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A REVIEW STUDY OF ANTI HYPERTENSIVE DRUGS USED IN PATIENTS WITH HYPERTENSION

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ABSTRACT

Drug utilization review can be defined as review of drugs used in a population to determine effectiveness, potential dangers, problems with drug interaction and other issues. It helps pharmacist to monitor, evaluate and suggest modification. In prescribing medicinal practitioners with the aim of making medical care rational and cause effective. Drug utilization review or survey aims that providing guidelines to doctors with respect to the rational use of drugs minimizing side effects, polypharmacy and exposure to potent drugs. Rational use of drugs minimizes polypharmacy, drug interaction in turn it minimizes the hospital stay. The study includes survey and treatment for geriatrics and pediatrics. Also, we focused on different parameters like various class of drugs given to the patients of different gender, age, etc. In conclusion, the use of antihypertensive drugs in the treatment of hypertension was almost found to be rational. Pharmacist is a key person in the better management of therapy based on stage and condition of the patient. Our aim in choosing this topic is to give a brief idea about the threatful disease hypertension and highlight the rational and cause effective use of the antihypertensive drugs. In the treatment of hypertension which if not rational may ultimately lead to poor patient outcome and significant wastage of money and resources. The impact of inappropriate use of medicine on the healthcare system is reduction of quality of medicine therapy leading and increased risk of unwanted effects viz., adverse medicine reaction. And it also leads to the decrease in patients of geriatrics and pediatrics in the population. We also compared the use of drugs, patients, side effects in patients of different ages and different gender. It has been a sincere effort by us, to minimize the anticipated untoward events in our dissertation. It shows negativity towards medicines.

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INTRODUCTION

Hypertension, types and causes

HYPERTENSION:

Hypertension is also known as high blood pressure. It is defined as transitory (short-lived) or chronic elevation of the blood pressure in the arteries. This elevation may lead to cardiovascular damage.

The two TYPES of hypertensions are essential or secondary. High blood pressure with an unknown cause is essential hypertension. High blood pressure with a known or direct cause is secondary hypertension. Some of the causes of secondary hypertension include kidney disease, tumours or medications such as use of birth control pills.

The most common causes of hypertension include smoking, obesity or being overweight, diabetes, having a sedentary lifestyle, lack of physical activity, high salt or alcohol intake levels, insufficient consumption of calcium, potassium or magnesium, a deficiency in vitamin D, stress, aging, chronic kidney disease and adrenal and thyroid conditions or tumours. Some individuals may also be genetically predisposed to hypertension.

Headaches, fatigue, confusion, dizziness, nausea, vision problems, chest pains, breathing problems, irregular heartbeat and blood in the urine are all symptoms of hypertension. However, many cases of high blood pressure are asymptomatic, which is why periodic blood pressure screenings are recommended.

Almost half of all adults in the United States have high blood pressure, but many are not aware of this fact. Hypertension is a primary risk factor for cardiovascular disease, including stroke, heart attack, heart failure, and aneurysm. Keeping blood pressure under control is vital for preserving health and reducing the risk of these dangerous conditions.

Hypertension is a global health problem. Worldwide, approximately 26.4% of the adult population in 2000 had hypertension (26.6% of men and 26.1% of women), and 29.2% were projected to have this condition by 2025 (29.0% of men and 29.5% of women). The estimated total number of adults with hypertension in 2000 was 972million; 333million in economically developed countries and 639million in economically developing countries. The number of adults with hypertension in 2025 was predicted to increase by about 60% to a total of 1.56billion.

High blood pressure (hypertension) is a common condition in which the long-term force of the blood against your artery walls is high enough that it may eventually cause health problems, such as heart disease.

OBJECTIVE:

To know the rational use of drugs in patients with hypertension in all groups adults children and geriatric.

REVIEW OF LITERATURE

INTRODUCTION TO BLOOD PRESSURE

BLOOD PRESSURE:

Blood pressure is broken into systolic and diastolic values. The systolic measurement is the peak pressure in the arteries, and the diastolic measurement is the minimum pressure in the arteries. Normal blood pressure is defined as being below 120/80, where 120 represents the systolic (maximum) measurement and 80 represents the diastolic (minimum) measurement. Hypertension occurs when the blood pressure reaches above 140/90. The risk for hypertension is increased in a condition known as prehypertension, which occurs when the blood pressure is between 120/80 and 139/89.

Blood pressure is determined both by the amount of blood your heart pumps and the amount of resistance to blood flow in your arteries. The more blood your heart pumps and the narrower your arteries, the higher your blood pressure. A blood pressure reading is given in millimetres of mercury.

INTRODUCTION TO HYPERTENSION

Hypertension is another name for high blood pressure. It can lead to severe health complications and increase the risk of heart disease, stroke, and sometimes death. Blood pressure is the force that a person's blood exerts against the walls of their blood vessels. This pressure depends on the resistance of the blood vessels and how hard the heart has to work.

