

A comparative cross-sectional study investigating prevalence and patterns of sexual dysfunction among hypertensive and non-hypertensive men

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ABSTRACT

Background and Aims: Erectile dysfunction is prevalent among men with hypertension, but there is paucity of data on prevalence of other domains of sexual dysfunction (SD) in hypertensives and the general population. The study compared the prevalence and patterns of SD among treated hypertensive male patients with normotensive men. The effect of antihypertensive drugs on different domains of sexual function was also investigated in our study.

Methods: A total of 195 participants (95 hypertensive and 100 non-hypertensive men) were recruited from the medical outpatient department of a secondary health care facility in Lagos, Nigeria. Sexual function was assessed using International Index of Erectile Function (IIEF) which measures erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction.

Results: Sexual dysfunction affecting at least one domain was present in 82.1% of the hypertensive subjects and 52% of nonhypertensive controls (P<0.001). The hypertensive patient had more severe dysfunction in the multiple domains (p< 0.001). The use of methyldopa, furosemide and β -blockers were associated with significantly lower scores while there was no significant difference in scores with the use calcium channel blockers, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, thiazide and potassium sparing diuretics. SD was higher in the older age group and with longer duration of hypertension and treatment.

Conclusion: SD is common in the adult male population with hypertension significantly increasing the risk. Hypertension is associated with involvement of multiple domains for sexual dysfunction. Use of methyldopa, furosemide and ß-blockers were associated with higher rates of SD in the hypertensive population.

Keywords: Sexual dysfunction, Hypertension, Erectile dysfunction, antihypertensive drugs

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INTRODUCTION

Sexual dysfunction (SD) is a disorder of sexual sensation and activity which affects one or more components of sexual response cycle. In men, SD manifests as loss of libido, erectile dysfunction (ED) and reduced sexual activity. SD is common, and has been shown to be a contributor to poor quality of life and marital disharmony (Kessler, Sollie, Challacombe, Briggs, & Van Hemelrijck, 2019).Prevalence of SD varies across populations, but it has been reported that about 50% of men between the ages of 40-70 year have SD (Chen et al., 2019). ED is one of the most commonly reported manifestations of SD, and global prevalence varies from 3-76.5% (Kessler et al., 2019). A community based study in South-Western Nigeria reported a prevalence rate of 58% among participants (Oyelade, Jemilohun, &Aderibigbe, 2016).

Risk factors for the development of SD include increasing age, the presence of diseases affecting the cardiovascular and neuroendocrine systems, previous urological surgery, psychological disorders, toxins and drugs (Chen et al., 2019). SD has been associated with specific drugs such as selective serotonin reuptake inhibitors (SSRI), alpha-5-reductase inhibitors and antihypertensive medications (Healy, Le Noury, & Mangin, 2018; Imprialos et al., 2018). Hypertension is one of the most common cardiovascular diseases affecting the adult population, therefore men with hypertension are expected to have a significantly higher risk of developing SD from complications of hypertension and as an adverse effect of therapy. A study reported that more than half of men using antihypertensive drugs experienced SD (Oshodi, Adeyemi, Oke, & Seedat, 2010). SD often leads to poor drug adherence and ultimately poor clinical outcome in the management of hypertension, this emphasizes the need to address this disorder (Oyelade et al., 2016; Chen et al., 2019; Kretchy, Boima, Agyabeng, Koduah, & Appiah, 2020).

It has been shown that nearly all classes of antihypertensive drugs can cause SD although different classes of drugs have varying degree of severity (Ekman, Hägg, Sundström, &Werkström, 2010; Akinyede et al., 2020). We have also previously reported the occurrence of SD with the use of different classes of antihypertensive drugs (Akinyede et al., 2020). A recent publication by the Working Group on Sexual Dysfunction and Arterial Hypertension of the European Society of Hypertension which reviewed antihypertensive drugs and ED, reported that thiazide diuretics, centrally acting sympatholytics and beta-blockers have the worst profile, whereas angiotensin receptor blockers (ARB) and nebivolol (a beta-blocker which is a nitric oxide donor) have the best profile on ED (Imprialos et al., 2018; Viigimaa et al., 2020). Calcium channel blockers and angiotensin converting enzyme inhibitors (ACEI) have however been shown to have neutral effects on sexual function (Burnett, 2019; Fogari & Zoppi, 2002).

