Original Article

Perimenopausal Females with High BP

Perimenopausal Females Continue to Have High Blood Pressure Spikes Inspite of Taking Regular Antihypertensive Use – Need to Manage the Symptoms Not the Cause

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ABSTRACT

Objective: To recognize the inability of antihypertensive medicine to control BP spikes during VMS in perimenopausal females.

Study Design: Observational cross sectional study

Place and Duration of Study: This study was conducted at the Rai Medical College Teaching Hospital, Sargodha from July 2022 to February 2023.

Materials and Methods: Females presenting to OPD for the control of HTN between 30-70 years of age using regular antihypertensive medicine and experiencing the Vasomotor Symptoms (VMS). STRAW staging system was used to define the menopause. After securing informed consent, applying inclusion and exclusion criteria Composite Symptoms Severity Score was assessed on the prescribed modified MENQOL questionnaire proforma. Average of all the available recorded readings (10 at least) of BP in the period since antihypertensive medicines are being used regularly was documented. In the absence of written record we recorded the values given by recall. Office reading of BP was taken within half hour of the VMS symptoms as per JNC7 guidelines at the time of the visit. antihypertensive medicines (by the group) being used by the patient were noted as per standard.

Results: We had 346 patients during the study period. We had 4% in 4th decade, 36% in 5th decade, 47% in 6th decade and 13% in 7th decade of life, this is expected and in accordance with the literature. We divided the patients in 3 groups, low score <50 composite severity score index (CSSI), intermediate score 50-100 CSSI, severe score >100 CSSI for the sake of convenience of interpretation. Most of the patients in 4th and 7th decade had low CSSI, 79% and 13%. Most of the patients in 5th and 6th decade had intermediate CSSI, 47% and 52%. High score was seen in relatively fewer patients in all 4 decades, 10%, 19%, 19% and 7%.Average home BP record mostly fell into hypertensive range (higher than 140/100 mmHg), matching the CSSI score in all three groups with wide fluctuation well reflected in SD while still regularly using antihypertensive medicine. Office BP measured after at least half hour of the hot flushes was still high in all age groups and all CSSI score groups.

Conclusion: These findings reinforce our hypothesis that antihypertensive medicines fails to control spikes of high BP during VMS symptoms in spite of good compliance. It must be appreciated that BP spikes are mediated through a different mechanism other than the classical aldosterone-renin-angiotensin mechanism of essential hypertension. A different approach is needed, if we control the VMS, BP swings will be minimized without antihypertensive medicine thereby avoiding unnecessary and wrong prescription.

Key Words: Peri-menopausal syndromes, vasomotor perimenopausal symptoms, hot flushes, hypertension.

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INTRODUCTION

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Every female is expected to experience the physiological changes of Menopause (MNP) anywhere after the age of 30 years to around 70 due to fading female hormones and around 50-80% do experience some of these with varying severity, ranging from a mild nuisance to disabling, during perimenopausal period lasting on average 5 to 7 years or more. This set of symptoms complex is called VMS consisting of hot flushes, sweating, palpitation and extreme fluctuation in BP. They peak around forties to mid-fifties and may have a circadian rhythm, nocturnal symptoms being more disturbing.[1,2] As these symptoms may start while females are still menstruating or long after cessation of

periods especially after hysterectomy, many a times females fail to appreciate or recognize them. Psychosocial, physical, and sexual symptoms are the other features.[3,4]

Wide swings in BP are very commonly associated with any internal unpleasant feeling or bodily hurt like headache or abdominal cramps. VMS when more than mild are quiet disturbing, these are expected to be associates with upshot in BP. This is compounded by the fact that BP swings are integral part of VMS with its own hormonal pathophysiology. The untended labelling of Hypertension in anxious and panicked patients and patients passing through different phases of menopause was documented in 2 related studies by the same lead author.[5,6]

The cyclical changes in follicle stimulating hormone, luteinizing hormone, estrogen and other hormones during the long fertile years gradually reset and fade. HTN and resulting cardiovascular diseases (CVD) are explained on the basis of altered estrogen and androgens proportion.[7] In menopause transition the loss of cardiovascular protection, HTN becomes more important along with other components of Metabolic Syndrome (MS) due to declining levels of estrogen. Lower estrogen levels in premenopausal years like in smoker females are associated with 7 fold higher risk of premature CHD. Before prescribing HRT it is mandatory to stratify CHD and CVS risks in women with a previous CHD event or stroke, current smoking and MS. It shall be definitely considered for specific urogenital complaints or osteoporosis. The use of HT is contraindicated in women at higher risk for breast cancer (previous history, family history).[8] During VMS phase, patient is labelled and is prescribed antihypertensive medicine for regular use. These are the patients who continue to have surges in BP during VMS phase in spite of good compliance, a perfect example of treating the symptoms without addressing the underlying pathophysiology.

Sample size: A minimum sample size of 220 was calculated to maintain a 5 percent margin of error, a 95 percent confidence interval and a 75 percent response distribution, using WHO sample size calculator.

Statistical Analysis: Data analysis was conducted using Statistical Package for Social Sciences software version 25. Descriptive statistics (i.e. frequency distribution, percentages, mean and standard deviations) were the primary analytical methods.

