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CLINICAL ANGER AND NEGATIVE EXPRESSIVITY - ARE THEY PREDICTORS OF COGNITIVE IMPAIRMENT IN PATIENTS WITH HYPERTENSION?

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Contribution

AG conceived, designed and did statistical analysis & manuscript writing. MM did data collection manuscript writing and did review final approval of manuscript

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ABSTRACT

Objectives: To examine association between clinical anger, emotion expressivity and cognitive performance of hypertensive patients.

Methodology: The study had cross sectional research design. Purposive sampling was used. Patients diagnosed with hypertension at Nishter Hospital Multan and Bahawal Victoria Hospital Bahawalpur, Pakistan and healthy individuals from community participated in the study during 1st April to 31st October 2016. Subjects completed clinical anger scale, Berkeley expressivity questionnaire and Mini mental status examination.

Results: Total of 80 hypertensive and 80 healthy individuals were included in the study. Patients with hypertension showed higher clinical anger (M ± SD patients 54.38 ± 3.87 vs. healthy individuals 10.15 ± 2.01) and expressivity of negative emotions (5.31 ± 1.02) than healthy individuals (2.23 ± 0.84). In contrast with healthy individuals, patients with hypertension showed cognitive impairment (14.63 ± 2.87 vs. 27.31 ± 1.57). Clinical anger (β=-.64, t=-7.41, $p<.001$) and negative expressivity (β=-.33, t=-3.84, $p<.001$) were significant predictors of cognitive performance in patients with hypertension $R2 = .90$, $F(12, 79) = 52.24$, $p<.001$.

Conclusion: Clinical anger and negative emotion expressivity are significant markers of cognitive decline associated with hypertension.

Key Words: Hypertension, Cognition, Anger, Emotion.

INTRODUCTION

Inadequate management of hypertension may lead to several life threatening diseases such as heart failure, stroke, coronary artery disease, kidney disease etc.[1] According to new guidelines of American Heart Association, systolic blood pressure (BP) between 130 –139 (mmHg) and diastolic BP80-89 (mmHg) is defined as stage 1 whereas systolic BP at least 140 (mmHg) and diastolic at least 90 (mmHg) is called stage 2 hypertension.[2] According to an estimate, 1 billion people around the world are hypertensive while the number will increase up to 1.56 billion in 2025.[3] The situation is alarming in Pakistan as 18% of population is affected by hypertension and every third person above 40 years of age is at risk of becoming hypertensive.[4] There is a growing evidence that hypertension has deleterious effects on cognition.[5] Studies have shown that high BP increases the risk of dementia.[6] Among several vascular risk factors (glycosylated hemoglobin, body mass index, high sensitive C-reactive protein, smoking, serum cholesterol) and demographic characteristics (gender, education), systolic BP showed 11% of variance in cognitive performance of midlife age group.[7] Review of studies showed that people with hypertension demonstrated worse performance on tests of cognitive functions such as attention, executive functions, learning, memory, psychomotor abilities, visuo-spatial and perceptual skills.[8] Hypertension affects cognitive performance in several ways, for instance patients with hypertension demonstrated reduced cerebral blood flow during cognitive performance as compared with normotensives. Inadequate cerebral blood flow leads to reduced cognitive performance in hypertensive patients.[9] Hypertension also increases cortisol level (stress hormone) which induces stress and in turn reduces cognitive performance.[10] Hypertension triggers accumulation of Amyloid-β peptide (Aβ) in brain vasculature through activation of Receptor for Advanced Glycation End products. CNS concentrations of Aβ is associated with dementia and cognitive impairment.[11]Reduced regional cerebral blood flow to frontal cortex and basal ganglia, white matter vascular lesions, decreased cerebral glucose utilization in hippocampus, and increased thickness of cerebral arteries are associated with cognitive impairment in hypertensive patients.[12] Animal model suggests that hypertension reduces synaptic plasticity, synaptic density and regulation of genes responsible to conduct synaptic function in mouse hippocampus representing aging phenotype. These structural alterations in neurons impair cognitive functions and contribute to pathogenesis and manifestation of cognitive decline.[13] Recent studies demonstrated aside Aβ pathology, tau hyperphosphorylation is also involved in cognitive decline related with hypertension. For instance it has been observed that in non-transgenic hypertensive rats, cerebral small vessel disease appears which increases brain concentrations of Aβ and intra-neuronal tau hyperphosphorylation.[14] Hypertension promotes cognitive decline by disrupting blood brain barrier and inducing capillary rarefaction resulting in neuroinflammation which impairs neurovascular coupling responses and stimulates genesis of cerebral microhemorrhages.[15] Hypertension not only modulates cognition, rather emotional disturbances have also been associated with high blood pressure.[16] Training to reduce anger and hostility in hypertensive patients helps lowering blood pressure and effectively improving cognitive (problem solving) and psychological (anxiety) resources.[17] Long term emotional, behavioral and cognitiveintervention improves health related quality of life, systolic and diastolic BP.[18] Patients with hypertension showed depression, anxiety and agitation which leads to high BP.[19] Studies have demonstrated that clinicians should pay attention to negative emotions in patients with hypertension because it leads tonon-adherence of medication.[20] People with high BP not only show mood swings, hostility and worry rather they perceive environment as hostile, demanding and noisy.[21] Behavioral studies suggest that patients with hypertensionexperience anger, though they try to control and suppress its' expression.[22] Neural correlates of anger and cognition overlap, for instance activation in prefrontal cortex (PFC) and hippocampus is positively associated with aggression and self- reported anger. Increased activity in hippocampus can predict subjective feelings of anger.[23] Regions of PFCare involved in regulation of anger as lesions of the frontal cortex are related with increased anger.[24] PFC and hippocampus process diverse cognitive functions.[25,26]

