



ROLE OF VARIOUS MODIFIABLE FACTORS AND DRUGS IN THE TREATMENT OF ISOLATED SYSTOLIC HYPERTENSION IN ELDERLY POPULATION.

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ABSTRACT Prevalence and severity of hypertension are strongly associated with the advancing age, women have lower systolic blood pressure as compare to men during early adulthood, however after menopause blood pressure increases in women to levels even higher than in men. In elderly population isolated systolic hypertension is a major health problem predisposing them to substantially increased risk for stroke, coronary artery disease and congestive heart failure. Adequate control of systolic blood pressure by life style modification and appropriate use of medicine can improve the quality of life and productivity in this population. The aim of the present study was to evaluate the effect of various modifiable factors and appropriate drug /drugs that is most suitable for controlling systolic blood pressure in elderly population. This was a retrospective observational study conducted on the patients attending medicine department of Hakeem Abdul Hameed Centenary Hospital, Delhi. Elderly hypertensive were included in the study. The prevalence of ISH in the study population was found to be 63.18 %, among of them men and women were 31.81% and 31.36%. Angiotensin receptor blockers were found to be the most appropriate drug in single drug regimen, whereas calcium channel blocker in combination with beta blocker produced best result in two drug combination therapy and calcium channel blocker plus ARB and hydrochlorothiazide provided best result where more than two drug was used. In our study various modifiable factors were strongly related to the development of ISH whereas only 6.36% study population were having family history of hypertension which suggest that hypertension and isolated systolic hypertension, both can be controlled with minor modification in our routine lifestyle.

KEYWORDS : isolated systolic hypertension, elderly, antihypertensive, modifiable factors.

Introduction

Hypertension exerts a considerable public health laden on cardiovascular health status and healthcare organizations in India [1, 2]. In a scrutiny of worldwide data for the global burden of Hypertension in India, it was found that 20.6% of men and 20.9% of women were agonize from hypertension in 2005 [3]. Isolated systolic hypertension (ISH), defined as an elevation in systolic blood pressure with normal diastolic pressure, was originally considered as part of aging like essential hypertension [4] but now it is reported that patients with isolated systolic hypertension are at substantially increased risk for stroke, coronary heart disease and congestive heart failure [5-6]. The prevalence and severity of the hypertension are strongly associated with the advancing age [7]. Women have lower systolic blood pressure levels than men during early adulthood, however, after menopause blood pressure increases in women to levels even higher than in men [8-9]. Obesity increases the risk of the development of hypertension and the occurrence of ISH may be higher among the subjects with obesity [10, 11, 12, 13]. The prevalence of coronary heart disease is significantly more in Hindu males as compared to the Muslims and is associated with a greater prevalence of diabetes and hypertension [14]. Occurrence of hypertension was highest among the low educated people, whereas it was minimum among the high educated individuals [15]. Several studies that have investigated the relationships between vegetarian diets and blood pressure have shown a lower blood pressure among vegetarians compared with non-vegetarians and red meat is the greatest risk factor for CVD [16, 17, 18]. Smoking is a strong independent risk factor for cardiovascular disease. Smoking causes an immediate increase in blood pressure and heart rate. The drastic effects of smokeless tobacco have been reported by increases up to 21 mm Hg in systolic blood pressure and 19 beats per minute in heart rate [19, 20, 21]. Prevention and treatment of ISH leads to lowering of cardiovascular morbidity and mortality [22]. Over the last few years, a paradigm shift has occurred, away from the prior concern over an elevation of diastolic pressure to our current awareness that an elevation of systolic pressure and, to an even greater extent, the combination of higher systolic and lower diastolic pressures (i.e. a widening of the pulse pressure) are the major determinants of cardiovascular risk in elderly [23]. Systolic hypertension has now been found to be related to the progression of peripheral atherosclerosis,

with lower progression rate among treated individuals. The high prevalence of mild systolic hypertension and its clear association with atherosclerotic disease and stroke suggest that older individuals with early systolic hypertension should be identified and treated [24]. However when the diastolic blood pressure are lowered too much by antihypertensive treatment similar increase in coronary event risk has been reported as due to high systolic hypertension [25]. Therefore the systolic blood pressure must be lowered but caution is needed not to lower already low diastolic pressure much further keeping these factors in mind the present study was undertaken to find out the drug or group of drug that can decrease the systolic blood pressure without much decrease in diastolic and pulse pressure and to evaluate the effect of various modifiable factors that may be associated with isolated systolic hypertension in elderly patients, implication of which may improve the quality of life and productivity in this population.

