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Duration of hypertension and antihypertensive agents in correlation with the phases of female sexual response cycle

Rozimah Abdul Latif[a], Rosediani Muhamad[a], Anne Yee Hway Ann[b], Hatta Sidi[c,*], Nik Ruzyanei Nik Jaafar[c], Marhani Midin[c], Srijit Das[d], Loh Huai Seng[e], Ng Chong Guan[b]

[a]*Department of Family Medicine, School of Medical Science, Universiti Sains Malaysia, Kota Bahru, Kelantan, Malaysia*
[b]*Department of Psychological Medicine, University Malaya Medical Centre, Kuala Lumpur, Malaysia*
[c]*Department of Psychiatry, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, 56000 Cheras, Kuala Lumpur, Malaysia*
[d]*Department of Anatomy, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia*
[e]*Department of Family Medicine, International Medical University, Kuala Lumpur, Malaysia*

Abstract

Objective: This cross-sectional study aimed to determine the construct of the phases of the female sexual response cycle (SRC) in women with hypertension and their association with the duration of hypertension and types of antihypertensive agents.
Methods: The sexual response phases were measured with a validated Malay version of the Female Sexual Function Index (FSFI). The correlations structure of the items of the SRC's phases (i.e. desire, arousal, orgasm, satisfaction and pain) was determined using principal component analysis (PCA), with varimax rotation method. The number of factors obtained was decided using Kaiser's criteria. A total of 348 hypertensive women were recruited for this study. Four constructs were extracted in the analysis of all subjects.
Results: Using the factor analysis, the six domains (i.e. sexual desire, arousal, etc.) of the women's SRC among hypertensive women merged into 4 constructs. They were composed of (i) sexual desire and arousal, (ii) orgasm and sexual satisfaction, (iii) vaginal lubrication and (iv) sexual pain. Interestingly, vaginal lubrication stood out alone as one construct, compared to the non-hypertensive women. It was also observed that the duration of hypertension, beta blocker and diuretic antihypertensive medications had different influence on the SCR (in terms of constructs).
Conclusion: Duration of hypertension and types of antihypertensive drugs may affect the components of the SRC. A clear understanding would help the clinician in strategizing the treatment approach of sexual dysfunction in women with hypertension.

1. Introduction

Sexual dysfunction in hypertension is commonly observed in clinical practice. It may be a consequence of the natural progression of the disease itself and/or the antihypertensive medications [1,2]. Although the theory of endothelial dysfunction and inflammatory markers is currently inconsistent [3], the effect of hypertension on vascular system and neural component of the genitalia, may cause a reduction in blood flow (secondary to hypertensive arteriosclerosis) and mucus secretion of the vagina, subsequently leading to sexual dysfunction [4]. Certain antihypertensive medications especially the diuretics and beta blockers may have negative impact on the sexual functioning [2,5]. This creates not only adverse biochemical (increased cortisol level) but psychological reactions, which in turn exacerbate the sexual dysfunction [6].

Over the past few years, there has been a growing understanding in the differences of the SRC between males and females. While the linear model of SRC as described by Masters and Johnson was readily applied in males, Basson introduced an alternative model, known as the intimacy-based model or SRC circular model to explain the SRC in females. According to this model when a sexually neutral woman faces intimacy, she is driven by both biological (subjective arousal from non-genital and genital stimulations) and psychological factors (to get emotional closeness to her partner) to experience sexual arousal. What follows is an ongoing enjoyable sexual sensation which can further

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* Corresponding author. Tel.: +1 603 91456142; fax: +1 603 91737841.
E-mail address: hattasidi@hotmail.com (H. Sidi).

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trigger and sustain a sexual desire which may eventually lead to sexual satisfaction [7].

In Malaysia, the local data support the theory of Basson's circular model of female [8,9]. In the present study, the sexual function of 230 married women was assessed by using the Malay-translated version of Female Sexual Function Index (MVFSFI). Using the PCA with varimax rotation, three factors were extracted from the analysis whereby sexual desire, arousal and lubrication were highly correlated and fell into one component. Orgasm and satisfaction fell into another construct. Lastly, pain items formed the third component.

The first component was described as a driving force followed by the achievement of positive outcome of sex as the second component. Pain was an isolated component which is considered as the negative outcome of sex. However, when the similar study was carried out in a group of depressed women in remission, the orgasm became highly correlated to sexual desire, arousal and lubrication but not sexual satisfaction. The author explained that the women with depression may adopt a different sexual model. Hence, depression which affects the SRC in women, has the most impact on sexual satisfaction [9].