Hypertension and antihypertensive drugs use are both associated with SD, the real magnitude of sexual dysfunction associated with hypertension and antihypertensive drug use may be overestimated because SD is also commonly seen among non-hypertensive men population Several studies have investigated prevalence of ED among the general population with only a few addressing SD. This may lead to under-recognition of the prevalence of SD especially in men who have other forms of SD without ED. There is also paucity of data on the effect of antihypertensive drugs on different domains of sexual function. This may mask the true pattern of antihypertensive drug induced SD which has implications for its pathophysiology and management.

This study investigated the prevalence, patterns, and determinants of sexual dysfunction in a cohort of hypertensive men on treatment and compared to non-hypertensive controls. It also determined the effect of antihypertensive drugs on the different domains of sexual function.

MATERIALS AND METHODS

Study design

This is an analytical cross-sectional study carried out at the General Hospital Ikorodu, Ikorodu, Lagos State. The hospital provides secondary level of healthcare to people living in Ikorodu and its environs.

Population

A total of 195 (95 patients and 100 control group) consecutively consenting male adults were recruited for this study. The subjects were sexually active male adults aged 25 to 80 years who were attending the medical outpatient's clinic and had been on treatment for hypertension for > 3 months. Patients with co-morbid disorders that could affect sexual function like diabetes mellitus, renal disease, stroke, heart failure, history of previous urological surgery and penile injury were excluded from the study.

Controls were men aged 25-80 years, sexually active, consenting males who were normotensive with no previous history of hypertension. Those with disorders that could affect sexual function and who were non-consenting were excluded from the study.

Ethical approval

Ethical clearance was obtained from the Lagos University Teaching Hospital Health Research Ethics Committee (CMUL HREC). Permission for use of the Ikorodu General Hospital was obtained from the Lagos State Health Service Commission. Informed consent was also obtained from each participant before inclusion in the study.

Methodology

All interviews were conducted privately, and anonymity of the participants was maintained. Information was obtained using a semi structured interviewer administered questionnaire to document their socio-demographic and clinical data. The International Index of Erectile Function (IIEF) questionnaire was used to assess sexual function over the previous four weeks prior to the clinic days. Antihypertensive agents used by each subject in the last 3 months prior to presentation were also documented. The blood pressure of participants was measured using a mercury sphygmomanometer.

International Index of Erectile Function

The 15-question International Index of Erectile Function (IIEF) Questionnaire is a validated, multi-dimensional, questionnaire

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that has been validated for use in the clinical assessment of erectile dysfunction. A score of 0-5 is awarded to each of the 15 questions. The IIEF has five domains: erectile function (q1,2,3,4,5,15), orgasmic function (q9,10), sexual desire (q11,12), intercourse satisfaction (q6.7), and overall satisfaction (q13.14) (Rosen et al., 1997). Scores were rated as mild, moderate and severe with lower scores suggesting the presence of SD in the domain measured. For erectile function, a score of 26-30 was regarded as normal, 17-25 signified mild erectile dysfunction (ED), 11-16 showed moderate ED while a score of 1-10 signified severe ED. Intercourse satisfaction was graded as normal for a score of 12-15, mild dysfunction (9-11), moderate (6-8), while a score of 0-5signified severe dysfunction. Orgasmic function, sexual desire, and overall satisfaction were graded as normal for a score of 9-10, mild dysfunction (7-8), and moderate (5-6). A score of 0-4 suggested severe dysfunction affecting orgasmic function while a score of 2-4 suggested severe dysfunction in sexual desire and overall satisfaction.

Data analysis

Data was analyzed using Statistical Package for Social Sciences (SPSS VERSION 21). The data was assessed for normality. Variables were expressed as means \pm standard deviation and

percentages. Association between variables were determined using Chi-Square, Mann Whitney U test and Spearman correlation analysis.