Material and Methods

This retrospective observational study was conducted on the patients attending medicine department between January-2015 to December-2016 at Hakeem Abdul Hameed Centenary Hospital, Jamia Hamdard, New Delhi, India. The study was designed to ascertain the prevalence of isolated systolic hypertension in the elderly population (≥ 50 years of age in male and female) and the most effective drug/drugs and various modifiable factors in treatment of isolated systolic hypertension in this population.

Inclusion Criteria: Elderly patients (≥ 50 years) / Patients with $> 150/90$ mm of Hg / All menopausal female with BP $> 150/90$ mm of Hg / Systolic blood pressure > 150 mm of Hg / Patients who agreed to give consent

Exclusion Criteria: Patient with age of < 50 years / Patients with $\leq 150/90$ mm of Hg / Patients with other chronic diseases (except diabetes / Patients who denied giving consent.

Data Collection: A case record form (CRF), was designed and reviewed by an expert panel, and was pre-tested on 25 patients and was scaled up for study. The data were collected using various data sources as OPD, IPD, and medicine ICU visited by the patients. Relevant clinical information were retrieved through personal interview with

the patients or his/her attendant, and medical prescribing records. Informed consent was taken from the patient prior to data collection. Social class was calculated using modified Kuppuswamy scale [26] in urban area. Classes 1 & 2 were considered as upper class and classes 3 & 4 were considered as middle class and 5 as lower class.

Result

Out of total 330 hypertensive elderly hypertensive enrolled for the study, 316 (96%) patients were followed and completed the study (11 were left and 3 died). The study sample comprised of 160 women (50.63 %) and 156 men (49.39 %). The prevalence of ISH in the study population was 39.87% (n = 126). For the analysis of association of ISH with various determinants, we compared subjects having ISH (n = 126) with total hypertensive with either both systolic and diastolic hypertension or diastolic hypertension alone (n = 316). Isolated systolic hypertension is more common in elderly female subjects 53.17% (n = 67) as compare to male 46.82% (n = 59), prevalence is significantly high in the age group of 61-70 years (41.26 %) [Table-1]

Role of various modifiable factors in the treatment of isolated hypertension in elderly:

The prevalence of isolated systolic hypertension was highest among the patients of group –IV socioeconomic class (i.e. upper-lower and lower-lower socioeconomic group) (42.84%), and among the patients whose education level were below graduation (48.41%) [Table -2]. Among the total 126) study subjects of isolated systolic hypertension 77.77% (n= 98) patients were obese and obesity was more common in female 62 (64.51%) compare to male 62 (64.51%) (Table-3). Prevalence of ISH was more common in which were red-meat eater 228 (72.15%).

Table.1: Relationship of ISH with age of the patient.

Age in Years	ISH (n = 126)	Total (n = 316)		
50-60	39	30.95%	106	33.54%
61-70	52	41.26%	138	43.67%
71- 80	31	24.60%	62	19.62%
>81	04	03.17%	10	03.16%

Table.2: Relationship with Socioeconomic class and level of Education with occurrence of ISH

Determinants	ISH (n = 126)	Total no of hypertensive (n = 316)			
		No	%	No	%
A. Socioeconomic class					
Upper Middle (II)	32	25.39	88	27.84	
Lower Middle (III)	40	31.74	102	32.27	
Upper Lower & Lower-lower (IV)	54	42.85	116	36.70	
B. Level of Education					
Illiterates	53	42.06	102	32.27	
Below Graduates	61	48.41	160	50.63	
Graduates	12	9.52	54	17.08	

Table-3: Relationship with obesity and ISH

Gender	Total Patients (n = 316)	Obese Patients	Obese with (ISH)
Male	156 (50.63%)	54 (34.61%)	36 (66.66%)
Female	160 (49.33%)	93 (58.12%)	62 (64.51%)
Total	316 (100%)	147 (46.51%)	98 (77.77%)

Table-4: Relationship with Non-vegetarian diet.