Previous studies showed that female sexual function may be disrupted by hypertension and/or its medications [2,5]. However, to the best of our knowledge, there are no studies which have identified the phases of SRC which the hypertension and antihypertensive medications affecting such. The present was the first of its kind to examine the association between hypertensive variables i.e. the duration of hypertension and antihypertensive medications and the correlations of the phases of SRC among the treated hypertensive women.

2. Materials and methods

Prior ethical approval was obtained from the Ethical Comittee, Universiti Sains Malaysia Hospital for conducting the research study.

2.1. Study design and setting

This cross-sectional, correlational study was conducted over a period of five months at a hypertension clinic of a teaching hospital in Malaysia. The data on sexual function was obtained using a self-administered questionnaire. Hypertensive women, aged 35–65 years, who were diagnosed more than a year ago using WHO criteria, were recruited for the study. They were selected via systematic random sampling in the ratio of 1:2 based on clinic attendance lists. The individuals who were excluded were those who were illiterate, were having active psychotic symptoms or were bedridden secondary to any underlying medical diseases.

2.2. Data collection

Subjects of this study were identified from the primary care and hypertension clinics in Universiti Sains Malaysia Hospital, Kelantan, Malaysia. Kelantan is a state that is situated at the north-east coast of Peninsular Malaysia with 1.7 million population. Nearly half of the population are women, with local Malays as the main ethnicity (i.e. 95%). Written consent was obtained from all recruited subjects after explaining the the nature and objectives of the study. Subjects were then interviewed in a privatre room to ensure their privacy and comfort. Female sexual dysfunction/response phases were assessed using the local Malay Version of the Female Sexual Function Index (MVFSFI). The basic socio-demographic data of the subjects were collected using a predesigned questionnaire. Medical record was reviewed to gather the patient's medical information (i.e., blood pressure, body mass index, duration of hypertension and type of medication prescribed).

2.3. Malay version of the female sexual function index (MVFSFI)

Female Sexual Function Index (FSFI) is a brief, multidimensional self-report measure of sexual functioning. It was validated on a clinically diagnosed sample of women with female sexual dysfunction. It consists of 19 items and were divided into 6 basic domains in female sexual dysfunction such as desire, subjective arousal, lubrication, orgasm, satisfaction and pain. Each of the domains had two to four questions with five to six options for patients to choose the most likely answer. These answers represented their sexual function within 4 weeks prior to the day before the questionnaire was administered [10,11].

The Malay Version of the Female Sexual Function Index (MVFSFI) is a validated and locally accepted questionnaire for use in the assessment of female sexual dysfunction in the Malaysian population. For this questionnaire, a total score of 55 was taken as the cut-off point for the MVFSFI to distinguish between women with and without sexual dysfunction (sensitivity = 99%, specificity = 97%). The cut-off score for each domain was also established for the MVFSFI [12].

2.4. Data analysis

Data were analyzed using SPSS version 13 for Windows (SPSS Inc., Chicago, IL, USA). The sum scores of all items in each phase were calculated. Principal component analysis (PCA) with varimax rotation method was used to explore the correlation structure of the phases. The number of factors or components to obtain was decided using Kaiser's criteria (a new factor or component was obtained if the eigenvalue of the factor was more than one).

3. Results

A total of 355 hypertensive female patients were recruited for this study. However, three of them refused to participate in the study and another four were unable to understand parts

of the questionnaire. Therefore, the overall response rate was 98% with total subjects being 348. The socio-demographics, marital, obstetric and gynaecological, and medical characteristics of 348 participants were shown in Table 1.

Table 2 showed the sexual function items among this group of women who were divided into four constructs. The first component consisted of sexual desire and sexual arousal times. The second component included only lubrication items. Orgasm and satisfaction fell into the third component. The last component was formed by the pain items.

Table 3 revealed those patients with hypertension for less than 10 years, had high correlation between sexual desire and sexual arousal. Hence, they were considered as one component, while lubrication was a standalone component. The third construct was composed of orgasm and satisfaction. Pain remained as the last component. However, for patients who had hypertension for more than 10 years, lubrication was shown to have merged with orgasm to become one component. Satisfaction, then became an individual component.