RESULTS

The study consisted of 95 patients and 100 non-hypertensive control group. The mean age for the hypertensive patients was 57.7 ± 12.6 years while that for the control subjects was 54.92 ± 8.73 years. The mean duration of hypertension was 75.26 ± 63.07 months while the mean duration of treatment was 69.7161.12 months. Blood pressure control was poor among the hypertensive population. Sexual dysfunction was significantly higher among the hypertensive population with a prevalence of 82.1% and 52% among control. (Table 1).

The hypertensive patient had more severe dysfunction in the different domains (p<0.001) and also were more likely to have involvement of multiple domains of sexual dysfunction. (Results are shown in Tables 1 - 3).

The patterns of antihypertensive drug used is documented in Table 4. Calcium channel blockers (CCB), angiotensin receptor

Variable	Patients n=95	Control n=100	P-value
Age			
Age range	25-79	25-80	<0.001*
Mean age	57.7 12.6	47.23 12.12	
Marital status			
Married	89 (93.7)	89 (89)	
Single	6 (6.3)	11(11)	
Educational Status			
Nil	11(11.6)	6(6)	
Primary	23(24.2)	14(14)	
Secondary	26(27.4)	35(35)	
Tertiary	35(36.8)	45(45)	
Mean Systolic BP	147.55 19.61	120.15 15.93	<0.001*
Mean Diastolic BP	90.93	79.40 9.98	<0.001*
Mean duration of HTN (months)	75.26±63.07		
Mean duration of treatment (months)	69.7161.12		
Sexual dysfunction			
Yes	78 (82.1)	52 (52)	<0.001#
No	17 (17.9)	48 (48)	
Number of domains affected per patient			
One domain	2 (2.1)	16 (16)	<0.001*
Two domains	4 (4.2)	6 (6)	
Three domains	2 (2.1)	2 (2)	
Four domains	8 (8.4)	5 (5)	
Five domains	62 (65.3)	23 (23)	

Patients=Hypertensive males on treatment, Control= Normotensive males, BP= Blood pressure, HTN= Hypertension *p values were calculated using Mann-Whitney U test, *p values were calculated using Chi square

Table 2. Table comparing IIEF scores among male patients on anti-hypertensive drugs and normotensive	
males.	

		Subje	ct		Contr	ol	P values
SD Domains	N	%	Mean score	n	%	Mean score	
Erectile dysfunction	72	75.79	17.12 9.97	29	48.33	23.83 6.55	<0.001*
Intercourse dissatisfaction	63	66.31	7.68 5.11	28	46.66	11.15 3.16	<0.001*
Orgasmic dysfunction	74	77.89	5.863.11	30	50	8.18 1.85	<0.001*
Sexual desire dysfunction	75	78.94	6.0 2.8	30	50	8.12 1.98	<0.001*
Overall dissatisfaction	73	76.84	6.182.91	20	33.33	8.23 1.99	<0.001*

SD = Sexual dysfunction, *p values were calculated using Mann-Whitney U test

Table 3. Table showing SD severity among hypertensive subjects and normotensive controls.

		Subje	cts n (%)			Cont	rol n (%)	
	NIL	Mild	Moderate	Severe	NIL	Mild	Moderate	Severe
Erectile dysfunction	23(24.2)	31(32.6)	12(12.6)	29(30.5)	65(65)	24(24)	8(8)	3(3)
Intercourse dissatisfaction	32(33.7)	13(13.7)	20(21.1)	31(32.6)	69(69)	20(20)	8(8)	3(3)
Orgasmic dysfunction	21(22.1)	27(28.4)	17(17.9)	31(32.6)	65(65)	26(26)	7(7)	2(2)
Sexual desire dysfunction	20(21.1)	21(22.1)	20(21.1)	33(34.7)	65(65)	19(19)	14(14)	2(2)
Overall dissatisfaction	22(23.2)	26(27.4)	17(17.9)	30(31.6)	77(77)	14(14)	5(5)	4(4)
SD = Sexual dysfunction								