Gender	Total no. Of patients	Non-veg eater (n=264)	
		Red meat eater	Non-red meat eater
Male	156 (50.63%)	120 (76.92%)	36 (23.07%)
Female	160 (49.33%)	108 (67.50%)	52 (32.50%)
Total	316 (100%)	228 (72.15%)	88 (27.84%)

Antihypertensive utilization pattern in elderly patients: In single drug therapy, telmisartan is the most commonly prescribed antihypertensive agent in elderly population (23.14%) whereas amlodipine with atenolol combination is most frequently prescribed two drug combination therapy (19.44%) and Cilnidipine with Telmisartan and hydrochlorothiazide in three drug combination therapy (5.55%) (table.5).

Table.5: Drug utilization pattern.

Drug/drugs	No. of male	No. of female	Total
Amlodipine	12	06	18 16.66%
Cilnidipine	05	05	10 9.25%
Telmisartan	11	14	25 23.14%
Amlodipine + Atenolol	08	13	21 19.44%
Olmesartan + Hydrochlorothiazide	04	09	13 12.03%
Olmesartan + Metoprolol	04	04	08 7.4%
Cilnidipine + Telmisartan + Hydrochlorothiazid	02	04	06 5.55%
Olmesartan + Amlodipine + Metoprolol	04	01	05 4.62%
Losartan + Hydrochlorothiazide + Clonidine	02	00	02 1.85%

Efficacy of antihypertensive drug in elderly population: Out of nine different drug regimen used in our study population Telmisartan produced significant reduction in systolic blood pressure ($P < 0.005$) and adequate control of diastolic and pulse pressure, on the other hand a combination of amlodipine with atenolol produced significant reduction of systolic blood pressure ($P < 0.005$) with adequate control of diastolic and pulse pressure and in three drug regimen a combination of Cilnidipine, Telmisartan and hydrochlorothiazide produced adequate control of systolic blood pressure (table-6).

Table: 6: Effect of anti-hypertensive drugs on blood pressure.

Drug/drugs	Dose (mg)	Average BP before medication			Average BP after medication		
		Systolic	Diastolic	Pulse pressure	Systolic	Diastolic	Pulse pressure
GROUP – 1							
Single drug therapy							
Amlodipine	5	162	94	68	136	84	52
Cilnidipine	10	170	94	76	144	82	62
Telmisartan	40	166	92	74	128	78	50
GROUP – 2							
Two Drug therapy							
Amlodipine + Atenolol	5 50	176	96	80	138	82	56
Olmesartan + Hydrochlorothiazide	40 12.5	188	92	96	146	86	60
Olmesartan + Metoprolol	40 50	178	90	88	150	82	68
GROUP - 3							
Triple drug therapy							
Cilnidipine + Telmisartan + Hydrochlorothiazid	10 40 12.5	192	96	96	138	88	50
Olmesartan + Amlodipine + Metoprolol	40 5 50	200	102	98	170	94	76
Losartan + Hydrochlorothiazide + Clonidine	50 12.5 100 µg	204	98	106	154	90	64

Discussion

Uncontrolled or poorly controlled systolic hypertension is a major risk factor for cardiovascular morbidity and mortality in the elderly

population^[8]. Proper control of isolated systolic hypertension by using appropriate medicine and proper care may improve quality of life and productivity of the elderly population^[9,10]. In this study, all the patients included were belong to the elderly category^[11-12]. The study concluded that post-menopausal female are more prone to have isolated systolic hypertension as compared to men because of many reasons such as hormonal changes, body fat more in females than men^[13-14] and in this age female group are more obese than men^[15]. Priscilla et al., 2008 also has been reported that women have lower systolic blood pressure levels than men during early adulthood, while the opposite is true after the sixth decade of life which has been seen in our study.^[16] The development of isolated systolic hypertension (ISH) with increasing age is explained by a slump of arterial compliance^[17-18]. Pinto et al., 2007 has also concluded that there exists a significant association of ISH with age. The prevalence was highest in age group above 50 years^[19]. In our study highest numbers of patients showing isolated systolic hypertension were from age group 56-65 years followed by 50-55 years age group and it shows a significant correlation between isolated systolic hypertension and age and by this we can conclude that as the age increases the incidence of isolated systolic hypertension also increases.

