive patients compared to HIV negative patients. Visceral fat, whole fat had low mean levels but skeletal muscle fat showed the highest mean levels in both HIV positive groups. All the blood pressures between HIV groups were on a normal range scale. Mean values of endothelin and nitric oxide are increased in HIV positive not on ART and HIV (+) on ART compared with the HIV negative group.

Conclusion

NO, ET-1, ART and HIV itself were associated with the pathogenesis of endothelinl dysfunction in HIV infection patients. Endothelinl markers were elevated, although these markers have deleterious effect on the endothelium but can also serve as up-regulator of hypertension.

Keywords

HIV-Infection; Antiretroviral Therapy; Endothelinl Dysfunction; Endothelin-1 (ET-1); Nitric Oxide (NO); Blood Pressures (BPs)

Introduction

Vascular endothelinl dysfunction has been implicated in the development of cardiovascular diseases and is closely associated with atherosclerosis and hypertension [1]. Vascular dysfunction has been attributed to impaired ability to vasoconstrictor or dilates [2]. The endothelium releases vasoactive agents such as nitric oxide (NO), prostacyclin (PGI2) and endothelium derived hyperpolarizing factor (EDHF) which are vasodilatory

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or vasoconstrictive factors such as thromboxane (TXA2) and endothelin-1 (ET-1) [3]. Endothelinl mediators like NO and ET1 are known counterparts in the regulation of vasoactive and an imbalance between the two may result in endothelinl dysfunction [4, 5]. Enhancement of ET-1 system coupled with lack of NO leads to significant up-regulation of blood pressure resulting in hypertension [6], The role of NO in regulating BP is also well established [6]. Enhanced ET-1 mediated vasoconstriction is also associated with overweight and obesity which contributes to endothelinl vasodilator dysfunction [7]. Evidence suggests that NO play a major role in regulating blood pressure and that impaired NO bioactivity is an important component of hypertension [8].

HIV-associated cardiovascular diseases have been widely described, but clinical studies aimed at establishing cause-effect relationships between HIV-associated cardiovascular disease and either the HIV infection or antiretroviral therapy have been problematic [9]. However these studies were only performed using animal model (FVB/n mice), therefore it is of great importance to illustrate its effect (anti-retroviral) on vascular endothelium in humans. Obesity has been identified as a major risk factor for hypertension, increased triglycerides, and elevated serum lipids including hypercholesterolemia [10]. Renal complications are likely long term effects of hypertension.

High levels of waist fat are a leading cause of possible inflammation in blood vessels [11]. Tissue capillaries undergo wall stress in the endothelium in particular thereby leading to impaired oxygen release to cells leading to waste products accumulation [12]. Atherothrombotic problems have been implicated in carotid artery insufficiency, strokes and circulatory problems [12].

Obesity itself has been clearly shown to disrupt the ET1 mediated vasoconstriction which further leads to endothelinl dysfunction resulting in increased prevalence of hypertension associated with elevated adiposity [7]. Previous study in HIV patients on HAART showed a prevalence of hypertension similar to HIV negative controls although this has been considered as a lesser evil [13].

The aim of the present study was to evaluate the effects of HIV infection, antiretroviral therapy and its possible implication in the etiology of hypertension and obesity and its association between endothelin and nitric oxide. The present study attempts to compare endothelin and nitric oxide between HIV groups using univariate and multivariate analysis; to determine the association between gender, blood pressure, body composition and endothelin in each group and to determine association between endothelin and nitric oxide according to the study groups.

Does HIV treatment or HIV itself contribute to changes in the levels of endothelin and NO in HIV positive patients and HIV positive patients on HAART treatment?

Materials and Methods

Study Design

This was a descriptive and comparative study.

Ethics Approval

Ethical and bio-safety clearance was obtained from Walter Sisulu University (protocol number: 023/2012) and the purpose of the study was explained orally and in writing to obtain consent from recruited participants. Participants were informed that they may refuse to participate or withdraw from the study at any time without fear of victimization. Participants were assured of total confidentiality and that there will be no information that identified them in any manner. They were informed that the information will only be utilized for the purposes as stipulated and all possible steps will be taken to ensure that the information remained confidential.

Sample Size

This study was conducted in a random manner, planned to convenience population according to inclusion and exclusion criteria and the expected sample size was 180 participants of different sex groups but 154 participants completed the study.