Number of drugs	N	%
One	7	7.4
Two	52	54.7
Three	25	26.3
Four	9	9.6
Five	2	2.1
Drug class		
ССВ	62	65.3
ARB	40	42.1
Thiazide	38	40
ACE	30	31.6
K sparing	29	30.5
Centrally acting sympa- tholytic	13	13.7
BB	12	12.6
Furosemide	7	7.4
Nitrate	1	1.1

converting enzyme inhibitor, ARB- Angiotensin receptor blocker, BB- beta blockers

blockers (ARB) and thiazide diuretics were the most commonly used antihypertensive drugs in this population. Other classes of antihypertensive used include angiotensin converting enzyme inhibitor (ACEI), beta blockers (BB) and centrally acting sympatholytic drugs (Methyldopa). Majority (54.7%) of the patients were on two medications (Table 4). The most common two drugs combination were CCB + ACEI in 15.8% and CCB + ARB in another 15.8% of the patients. Other combinations include CCB and thiazide in 4 (4.2%) patients and CCB + BB in 3 (3.2%). In patients on three drug combination the most frequent combination was CCB + ARB + thiazide which was seen in 4(4.2%) of the subjects.

The use of centrally acting sympatholytic (alpha methyl-dopa) significantly affected all domains, B-blockers affected all except sexual desire score (SDS). Furosemide, a loop diuretic significantly affected all domains of sexual function except erectile function score (EFS) (Table 5).

The age of the patient, duration of hypertension and duration of treatment in subjects were negatively correlated with sexual function among the hypertensive population in the study (p<0.001) (Table 6).

DISCUSSION

The study showed that sexual dysfunction was prevalent among both hypertensive and normotensive men with more than half of both populations affected, the prevalence was however higher among the hypertensive population. About 82% of men in the hypertensive group had sexual dysfunction affecting at least one domain of SD, in comparison to about half of non-hypertensive males (Table 1). This is in consonance with previous studies, a study involving over 3000 community

				EFS		ISS		OFS		SDS		055	
Drug	Use	z	%	Mean + SD	٩	Mean+ SD	4	Mean+ SD	٩	Mean+ SD	٩	Mean + SD	٩.
CCB	Yes	62	65.3	17.29±10.45	0.677	7.81±5.43	0.712	5.85±3.28	0.865	6.05±2.99	0.791	6.16±3.07	0.968
	No	33	34.7	16.79 ±9.15		7.45±4.54		5.88±2.79		5.91±2.47		6.21±2.62	
ACEI	Yes	30	31.6	19.03±10.43	0.185	8.80±5.39	0.136	6.63±3.21	0.084	6.67±2.95	0.119	6.63±3.12	0.241
	No	65		16.23 ± 9.69		7.17±4.94		5.51±3.02		5.67±2.70		5.97±2.80	
ARB	Yes	40	42.1	18.78±9.16	0.192	8.28±4.87	0.371	6.13±2.95	0.513	6.33±2.66	0.360	6.68±2.75	0.166
	No	55		15.91±10.43		7.25±5.29		5.67±3.23		5.76±2.91		5.82±2.99	
B-blockers	Yes	12	12.6	11.58±8.20	0.032*	5.17±3.61	0.046*	4.08±2.19	0.016*	4.75±2.18	0.089	4.67±2.39	0.046*
	No	83		17.92±9.99		8.05±5.21		6.12±3.14		6.18±2.85		6.40±4.67	
Central	Yes	13	13.7	9.31±7.79	0.003*	4.00±4.06	0.006*	3.77±2.49	0.007*	4.31±2.32	0.018*	4.46±2.90	0.025*
acting	No	82		18.35±9.75		8.27±5.04		6.20±3.08		6.27±2.79		6.45±4.46	
Thiazide	Yes	38	40	17.89±9.53	0.596	8.24±4.81	0.429	6.16±2.82	0.552	6.13±2.61	0.689	6.42±2.65	0.639
	No	57		16.60±10.30		7.32±5.32		5.67±3.29		5.91±2.95		6.02±3.09	
K- sparing	Yes	29	30.5	17.86±8.41	0.820	7.69±4.28	0.887	5.93±2.51	0.838	5.86±2.31	0.692	6.14±2.39	0.743
	No	99		16.79±10.62		7.68±5.47		5.83±3.35		6.06±3.01		6.20±3.13	
Furosemide	Yes	7	7.4	10.29±7.82	0.054	3.71±3.14	0.030*	3.29±1.80	0.015*	4.00±1.63	0.047*	4.00±1.92	0.033*
	No	88		17.66±9.95		8.00±5.12		6.07±3.10		6.16±2.82		6.35±2.91	