Several modifiable socioeconomic determinants, such as literacy, education and occupation, are incorporated with hypertension. Supplementary socioeconomic status markers such as urban or rural billet and individual, local, national and international economic state are also correlated with hypertension, although these associations are knotty and at times somewhat conflicting. Possible clarification for this impact include awareness of hypertension prevention, control and superior accessibility and fidelity to medical treatment among higher socioeconomic status groups, as well as higher job stress more prevalent among lower socioeconomic status groups^[27]. In our study of socioeconomic status, 55.90% patients were from class IV followed by 30% patients were from class III and a negative correlation between socioeconomic status and systolic blood pressure was observed. Cue from the previous outcomes shows that lower socioeconomic status leads to higher probability of hypertension which resembles with our inferences.

In this study, out of 220 hypertensive patients maximum number of patients were from Hindu patients (72%) followed by Muslim patients (28%). Gupta R et al., 2002 has also supported that prevalence of Coronary heart disease is significantly more in Hindu males as compared to the Muslims and is associated with a greater prevalence of diabetes and hypertension^[28]. In Islam religion, Salah is the fundamental religious commitment of every Muslim to do five times a day at schedule time and conditions by following a proper order. The Salah positions have resembles Yoga positions the utmost effect of Salah on psycho-physiological and physical efficiencies of people offering regular Salah as provided by Yoga^[29].

Patient education has been influential and essential in bringing about stupendous improvements in mortality, morbidity, life expectancy, and life quality for society as a whole and for the individual^[30]. Gupta R et al., 2002 concluded in his study that the prevalence of illiteracy was high among the hypertensive population. Our findings also supported that illiterate patients are more prone to have hypertension as compared to literate patients. Hence, there is negative correlation between systolic blood pressure and education. The results mentioned above fit well into the wide array of studies that have examined the therapeutic value of patient education.

Obesity is strongly associated with hypertension and cardiovascular disease. Obese individuals are at higher risk of hypertension, renal failure, diabetes, and other cardiovascular diseases. Clinical and animal studies have established a strong relationship between obesity and hypertension^[31]. Accumulating evidence indicates to visceral obesity as the most important risk factor for hypertension and cardiovascular disease^[32-34]. David W. Harsha et al., 2008 has concluded that overweight and obesity are entrenched risk factors for cardiovascular disease, noninsulin dependent diabetes, stroke, certain cancers, and countless other disorders. It is also a risk factor for hypertension^[35]. In our study, among 220 hypertensive patients 134 (60.90%) were obese in which 65.67% female and 34.32% male.

There is a significant relation between obesity and isolated systolic hypertension. As previous studies depicted that fat contents are more in women than in men^[36] and after menopause in women, weight gain is also reported^[37] so these may be the primary reason for obesity in post-menopausal females. Smoking is a strong independent risk factor for cardiovascular disease. Smoking leads to an immediate increase in blood pressure and heart rate that remains for more than 15 minutes after one cigarette. People who smoke show raised ambulatory blood pressure levels than non-smokers. The drastic effects of smokeless tobacco have been reported by increases of up to 21 mm Hg in systolic blood pressure and 14 mm Hg in diastolic blood pressure and by an average increase of 19 beats per minute in heart rate^[24]. Various factors are associated with ISH, including smoking status, hence lifestyle modifications will be of benefit in the control of ISH^[38]. Quitting is conceded to be one of the most effective lifestyle interventions for intercepting cardiovascular disease and premature deaths. In our study out of 220 hypertensive patients, 90 patients (41%) were tobacco user, it indicates significant correlation was seen between tobacco user and isolated systolic hypertension which is in line with the aforementioned findings.