Table 4 showed that participants who were on beta blockers had all the sexual items merged into 1 component. However, for those who were not on beta blockers, the three constructs which were sexual desire, sexual arousal and lubrication remained as one component, while orgasm and satisfaction fell into another component. Pain items were found in the last component.

Table 5 revealed that participants who used diuretics had only 3 constructs which consisted of sexual desire, sexual arousal and lubrication as one component. Orgasm and satisfaction became another component, while pain items remained as the last component.

The factor loadings of sexual function items among the participants who used calcium channel blockers, angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB), were similar to those in the group who had less than 10 years of hypertension.

Table 1
Socio-demographics and medical characteristic of participants (N=348).

Variables	Mean (SD)	n (%)
Age (year)	53.50 (7.16)	
Duration of marriage (years)	31 (9.9)	
Race		
Malay		338 (97.1)
Non-Malay		10 (2.9)
Education level		
None		20 (5.7)
Primary		73 (21.0)
Secondary		217 (62.4)
Tertiary		38 (10.9)
Employment		
Employed		115 (33.0)
Unemployed		233 (67.0)
Monthly family income (RM)		
<1000		171 (49.1)
1000–1999		75 (21.6)
2000–3000		33 (9.5)
>3000		69 (19.8)
Parity		
≤ 2 children		50 (14.4)
3–5 children		180 (51.7)
> 5 children		118 (33.9)
Menopause		
Yes		202 (58.0)
No		146 (42.0)
Duration of hypertension		
≤10 years	242 (69.5)	
>10 years	106 (30.5)	
ACE I		
Yes	130 (37.4)	
No	218 (62.6)	
B Blocker		
Yes	128 (36.8)	
No	220 (63.2)	
Calcium channel blocker		
Yes	223 (64.1)	
No	125 (35.9)	
Diuretics		
Yes	92 (26.4)	
No	256 (73.6)	
ARB		
Yes	96 (27.6)	
No	252 (72.4)	
Body mass index (kg/m^2)		
Normal weight	58 (16.7)	
Overweight	290 (83.3)	
Diabetes Mellitus		
Yes	120 (34.5)	
No	228 (65.5)	
Hyperlipidemia		
Yes	259 (74.4)	
No	89 (25.6)	

4. Discussion

Using the principal component analysis with varimax rotation, we found that the six domains of the women's sexual response could be divided into four constructs or concepts among hypertensive women. The first construct was composed of highly correlated sexual desire and arousal. The second construct only included lubrication. The third construct was orgasm and sexual satisfaction. Pain remained as the last component. Interestingly, the domains for lubrication stood out alone as one construct, when compared to the non-hypertensive women study [8] in which lubrication was highly correlated with sexual desire and arousal. In this study, we also found out that the duration of hypertension, beta blocker and diuretic antihypertensive medications had different influence on the SCR (in term of constructs) in this group of women.

Previous studies had shown that hypertension was associated with increased sexual dysfunction in women. These included reduced sexual desire and arousal, inadequate lubrication, difficulty attaining orgasm, dyspareunia and lack of sexual satisfaction [2,13]. Duncan et al., in a study of premenopausal Caucasian women, found that 24.1% of the hypertensive women had vaginal dryness

Table 2
Factor loading of sexual function items on four components among hypertensive participants.*

Domain	Item	Component†			
		1	2	3	4
Desire	D1	0.781			
	D2	0.809			
Arousal	A3	0.775	0.307		
	A4	0.833			
	A5	0.793	0.306		
	A6	0.752	0.388		
Lubrication	L7	0.431	0.702		
	L8	0.313	0.814		
	L9		0.747		
	L10		0.821		
Orgasm	O11	0.357	0.492	0.781	
	O12	0.324	0.612	0.809	
Satisfaction	S13	0.308	0.317	0.775	0.307
	S14	0.340		0.833	
	S15			0.793	0.306
	S16			0.752	0.388
Pain	P17			0.431	0.702
	P18			0.313	0.814
	P19				0.747

* Using principal component analysis with varimax rotation (loadings less than 0.3 are omitted in presentation for simplicity).
† Four components were formed using Kaiser's criteria.

