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A COMPARATIVE ASSESSMENT OF THE EFFICACY OF VARIOUS ANTIHYPERTENSIVE DRUGS ON ISOLATED SYSTOLIC BLOOD PRESSURE IN ELDERLY.

[1]Sana Rehman, *[1]Razi Ahmad and [2]Anwar Habib

[1]Department of Pharmacology, HIMSR, Jamia Hamdard, New Delhi.
[2]Department of Medicine and Head Dialysis Unit, HIMSR, Jamia Hamdard, New Delhi.

***Corresponding Author: Dr. Razi Ahmad**
Department of Pharmacology, HIMSR, Jamia Hamdard, New Delhi.

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ABSTRACT
Isolated systolic hypertension (ISH), is defined as an elevation in systolic pressure but normal diastolic pressure, and was originally considered part of aging like essential hypertension. Patients with isolated systolic hypertension are at substantially increased risk for stroke, coronary heart disease and congestive heart failure, elderly population is at increased risk Isolated systolic hypertension is a major problem in the elderly population, The prevalence and severity of the hypertension are strongly associated with the advancing age. 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. Uncontrolled or poorly controlled systolic hypertension is a major risk factor for cardiovascular morbidity and mortality in the elderly population. Proper control of isolated systolic hypertension by using appropriate medicine and proper care may improve the quality of life and productivity of the elderly population. Most of the drug used for the treatment of hypertension affect both systolic and diastolic blood pressure. In elderly population a 10mm Hg increase in pulse pressure increases the risk of cardiovascular complication and mortality by nearly 20%. The aim of the present study was to find out drug or combination of drugs that is most appropriate in controlling systolic blood pressure with adequate maintenance of pulse pressure and we found that angiotensin receptor blocker (Telmisartan), as single drug therapy, calcium channel blocker (amlodipine) in two drug combination therapy and calcium channel blocker in combination of ARB and hydrochlorothiazide provided appropriate control of systolic blood pressure and pulse pressure, further study is needed to establish their long-term morbidity and mortality profile.

KEYWORDS: isolated systolic hypertension, Elderly, antihypertensive.

INTRODUCTION
Isolated systolic hypertension is the predominant type of hypertension in elderly and is associated with increased risk of cardiovascular complications such as stroke, coronary artery disease and congestive heart failure.[1,2,3,4,5]

The prevalence and severity of the hypertension are strongly associated with the advancing age.[6] 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.[7-8]

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.[9] 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 suggest that older individuals with early systolic hypertension should be identified and treated. However when the lower diastolic blood pressure are lowered too much by antihypertensive treatment similar increase in mortality rates has been reported as due to high systolic hypertension there for the systolic blood pressure must be lowered but caution is needed not to lower already low diastolic pressure much further. Therefore the main aim of this study was to find the drug or group of drug that can decrease the systolic blood pressure without much decrease in diastolic and pulse pressure.[10]

Study design and Methodology

The study was conducted at Hakeem Abdul Hameed Centenary Hospital, Jamia Hamdard, New Delhi, India after the approval of IRB (27-July, 2015 (13/16). It was a single centered prospective observational study conducted between August-2015 to July-2016 (one year) the study was designed to ascertain the prevalence of hypertension in elderly population (> 50 years of age) in the south Delhi, a capital city in India and the most effective drug or group of drug in controlling systolic blood pressure and pulse pressure.

