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Abuse, Nocturnal Stress Hormones, and Coronary Heart Disease Risk Among Women with HIV

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Abstract

This study investigated the relationships among abuse, nocturnal levels of cortisol and norepinephrine (NE), and coronary heart disease (CHD) risk as measured by the Framingham Risk Score (FRS) among women with HIV. Participants (n=53) from the Chicago Women's Interagency HIV Study, a longitudinal prospective cohort study initiated in 1994, were enrolled in this study during 2012. At WIHS baseline and annual follow-up visits women were asked about recent experiences of abuse. Summary variables captured the proportion of visits for which women reported recent (past 12 months) physical, sexual, and domestic abuse. Cortisol and NE were assayed in overnight urine samples and adjusted for creatinine levels. Recent abuse was not significantly associated with levels of cortisol, NE, or NE/cortisol ratio. However, higher NE/cortisol ratio was significantly related to higher CHD risk score, higher cortisol was significantly related to lower CHD risk score, and NE was not associated with CHD risk score. In addition, higher proportions of visits with recent sexual abuse, physical abuse, and domestic abuse were significantly related to higher CHD risk score. The association between abuse exposure and CHD risk in the context of HIV infection is likely complex and may involve dysregulation of multiple neurobiological systems. Future research is needed to better understand these relationships and prevention and intervention efforts are needed to address abuse among women with HIV.

Keywords

abuse; HIV; women; norepinephrine; cortisol

Women living with human immunodeficiency virus (HIV) (WLWH) who adhere to antiretroviral therapy (ART) are living longer and are at increased risk for heart disease compared to women without HIV (Womack et al., 2014; Sackoff, Hanna, Pfeiffer, & Torian, 2006). Coronary heart disease (CHD) is the most common type of heart disease (Go et al., 2013) and increased risk for CHD among WLWH may in part be linked to taking ART (Currier et al., 2003). Other CHD risk factors in people with and without HIV include

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genetics, diet, hypertension, diabetes, cigarette smoking, and the management of psychosocial stress (Krantz & McCeney, 2002; O'Toole, Conklin, & Bhatnagar, 2008; Dong et al., 2004). There is a high prevalence of abuse histories among women with HIV such as a 55.3% estimated rate of intimate partner violence (Machtinger, Wilson, Haberer, & Weiss, 2012).

Abuse may lead to dyregulation in the hypothalamic-pituitary-adrenal (HPA) axis and the sympathomedullary pathway and their associated stress hormones cortisol and norepinephrine, which in turn may lead to increased risk for CHD (Hulme, 2011; Jokinen & Nordstrom, 2009). Increased NE and cortisol levels prepare the body to cope under acutely stressful conditions, and histories of abuse are reportedly linked to both ongoing high stress hormone levels and to low stress hormone levels (Friedman et al., 2007; Yehuda et al., 2001). Inconsistencies may be due to variations in abuse measurement, the context/timing in which hormones are measured, and whether they are analyzed in isolation or relative to each other. The NE/cortisol ratio has previously been found to distinguish between Post-traumatic Stress Disorder (PTSD) and non-PTSD diagnoses: male patients with PTSD had a higher NE/cortisol ratio than male patients without PTSD (Mason et al., 1988). Night-time has been noted as the period most sensitive to chronic stress, and removes the confounding impact of daily activities such as work (Mellman, Kumar, Kulick-Bell, Kumar, & Nolan, 1995).

The present study added to the existing literature by investigating the relationships among abuse histories, levels of nocturnal NE and cortisol, and CHD among women with HIV who have a high prevalence of abuse and may be at increased risk for CHD. We hypothesized that abuse histories would be associated with higher CHD risk and explored whether and in what ways nocturnal urinary levels of NE, cortisol, and NE/cortisol ratio were significantly associated with CHD risk and abuse histories.

Methods

Participants and Procedure

Fifty-three WLWH at the Chicago Women's Interagency HIV Study (WIHS) site participated in this study during 2012. Barkan (1998) and Bacon and colleagues (2005) described WIHS methods and baseline characteristics of participants. Women provided written informed consent and were given transportation support, childcare, and a $25 honorarium. The study protocol was approved by the Cook County Health and Hospital System and Boston University Institutional Review Boards and the WIHS Executive Committee.

Measures

Domestic Violence, Physical Abuse, and Sexual Abuse Histories—Women were asked questions about prior adult or childhood experience of sexual abuse, physical abuse and domestic violence at their WIHS initial visit and then again each year over the course of their participation in WIHS (range 1–17 years). Summary variables were created to capture the proportions of visits for which women reported recent physical abuse, sexual abuse, and domestic violence.