Place of Research

Participants were recruited from Clinics (Gateway and Infectious disease clinic), Nelson Mandela Academic Hospital (NMAH) in KSD Municipality, in the Eastern Cape Province, South Africa.

Inclusion Criteria

HIV patients were considered eligible for inclusion in the study if at the time of data collection they accept to participate in the study by filling in questionnaire and signing consent form. The age range of participants was between 20-50 years old, female and males of equal ratio.

Exclusion Criteria

Excluded from participation were individuals who were under treatment for hypertension, had used anti-diabetic agents, steroids, growth hormone, oral contraceptives pills, or any anabolic agent, substance abuse, appetite suppressor, pregnant, or had breast-fed in the past year, who have or who had an acute infection within 3 months of the study.

Grouping

154 participants took part in the study and were categorized into the following groups: 57 HIV (+) participants on HAART (Group A), 40 HIV (+) not on HAART participants (Group B), and 57 HIV (-) participants (Group C as controls).

Methodology

Questionnaires forms (self designed and tested) were issued to the participants. Body composition indices were measured using anthropometry, bioelectric impedance analysis (BIA) and also by the use of medical equations [14]. The measurements of weight were performed before the use of bioelectric impedance analysis. Height was taken to the nearest 1 cm with the aid of Electronic body scale for weight and height (model: TCS-200-RT, China) with patients wearing light clothes without shoes [14].

Weight (kg), body mass index (BMI in kg/m2), body fat (%), visceral fat levels (%), resting metabolism rate (calorie expenditure of resting body) all were automatically obtained using Omron body composition monitor BF 500 (Omron, Tokyo ,Japan) [15]. Blood pressure was measured using sphygmomanometer (Automatic blood pressure monitor: Model: KD-525E, Zhe Jiang, China) [14].

JNC-7 Classification and management of blood pressure : Hypotension (< 90 mmHg systolic pressure and <60 mmHg diastolic pressure), normal (90-119 mmHg systolic pressure and 60-79 mmHg diastolic pressure), pre hypertension (120-139 mmHg systolic pressure and 80-89mmHg diastolic pressure), stage 1 hypertension (140-159 mmHg systolic pressure and 90-99 mmHg diastolic pressure), stage 2 hypertension (160-179 mmHg systolic pressure and 100-119 mmHg diastolic pressure) and hypertensive crisis (≥ 180 mmHg systolic pressure and ≥ 120 mmHg diastolic pressure) [16].

5 milliliters of venous blood was drawn at 08:00 am before breakfast after 8-12 hrs overnight fast. Fasting blood was collected in tubes containing 50 mmol of EDTA as an anticoagulant. Blood was centrifuged for 15 minutes at 1000 x g within 30 minutes to separate serum from the whole blood. Serum samples were stored at -80° C refrigerator in the fridge until the time for analysis. Endothelin assay is an immunometric (i.e. sandwich) EIA that permits endothelin measurement within the range of 0-250 pg/ml [17]. The Griess reagent system will ensure an accurate Nitric Oxide quantization, by preparing a reference curve with the Nitrite Standard for each assay [18].

Statistical Analysis

Data was analyses using SPSS version 19 for Windows (SPSS, Chicago, U.S.A.). Multiway analysis of variance (MANOVA) and covariance (ANCOVA) were used to explore the association between blood pressure groups, body composition and age, and gender. In addition, these statistics were used to explore the effect of the study variables on the log-transformed hormone levels of ET-1, and NO. Turkey's multiple comparison post-hoc analysis was subsequently used. Descriptive statistics and Comparism study was used to calculate mean ± SD of all variables. Correlation analysis will also be used to look for the degree of correlation between ET-1, NO levels, body composition and arterial blood pressure. A P-value of <0.05 was considered significant.

Results

Among the study population comprising 154 participants, 47 were males and 107 females with sex ratio of 2 females: 1 male (Figure 1), women were 2/3 (69.48% n=107) and men were 1/3 (30. 52 % n=47). HIV positive patients on HAART (sex ratio almost 2 males: 3 females), HIV positive patients not on HAART (sex ratio 1 male: 3 females) and HIV negative patients (sex ratio almost 1 male: 2 females.