Inclusion criteria

a) Elderly patients both male and female of ≥ 50 years of age
b) Patients with > 160/90 mm of Hg
c) Systolic blood pressure >160 mm of Hg
d) Patients who agreed to give the consent were included

Exclusion Criteria

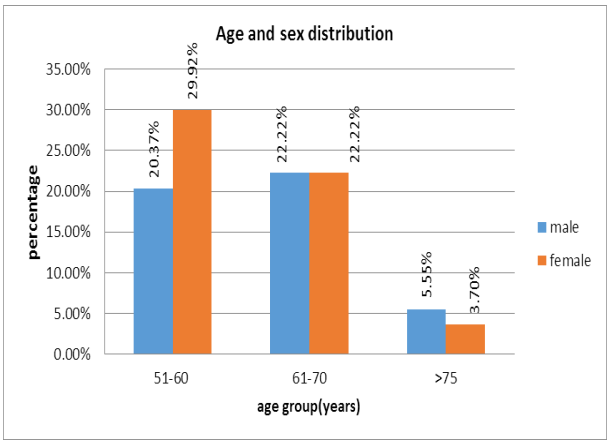
a) Patient with age of < 50 years
b) Patients with ≤ 160/90 mm of Hg
c) Those patients who will not agree to give his consent
d) Patients with other chronic diseases

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/MICU visited patients. Relevant clinical information were retrieve through personal interview with patients or his/her attendant, Medical prescribing records, patient's medication profile/treatment chart and Laboratory investigation reports (if available). Informed consent was taken from the patient prior to data collection.

RESULT

A total 290 hypertensive patients attended the medicine clinic of HAHC hospital during the study period 117 were having isolated systolic hypertensive (40.34%). Out of 117 patients with isolated systolic hypertension (ISH) enrolled 108 (92.3%) were followed and completed the study (8 were left and one died in road traffic accident). The study sample comprised of 56 female (51.85%) and 52 male (48.1%) fig.1.



Antihypertensive utilization pattern in elderly patients

Telmisartan was the most commonly prescribed antihypertensive agent in elderly population (23.14%) whereas amlodipine with atenolol (19.44%) prescribed two drug combination therapy and Cilnidipine with Telmisartan and hydrochlorothiazide (5.55%) in three drug combination therapy (table.1).

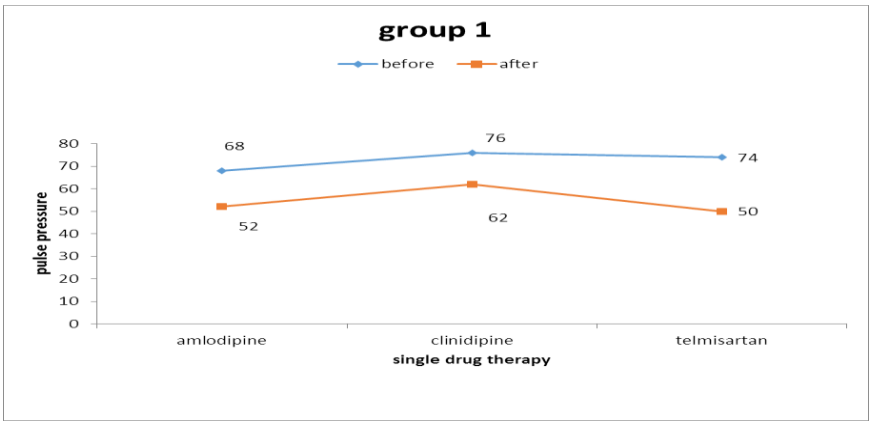
Table.2: Drug utilization pattern.

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 + Hydrochlorthiazide	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 + Hydrochlorthiazide + Clonidine	02	00	02	1.85%

