

**YOUNG HYPERTENSION**

The definition of young adults is a matter of debate. While the American motion picture “Young Adult” features a 37-year-old lady as its heroine, the Framingham Offspring Study on ‘young’ hypertension includes 2027 men and 2267 women aged 20 to 49 years.<sup>1</sup> We therefore use the same age group to define ‘young’, in the context of adult hypertension. Young hypertensives have unique biomedical, psychological and social attributes, which are important determinants of their risk factors, clinical features, motivational cues, and therapeutic outcomes. A thorough understanding of these issues is important to ensure appropriate screening, diagnosis and management of young adults with hypertension.

**PATIENT-CENTRED APPROACH**

Patient centricity is encouraged by management guidelines on diabetes and dyslipidemia, but not by current hypertension treatment recommendations. In blood pressure care, patient centeredness implies active involvement of patients in their own care, by using modern technology such as ambulatory blood pressure monitoring and home blood pressure monitoring. There has been no use of the phrase “patient centered choice of targets” in blood pressure treatment recommendations.

Hypertension management, especially in young persons, needs patient centered goals, strategies and targets. The Eighth Joint National Committee (JNC 8) panelists<sup>2</sup> write: “{their} recommendations are not a substitute for clinical judgment, and decisions about care must carefully consider and incorporate the clinical characteristics and circumstances of each individual patient”. This suggestion forms the noesis of this chapter.

Both American Diabetes Association (ADA)<sup>3</sup> and European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)<sup>4</sup> convey the message of choosing patient-centered targets and goals while managing hypertension. The general target for blood pressure may be made more stringent for ‘younger’ individuals with longer life expectancy and additional risk factors (smoking, obesity, dyslipidemia); high risk of stroke or progression of albuminuria. Such a step should be contemplated only if therapy is well tolerated, and does not pose an unacceptable cost or bill burden upon the patient.

Younger patients who complain of symptoms suggestive of high blood pressure, such as headache, anger and irritability, may benefit from lower blood pressure levels,

provided they remain asymptomatic, and enjoy better quality of life. Asymptomatic patients may be managed using conventional targets (<140/90 mm Hg).

**DIAGNOSIS**

The diagnostic criteria for various grades of hypertension are similar in younger and older adults.<sup>2,4</sup> The methods of evaluation and diagnosis are similar. It must be noted, however, that many forms of secondary hypertension, such as renal hypertension (renal artery stenosis) adrenal disorders (pheochromocytoma, Conn’s syndrome) and other endocrine disorders (acromegaly, hyperthyroidism, hypothyroidism, hyperparathyroidism, hypogonadism, polycystic ovary syndrome) are more common, or are first diagnosed in, young adulthood. Thus, young hypertensives need thorough evaluation prior to being labeled as having essential hypertension.

**RISK FACTORS**

Hari Kumar et al have described the Ominous Octet of S’s which are risk factors for the development of non-communicable disease are in general, and cardiovascular diseases in particular. These include sex, salt, sugar, sleep, smoking, stress, sunlight and sedentary behavior.<sup>5</sup> The same authors have added saturated fat to complete the Nasty Nine, and prolonged sitting to create the list of Terrible Ten. Some of the terrible ten have a bidirectional relationship with high blood pressure, others contribute to or are risk factors for hypertension, and yet others are worsened by hypertension. Understanding of these associations helps in chalking out preventive and therapeutic strategies for hypertension.

Rates of hypertension are higher among young men than among women,<sup>1</sup> increasing threefold from the second to the fifth decade in men and eight-fold in women. Under age 40, men are twice as likely as women to develop hypertension, but after age 40, 8-year incidence rates were similar in men (14.2%) and women (12.9%). Adiposity ( $P < 0.01$ ), heart rate ( $P < 0.01$ ), and triglyceride ( $P < 0.05$ ) are significant independent predictors of hypertension in men, while adiposity ( $P < 0.001$ ), heart rate ( $P < 0.01$ ), hematocrit ( $P < 0.05$ ), and alcohol consumption ( $P < 0.05$ ) are independent contributors in women. Adiposity is a major modifiable contributor to hypertension.