Limiting dietary sodium and use of the Dietary approaches to stop Hypertension (DASH) have been shown to be effective in reducing blood pressure in hypertensive individuals^[39]. Reduction of red meat consumption may be a promising method for hypertensive patients to manage their blood pressure and improve their health. The connection between red meat and hypertension is important across cardiovascular dietary studies. Several dietary studies have shown that increased red meat i.e. beef, veal, pork consumption leads to increased blood pressure^[40-42]. In our study 152 (69.09%) patients were non-veg eater and among them 128 (58.18%) were red meat eater.

Among the non-veg eater, male patients were found comparatively higher than female patients. A significant correlation was found between non-veg eater and SBP. Several studies that have investigated the relationships between vegetarian diets and blood pressure have shown a lower blood pressure among vegetarians compared with non-vegetarians which confirm our findings^[39,43,44]. In this study 190 (86.36%) patients were junk food eater out of 220 hypertensive patients. There was a positive correlation between junk food eater and isolated systolic hypertension. Junk food contains high level of white flour, refined sugar, salts, polyunsaturated fats and numerous food additives, but lacking in protein, vitamin and fibers^[45] and all this leads to obesity which is directly correlated with HTN. Junk food or fast food both correlated with obesity and low nutrient quality which leads to increase in hypertension indirectly^[46,47]. Evidence from the previous investigations supports our upshots that junk food plays a significant role in the development of hypertension.

Recent work suggests that a high pulse pressure is an important risk factor for heart disease. A meta-analysis in year 2000, which combined the results of several studies of 8,000 elderly patients in all found that a 10 mm Hg increase in pulse pressure increased the risk of major cardiovascular complications and mortality by nearly 20%^[7,20]. The authors of the meta-analysis suggest that this helps to explain the apparent increase in the risk of heart disease sometimes associated with low diastolic pressure and warn that some medications for high blood pressure may actually increase pulse pressure and risk of heart disease. In our study we found that calcium channel blocker (amlodipine or Cilnidipine) alone or in combination with beta-blocker (atenolol) or ARB (Telmisartan) and thiazide diuretic (Hydrochlorothiazide) produced good control of systolic blood pressure with adequate changes in diastolic pressure and pulse pressure. As per JNC-7 criteria the drug of choice for the treatment of systolic hypertension is a combination of low dose thiazide diuretic with calcium channel blocker but in our study this combination is not used which may be due to physician experience with these drugs because use of hydrochlorothiazide may benefit these patients especially post-menopausal women to prevent development of osteoporosis. Further study is needed to see the long-term morbidity and mortality in these patients provide better evidence of drug of choice in these patients.

Conclusion

This study concluded that elderly population is at higher risk of high

systolic blood pressure with increased risk of cardiovascular and cerebrovascular complications and various factors like increasing age, higher BMI values, junk food, red meat or non-vegetarian diet, literacy, socioeconomic status and smoking were significant independent predictors of ISH as revealed by this study. Proper treatment by single drug or combination of drugs that maintains systolic blood pressure with adequate control of pulse pressure like angiotensin receptor blockers (e.g. Telmisartan, olmesartan etc.) or a combination therapy calcium channel blocker, ARB and Hydrochloro thiazide especially in post-menopausal women who are at greater risk of systolic hypertension as it provides additional beneficial in prevention of osteoporosis. Further study is needed to see the long-term effect of these drugs.

This study emphasizes the need for further research on drugs which are available and showing splendid effect out of other anti-hypertensive drugs to document the impact of modifiable risk factors of ISH and the effect of primary prevention in bringing down the burden of ISH by preventing at the initial stage and improving the effect of anti-hypertensive drugs for resistant hypertension. By running the educative program on television or radio network regarding weight reduction and cessation of smoking may be considered as a cost effective public health approach in dealing with the morbidity attributed to ISH and cardiovascular diseases and this approach will reduce the risk of cardiovascular disease associated with ISH. This was a Retro prospective observational study designed to formulate the hypothesis for future research. This study is only a start for the upcoming research in the field of non-communicable diseases and indicates the insidious presence of ISH in the elderly population and the underlying factors, which may be responsible for its occurrence.

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