Influence of Gender

Table 1 below represents the characteristics in the study population and the impact of gender on general characteristics in these adults females and males presented similarities in age, waist/hip ratio, systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP) and Endothelin but there was a significance when it comes to weight, height, waist circumference (WC), hip circumference (HC),skeletal muscle fat (SMF), whole fat (WF), body mass index (BMI), resting metabolism (RM) and nitric oxide (NO) respectively.

Figure 1: Percentage of Patients in Different Study Groups

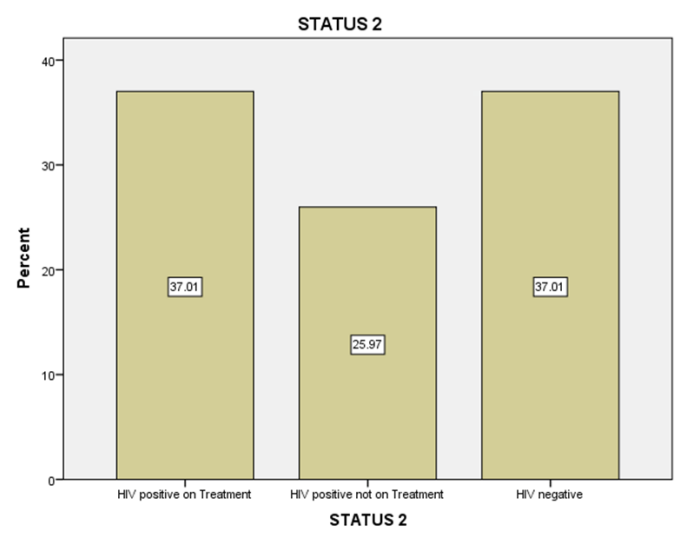


Table 1: Mean levels of Variables by Gender in all

Variables of	Males n=47	Females n=107	ANOVA
Interest	mean±SD	mean±SD	P-value
Weight (kg)	64.2±12.2	71.3±16.5	(0.009)
Height (m)	1.691±0.08	1.581±0.07	(<0.0001)
Waist circ (cm)	82.31±9.8	91.6±12.9	(<0.0001)
Hip circ (cm)	93.5±10.2	107.4±12.9	(<0.0001)
SMF (%)	37.7±6.7	25±4.3	(<0.0001)
Whole fat (%)	19.8±10.4	41.3±9.1	(<0.0001)
BMI (Kg/m^2)	22.5±4	28.4±6.1	(<0.0001)
RM (Kcal)	1503.8±168.8	1383.4±163	(<0.0001)
NO (nmol)	15.5 ±5.4	17.9±5.5	(0.048)
Age (years)	37.8±12.7	36.9±11.4	0.672
W/H ratio	0.883±0.075	0.856±0.09	0.078
SBP (mmHg)	131.8±28.3	128.1±22.4	0.385
DSP (mmHg)	84.9±13.1	84.9±13.4	0.994
PP (mmHg)	83.7±22.3	84.1±15.1	0.906
Endothelin (pg/ml)	8.1±3.5	8.6±3.4	0.325
DSP (mmHg)	84.9±13.1	84.9±13.4	0.994
PP (mmHg)	83.7±22.3	84.1±15.1	0.906
Endothelin (pg/ml)	8.1±3.5	8.6±3.4	0.325

Influence of Aging

The largest percentage seemed to be in middle age group and older group (30-39 and >=40) (66%). The lowest percentage is found in young age group (34%). The impact of aging on the general characteristics profile is shown in Table 2. There was no significant (P>0.05) influence on height, HC, SMF, WF, RM, SBP, PP, endothelin and NO. However, Waist Circumference (<0.0001), Waist/Hip ratio (<0.005), and Diastolic Blood Pressure (<0.0001) were significantly increased with age.