Therefore, the present study was designed to compare clinical anger, emotion expressivity and cognitive performance of patients with hypertension and healthy individuals. Second objective was to assess predictor of cognitive performance in patients with hypertension. It was hypothesized that patients with hypertension would show higher clinical anger than healthy individuals. Patients with hypertension would express negative emotions and impulse strength frequently than healthy individuals. On contrary, healthy individuals would express positive emotions frequently than hypertensive patients. Patients with hypertension would show cognitive impairment in contrast with healthy individuals. Clinical anger and negative expressivity would predict cognitive performance.

METHODOLOGY

The study had a cross sectional research design. Patients diagnosed with hypertension at Nishter hospital Multan and Bahawal Victoria hospital Bahawalpur from 1st April 2016 until 31st October 2016 participated in the study. Healthy individuals from local community took part in the study. Participants were screened for not having (i) depression through Geriatric Depression scale -GDS (score 0-4/15) (ii) psychiatric disorder assessed through Mini International

Neuropsychiatric Interview (iii) history or present physiological disease such as diabetes, stroke, head injury, etc. (iv) unhealthy life style including as smoking, exercise, obesity.[27,28]

Clinical Anger Scale-CAS was used to assess syndrome of clinical anger. It is a 21 item questionnaire rated on a 4-point Likert scale (A=0 to D=3).[29] Total score ranges from 0-63. Higher score shows greater clinical anger. Scores are interpreted as 0-13/63 minimal, 14-63 clinical anger. The scale is highly reliable (β 0.94) and valid to screen anger symptomology in both clinical and non-clinical settings. Berkeley Expressivity Questionnaire BEQ(16 items) was administered to assess three aspects of expressivity: positive (4 items), negative (6 items) and impulse strength (6 items) on 7 point scale (1=strongly disagree to 7=strongly agree).[30] Score on each subscale is a mean of scores on corresponding items. Higher scores reflect higher expressivity pertaining to the subscale. Questionnaire has good psychometric properties.Mini Mental Status Examination-MMSE was administered to assess cognition. The test consists of 11 items assessing orientation, registration, attention and calculation, recall, and language.[31] Score equal to 23 or below reflects cognitive impairment. The test is highly reliable and valid tool to assess cognitive status in clinical settings.

The study was approved by board of studies of The Islamia University of Bahawalpur. All participants gave written informed consent for their participation in the study. Blood samples were collected after at least 8 hour fasting. Following, participants completed Clinical Anger Scale, Berkeley Expressivity Questionnaire and Mini Mental Status Examination.

