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Review Article

Isolated Systolic Hypertension

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Abstract

Isolated systolic hypertension (ISH) is a problem of major public health concern as its incidence is increasing. It is difficult to control and is an important risk factor for cardiovascular disease. This article discusses the pathophysiology behind ISH and how to go about treating this condition. The article also discusses about ISH in the young, which is a totally different entity with respect to pathophysiology and treatment.

Key words: Hypertension, systolic, isolated

Introduction

Isolated systolic hypertension (ISH) is defined as systolic blood pressure (SBP) of >140 mmHg with a diastolic blood pressure (DBP) of <90 mmHg.[1] It is the most common and the most difficult form of hypertension and is a public health problem of major proportion. If we consider the frequency of untreated hypertension according to subtype and age, ISH is the most common form of untreated hypertension above the age of 50 years. Above the age of 80 years, more than 90% of all untreated hypertension is ISH.[2]

There are several unanswered questions about ISH. Does ISH develop *de novo* in older people or is it a naturally occurring stage in the hypertensive process? Data from Framingham study showed that about 40% of patients with ISH were conversion from untreated or poorly controlled diastolic HTN at young age. The majority acquired ISH without going through a stage of elevated DBP.[3]

SBP

Elevation of both SBP and DBP predicts an increased risk of cardiovascular (CV) events. However, raised SBP is more important and the prognostic value of SBP increases with age.[4] It becomes greater than DBP in the elderly individuals.[5] Raised SBP was once thought to be benign accompaniment of aging. However, now, we know that it increases the risk of CV events. Recent guidelines, therefore, give more importance to SBP in the diagnosis and treatment of HTN, especially in the elderly.[6]

SBP increases progressively with advancing age, while DBP tends to decline from the sixth decade, irrespective of ethnicity and sex.[4] Thus, there is an increase in the prevalence of ISH with age. 60% of older patients with HTN have ISH. Elevated SBP is the key risk factor for CV disease, CV, and all-cause mortality and declines in renal function.[7] Lowering elevated SBP improves CV and renal outcomes regardless of any concomitant reduction in DBP.[8]

As SBP goes up and DBP comes down, the pulse pressure (PP) starts widening. For each 10 mmHg increase in PP, there was an 11% increase in the risk of stroke.

For each 10 mmHg increase in mean arterial pressure (MAP), there was an independent 20% increase in the risk of stroke. Thus, both PP and MAP are independent predictors of stroke and all-cause mortality.[9]

Independent predictors of incident ISH include older age, female gender, higher baseline SBP, lower baseline DBP, longer duration of hypertension, greater arterial stiffness, higher intima-media thickness of the carotid artery, and higher cardiac mass.[10]

DBP

The invariable result of aggressive control of SBP in ISH is the excessive fall in DBP. Secondary analysis of elderly SPRINT[11]

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participants showed that DBP in the intensive-therapy arm fells to 62 mmHg. There was no trend toward myocardial damage or CHD among those with DBP <60 mmHg and SBP <120 mmHg. Maybe the low systolic pressure, by reducing the myocardial oxygen demand, protected against a low diastolic pressure.

Vascular Changes with Aging

Normal aging causes generalized arterial stiffening. Elastin becomes thinner, fragmented, and degraded and is replaced by collagen, which is much stiffer. Pressure wave now travels faster along the stiffened arterial system.

Vascular inflammation, fibrosis, hypertrophy, collagen deposition, and elastin degradation occur with aging. These processes dilate the vessel lumen and increase the wall thickness.[12] There are a loss of arterial elasticity and a reduction of compliance. There is also loss of endothelial function. This results in reduced production of vasodilator factors (nitric oxide, natriuretic peptides, and so on) and increased production of vasoconstrictor substances (endothelins, norepinephrine, and so on).[13] Alterations in large artery structure and function are accelerated by risk factors such as hypertension, diabetes, and dyslipidemias. This results in early vascular aging in people with uncontrolled risk factors.[14]

The Pulse Wave

The morphology of any pulse wave is the summation of incident (forward-traveling) and reflected (backward-traveling) pressure waves. Timing of backward travelling wave depends on the pulse wave velocity and the distance to the predominant or "effective" reflecting site. In young healthy adults, SBP and PP at the brachial artery are higher than in the ascending aorta. This is because the reflected wave reaches brachial artery earlier, in systole itself. By the time it reaches the ascending aorta, it has become diastole. Hence, the brachial artery systolic pressure is the sum of forward wave and reflected wave, while SBP in the ascending aorta is only forward wave. Hence, there is pressure amplification from the aorta to the brachial artery. The other reasons for the higher pressure in the brachial artery include the increase in arterial stiffness as we go from the elastic ascending aorta to the stiffer peripheral vessels and the smaller diameter of the peripheral vessels.[15] As age advances, vessels become stiff and inelastic. Hence, the SBP starts going up. The vessels cannot dilate to accept the cardiac output in systole without increasing the pressure. Furthermore, the inelastic vessels have a higher pulse wave velocity. The reflected wave, hence, reaches the ascending aorta in systole itself, augmenting the SBP. The DBP falls because the normal support given by the reflected wave is absent in diastole. The PP rises.