	EFS		ISS		OFS		SDS		0SS	
	rho	P- value								
Age	-0.560	<0.001*	-0.586	<0.001*	-0.557	<0.001*	-0.536	<0.001*	-0.522	<0.001*
No of antihypertensive	-0.021	0.838	-0.039	0.71	-0.074	0.477	-0.054	0.605	-0.05	0.632
Diastolic blood pressure	-0.042	0.590	-0.030	0.710	-0.028	0.732	-0.020	0.809	-0.054	0.509
Systolic blood pressure	-0.097	0.205	-0.096	0.211	-0.073	0.352	-0.057	0.467	-0.086	0.274
Hypertension duration	-0.370	<0.001*	-0.415	<0.001*	-0.329	<0.001*	-0.349	<0.001*	-0.456	<0.001*
Treatment duration	-0.315	<0.001*	-0.317	<0.001*	-0.357	<0.001*	-0.275	<0.001*	-0.294	<0.001*

Akinyede et al. Patterns of sexual dysfunction in hypertensive men

dwelling adults aged 57-85 in the USA showed that treated hypertensive male patients had significantly higher rates of SD (69.1%) compared to untreated hypertensives (57.7%), and non-hypertensives (54.3%) (Spatz, Canavan, Desai, Krumholz, & Lindau, 2013). Another study carried out in treated hypertensive male patients in France reported a prevalence of 49% (Hanon et al., 2002). A study at a tertiary centre in Lagos, Nigeria documented a prevalence of 56.7% in both male and female patients on antihypertensive drugs (Oshodi et al., 2010).

The study also showed that about half of the non-hypertensive men have sexual dysfunction affecting at least one domain. Prevalence of sexual dysfunction is highly variable among different populations, a study reported a range of 25- 61% with the higher rates found in older population (Derogatis & Burnett, 2008). Other studies have however reported lower prevalence. A multidisciplinary committee review reported that about 20-30% of adult men have SD affecting at least one domain (Lewis et al., 2010). The prevalence rates reported among non-hypertensive control in this study appears high but falls within the range found in previous studies. The age of study population and the instrument used to investigate sexual function are major determinants of prevalence rates of SD and may explain the variation in results across different studies (Derogatis & Burnett, 2008; Lewis et al., 2010).

In this study, hypertensive patients were more likely to have involvement of multiple domains compared to controls. In the hypertensive patients, about 73.3% of the 82% with SD had involvement of 4 or 5 domains pointing to an overlap of domains in the same patient. A total of 75.8 % reported ED which is comparable to other domains like orgasmic dysfunction (77.9%) and problems with sexual desire (78.9%) and is in consonance with a previous study (Akinyede et al., 2020). This suggests that any of these domains may be used singly as screening for SD in hypertension since there is involvement of multiple domains concurrently in same patient. The utility of a single domain for the assessment of SD in the normotensive population may however lead to underreporting of SD.

The differences in domains involved may be a pointer to the aetiopathogenesis of SD especially in the non-hypertensive populations. Problems with sexual desire and orgasm have been linked to neuroendocrine changes (Krüger et al., 2003; Motofei & Rowland, 2005). On the other hand, ED has been attributed to vascular, endocrine and neurological dysfunction (Bleustein, Arezzo, Eckholdt, &Melman, 2002; Santi et al., 2016; Burnett, 2019), although ED associated with hypertension is mainly related to vascular dysfunction (Nilsson, Viigimaa, Giwercman, &Cifkova, 2020).

Several studies have reported a high prevalence of ED among hypertensive patients. A study carried out in the same geographical region as ours showed a prevalence of 65.8% which is similar to our report (Fafiolu, Adebayo, Akande, & Akinboboye, 2014). Another study in Italy among hypertensive patients attending clinics reported a prevalence of 50.6% (Artom et al., 2016). Although a much lower prevalence of 35.2% among hypertensive patients was reported in Greece, it was significantly higher compared to the normotensive population that had a prevalence of 14.1% (Doumas et al., 2006).There is paucity of data comparing other domains of SD.