Table 2: Influence of Aging on the Mean Levels of Variables in all

Variables of	<30 years	30-39 years	≥40 years	ANOVA
interest	mean±SD	mean±SD	mean±SD	P-value
Weight (kg)	63.9±15	70±16.9	72.5±14	0.021
Height (m)	1.626±0.09	1.615±0.09	1.610±0.09	0.525
Waist circ (cm)	84±13.3	87.6±12.6	93.8±10.8	(<0.0001)
Hip circ (cm)	100±12.5	100.4±14.1	105.4±14	0.143
W/H ratio	0.840±0.076	0.853±0.108	0.894±0.069	(0.005)
SMF (%)	29.2±8	29.8±8.1	27.8±7.3	0.388
Whole fat (%)	32.7±13.2	34.3±13.8	36.8±13.9	0.328
BMI (Kg/m^2)	24.6±5.5	26.6±6	28.3±6.5	0.009
RM (Kcal)	1374.6±166.1	1430.1±182	1447.6±165.9	0.096
SBP (mmHg)	127.5±26.4	124.5±20.4	135.2±25.2	0.060
DBP (mmHg)	80.4±8.7	82.8±12	90.7±15.5	(<0.0001)
PP (mmHg)	80.4±19.7	88.1±12.9	82.9±19.6	0.087
Endo (pg/ml)	9.5±4.6	8±2.8	8±2.6	0.051
NO (nmol)	15.6±4.7	18±6.1	17.6±5.5	0.082

Table 3: Levels of Continuous Variables in all and by HIV Status Groups

Variables of	All	HIV+ on ART	HIV+ not on HAART	HIV (-)	ANOVA
Interest	mean±SD	mean±SD	mean±SD	mean±SD	P-value
Age (years)	37.2±11.8	37.4±10.6	34.1±10.4	39.1±13.4	0.111
Weight (kg)	69.1±15.6	66.4±15.8	65.7±11.8	74.3±16.7	0.007
Height (m)	1.615±0.089	1.623±0.084	1.601±0.088	1.617±0.098	0.483
WC (cm)	88.8±12.8	86.1±12.4	88.8±11.4	91.4±13.6	0.079
HC (cm)	103.1±13.7	100.2±13.4	100.4±11.8	108.1±14	0.002
WHR	0.864±0.089	0.862±0.080	0.900±0.108	108.1±14	0.080
BMI (kg/m^2)	26.7±6.1	25.1±5.2	25.9±5	28.8±7.1	0.003
SMF (%)	28.9±7.8	30.7±8.1	28.7±6.7	27.1±7.8	0.048
Whole fat (%)	34.7±13.7	31.5±14	34.1±12.1	38.4±13.8	0.023
RM (Kcal)	1420.1±173.3	1396.1±162.5	1383.1±144.2	1470.1±192.6	0.021
SBP (mmHg)	127.1±20.5	121.5±21	129.1±18.6	131.3±20.3	0.029
DBP (mmHg)	84.7±13.4	81.4±14	85.6±15	87.5±10.8	0.044
PP (mmHg)	86.9±12.8	87.1±12.8	6.9±2.5	84.7±12.7	0.189
Endo (pg/ml)	8.2±3.9	9.7±3.8	6.9±2.5	7.6±4.2	<0.0001
NO (nmol)	18.1±5.8	19.6±7.5	19.6±4.5	15.6±3.6	<0.0001

Table 4: BP and Body Mass Index Interactions across the Study Group

Groups of	SBP	DBP	PP
Interaction	Mean±SD	Mean±SD	Mean±SD
HIV(+) on ART			
Obesity	129.1±28.2	85.6±18.2	87.0±8.1
Overweight	129.2±20.4	86.3±15.1	86.1±12.2
Normal	116.8±15.0	79.1±9.5	87.4±14.1
Underweight	108.0±29.5	67.3±10.0	89.0±23
HIV(+) not on ART			
Obesity	134±17.4	95±10.0	88.2±9.7
Overweight	133.7±25.4	86.3±20.2	88.6±12.8
Normal	122.6±11.3	80.3±9.7	86.4±10.7
Underweight	178.4±37.4	74.6±32.6	108.8±19.1
HIV (-)			
Obesity	130.0±15.8	87.7±11.3	84.3±18.6
Overweight	138.7±32.0	91.0±12.2	82.1±13.6
Normal	125.2±9.8	83.4±8.9	61.9±25
Underweight	119.0±17	77.5±3.5	74.0±4.2
ANOVA	0.018	<0.0001	<0.0001

Table 5: Univariate Associated Factors with presence of Arterial Hypertension (n=54)