Inclusion Criteria: All female presenting to the OPD for the control of HTN and receiving regular antihypertensive medicine between 30-75 years was assessed for the perimenopausal status and presence of VMS, were invited to participate in this study. Patients not menstruating due to surgical hysterectomy but still having vasomotor symptoms were included.

Exclusion Criteria: Pre-menopause, Medical and Iatrogenic conditions that can masquerade as Hot Flushes like Anxiety disorders, Autoimmune disorders, Carcinoid syndromes, Diabetic autonomic dysfunction/hypoglycemia, Epilepsy, any Infection or febrile illness, Insulinoma/pancreatic tumors, Leukemia/lymphoma, cancer survivors, mast-cell disorders, New-onset hypertension, Thyroid disease, Tuberculosis, Use of selective-reuptake inhibitors or serotonin norepinephrine-reuptake inhibitors.Hormonal (HRT) or non-hormonal replacement (Tibolol) therapy.[9] Major psychotic disorder, substance abuse, already taking antidepressants and anxiolytics.

MATERIALS AND METHODS

This study was conducted on the females presenting to OPD for the control of HTN between 30-70 years of age using regular antihypertensive medicine and experiencing the cardinal VMS symptoms, fluctuating BP, hot flushes, palpitation and sweating. STRAW staging system was used to define the menopause.[3] After securing informed consent, applying inclusion and exclusion criteria, frequency and severity of VMS perimenopausal symptoms was recorded with the help of trained paramedical staff on the prescribed modified MENQOL questionnaire proforma limited to the vasomotor domain, hot flashes, sweating, palpitation and hypertension. The composite score was calculated by multiplying the average weekly occurrence of symptoms with severity score for each symptom.[4] Average of all the available recorded readings of BP (10 at least) in the period since antihypertensive medicines are being used regularly was documented. In the absence of written record we recorded the values given by recall. Office reading of BP was taken within half hour of the VMS symptoms as per JNC7 guidelines at the time of the visit.[10] The group/s of antihypertensive medicines being used by the patient were noted as per standard.

RESULTS

We had 346 patients during the study period. We had 4% in 4th decade, 36% in 5th decade, 47% in 6th decade and 13% in 7th decade of life, this is expected and in accordance with the literature.

Table No. 1: Demography (N = 346)

Age Group	N	BP VMS, CSSI < 50	BP VMS, CSSI > 51 < 100	BP VMS, CSSI > 100
30-40	14	78.57 + 0.53%	14.29 + 0.07%	7.14 + 0.02%
41-50	125	33.60 + 0.02%	47.20 + 0.08%	19.20 + 0.12%
51-60	163	28.83 + 0.13%	52.15 + 0.04%	19.02 + 0.20%
61-70	44	59.09 + 0.33%	34.09 + 0.15%	6.82 + 0.04%

Table No. 2: Home Monitoring of BP (N = 346)

Age Group	N		BP VMS, CSSI < 50	BP VMS, CSSI > 51 < 100	BP VMS, CSSI > 100
30-40	14 (4%)	Range	135-180/95-100	135-180/95-100	135-200/100-110
		Mean	156.8+5.1/97.2+2.3	158.4+4.4/97.7+3.8	165.6+6.5/103.7+5.4
		Mode	155.3/96.5	158.0/96.6	164.6/102.2
		Median	155.7/96.9	158.1/97.2	165.2/102.7
41-50	125 36.13%	Range	135-180/95-100	150-220/95-120	150-240/105-120
		Mean	157.2+4.4/97.7+3.9	187.1+5.5/109.2+6.1	194.8+4.9/113.3+4.7
		Mode	156.5/97.1	186.1/108.3	193.3/112.0
		Median	157.1/97.3	186.6/109.1	193.8/112.6
51-60	163 47.11%	Range	135-180/95-100	170-220/95-120	150-240/105-120
		Mean	157.9+4.9/98.1+5.2	193.9+4.9/110.8+6.9	195.8+4.6/113.4+5.7
		Mode	156.7/96.8	192.1/109.5	194.1/112.6
		Median	157.4/97.3	192.7/109.9	194.7/113.2
61-70	44 12.72%	Range	135-180/95-100	165-220/105-120	150-240/105-120
		Mean	163.2+5.3/108.1+7.7	195.4+4.5/111.1+3.9	196.6+4.9/109.3+6.4
		Mode	160.4/107.2	194.7/109.6	194.5/107.9
		Median	161.4/107.6	195.0/110.3	195.1/108.4

We divided the patients in 3 groups, low score <50 composite severity score index (CSSI), intermediate score 50-100 CSSI, severe score >100 CSSI for the sake of convenience of interpretation. Most of the patients in 4th and 7th decade had low CSSI, 79% and 13%. Most of the patients in 5th and 6th decade had intermediate CSSI, 47% and 52%. High score was seen in relatively fewer patients in all 4 decades, 10%, 19%, 19% and 7%.