Demographic and clinical variables were assessed through t-test. Univariate analysis of variance (ANOVA) was conducted with scores on CAS as dependent factor and Group as fixed factor to assess group differences on clinical anger. Repeated measures ANOVA was conducted with Expressivity 3 (negative vs. positive vs. impulse strength) x Group 2 (patients with hypertension vs. healthy individuals) to examine group differences on BEQ. Univariate ANOVA was conducted to analyze group differences on MMSE with scores on MMSEas dependent factor and Group as fixed factor. Regression analysis was conducted to assess predictors of mental status (dependent variable) with systolic BP, diastolic BP, serum cholesterol, serum LDL-cholesterol, serum LDL-cholesterol, triglycerides, clinical anger, negative expressivity, positive expressivity, impulse strength and geriatric depression as independent factors.

RESULTS

Results showed that patients with hypertension had higher BP and lipid profile than healthy individuals whereas there was no difference between patients and healthy individuals on demographic variables (Table 1).

There was significant difference between patients and healthy individuals F (1, 159) =8205.98, $p<0.001$, βp2=.98 on clinical anger. Patients with hypertension showed higher clinical anger than healthy individuals (M ± SD patients 54.38 ± 3.87 vs. healthy individuals 10.15 ± 2.01). Repeated measures ANOVA revealed significant main effects of Expressivity F(2, 158) =169.67, $p<0.001$, βp2=.51 and Group F(1, 158) =229.32, $p<0.001$, βp2=.59.There was significant main interaction between Expressivity x Group F(2, 158) =718.30, $p<0.001$, βp2=.82. Patients showed higher negative expressivity and impulse strength than healthy individuals. In contrast, healthy individuals scored higher on positive expressivity (Table 1).There was significant cognitive impairment in patients with hypertension in contrast with healthy individuals (F1, 159) =1194.97, $p<0.001$, βp2=.88 (Table 1).Regression analysis showed clinical anger standardized β=-.64, t=-7.41, $p<.001$ and negative expressivity standardized β=-.33, t=-3.84, $p<.001$ as significant predictors of cognitive impairment in patients with hypertension R2= .90, F(12, 79)= 52.24, $p<.001$. In contrast, age standardized β=-.00, t=-.03, p=.96, SBP standardized β=.01, t=.31, p=.75,DBP standardized β= -.02, t= -.55, p=.58, serum LDL-cholesterol standardized β= .05, t= -.55, p=.58, serum HDL-cholesterol standardized β= -.00, t= -.14, p=.88, cholesterol β= -.08, t=- .82, p=.41, triglycerides β= .03, t= .74, p=.45, positive expressivity β= -.03, t=- .72, p=.47, impulse strength β= .05, t= 1.30, p=.19and geriatric depression β= -.02, t=- .49, p=.62.

Table 1: Demographic and Clinical Characteristics

	Patients with Hypertension (n=80)		Healthy Individuals (n=80)		p value
	M ±SD	Range	M ±SD	Range	
Age	58.27 ± 2.49	5.001-60.00	57.68 ± 2.57	51.00-60.00	t(79)=1.82, p=.07
Gender (m:f)	40:40		40:40		
SES					
High	20		20		
Middle	20		20		
Low	20		20		
Education					
Postgraduate	20		20		
Graduate	20		20		
Higher Secondary/O' level	20		20		
GDS	12.12 ± 1.12	10.00 -15.00	3.26± 0.68	1.00 -5.00	
SBP (mmHg)	162.00 ±5.88	150.00 -171.00	119.00 ± 2.48	110.00 -125.00	t(79)= 77.18, p<.001
DBP (mmHg)	110.00 ± 7.33	100.00 -130.00	80.00 ± 1.18	79.00 -85.00	t(79)= 34.51, p<.001
Serum cholesterol (mg/dl)	224.00 ± 20.51	170.00 -260.00	164 ± 17.20	137.00 -198.00	t(79)= 19.62, p<.001
Serum HDL-cholesterol (mg/dl)	48.16± 2.14	43.00 -56.00	44.00 ± 2.53	40.00 -49.00	t(79)= 9.17, p<.001
Serum LDL-cholesterol (mg/dl)	176 ± 9.07	160.00 -190.00	89.00 ± 11.28	70.00 -103.00	t(79)= 51.72, p<.001
Serum Triglycerides (mg/dl)	176.45 ± 18.02	140.00 -200.00	126.00 ± 11.17	100.00 -145.00	t (79)= 20.20, p<.001
CAS	54.38 ±3.87	45.00 -61.00	10.15 ± 2.01	6.00 -13.00	
NE	5.31 ± 1.02	4.00 -7.00	2.23 ± 0.84	1.00 -3.00	
PE	3.86 ± 0.59	3.00 -5.00	6.01 ± 0.41	5.00 -6.90	
IS	5.92 ± 0.45	5.00 -6.90	3.94 ± 0.42	3.10 -4.50	
MMSE	14.63 ± 2.87	10.00 -20.00	27.31 ± 1.57	25.00 -30.00	