Variables of	presence of hypertension	non hypertension	ANOVA
Interest	mean±SD	mean±SD	P-value
Age (years)	41.2±11.5	35±11.4	0.002
Weight (kg)	74.3±14.6	66.4±15.5	0.003
BMI (Kg/m^2)	28.9±7	25.4±5.3	<0.001
SBP (mmHg)	148.9±27.8	118.6±13.1	<0.001
DBP (mmHg)	98.4±11.3	77.6±7.2	<0.0001
PP (mmHg)	89.5±17.5	81±17.2	0.004
Endothelin (pg/ml)	5.6±1.7	7.9±.3.9	0.002
Nitric oxide (nmol)	17.9 ±5.5	16.7±5.6	0.211

Influence of HIV and HIV on Treatment on Variables

Out of the study population, 57 (37.01%), 40 (25.97%), and 57 (37.01%) participants were HIV positive on treatment, HIV positive not on treatment and HIV negative respectively (Figure 1). Most of the variables presented show no significant difference between the three study groups. However, endothelin and NO levels were significantly different between the study groups (P<0.0001) in table 3. Interaction of blood pressure and Body Mass Index across the HIV status groups are shown in table 4. There was no significant difference in SBP among the different groups. . There was a significant difference in DBP and PP between the study groups (p<0.0001). Table 5 shows associated factors attributed by the presence of arterial hypertension in few participants (n=54). There was no significant variation of mean values of nitric oxide or endothelin between hypertensive and

non-hypertensive patients. However, there was significant association in other variables presented. Endothelin levels were higher in non hypertensive patients who are on HAART treatment. In HIV positive not on treatment, the values of endothelin were significantly higher (P<0.0001) hypertensive's (9.8±1.4 mmHg) than non hypertensive's (6.9±2.5 mmHg), whereas the values of NO did not vary (P=0.403) between hypertensive's (19.9±3.1 units) and non hypertensive's (18.8±4.7 mmHg). In HIV negative patients, the mean endothelin was higher (P<0.0001) in hypertensive's (9.2±1.6 mmHg) than non hypertensive's (6.1±2.3 mmHg), but NO values were similar between hypertensive's (P=0.448) (15±3.2 mmHg) and non hypertensive's (14.4±2.9 mmHg).

Discussion

This study is a descriptive and comparative study, with a large number of participants (154) gathered into different groups of HIV status, age (18-60 years) and gender (males and females). A large number of the patients were females (69.48%) compared to males (30.52%) (Sex ratio 2 females: 1 male). This support the fact that in South Africa, a large percentage of attendees in the public or private hospitals are females and are also the most willing to participate in all kinds of research that can facilitate good health.

Gender showed significant impact on different variables which include weight, waist circumference, and hip circumference. These variables are prone to be found high in females all over the world. For total body fat in our study we included skeletal muscle fat and whole body fat which both have shown to be significantly high in females compared to males. Obesity and its role in the causation of hypertension, elevated triglycerides and hypercholesterolemia are well known [10]. Waist fat is particularly known to be implicated in inflammations in blood vessels.

Body mass index as expected was high in females with its mean value range being 28.4±6.1, which depict overweight and as a sign of early obesity stage. Obesity is one of the earlier markers of renal function disorders [11], other complications of hypertension in obesity, such as cardiac remodeling and heart failure [19]. Then we continued and looked at the age range in all, our results have shown a significant trend between age and weight, age and waist circumference, age and waist/hip ratio, and also age and diastolic pressure. All these variables increase steadily as age increases from middle age to older age group, so this clearly stipulate high risk of cardiovascular diseases in older participants. However, there was no significance trend to the rest of variables. The results also describe some evidence that males were slightly older than females but not significant.

Impact of Haart and HIV Itself on the Study Variables

There is not much significance presented when comparing HIV positive participant on treatment and HIV positive participant not on treatment to weight but greatly reduced when both are compared to negative participants. This therefore means, HIV itself may have an impact on the weight of HIV positive participants.

HIV positives on treatment and HIV positive not on treatment had levels of BMI, whole fat, SMF, resting metabolism, similar to those of HIV negatives, the levels indicate overweight of the participants. This suggests that all the groups are in risk of pre exposure to type II diabetes, hypertension, urinary stress, sleep apnea because of elicited BMI. A high BMI is a risk factor for mortality from overall cardiovascular disease.