Average home BP record fell into hypertensive range (higher than 140/100 mmHg) in all the patients. The rise in BP roughly matched the CSSI score in all three groups with wide fluctuation well reflected in SD. All were using antihypertensive medicine regularly. ACE Inhibitors or AT2R blockers were the commonest medicine followed by Beta Blockers and the Calcium Channel Blockers. More than 50% were using combinations, diuretics were least frequently used medicines. We could not make formal calculation as patients kept on switching medicine from time to time.

Office BP measured after at least half hour of the hot flushes were still high in all age groups and all CSSI score groups.

Table No. 3: Office Reading within Half Hour of VMS BP (N = 346)

Age Group	N		BP VMS, CSSI < 50	BP VMS, CSSI > 51 < 100	BP VMS, CSSI > 100
30-40	14 (4%)	Range	135-150/95-100	135-150/95-100	135-200/100-105
		Mean	143.2+5.6/97.8+3.9	144.2+5.3/98.0+4.7	169.9+5.2/102.3+4.4
		Mode	142.3/96.4	143.3/97.1	168.5/100.8
		Median	142.6/97.1	143.6/97.5	169.2/101.4
41-50	125 36.13%	Range	135-150/95-100	150-180/95-120	150-180/100-105
		Mean	144.4+4.8/96.8+6.9	164.7+5.8/109.4+4.2	165.5+4.7/102.8+6.2
		Mode	143.4/95.6	162.6/108.4	164.8/101.4
		Median	144.2/96.3	163.9/109.0	165.0/102.1
51-60	163 47.11%	Range	135-180/95-100	170-220/95-120	150-240/105-120
		Mean	159.3+6.1/98.2+3.9	195.8+5.1/112.6+6.6	198.3+5.7/108.4+7.1
		Mode	157.7/97.1	194.5/111.4	196.7/107.8
		Median	158.4/97.7	195.1/111.6	197.1/108.0
61-70	44 12.72%	Range	135-180/95-100	165-220/105-120	150-240/105-120
		Mean	156.9+5.8/96.8+6.1	196.4+4.5/108.8+5.1	196.2+4.9/113.6+4.9
		Mode	156.1/95.4	194.7/108.0	194.6/112.3
		Median	156.5/96.2	195.6/108.4	195.6/112.8

DISCUSSION

These findings reinforce the hypothesis that antihypertensive medicines fails to control spikes of high BP during VMS symptoms in spite of antihypertensive medicines. All of our patients were regularly using antihypertensive medicine, ACE inhibitors/ AT2RBs most frequently followed by Beta Blockers and calcium Channel Blockers either alone or in combination. These are the patients who continue to have surges in BP during VMS phase in spite of good compliance, a perfect example of treating the symptoms without addressing the underlying pathophysiology. Role of coexisting anxiety and panic attacks must be taken into consideration. It is agreed that essential HTN presents in the same age group and the history of pre-eclepmsia or eclepmsia, gestational HTN and presence of VMS is associated with higher risk of developing HTN in future. This study by no means undermines the importance of genuine HTN in these patients, such patients must be carefully evaluated to prescribe proper lifestyle modifications and compliance with antihypertensive treatment. It must also be appreciated that some very important determinants of perimenopausal symptoms like lower socioeconomic class, racial differences (Afro-American, Hispanics, Asians) smoking, being overweight with underlying insulin resistance, higher alcohol intake and reduced physical fitness are also considered significant in the development of HTN. On this very basis one is likely to have both components active in same patient, there is underlying essential HTN and VMS phase adds to it in causing wide swings in BP. Antihypertensive medicine may be able to keep BP in normal range but it shots up during VMS complex. This is misinterpreted and leads to a kneejerk response of increase in the dose of present antihypertensive medicine or addition of a new drug. Many a times symptoms like non-specific chest pain, mood changes, sleep disturbances, headaches, palpitations, hot flushes, anxiety, depression, tiredness have an overlap with VMS and are likely to be misinterpreted. These need to be addressed on their own merit keeping in mind that our society is getting intolerant and anxiety is getting more and more common in general population. Anxiety and panic attack are the most common medical conditions which cause a temporary rise in BP. White coat hypertension is a well-known entity. Every hypertensive must be thoroughly evaluated for anxiety. The very common notion that I know from my symptoms that my BP is high is a sure sign that underlying mood disorders are operating.

It must be appreciated that BP spikes are mediated through a different mechanism other than the pathophysiological aldosterone-renin-angiotensin mechanism of essential hypertension. A different approach is needed, if we control the VMS, BP swings will be minimized without antihypertensive medicine. Hormone replacement therapy is known to control all symptoms of VMS including HTN. There is a large data available to support use of non-hormonal replacement therapy (Tibolol) and Selective Serotonin Reuptake Inhibitors SSRIs or NNSRIs to control VMS. The effectiveness of HRT, non HRT and antidepressants in controlling the VMS symptoms is abundantly documented in the literature and is a testimony to our hypothesis.

CONCLUSION

BP spikes are mediated through a different mechanism other than the pathophysiological aldosterone-renin-angiotensin mechanism of essential hypertension. A different approach to treat the underlying cause is needed. HRT, non HRT and antidepressants are very effective in controlling the VMS symptoms.

Author's Contribution:

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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