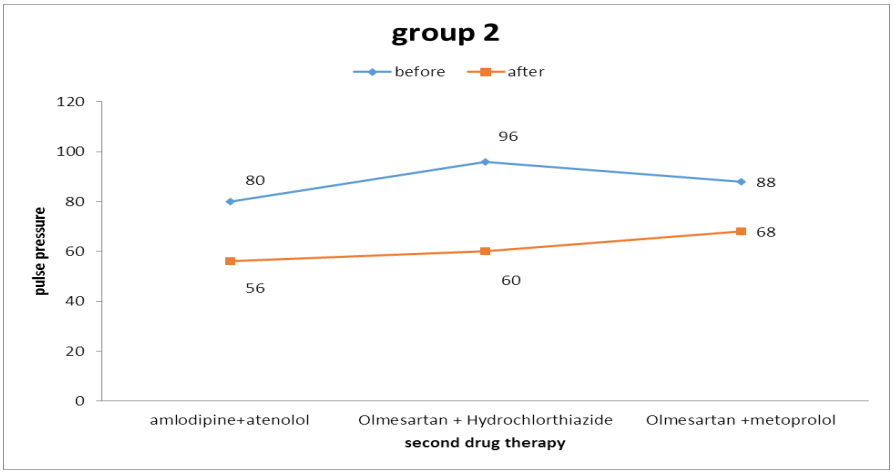
Efficacy of antihypertensive drug in elderly population: out of nine different drug regimen used in our study population Telmisartan produced significant reduction in systolic blood pressure (P < 0.005) and adequate control of diastolic and pulse pressure, on the other hand a combination of amlodipine 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-3a,b,c).

Table: 3-a. Effect of anti-hypertensive drugs on blood pressure.

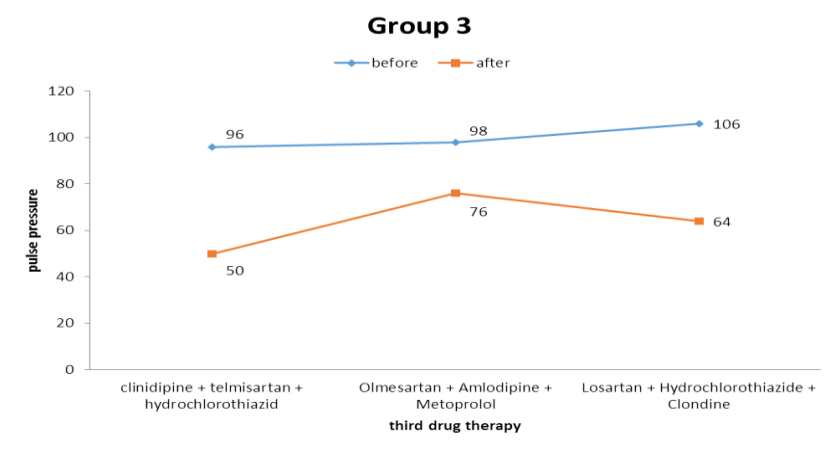
Drug/drugs	Dose (mg)	Average BP before medication			Average BP after medication		
		Systolic	Diastolic	Pulse pressure	Systolic	Diastolic	Pulse pressure
GROUP – 1							
Single drug therapy							
Amlodipine	5	162	94	68	136	84	52
Cilnidipine	10	170	94	76	144	82	62
Telmisartan	40	166	92	74	128	78	50



GROUP – 2							
Two Drug therapy							
Amlodipine + Atenolol	5 50	176	96	80	138	82	56
Olmesartan + Hydrochlorthiazide	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 + Hydrochlorthiazide + 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 controlled of isolated systolic hypertension by using appropriate medicine and proper care may improve the quality of life[9] and productivity of the elderly population.[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, many reasons are there, 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 is in agreement with our findings.[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 and age. The prevalence was highest in ≥50 year's age group.[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 which is consort with the aforementioned upshots.

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 risk 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 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 first choice for the treatment of systolic hypertension a combination of low dose thiazide diuretic with calcium channel blocker but in our study this combination is not used this may be because of 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 patient provide better evidence of drug of first choice in these patients.

CONCLUSION

This study concluded that elderly population is at higher risk raised systolic blood pressure with increased risk of cardiovascular and cerebrovascular complications and needs proper treatment by drug or combination 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 Hydrochlorothiazide especially in post-menopausal women who are at greater risk of systolic hypertension and hydrochlorothiazide will provide additional beneficial in prevention of osteoporosis. Further study is needed to see the long-term effect of these drugs. post-menopausal women are at increased risk of raised systolic blood pressure and needs proper care with drug like.

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