In modern medicine, asymptomatic organ damage is assessed for risk stratification. Four markers (micro albuminuria, increased pulse wave velocity, left ventricular hypertrophy and carotid plaques) are considered important risk prognosticators. Among

investigations, echocardiography with Doppler is considered to have the highest predictive value, while electrocardiography, estimation of glomerular filtration rate, micro albuminuria, carotid intima-media thickness, arterial stiffness, ankle-brachial index and fundoscopy are considered useful, reproducible, easily available, and cost-effective alternatives.

### THERAPEUTIC TARGETS AND TOOLS

In the general population, the blood pressure threshold for initiating pharmacologic treatment is  $\geq 140/90$  mm Hg in those aged less than 60 years, and  $\geq 150/90$  in those aged 60 or above. While the therapeutic target is a blood pressure of  $< 140/90$  mm Hg or  $< 150/90$  mm Hg respectively, persons who are asymptomatic on therapy which achieves lower levels do not require adjustment of medication.

In all persons aged  $\geq 18$  years, with either diabetes or chronic kidney disease (CKD) (till age 70) the threshold of  $\geq 140/90$  mm Hg, and target of  $\leq 140/90$  mm Hg will apply. JNC 8 reiterates that a person who has lower blood pressure should not modify therapy, as long as it is well tolerated.

JNC 8 panelists do recommend ethnicity based choice of therapy including thiazide type diuretic or calcium channel blocker (CCB) for the general black population (including those with diabetes), and ACEi or ARB for blacks with CKD. However, no specific guidance is provided for South Asians.

ADA suggests a target of  $< 140/90$  mm Hg for all people with diabetes, but advocates lower targets in “younger patients”, those with albuminuria, and/or those with one or more additional atherosclerotic cardiovascular disease risk factors (dyslipidemia, obesity, and smoking). Such targets are proposed only if they can be achieved ‘without undue treatment burden’. Lower targets are especially important in persons with a high risk of stroke (systolic blood pressure control) or worsening of albuminuria, and ‘long life expectancy’. The threshold for beginning non-pharmacological intervention is also lower, at  $> 120/80$  mm Hg.

ADA favors the use of renin angiotensin system (RAS) inhibitors. Mention is made of outcome benefits with perindopril + indapamide<sup>6</sup> and benazepril + amlodipine combinations. ACEi and ARB may be substituted for each other, if one class is not tolerated. Serum creatinine/eGFR and serum potassium levels should be monitored during long term of RAS blockers. ADA suggests administration of one or more antihypertensive medications at bed time.

The 2013 ESH/ESC guidelines suggest institution of pharmacotherapy above a threshold of  $140/90$  mm Hg, in all patients with low-moderate cardiovascular risk, or previous stroke/transient ischemic attack, or coronary heart disease or diabetic/non-diabetic kidney disease. The only exception is made for the elderly (who are offered a higher systolic target) and for diabetes (who are given a lower diastolic target).

### PSYCHOSOCIAL FACTORS

In the modern world, young adults face high stress levels. Whether related to domestic, work or travel issues, stress is a ubiquitous part of today’s life; and is a major contributor to young hypertension. Treatment strategies need to take this into account.<sup>7</sup> Busy and erratic schedules also mean that drugs with long half-lives, which can be administered at any time of the day, without regards to the clock or to meal timing are preferred.

### PERCEIVED COMPLICATION RISK

Hypertension needs to be managed not only for symptom relief, but also for maintenance of vascular health.<sup>8</sup> Prevention or delay of vascular events such as stroke and myocardial infarction are important motivating factors for elderly persons with high blood pressure. Such illnesses may appear remote or unlikely to a young person. However, more immediate, and more worrisome, is the possibility of complications such as sexual dysfunction. Counselling regarding the role of good blood pressure control in maintaining sexual function, and prescription of “sexually neutral” drugs are important in this regard.<sup>9</sup> Such counseling and choice of drugs may help improve adherence to prescribed anti-hypertensive therapy.