Note. ReadGDS=Geriatric depression scale; SBP= systolic blood pressure; DSB=diastolic blood pressure; CAS=clinical anger scale; NE= negative expressivity; PE= positive expressivity; IS= impulse strength; MMSE=Mini mental status examination.

DiSCUSSION

The present study was conducted with the objective to compare clinical anger, emotion expressivity and cognitive performance between hypertensive patients and healthy individuals. Second aim was to examine association between clinical anger, emotion expressivity and cognition in patients with hypertension. There were several important results. Patients with hypertension showed cognitive impairment in contrast with healthy individuals. Hypertension has been associated with cognitive decline and dementia.[5,6] High BP is a strong risk factor for cognitive decline among various vascular and demographic characteristics, for example cholesterol, age, smoking.[7] Cognitive impairment related with hypertension encapsulates several cognitive domains including executive functions, memory, perception, attention.[8] Hypertension affects cognition through several mechanisms such as reduced cerebral blood flow9, increased cortisol levels, deposition of Aβ in brain vasculature, reduced regional blood flow to brain areas critical for cognition such as frontal cortex and basal ganglia, decreased glucose utilization in hippocampus, vascular lesions of white matter, and increased thickness of cerebral arteries.[10-12] There are

evidences from animal model studies of reduced synaptic plasticity and density, deregulation of genes involved in synaptic functions, proliferations of brain Aβ and intraneuronal tau hyperphosphorylation, neuroinflammation and disruption of blood brain barrier in hypertension triggering cognitive impairment.[13-15]

Results of the present study also demonstrated that patients with hypertension showed higher clinical anger than healthy individuals. Hypertensive patients had differential emotion expressivity as compared with healthy individuals. Patients reported higher expressivity of negative emotions and impulse strength. On contrary, healthy individuals reported higher positive expressivity than negative emotion expressivity and impulse strength. Previous studies indicated emotional disturbances and presence of negative emotions (e.g., agitation, depression) in hypertensive patients16,19 which stimulates medication non-adherence, cognitive impairment and deteriorates quality of life.[18,20] Our results demonstrated that patients not only express negative emotions frequently rather there is disinhibition of emotional impulse. As a result, expression of negative emotions becomes frequent. In contrast, healthy individuals have more control over emotional impulse, thus expression of negative emotions turns out to be less frequent. Model of relationship between negative emotions and hypertension suggests that negative emotions deteriorate biological and behavioral processes affecting sympathetic/ parasympathetic nervous system and hypothalamic pituitary adrenal axis resulting in high blood pressure. Thus, regulation of negative emotions is necessary to restore biological-behavioral processes.[32] It has been found that people with high blood pressure show high emotional reactivity than controls33 which can be reduced with training improving cognition.[17]

Results of the current study indicated expressivity of negative emotions and clinical anger as determinant of cognition in hypertension among several other risk factors such as lipid profile, depression, etc. This result can be seen in the context of overlapping neural correlates of anger and cognition. For instance frontal cortex is involved in emotion regulation and higher order cognitions.[24,25] Our results demonstrated that higher clinical anger and higher expressivity of negative emotions contribute to cognitive impairment in hypertension.

LIMITATIONS

Results may be limited due to small sample size of the study. Patients were selected from two hospitals only in Pakistan. Future studies might consider larger sample size with selection of patients from several hospitals to increase generalizability.

CONCLUSIONS

This study demonstrated that clinical anger and expression of negative emotions are determinants of cognitive performance in patients with hypertension. Early detection of clinical anger and negative expressivity could prevent cognitive decline in hypertensive patients. Clinicians and primary health care professionals must consider screening of clinical anger and expression of negative emotions at the time of diagnosis. In addition, therapeutic intervention to reduce clinical anger and negative expressivity should be considered along with antihypertensive medication.

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