



Efficacy of Monotherapy Versus Combination Therapy in Isolated Systolic Hypertension

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Abstract

OBJECTIVE: To assess the efficacy of monotherapy and combination drug therapy on Isolated Systolic Hypertension in Elderly. **MATERIALS AND METHODS:** A cross sectional study was conducted among patients attending the geriatric outpatient department in a tertiary care hospital. The medical records of a total of 530 subjects were screened, out of which 124 individuals were found to have Isolated Systolic Hypertension as per the inclusion criteria. Due to poor drug compliance 24 patients were excluded from the study. 100 patients with ISH were categorized on the basis of the antihypertensive drugs they were receiving. The response to therapy was measured in terms of Control of BP. The study was conducted over a period of 6 months. A detailed history was obtained from all patients including their complaints, co-morbid illnesses, medications and personal history. The blood pressure response to various drugs was analysed. **RESULTS** In the total study population of 100 patients 32 patients were on monotherapy and 68 patients were on a combination of antihypertensive drugs. Among patients receiving monotherapy, 56.25 percent were on Calcium channel blockers, 31.25 percent on ACE inhibitors and 12.5 percent on Beta blockers. BP control was comparatively higher among those on calcium channel blockers. In subjects on a combination of antihypertensives, 54 percent were on ACE inhibitors and Calcium Channel Blockers and 46 percent on ACE inhibitors, Calcium channel blockers and Beta blockers. The former group was found to be more effective in BP control. **CONCLUSION** In patients receiving monotherapy, Calcium channel blockers were found to have better efficacy when compared to other drug groups. In combination therapy, patients on ACE inhibitors and Calcium channel blockers were found to be more effective.

Keywords: Isolated Systolic Hypertension, Blood Pressure, Antihypertensive drugs

Introduction

Until the 1980's the diastolic blood pressure (DBP) was assumed to be the most relevant hemodynamic parameter for prognosis of hypertensive patients and elevated systolic pressure was considered as an inevitable consequence of aging.

There was a radical change in thinking based on epidemiological studies which led to recognition of elevated systolic blood pressure (SBP) as an important prognostic factor in Cardiovascular morbidities. The term isolated systolic hypertension (ISH) has been introduced particularly in elderly subjects, since SBP is known to rise with advancing age where as diastolic blood pressure (DBP) usually levels off and tends to decrease in elderly. According to the National Health and Nutrition Examination Survey (NHANES) III, ISH is the most prevalent type of untreated hypertension over 60 years of age. ISH represents a substantial health care problem as the target BP is very difficult to attain by drug therapy. Increased arterial stiffness is the vascular phenotype of systolic hypertension, especially of the large arteries. Elevated systolic blood pressure is even more associated with cardiovascular morbidity and mortality than diastolic blood pressure. Treatment of systolic hypertension in the elderly should be based on nonpharmacological measures and medical therapy if the systolic hypertension cannot be controlled by conservative therapy alone. The HYVET study (4) provided evidence-based medicine data showing that, in the very elderly, lowering blood pressure to a level of 150/80 mmHg is still very beneficial. Antihypertensive therapy needs to be tailored in the elderly because of comorbid conditions, such as ischemic heart disease, heart failure, atrial fibrillation, renal insufficiency and diabetes. Angiotensin-converting enzyme inhibitors or angiotensin II-receptor blockers should be considered in combination with diuretics or with a dihydropyridine calcium antagonist. Beta blockers seem to be less effective for cardiovascular disease protection in comparison with other antihypertensive drug classes, such as diuretics, dihydropyridines, angiotensin converting enzyme inhibitors or angiotensin II-receptor blockers. Major effort is required to reduce the therapeutic inertia and increase therapeutic adherence for better blood pressure control in the elderly with systolic hypertension.

Materials and Methods

A cross sectional study was conducted among patients attending the geriatric outpatient department in a tertiary care hospital. The medical records of a total of 530 subjects were screened, out of which 124 individuals were found to have Isolated Systolic Hypertension as per the inclusion criteria.

Due to poor drug compliance 24 patients were excluded from the study. The inclusion criteria for the study was as follows: Patients aged 65 years and above with blood pressure of systolic BP>140 mmHg and diastolic BP <90 mm Hg, at initial diagnosis, with good drug compliance. The study was conducted over a period of 6 months. A detailed history was obtained from all patients including their complaints, co-morbid illnesses, medications and personal history. Blood pressure readings were taken at two visits and averaged. The blood pressure response to various drugs was analysed.