Impact on Target Organs

The high SBP and low DBP lead to excessive pulsatility. The high pulsatile BP/flow is not absorbed by the large artery walls and is transmitted to the microcirculation of the brain, kidney, and heart. This causes structural damage to the tissues and functional derangement of the organs.[16] An increase in SBP also increases left ventricle (LV) afterload and oxygen demands. Final result will be LV hypertrophy and failure, myocardial ischemia, chronic heart failure, and arrhythmias.[17]

The increased pulsatility and the reduced ability of the vessels to distend enhance the traumatic effect on the large artery wall and favor an increase in endothelial permeability and initiate formation of an atherosclerotic plaque.[13]

Evidence for the Benefits of Treatment in Ish

The first major trial in ISH was the systolic hypertension in the elderly program (SHEP).[18] This was the first clinical trial to demonstrate the beneficial effects of treatment in ISH. Chlorthalidone (with the addition of a beta blocker if needed) was the treatment regimen used. SBP was reduced by approximately 26 mmHg. There was a significant reduction in stroke (36%), coronary heart disease (25%), and heart failure (49%). Other important trials, which showed benefits of treatment, include systolic hypertension in Europe study,[19] systolic hypertension in China study,[20] the Swedish trial in old patients with hypertension (STOP-hypertension-2),[21] and hypertension in the very elderly trial.[22] Even though the drugs used in these trials were different, the results were identical. This proved that reducing SBP was important in the elderly with ISH, irrespective of the drug used. Substudy on the elderly in the SPRINT[11] also showed benefits of aggressive SBP reduction, especially in reducing the incidence of heart failure.

Management

Dihydropyridine calcium channel blockers (CCBs) and thiazide-like diuretics are the preferred first-line drugs. ACEI/ARB should be used in situations with compelling indications such as heart failure, post-myocardial infarction, or albuminuria. Beta-blockers are better avoided. Optimal blood pressure has not been well studied, but SBP goal of <140 mmHg is generally accepted. It is better to individualize the target for each patient depending on the comorbidities and the tolerability and the clinical response.[23]

Atrial Fibrillation (Af) and ISH

The prevalence of AF increases with age and approximately doubled for every 10-year increment in the age beyond 50 years. The prevalence is around 5% above the age of 70 years.[24]

Arterial hypertension is an independent risk factor for developing AF.[25] In the SHEP trial, 2.06% developed AF over 4.5-year follow-up, 1.82% in the active treatment group, and 2.32% in the placebo group ($P = 0.2$). The mean of all systolic BP measurements during 4.5 years of follow-up was significantly higher in the AF group. Poor blood pressure control increased the risk of developing AF. Subjects who developed AF were significantly older, had more electrocardiography abnormalities at baseline, and were more likely to experience CV events, left

ventricular failure, and rapid death. All-cause and total CV mortality were significantly increased in the hypertensives who developed AF at both 4.7-year and 14.3-year follow-up.[26]

ISH in the Young

Clinical significance of high SBP in the first decades of life is debatable. There is a lack of a consistent definition of young age. The prevalence of ISH in the general adult population follows a typical J-shaped pattern with a nadir in the fifth decade. There is a steep increase in SBP after 70 years of age. There is an earlier peak, though of lower magnitude, below 30 years of age. There is a steep increase in SBP during childhood, followed by a plateau phase between 20 and 40 years, and then a subsequent increase. PP decreases in the age range between 20 and 40 years.[27,28] Higher baseline SBP predicts steeper increases in aortic stiffening and the future risk of hypertension in both adolescence and adulthood.[29] ISH in individuals <16 years is defined as SBP at least 95th percentile and DBP <90th percentile for the age, sex, and height.[30] It is often correlated to overweight and obesity.

ISH in the young is thought to have different mechanisms than ISH of the elderly. It is a very heterogeneous condition and includes individuals with totally different genetic background and clinical characteristics. It remains unclear as to whether this condition implies a worse outcome or needs antihypertensive treatment. ISH in the young is associated with and caused by multiple factors that can operate in isolation or interact. These include a hyperkinetic heart, a selective increase in heart rate or stroke volume, and an increase in arterial stiffness above the values regarded as normal for young age ranges.[31]

Isolated SBP elevation at the level of the brachial artery with normal central BP did not exhibit a greater CV risk or progression to systolic–diastolic HTN. Antihypertensive treatment is recommended if target organ damage is present or if central aortic BP is also raised.[31] The 2013 European guidelines recommend following these people closely, modify risk factors by lifestyle changes, and avoid antihypertensive drugs.[6]

Conclusion

ISH is increasing in prevalence as the population of the elderly increases. It is difficult to treat and is an important risk factor for CV and renal diseases. The basic pathology is increased arterial stiffness. Several trials have shown benefit, even in the elderly, by treating ISH. Very low DBP is a concern, but elderly subgroup analysis of SPRINT showed no adverse effects with a DBP of 60 mmHg. CCBs and diuretics are the drugs of choice. ISH in the young is a different entity with different pathologies and different prognoses. ISH in the young has to be treated only if the central aortic blood pressure also is high or if there is evidence of target organ damage.

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