Coronary Heart Disease (CHD) risk measures—The composite 10-year Framingham CHD Risk score (FRS), the gold standard for composite scoring methodology in cardiovascular research, was used to assess overall CHD risk (Wilson et al., 1998). The FRS is highly sensitive in predicting a diagnosis of CHD (Ketola, Laatikainen, & Vartiainen, 2009). The FRS includes measures of systolic blood pressure, diastolic blood pressure, total blood cholesterol, high-density lipoprotein cholesterol, age, diabetes, and smoking.

Collection of Nocturnal Urinary Cortisol and Norephinephrine—Urine was collected during the mid-follicular phase (5–10 days following first day of menses) of cycling women's menstruation and at any time for post-menopausal women. Participants collected overnight urine between 6pm and 9am or until their first morning void. Participants were asked to refrain for 12 hours prior to the urine collection from intake of nicotine, alcohol, caffeine and diuretics. Research staff administered a questionnaire on any medications taken, substances used, smoking, and drinking of tea/coffee during collection.

Assay of Urinary Cortisol and Norephinephrine—Quest Nichols Specialty Lab used a liquid chromatography-tandem mass spectrometry (LC-MS/MS) method for urinary cortisol assay and a high-performance liquid chromatography with electrochemical detection for urinary NE assay. Both cortisol and NE levels were adjusted for urinary creatinine (a measure of kidney function) by dividing cortisol or NE concentrations by creatinine concentration.

Data Analyses

SPSS version 21.0 was used for data analyses. Due to skewness and a few outliers, cortisol and NE levels were log-10 transformed and these transformations were used in subsequent analyses. Further, a ratio of log-10 NE/ log-10 cortisol was derived. For nine participants, catecholamines (NE levels) were undetectable from their urine, and seven participants were missing cholesterol data needed to compute CHD risk score. Participants with missing data were excluded from relevant analyses using pairwise deletion.

Results

The majority of the 53 participants were African American and their median annual household income was $6,001-$12,000. Table 1 provides descriptive statistics on sociodemographic characteristics of the sample and all predictors (i.e. abuse) and outcome variables (e.g. CHD risk score [mean = 4.21, SD= 6.35, range -12 (low risk) to 17 (intermediate risk]).

Table 2 displays **r**esults from Pearson and partial correlations. Sociodemo-graphic variables with significant relationships to outcomes were controlled in all relevant analyses.

Higher CHD risk composite score was positively correlated with proportions of visits in which recent sexual abuse (r=.29, p=.03), physical abuse (r=.42, p=.002), and domestic violence (r=.35, p=.01) were reported. Abuse histories were not significantly associated with levels of cortisol, NE, or NE/cortisol ratio. Higher cortisol levels negatively correlated with

CHD risk score (r= −.56, p= .001). In contrast, higher NE/cortisol ratio positively related to CHD risk score (r= .42, p= .008). NE alone was not associated with CHD risk score.

Discussion

Findings indicate that in women with HIV, higher CHD risk was related to higher NE/cortisol ratio and lower cortisol levels. The relationship between CHD risk and a high NE/cortisol ratio is a new contribution to the literature. In addition, the present study's finding that higher cortisol levels predicted lower CHD risk score supports previous literature noting the anti-inflammatory properties of cortisol (Fantidis et al., 2002; Straub et al., 2002).

A higher proportion of visits in which women reported abuse was significantly related to higher CHD risk. Few studies have reported an association between abuse and heart disease risk for women (Dong et al., 2004) and none have been among women with HIV who are at increased risk for heart disease. Abuse histories may lead to increased heart disease risk by way of established associations with components of the FRS (i.e. smoking, high blood pressure, and diabetes) and factors not captured by the FRS (e.g. inflammation, obesity) (Huffhines, Noser, & Patton, 2016; Petrov et al., 2016; O'Cleirigh et al., 2015). Abuse may also increase CHD risk via elevated levels of stress hormones.

In the present study, abuse histories were not significantly associated with levels of NE, cortisol, or NE/cortisol ratio. Previous literature has indicated that trauma/abuse histories have been associated with higher NE and both lower and higher cortisol levels (Elzinga, Schmahl, Vermetten, van Dyck, & Bremner, 2003; Mason et al.,1988; Yehuda et al., 2001). Perhaps the complexity of the HPA in combination with our relatively small sample size account for these null findings.

Limitations

The cross-sectional study design prevents conclusions about causality. Also self-report measures to assess abuse may have been affected by social desirability constraints resulting in under-reporting; however staff with established rapport with participants administered the measures. Stress hormone levels were assessed via pooled random sampling of overnight urine collection, however using repeated measures over the course of one day or more may yield useful information (Vedhara et al., 2006). In addition, while the FRS is a gold-standard measure for CHD risk it is not a proxy for CHD or representative of real CHD events. Obesity and inflammation have been associated with abuse histories (Petrov et al., 2016; Wang, Wu, Yang, & Song, 2016) and may have a role in the findings and therefore should be addressed by future research.