Data Analysis

Category	Systolic Blood Pressure (MmHg)	Diastolic Blood Pressure (MmHg)
Optimal blood pressure	<120	<80
Normal blood pressure	<130	<85
High-normal blood pressure	130-139	85-89
Grade 1 hypertension (mild)	140-159	90-99
Grade 2 hypertension (moderate)	160-179	100-109
Grade 3 hypertension (severe)	>= 180	>= 110

The data collected for 100 subjects with ISH was analysed. The patients were classified according to the severity of isolated systolic hypertension. They were then categorised based on the type of medication (monotherapy versus multiple drugs). The response to therapy was taken as Controlled BP (Systolic BP<140mm Hg and Diastolic BP <90mmHg) or Uncontrolled BP (Systolic BP>=140 mmHg and Diastolic BP >=90 mmHg)

Results

1. The mean age of the study population was 69.2 years.

2. 55% of the subjects were men and 45% were women.

3. 32% of the group had stage 1 ISH, 48% had stage 2 ISH and 20% had stage 3 ISH.

4. 32% of the study population were on monotherapy and 68% were on a combination of antihypertensive drugs.

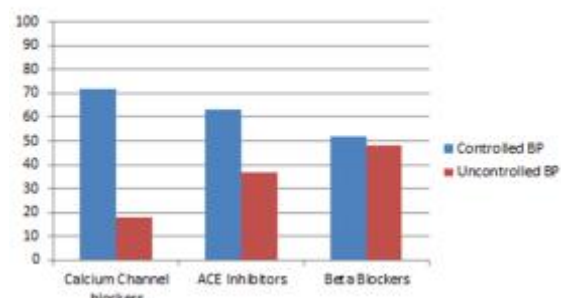
5. Among patients receiving monotherapy, 56.25% were on Calcium channel blockers, 31.25% on ACE inhibitors and 12.5% on Beta blockers.

6. The proportion of patients with Controlled BP and Uncontrolled BP in monotherapy: -Calcium channel blockers group (72% vs 18%)

-ACE Inhibitors (63% vs 37%)

-Beta Blockers (52% vs 48%)

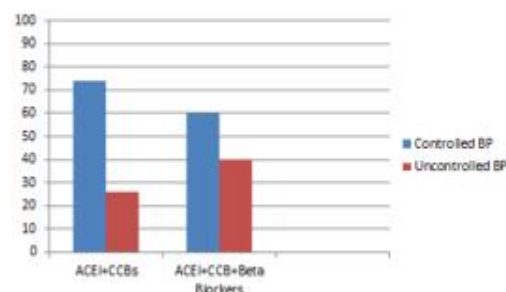
MONOTHERAPY IN ISH



7. In subjects on a combination of antihypertensives, 54% were on ACE inhibitors and Calcium Channel Blockers and 46% on ACE inhibitors, Calcium channel block and Beta blockers

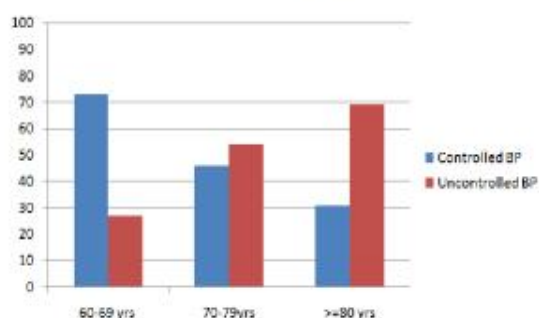
8. The proportion of patients with Controlled BP and Uncontrolled BP in the following groups on combination therapy was-
 -ACE inhibitors, Calcium Channel Blockers (74% vs 26%)
 -ACE inhibitors, Calcium channel blockers and Beta Blockers (60% vs 40%)

