

## SYSTOLIC BLOOD PRESSURE

Systolic Blood Pressure (SBP) results from gradual decrease in diameter and stiffening of the proximal to the distal arterial vessels and mostly of the modification in the transit of wave reflections. The importance of central SBP (cSBP) is greater than brachial pressure as it is more closely associated with left ventricular hypertrophy and carotid atherosclerosis; it is a marker of end-organ impairment in hypertensive patients (Figure 1).

## SIGNIFICANCE OF SBP

SBP has steadily gained importance in the last 10 to 15 years as many studies have revealed that it is a better indicator of cardiovascular disease in individuals above 50 years of age. The stiffening of the larger arteries in the elderly leads to elevation of SBP. The measurement of SBP is more precise than the measurement of diastolic blood pressure (DBP). If the hazards of high BP are concentrated on the former aspect, the clinicians will have greater clarity in measuring thresholds and setting objectives for their patients.

## THE NEED FOR EMPHASIS ON SBP CONTROL

According to 2013 ESH/ESC Guidelines for the management of arterial hypertension, hypertension (HTN) is described as BP measurement  $\geq 140/90$  mmHg. SBP in individuals suffering from pre-hypertension is between 120-139 mmHg. The prospects of major cardiovascular events like myocardial infarction (MI),

stroke and congestive heart failure (CHF) are also high in such population (supplementary hazards like diabetes mellitus, high body mass index (BMI) and physical inactivity are other contributing factors).

## CHALLENGES IN CONTROLLING SBP

The main factors that hinder the control of high SBP in are:

1. Stiffening of large arteries: The basic mechanism for the progressive rise in systolic blood pressure with age is the loss of distensibility and elasticity in the large capacitance vessels.
2. Reflected wave: As the pulse waves travel more rapidly and are reflected backwards from the periphery more quickly, a secondary boost is seen during systole in older patients. The early return of reflection increases pressure in late systole, leading to a progressive rise in systolic pressure,
3. Low renin activity: As people age, there is a progressive loss of functioning nephrons; therefore, the circulating renin level, measured as plasma renin activity typically falls in older people with hypertension

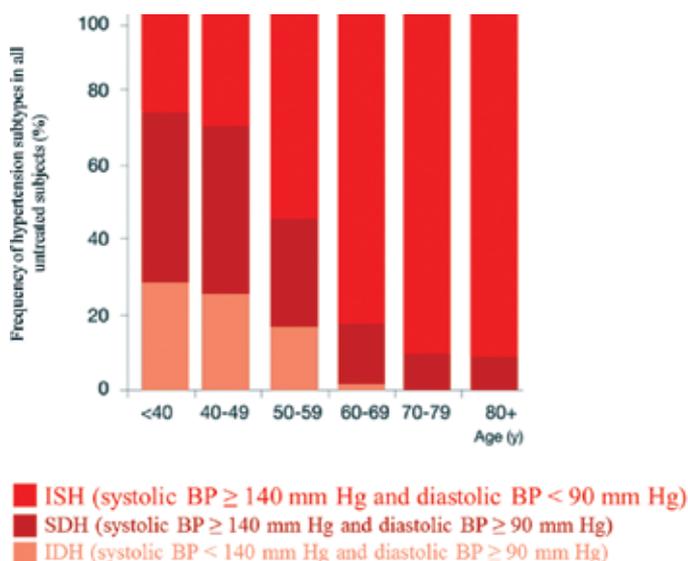
Shortcomings in compliance to official guidelines- some clinicians give importance to only diastolic pressure when considering their patients' health also hinders the control of SBP.

The SF-36 questionnaire (a routine questionnaire for evaluating a patient's health comprises of functional capacity, bodily pain, mental health etc.) evaluates the Health-Related Quality of Life (HRQoL) scores in hypertensive individuals with and without any existing complications. It has exhibited that the harshness of the resultant diseases due to HTN is directly involved in an individual's QoL, rather than uncontrolled SBP itself.

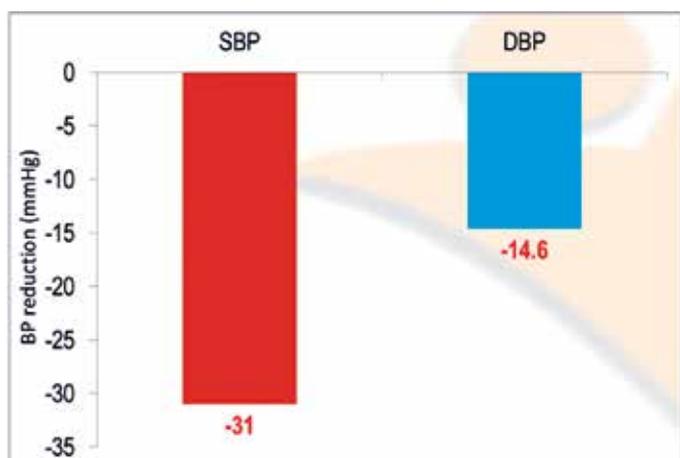
## THE POWER STUDY

Nair *et al.*, conducted a trial with Indian patients to evaluate the response of hypertensive patients on a sustained release (SR) indapamide (1.5 mg) tablet as monotherapy along with the administration of various antihypertensive drugs. The parameters evaluated were minimisation of BP along with well-being of the patients.