The significant value presented by both pressures (SBP and DBP) showed not much correlation. Beneficiary effects of HAART as a whole in reducing the mortality rate in HIV+ patients is to be recognized although the prevalence of hypertension in these patients is to be considered as a minor side effect [13]. In our study, in all groups of participants small number (n=54) were presented with arterial hypertension. However, the other variable did not vary significantly across these three groups.

Relationship of Endothelin, Nitric Oxide to HIV Status

Imbalance between the endothelinl mediators like ET-1 and NO, which are natural counterparts in vascular functions, are likely to be the causative factors in the progression of vascular disease [5]. In our study both endothelin and nitric oxide showed significant correlation among HIV groups. In HIV positive patients on treatment, the levels of endothelin were significantly increased. This clearly demonstrates that treatment also has a role in progression of hypertension. Elevated endothelin may pre dispose participants to vascular remodeling (change in the vessel structure), vascular hypertrophy, cardiac hypertrophy and endothelinl dysfunction.

Figure 2: Cellular Signalling Pathway of Endothelin and NO [20]

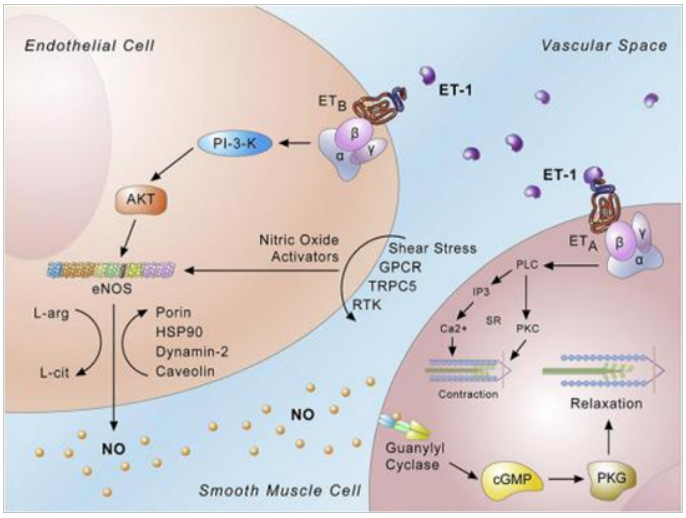
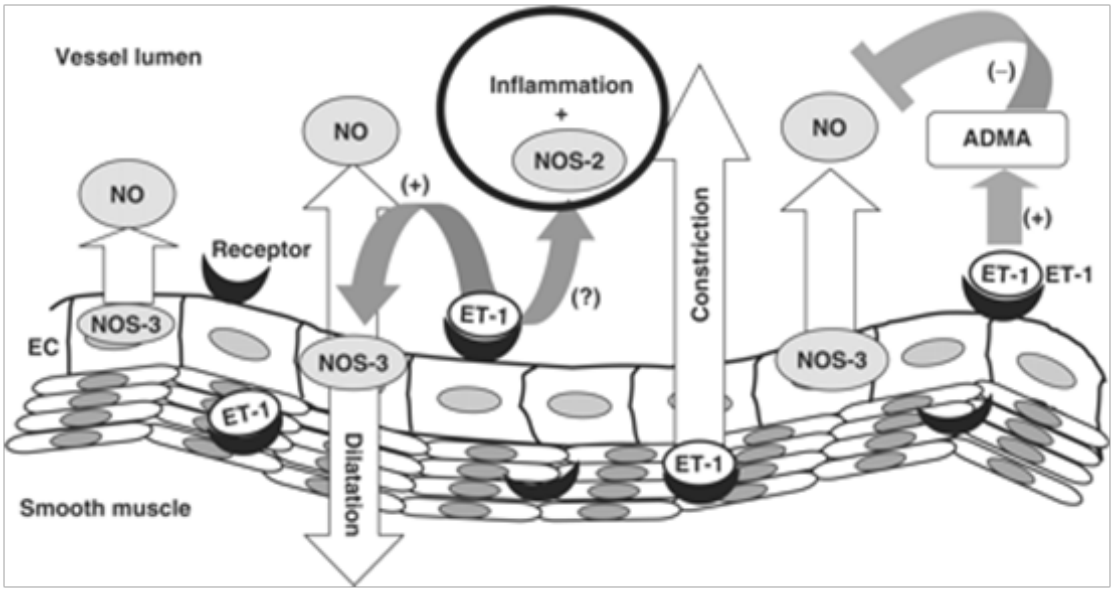


Figure 2 shows activation of eNOs, due to ET-1 activation of ET-B receptor and intracellular signaling pathway. G-protein coupled receptors & TRPC, RTK are also activators of eNOs. This probably leads to diffusion of NO to stellate cell, production of GMP and activation of PKG these results in relaxation of stellate cells which offset the ETs constrictor effects on stellate cells [20].