COMBINATION THERAPY IN ISH



9. With increasing age, the proportion of patients with uncontrolled BP was found to increase.

AGE AND ISOLATED SYSTOLIC HYPERTENSION



Discussion

In our study 32% of the study population was found to have blood pressure not controlled with medication. According to the analysis based on National Health and Nutritional Examination Survey (NHANES III) a study on Predominance of Isolated Systolic Hypertension Among Middle-Aged and Elderly US Hypertensives revealed that isolated systolic hypertension was the most frequent subtype of uncontrolled hypertension (65%). In the Systolic Hypertension in Elderly (SHEP) trial (1)(3), mean age of all the patients was 72 years and mean BP was 170/77 mm Hg. In the present study the mean age of all patients with Stage I ISH was 67.5 years, Stage II ISH was 73.1 years and Stage III ISH was 76.9 years. Messerly FH et al and Anery A et al found that the prevalence of ISH increases with age from 5% in subjects at 60 years to 25% in subjects aged 80 years. Among the patients who were receiving monotherapy, majority of the subjects were on calcium channel blockers. A higher proportion of cases were found to have adequate BP control in the Calcium channel blockers group (72%) when compared to ACE inhibitors (63%) and Beta Blockers (52%). According to the Systolic Hypertension in Europe (SYST-EUR) Trial (2) active treatment with the calcium antagonist nitrendipine (with optional add on enalapril and /or hydrochlorothiazide) was compared with placebo, in a double blind randomized design. A significant reduction (by 42%) in the incidence of stroke and vascular dementia (by -50%) by nitrendipine treatment was found. In the present study, among patients receiving combination drug therapy for ISH, the results were as follows: In the group on ACE inhibitors and calcium channel blockers, BP control was seen in 74% subjects. In the second group on ACE inhibitors, Calcium channel blockers and Beta Blockers adequate control of BP was found in 60% subjects.

Conclusion

In patients receiving monotherapy, Calcium channel blockers were found to have better efficacy when compared to other drug groups. In combination therapy, patients on ACE inhibitors and Calcium channel blockers were found to be more effective in achieving BP control. Isolated Systolic hypertension is a major health concern in the geriatric population. It gains importance due to the fact that it is highly prevalent in the ageing population, it is difficult to treat with both conservative and medical therapy and it is a risk factor for various co-morbidities like Coronary Heart Disease, Stroke, Chronic Kidney disease etc. Apart from diet control, avoidance of smoking and adequate physical exercise, antihypertensive drugs especially calcium channel blockers have been found to be useful in ISH. A combination of drugs is usually required according to the comorbidities present in the individual.

References

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1. Were your patients already on antihypertensives? If so, then your inclusion criteria is incorrect.

Ans. The patients included in this study were known cases of Isolated Systolic hypertension. We have examined their medical records in which their Blood pressure at initial diagnosis was Systolic BP >140 mmHg and diastolic BP <90 mmHg and were started on antihypertensives then itself. We have done a cross sectional study to see the level of BP control they have achieved with different groups of antihypertensives.

2. What were their comorbidities, which will influence your choice of drugs?

Ans. 64 out of 100 patients with ISH were found to have the following comorbidities. Coronary Artery disease (38 patients), stroke (13 patients), Diabetes mellitus (42 patients), Chronic Kidney Disease (20 patients), Chronic obstructive pulmonary disease (12 patients), Dyslipidemia (18 patients), Atrial Fibrillation (3 patients)

3. Read up JNC 8 and uptodate on Treatment of hypertension in the elderly.

Ans. According to uptodate and the recent JNC 8 guidelines, in patients 60 years or over, treatment should be started if systolic BP \geq 150 mmHg or Diastolic BP \geq 90 mmHg. Our study was carried out before these guidelines were brought out. We have taken a cut off of 140 /90 mmHg for BP control.

4. How did you measure compliance?

Ans. Compliance of patients was assessed by the following: Regular visits to the OPD, Monthly BP recordings, Blood Investigations as and when necessary, Patient's knowledge regarding dosage and timing of drugs.

5. How many patients needed more than one drug. Did you rule out secondary causes of hypertension.

Ans. 68 patients needed more than one drug and 32 patients were on monotherapy. We did not evaluate the patients for secondary causes of hypertension.

6. Why did you choose only Ca channel blockers, ACE inhibitors and Beta blockers?

Ans. We have used these drugs as they were the only ones available in the hospital during the study period.

7. 7. Did you give them advice on lifestyle modification?

Ans. Lifestyle modification measures such as salt restricted diet, weight reduction, physical exercise, avoidance of smoking are advised to all patients before starting them on antihypertensive medications.

8. 8. When did you add the second and third drug?

Ans. When BP control was not achieved with lifestyle modification and single antihypertensive drug therapy, the second and third drugs were added according to their comorbidities. This was done already prior to the start of this study.