Conclusion

In a sample of WLWH this study presents a new finding that higher NE/cortisol ratio significantly related to higher CHD risk and also confirmed existing literature in that (a) histories of abuse significantly related to higher CHD risk and (b) lower nocturnal urinary cortisol levels are significantly associated with higher CHD risk. Additional research studies with larger samples are needed to better understand these complex relationships. Prevention and intervention efforts are needed to decrease abuse among women with HIV and to lessen

the negative impact of stress hormones and abuse histories on the cardiovascular health of women with HIV.

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References

Bacon MC, von Wyl V, Alden C, Sharp G, Robison E, Hessol N, Young MA. The Women's Interagency HIV Study: an observational cohort brings clinical sciences to the bench. Clinical and Diagnostic Laboratory Immunology. 2005; 12(9):1013–1019. doi: 12/9/1013 [pii]10.1128/CDLI.12.9.1013-1019.2005. [PubMed: 16148165]

Barkan SE, Melnick SL, Preston-Martin S, Weber K, Kalish LA, Miotti P, Feldman J. The Women's Interagency HIV Study. WIHS Collaborative Study Group. Epidemiology. 1998; 9(2):117–125. [PubMed: 9504278]

Currier JS, Taylor A, Boyd F, Dezii CM, Kawabata H, Burtcel B, Hodder S. Coronary heart disease in HIV-infected individuals. Journal of Acquired Immune Deficiency Syndromes. 2003; 33(4):506–512. [PubMed: 12869840]

Dong M, Giles WH, Felitti VJ, Dube SR, Williams JE, Chapman DP, Anda RF. Insights into causal pathways for ischemic heart disease: adverse childhood experiences study. Circulation. 2004; 110(13):1761–1766. DOI: 10.1161/01.CIR.0000143074.54995.7F [PubMed: 15381652]

Elzinga BM, Schmahl CG, Vermetten E, van Dyck R, Bremner JD. Higher cortisol levels following exposure to traumatic reminders in abuse-related PTSD. Neuropsychopharmacology. 2003; 28(9):1656–1665. DOI: 10.1038/sj.npp.1300226 [PubMed: 12838270]

Fantidis P, Perez De Prada T, Fernandez-Ortiz A, Carcia-Touchard A, Alfonso F, Sabate M, Macaya C. Morning cortisol production in coronary heart disease patients. European Journal of Clinical Investigation. 2002; 32(5):304–308. [PubMed: 12027868]

Friedman MJ, Jalowiec J, McHugo G, Wang S, McDonagh A. Adult sexual abuse is associated with elevated neurohormone levels among women with PTSD due to childhood sexual abuse. Journal of Traumatic Stress. 2007; 20(4):611–617. DOI: 10.1002/jts.20221 [PubMed: 17721974]

Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, Turner MB. Heart disease and stroke statistics—2013 update: a report from the American Heart Association. Circulation. 2013; 127:e6–e245. [PubMed: 23239837]

Hulme PA. Childhood sexual abuse, HPA axis regulation, and mental health: an integrative review. Western Journal of Nursing Research. 2011; 33(8):1069–1097. DOI: 10.1177/0193945910388949 [PubMed: 21148463]

Jokinen J, Nordstrom P. HPA axis hyperactivity and cardiovascular mortality in mood disorder inpatients. Journal of Affective Disorders. 2009; 116(1–2):88–92. DOI: 10.1016/j.jad.2008.10.025 [PubMed: 19054568]

Ketola E, Laatikainen T, Vartiainen E. Evaluating risk for cardiovascular diseases--vain or value? How do different cardiovascular risk scores act in real life. European Journal of Public Health. 2009 ckp070 [pii]10.1093/eurpub/ckp070.

Krantz DS, McCeney MK. Effects of psychological and social factors on organic disease: a critical assessment of research on coronary heart disease. Annual Review of Psychology. 2002; 53:341–369. DOI: 10.1146/annurev.psych.53.100901.135208

Machtinger EL, Wilson TC, Haberer JE, Weiss DS. Psychological trauma and PTSD in HIV-positive women: a meta-analysis. AIDS and Behavior. 2012; 16(8):2091–2100. DOI: 10.1007/s10461-011-0127-4 [PubMed: 22249954]

Mason JW, Giller EL, Kosten TR, Harkness L. Elevation of urinary norepinephrine/cortisol ratio in posttraumatic stress disorder. Journal of Nervous and Mental Disease. 1988; 176(8):498–502. [PubMed: 3404142]