Table 4
Factor loading of sexual function items on three and four components among hypertensive participants (comparing between the use of beta blocker).*

Domain	Item	No beta blocker			Use beta blocker			
		Component†			Component††			
		1	2	3	1	2	3	4
Desire	D1	.774			.776	−.377		
	D2	.785			.803	−.316		
Arousal	A3	.798			.842	−.337		
	A4	.826			.787	−.332		
	A5	.811			.867			
	A6	.825			.845			
Lubrication	L7	.698	.469		.797			
	L8	.687	.393		.732	.383	−.333	
	L9	.633	.433		.720	.337		−.337
	L10	.680	.449		.762	.397		
Orgasm	O11	.513	.606		.827			
	O12	.556	.519		.808			
Satisfaction	S13	.371	.760		.796		.366	
	S14	.351	.771		.726		.423	
	S15		.840		.764		.508	
	S16		.799		.755		.480	
Pain	P17			.796	.572	.481		.401
	P18			.784	.562	.534		.416
	P19	.329		.772	.607	.477		.368

* Using principal component analysis with varimax rotation (loadings less than 0.3 are omitted in presentation for simplicity).
† Three components were formed using Kaiser's criteria.
†† Four components were formed using Kaiser's criteria.

which led to dyspareunia [14]. Although there is a paucity of literature on how the hypertension mediates the sexual responses in female, it has been suggested that the hypertension, as the systemic disease that affects the blood vessels in the entire body, could affect the vascularisation of the genital area. Physiologically, lubrication would take place during sexual arousal as a result of increased blood flow in the genital area. Therefore, if the blood vessels were affected by hypertension, inadequate vaso-congestion

Table 3
Factor loading of sexual function items on four components among hypertensive participants (Comparing between duration of hypertension more or less than 10 years).*

Domain	Item	Less than 10 years				More than 10 years			
		Component†				Component†			
		1	2	3	4	1	2	3	4
Desire	D1	0.768				0.833			
	D2	0.813				0.801			
Arousal	A3	0.807				0.688	0.337	0.417	
	A4	0.819				0.828		0.305	
	A5	0.792		0.323		0.791			
	A6	0.745		0.389		0.770	0.377	0.314	
Lubrication	L7	0.454	0.310	0.688		0.397	0.712		
	L8	0.356		0.806			0.809		0.318
	L9			0.734			0.783		
	L10	0.311		0.817			0.819		
Orgasm	O11	0.326	0.557	0.478		0.472	0.495	0.430	
	O12	0.356	0.400	0.570			0.670	0.340	
Satisfaction	S13		0.767			0.364	0.334	0.702	
	S14	0.306	0.779			0.401		0.765	
	S15		0.847					0.851	
	S16		0.795					0.811	
Pain	P17				0.806				0.771
	P18				0.799				0.815
	P19				0.773				0.804

* Using principal component analysis with varimax rotation (loadings less than 0.3 are omitted in presentation for simplicity).
† Four components were formed using Kaiser's criteria.

Table 5
Factor loading of sexual function items on four components among hypertensive participants (comparing between the use of diuretic).*

Domain	Item	No Diuretic				Use Diuretic		
		Component†				Component††		
		1	2	3	4	1	2	3
Desire	D1	.778				.707	.534	
	D2	.826				.652	.519	
Arousal	A3	.760	.318			.710	.549	
	A4	.851				.716	.493	
	A5	.816				.722	.464	
	A6	.739	.411			.726	.491	
Lubrication	L7	.418	.712			.783	.323	
	L8	.312	.805			.813		.387
	L9		.746			.790		
	L10		.824			.783		.439
Orgasm	O11	.330	.545	.509		.493	.609	.340
	O12	.315	.655	.354		.558	.410	.333
Satisfaction	S13		.334	.740		.349	.748	
	S14	.325		.779			.786	
	S15			.859			.830	
	S16			.816			.755	
Pain	P17				.794		.305	.743
	P18				.805			.803
	P19				.791	.326		.782

* Using principal component analysis with varimax rotation (loadings less than 0.3 are omitted in presentation for simplicity).
† Four components were formed using Kaiser's criteria.
†† hree components were formed using Kaiser's criteria.

during sexual arousal would result in decreased lubrication and dyspareunia [15]. This in turn may explain why lubrication had become a single entity among women who had hypertension.