### TOLERABILITY OF DRUGS

While efficacy of drugs is taken for granted today, emphasis is laid upon tolerability. Various classes of drugs may be associated with side effects such as edema, increased micturition, fatigue, cough, postural hypertension, and sexual dysfunction. The young hypertensive may find these side effects intrusive and inconvenient. Discussing these issues prior to prescription of therapy, and choosing management strategies and goals in a patient-centered manner will help improve acceptance of drug treatment.

### NON-PHARMACOLOGICAL THERAPY

Strong emphasis should be laid on non-pharmacological therapy in young persons with hypertension.<sup>9</sup> Regular physical activity, a healthy diet low in salt and saturated fat, avoidance of tobacco, excessive alcohol and abuse of drugs, stress management and adequate sleep are important components of such therapy. Yoga and meditation may be encouraged in such persons.<sup>10</sup>

### PHARMACOLOGICAL THERAPY

The choice of anti-hypertensive drugs is similar in young and relatively older individuals. As per current guidelines, diuretics, calcium channel blockers and renin angiotensin system (RAS) blockers are drugs of choice.<sup>2-4</sup> A patient-centered approach should be followed while choosing drugs for blood pressure management. Low dose thiazide diuretics, like indapamide SR and chlorthalidone, or thiazides in relatively higher dose, such as hydrochlorothiazide are economical choices, but increase urine output. Calcium channel blockers are effective blood pressure lowering drugs, but can cause edema. Angiotensin converting enzyme (ACE) inhibitors, especially enalapril and ramipril, may be associated with a high incidence of cough. Because of these factors, tolerability plays an important role in choice of therapy.

652 Efficacy is equally important, too there is a trend towards preference of once daily drugs with longer half-lives, which are able to achieve both day time and nocturnal normotension.

### PRO-METABOLIC THERAPY

A large number of young persons with hypertension have comorbid conditions such as diabetes,<sup>2</sup> obesity, dyslipidemia and hyperuricemia. The choice of antihypertensive drug should be such that it should preferably improve, and at the least be neutral to, other metabolic parameters. Renin angiotensin system blockers, for example, are able to enhance insulin sensitivity, and thus possibly attenuate the dysfunction noted with metabolic syndrome. The 2013 ESH/ESC authors list metabolic syndrome and glucose intolerance as possible contraindications for thiazide diuretics and beta-blockers, but refrain from describing these contraindication as compelling.

### COMBINATION THERAPY

Monotherapy may not be sufficient to normalize blood pressure in many patients, especially those with comorbid conditions such as diabetes, chronic kidney disease, and stress. A combination of drugs is required in such cases. The maximum time frame for intensification of therapy (either by up titration of dose or addition of an extra drug), if goals are not achieved, is one month.

Some JNC 8 panelists recommend initiation of combination therapy (2 or more drugs) when blood pressure is > 160/100 mm Hg or when it is > 20/10 mmHg above goal. Titration of drug treatment can be done by maximizing dosage, adding a second medication, or starting a fixed dose combination. They reiterate that more than one class of drugs will frequently be necessary and advocate use of thiazide-like diuretics, ACE or ARB and CCB, in varying combinations. Only if these three classes prove inadequate, along with lifestyle modification, do they recommend addition of beta blockers, aldosterone antagonists or other classes. Fixed dose combination (FDCs) of rational and complementary molecules are helpful in such cases. Examples include FDCs of RAS blockers, amlodipine and diuretics, in dual or triple combination.

### TECHNOLOGY

The average young hypertensive is more technology savvy than his elder counterparts. Blood pressure care provides digital health solutions for preventative and curative interventions, as well as non-pharmacological and drug related therapies. Mobile applications and gadgets which monitor diet and physical activity patterns,

support adherence to treatment by reminding the user to take his /her medication regularly. Tele-health projects offer counseling services related to various aspects of hypertension, enhancing patient and community awareness, and offer simple advice which facilitates patient empowerment and appropriate decision making. The YUVA helpline, recently launched from Hyderabad, is one such useful service (phone 07097066606).

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