Mellman TA, Kumar A, Kulick-Bell R, Kumar M, Nolan B. Nocturnal/daytime urine noradrenergic measures and sleep in combat-related PTSD. Biological Psychiatry. 1995; 38(3):174–179. doi: 0006-3223(94)00238-X [pii]10.1016/0006-3223(94)00238-X. [PubMed: 7578660]

O'Toole TE, Conklin DJ, Bhatnagar A. Environmental risk factors for heart disease. Reviews on Environmental Health. 2008; 23(3):167–202. [PubMed: 19119685]

Sackoff, Judith E., Hanna, David B., Pfeiffer, Melissa R., Torian, Lucia V. Causes of Death among Persons with AIDS in the Era of Highly Active Antiretroviral Therapy: New York City. Annals of Internal Medicine. 2006; 145(6):397–406. [PubMed: 16983127]

Straub RH, Gunzler C, Miller LE, Cutolo M, Scholmerich J, Schill S. Anti-inflammatory cooperativity of corticosteroids and norepinephrine in rheumatoid arthritis synovial tissue in vivo and in vitro. FASEB Journal. 2002; 16(9):993–1000. DOI: 10.1096/fj.02-0085com [PubMed: 12087060]

Vedhara K, Tuinstra J, Miles JN, Sanderman R, Ranchor AV. Psychosocial factors associated with indices of cortisol production in women with breast cancer and controls. Psychoneuroendocrinology. 2006; 31(3):299–311. DOI: 10.1016/j.psyneuen.2005.08.006 [PubMed: 16183206]

Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. Circulation. 1998; 97(18):1837–1847. [PubMed: 9603539]

Yehuda R, Halligan SL, Grossman R. Childhood trauma and risk for PTSD: relationship to intergenerational effects of trauma, parental PTSD, and cortisol excretion. Development and Psychopathology. 2001; 13(3):733–753. [PubMed: 11523857]

Table 1

Sample characteristics and socio-demographic statistics of 53 women living with HIV

Characteristics	Mean/N (*SD/%*)
Race	
White / non-Hispanic	3 (5.7)
White / Hispanic	2 (3.8)
African-American / non- Hispanic	46 (86.8)
Other / Hispanic	1 (1.9)
Other	1 (1.9)
Age	48.33 (8.92)
Education	
Grade 11 or less	22 (41.5)
Completed high school	19 (35.8)
Some college	11 (20.8)
Attended/completed graduate School	1 (1.9)
Income	
$6,000 or less	15 (28.3)
$6,001–$12,000	24 (45.3)
$12,001 or more	14 (26.4)
Unemployed	46 (86.8)
Marital Status	
Legally/common-law marriage	3 (5.7)
Not married but living w partner	2 (3.8)
Widowed	7 (13.2)
Divorced/Annulled	8 (15.1)
Separated	6 (11.3)
Never married	27 50.9)
Proportion of visits women reported recent domestic violence	.07 (.13)
Proportion of visits women reported recent physical abuse	.05 (.11)
Proportion of visits women reported recent sexual abuse	.03 (.11)
Women who reported recent sexual abuse (at least once) during 18th year period	20.8%
Women who reported recent physical violence (at least once) during 18th year period	32.1%
Women who reported recent domestic violence (at least once) during 18th year period	37.7%
Coronary Heart Disease risk score	4.21 (6.35)
Cortisol	21.58 (32.19)
Norepinephrine	24.26 (12.16)

Table 2

Partial correlations among, abuse histories, stress hormones and coronary heart disease risk

Variable	1	2	3	4	5	6	7
1. Proportion of visits women reported recent domestic violence[a]	--	.89***	.72***	.06	.10	−.05	.35**
2. Proportion of visits women reported recent physical abuse[a]		--	.63***	−.03	.19	.03	.42**
3. Proportion of visits women reported recent sexual abuse[a]			--	.16	.22t	−.12	.29*
4. Cortisol log10 transformed[b]				--	.09	−.81***	−.56***
5. Norepinephrine log10 transformed					--	.12	.16
6. NE/Cortisol Ratio[c]						--	.43**
7. CHD risk score[d]							--

Note. All tests are one-tailed. Covariates differed by analyses and are noted below. NE = Norepinephrine and CHD= Coronary Heart Disease risk score computed based on the Framingham Risk Score guidelines.

*$p < .05$.

**$p < .01$.

***$p < .001$.

t$p < .10$.

[a]Analyses controlled for age.

[b]Analyses controlled for lifetime history of crack/cocaine/heroin.

[c]Analyses controlled for beta blockers and lifetime history of crack/cocaine/heroin.

[d]Analyses controlled for age and employment.

[g]Analyses controlled for income and education.