Sexuality in women is complex. It is not only coordinated by vascular, hormonal and neurological factors, but it is also interplayed by socio-psychological factors. Well known psychological factors such as poor self-esteem, poor body image, poor quality of relationship with her partner, depression and anxiety, are all associated with female sexual dysfunction [15]. In this study, women who had more than 10-year history of hypertension had their sexual satisfaction separated from the lubrication and orgasm domains. These findings are similar to a previous study [8] which showed that orgasm and sexual satisfaction were highly correlated to form a single construct. Davison et al. reported that women with lower psychological well-being had more complaints of sexual dissatisfaction [16]. Therefore, sexual satisfaction is believed to be associated more with personal psychological, relationship and social factors rather than the sexual activity.

There have been studies to show that antihypertensive medications particularly the beta blockers and diuretics are associated with increased sexual dysfunction. In a systemic review of 14,897 patients [5], it was reported that the frequency of sexual dysfunction was 21.6% in the beta blocker group and only 17.4% in the placebo group. Fogari et al. found that in a group of hypertensive premenopausal women, who were treated with beta blocker, there were reduced sexual desire and libido [17]. Interestingly, in the present study, sexual desire, arousal, lubrication, orgasm, satisfaction and pain were strongly correlated to each other and integrated into one construct in those patients who were treated with beta blocker. This suggests that this group of patients were no longer able to clearly differentiate between the phases of SCR. Stahl hypothesized that sexual arousal was mainly increased by the elevated levels of dopamine, norepinephrine, oxytocin and testosterone; and was inhibited by increased level of serotonin at the mesolimbic, hypothalamus and prefrontal cortex [18,19].

It is well-known fact that beta blocker is a drug which interacts with the neurotransmitters and hormones (mainly norepinephrine and testosterone). This in turn may "confuse" the brain in differentiating the phases of SCR. Hence this may also explain why patients who are on antihypertensive medications such as calcium-channel blocker, ACEI and ARB, have less interaction with norepinephrine or testosterone, and have fewer problems with sexual function [17]. Earlier studies reported peripheral vasodilation and potentiation of α-adrenergic activity in the male sexual organs like penis [20]. These results in less blood blow to the genital organ and it may be an important cause of sexual dysfunction.

Another question which may be raised is the duration of the hypertensive use which can influence the results. Furthermore,the present study also found that the factor loading of sexual function items in this group of patients followed a similar pattern compared to those who had hypertension for less than 10 years.

Diuretics, mainly thiazides, are the most commonly used antihypertensive medications to treat hypertension. Diuretics are effective and less costly but they are associated with some unwanted effects in sexual function, particularly, reduced libido and vaginal lubrication. There are reports of long term use of diuretics leading to general fatigue and reduced sexual functions [21]. The exact mechanism still remains unclear. Possible mechanisms may also involve the vascular or central nervous system (CNS). If there is involvement of the CNS, then cognitive functions may be affected. Sexual impulses are also under nervous control and they can be altered once the drug acts on the CNS.

It has been proposed that diuretics interfere with smooth muscle relaxation and provoke decreased response to catecholamine (norepinephrine and epinephrine) which may cause reduced sexual arousal and desire. Interestingly, diuretics also cause reduced vaginal lubrication [22]. This could probably explain why the participants in the present study who were on diuretics, could not differentiate between sexual desire, arousal and lubrication. Therefore, while using factor analysis on the MVFSI, we found that sexual desire, arousal, and lubrication were highly correlated and formed one construct in this group of participants.

There were few limitations in this research study. The sample population was mainly comprosed of local Malays. This could reflect a sampling bias which limited the findings'

generalizability. There was a lack of data on sexual functioning of the subject's husbands which may have affected the women's sexual responses. There may be a possibility that the participants in this study were reluctant to openly reveal their sexual problems due to cultural inhibitions. Some of the problems that might be of concern would be the lack of assessment of the subjects' mental state. Research has shown the subjects' mental health status may influence their sexual functioning [23,24]. We did not discriminate peri-menopausal period amongst the recruited hypertensive women aged between 35 and 65 years. We also admit that the components which constitute metabolic syndrome were not analyzed. Finally, the beta-blockers used in our patients were not homogenous. Thus, there may not be any evidence of a class effect in this group.

5. Conclusion

It is advised that female sexual dysfunction may always be kept in mind while prescribing antihypertensive medications. This may also influence the quality of life of the patients. The SRC of hypertension women is highly affected by the duration of the disease and different types of antihypertensive medications. Keeping these facts in mind, clinicians should treat hypertension judiciously and offer the patients with antihypertensive medications which have the least influence on their SRC.

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