Antihypertensive medications are known to cause SD, the study therefore compared IEEF scores in different domains in patients who used specific classes of hypertensive drugs compared to those who did not use these drugs. The study showed that patients who were on antihypertensive combinations containing furosemide, ß-blockers and methyldopa had a significantly higher risk of SD compared to other groups of antihypertensive in this study (Table 5). It has been reported that drugs like diuretics, centrally acting sympatholytic and beta-blockers are notorious for SD (Nicolai et al., 2014; Kretchy et al., 2020). This study follows same trend except for the profile of diuretics which appears to deviate from reported patterns. The only diuretic significantly associated with SD in this study was furosemide (a drug which is used infrequently in the management of hypertension). Potassium sparing diuretics has not been linked to high rates of SD, this was replicated in our study (Nicolai et al., 2014). Thiazide diuretic use was however not associated with higher rates of SD, which conflicts with previous data (Nicolai et al., 2014; Artom et al., 2016). The reason for this is unknown, but it appears the combination of drug may influence the adverse effect profile, majority of the patients were on a combination of ARB and thiazide. ARBs have been reported to be protective against SD and the combination with of thiazide and ARB may be protective against SD in this study (Ismail et al., 2019).

β-blockers, methyldopa and furosemide are not recommended as first line drugs in blacks, as such were more likely to be given in combination with two or more drugs. It could be argued that the high rate of SD associated with these drugs was secondary to a higher number of pills co-medicated in our study. Higher drug loads have been associated with a higher prevalence of developing SD although a few studies have reported conflicting reports (Doumas et al., 2006; Hanon et al., 2002; Oshodi et al., 2010). Our study however found no association between number of antihypertensive drugs and scoring on IIEF index (Table 6).

Other variables significantly associated with higher prevalence of SD in this study include increasing age, and a longer duration of hypertension and treatment, this has been consistently replicated in several studies (Hanon et al., 2002; Doumas et al., 2006; Oshodi et al., 2010). Variables like systolic and diastolic BP on the other hand showed inconstant finding as regards the development of SD in both men and women (Hanon et al., 2002;Doumas et al., 2006; Oshodi et al., 2010; Foy et al., 2016). This study found no association between SD and blood pressure control.

The higher risk of SD with advancing age and longer duration of hypertension is a sequela of multiple processes which include a progressive in endothelial dysfunction. Normal endothelial function is required to maintain erectile function, secretion of gonadal hormones and spermatogenesis that is required for normal sexual function (Santi et al., 2016; Burnett, 2019). In the physiological state, endothelial cells release NO which enters the corpus cavernosum smooth muscle cells of the penis, to activate guanosine cyclase. Guanosine cyclase converts guanosine triphosphate into cyclic guanosine monophosphate (cGMP) which further activates protein kinases downstream leading to the relaxation of the smooth muscle cells. This process favours increased blood flow into the penile shaft to maintain tumescence (Burnett, 2019). One or more of this pathway is disrupted in when there is a reduction in NO production.

One of the strength of this study is the use of IIEF which assessed different domains of sexual function and also included a control population which helped to give a more holistic assessment of the SD in the population studied (Rosen et al., 1997). Although this study investigated the effect of each class of antihypertensive drug on SD by comparing patients who were on specific drug class to those who were not, it is still difficult to distinguish between patterns of SD caused by hypertension alone or SD associated with antihypertensive drugs. The introduction of an untreated hypertensive population would help to address this. Another limitation to the study is that the control population were relatively younger than the hypertensive population. Since SD has been shown to be more severe with advancing age, the actual prevalence among the older population who are not hypertensive might be much higher. In addition, the patterns of SD may be different across age groups. Further studies involving age-matched controls are needed.

SD is common in both normotensive and hypertensive adult males although prevalence is higher in the hypertensive males. The use of antihypertensive drugs, like methyldopa, furosemide and ß-blockers was associated with higher degrees of sexual dysfunction among the hypertensive population.

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