On the other hand NO exerts its effects through activation and allosteric modification of sGC, a hetrodimer NO receptor resulting in enhanced catalytic activity [21]. The second messenger pathway in this activation seems to be PKGs [22]. PKG-1 has been reported to be the predominant in CVS and its possible cellular action in mediating the anti-proliferative effects of cGMP has been proposed [23]. PKG exerts its effects through various means, including IP3 receptor, eventually activating Calcium and Potassium channels [23]. NO also exerts its effects through mediation of tyrosine residues [24].

Vasoconstrictor activation via ETA receptor located on the vascular smooth muscles and simultaneously activating ETB receptor subtype leads to vasodilatation by inducing release of NO and PGI2 [25]. ET-1 effects were found to be different if blood vessels were denuded or when hemoglobin was present which supposedly has a scavenging effect on NO. It has also been shown that vasomotion may be directly related to NO synthesis [26]. However, this interaction between ET-1 an1 may induce NO synthesis by the endothelinl NOs as well as increasing the production of NOs inhibitors, asymmetric dimethylarginine (ADMA). ADMA has been proven to potentially decrease the NO bio-availability [26]. Based on the above mechanisms the ET-1 and NO are shown to be causative factors in inflammatory diseases like asthma, arthritis etc [26].

Figure 3: Synthesis of Both ET and NO and Formation of Inflammation [26]



There are many physical factors that influence arterial pressure. Each of these may in turn be influenced by physiological factors, such as diet, exercise, disease, drugs or alcohol, stress, obesity, hormonal change and so-forth [11].

Nitric oxide also stipulated a steady increase in both HIV positive participants on treatment and HIV positive participants not on treatment, this demonstrate that not only changes in BMI can facilitate an increase in nitric oxide but also HIV itself and HIV status plays huge role [27].

The present findings constitute a preliminary scientific background to understand the path physiology, the clinical spectrum, and the prevention of HIV/AIDS-related atherogenesis. The study brought to light an evidence-based knowledge on the impact of gender, aging, HIV infection itself, HAART, and BMI changes across the HIV groups and interaction between endothelin and nitric oxide.

Pathophysiology

The existence and nature of a communication between HIV infection, HAART and the impact of relationship between endothelin, nitric oxide pathogenesis of hypertension warrants further investigations in these black patients. Future studies may better elucidate the mechanism of atherogenesis when HIV infected patients are recovering normal weight. Of particular importance is the need to elucidate the protective role of endothelin and nitric oxide against hypertension in HIV positive patients.

Indeed, the present study showed that there is an uneven relationship between endothelin, nitric oxide levels and also these two are associated with overweight/obesity and blood pressure. The findings reveal that the positive relationship was lost in both HIV positives not on treatment and HIV positives on HAART, possibly due to changes in the endothelium, HIV itself and HIV treatment. Further studies are needed on the relationship between endothelin, lipid profile, blood pressure and glucose levels in HIV positive patients.

Endothelin and nitric oxide therapy in case of deficiency states may assist in the future management of hypertension on both HIV positive and HIV positives on HAART. Studies on the effects and safety of status (lowering-endothelin or lowering-nitric oxide drugs) should be taken in our hospitals. Health professionals who are in charge of HIV infected patients have to monitor BMI, fat redistribution, blood pressure and drug toxicity regularly when these patients visit their clinics/Hospitals. Appropriate diet (5 different fruits intake/day), physical activity, and avoidance of known behavioral risk factors (smoking, excessive alcohol, fat and sugar intake) should be recommended to HIV infected patients.

Conclusion

The present study might be limited to some degree by its design (case-control study) to demonstrate a causal association. The study was limited by age distribution and over representation of females that made it difficult to generalize the ability of the results, the strength of this study comes from strong and significant associations using statistical analysis as well as from valid and standardized measurements of anthropometric/body composition, blood pressure, nitric oxide and endothelin.

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