In this multicentric trial, 1545 Indian patients (between 40 and 70 years of age) were included after obtaining their written informed consent. The patients had uncontrolled HTN and were administered indapamide



**Fig. 1: Raised systolic BP: accountable for the majority of hypertensive diagnosis**



\* 30% patients were on Indapamide SR monotherapy, in 70% patients Indapamide was given over and above existing anti-hypertensive

**Fig. 2: SBP and DBP reduction in POWER trial**

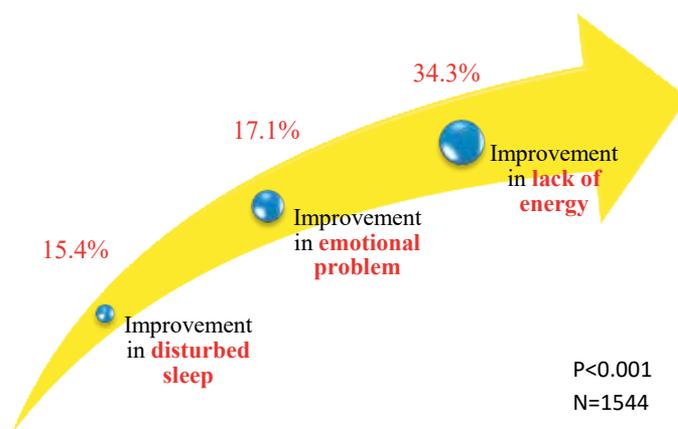
SR 1.5 mg once-daily as monotherapy or along with the continuing medication for 90 days. The variation in well-being was evaluated using the Nottingham general health questionnaire. The entire patient population was re-evaluated after 30, 60 and 90 days of the treatment regimen.

The treatment with Indapamide SR either as a monotherapy or over and above other existing anti-hypertensive agent lead to a reduction in SBP by 30 mmHg and a reduction in DBP by 15 mmHg, this reduction in BP was accompanied by overall improvement in well-being (Figures 2 & 3). The improvement in well-being was better in patients who could achieve the target BP.

### INDAPAMIDE SR- AN IDEAL DRUG TO CONTROL SYSTOLIC BP

Indapamide is an antihypertensive medication belonging to the class of thiazide like diuretics. Indapamide SR is well-tolerated in humans with no effect on the metabolic pathways. The antihypertensive property is due to an increased arterial compliance along with inhibition of the total and arteriolar peripheral resistance and sub clinical diuresis. It controls BP for the entire 24-hour time period. Indapamide even diminishes the occurrence of microalbuminuria in hypertensive patients with type-2 diabetes. The ESH 2013 guidelines advocate the administration of diuretics as the initial treatment in hypertensive patients which include the elderly suffering from HTN, hypertensive patients who suffer from periodic strokes as well as heart failure patients who are at risk.

The vascular action of indapamide involves the reduction of unusually high cardiovascular noradrenaline reactivity without inducing a corresponding increase in the adrenergic nervous activity. Hence, vasorelaxation occurs in hypertensive patients which decrease their BP. In the HYVET trial, Beckett et al included 3845 patients from Europe, China, Australasia and Tunisia ( $\geq 80$  years of age) who were randomised into 2 groups: 1<sup>st</sup> group was administered indapamide SR (1.5 mg) and the 2<sup>nd</sup> group



P<0.001

N=1544

**Fig. 3: Improvement in patient parameters after 90 days of treatment**

was given a placebo. Perindopril (an ACEI) (2 or 4 mg) was also incorporated, if required, to attain BP of 150/80 mmHg.

The trial results established that in very elderly individuals, antihypertensive treatment with indapamide (sustained release), with or without perindopril is beneficial as it causes reduction in the probability of deaths due to stroke by 39% and heart failure by 64%.

### BENEFITS OF INDAPAMIDE OVER CHLORTHALIDONE

1. Indapamide SR 1.5mg has proven life-saving benefits, whereas chlorthalidone shows life saving benefits only when given in higher dosage (25mg and above), but at such high dose the risk of metabolic imbalance is also very high.
2. Indapamide is glucose neutral hence there is no risk of new-onset diabetes, whereas chlorthalidone increased the relative risk of new onset diabetes by 43% in ALLHAT. This can be a big risk in diabetes prone Indian hypertensive patients.

SBP results from the reduction in diameter and hardening of the arterial vessels. The probabilities of major cardiovascular events like MI and CHF increases in the hypertensive population. Indapamide is an antihypertensive thiazide like diuretic, which exhibits good tolerability in humans as it is metabolically neutral. Various studies have established the efficacy of indapamide in controlling SBP in hypertensive patients above 50 years (POWER study, HYVET trial etc.). Its benefits like long term protection from CV death, stroke etc and metabolic neutrality, give it an edge over chlorthalidone in the Indian market.

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