HISTORY

The modern **history of hypertension** begins with the understanding of the cardiovascular system based on the work of physician William Harvey (1578–1657), who described the circulation of blood in his book De motu cordis. The English clergyman Stephen Hales made the first published measurement of blood pressure in 1733.[1][2] Descriptions of what would come to be called hypertension came from, among others, Thomas Young in 1808 and especially Richard Bright in 1836.[1] Bright noted a link between cardiac hypertrophy and kidney disease, and subsequently kidney disease was often termed Bright's disease in this period.

The term essential hypertension ('Essentielle Hypertonie') was coined by Eberhard Frank in 1911 to describe elevated blood pressure for which no cause could be found.[11] In 1928, the term malignant hypertension was coined by physicians from the Mayo Clinic to describe a syndrome of very high blood pressure, severe retinopathy and inadequate kidney function which usually resulted in death within a year from strokes, heart failure or kidney failure.[12] A prominent individual with severe hypertension was Franklin D. Roosevelt.[13] However, while the menace of severe or malignant hypertension was well recognised, the risks of more moderate elevations of blood pressure were uncertain and the benefits of treatment doubtful. Consequently, hypertension was often classified into "malignant" and "benign". In 1931, John Hay, Professor of Medicine at Liverpool University, wrote that "there is some truth in the saying that the greatest danger to a man with a high blood pressure lies in its discovery, because then some fool is certain to try and reduce it".[14][15]

This view was echoed in 1937 by US cardiologist Paul Dudley White, who suggested that "hypertension may be an important compensatory mechanism which should not be tampered with, even if we were certain that we could control it".[16] Charles Friedberg's 1949 classic textbook "Diseases of the Heart",[17] stated that "people with 'mild benign' hypertension. [defined as blood pressures up to levels of 210/100 mm Hg] ... need not be treated".[15] However, the tide of medical opinion was turning: it was increasingly recognised in the 1950s that "benign" hypertension was not harmless.[18] Over the next decade increasing evidence accumulated from actuarial reports[2][19] and longitudinal studies, such as the Framingham Heart Study,[20] that "benign" hypertension increased death and cardiovascular disease, and that these risks increased in a graded manner with increasing blood pressure across the whole spectrum of population blood pressures. Subsequently, the National Institutes of Health also sponsored other population studies, which additionally showed that African Americans had a higher burden of hypertension and its complications.[21]

SIGNS AND SYMPTOMS

Hypertension does not usually cause any noticeable symptoms. When it does, you might experience dizziness, shortness of breath, headaches, and nosebleeds, which could indicate that your blood pressure is high.(21). Complications such as heart disease, stroke, and kidney failure can occur if long-term hypertension is not adequately treated. A hypertensive emergency, which is an uncommon and dangerous event, may cause blurry vision, nausea, chest pain and anxiety.(22).

Frequent Symptoms

Overall, the vast majority of people who have hypertension, which is described as chronically high blood pressure (>130 mm Hg or diastolic pressure >80 mm Hg), do not experience any symptoms of the condition. It is usually diagnosed in the doctor's office with a simple blood pressure measurement using a blood pressure cuff.

Symptoms that do occur, if present, may indicate temporary fluctuations or elevations in blood pressure, and can be related to the timing of medication doses. Generally, the symptoms of hypertension can happen at any time, do not last for long, and may recur. They include:

Recurrent headaches:

Headaches are fairly common among people with or without hypertension. Some people with hypertension notice changes or worsening of headaches when medications are skipped or when the blood pressure becomes higher than usual. Headaches associated with hypertension can be mild, moderate, or severe and can be of a throbbing nature. (23).

Dizziness:

People with hypertension may notice dizziness in relation to medication doses and blood pressure fluctuations.

Shortness of breath:

Hypertension can cause shortness of breath as a result of the effect on the heart and lung function. (24). Shortness of breath is more noticeable with physical exertion or exercise.

Nosebleed:

You may be more prone to nosebleeds if you have hypertension, although, in general, nosebleeds are not a classic sign of high blood pressure.

Rare Symptoms

Extremely high blood pressure that occurs suddenly is more likely to produce noticeable symptoms than chronic hypertension. However, it is important to know that even very high blood pressure may not produce symptoms.

Severe high blood pressure is defined as systolic pressure of >180 mm Hg or a diastolic pressure of >120 mm Hg. People with severe high blood pressure can develop symptoms quickly, including:

Blurry vision or other vision disturbances:

Blurred vision and vision changes are warning signs that you could be at risk of a serious health problem, such as a stroke or a heart attack. (25).

Headaches:

Headaches associated with very high blood pressure tend to be throbbing in nature and can develop rapidly.

Dizziness:

The dizziness of very high blood pressure is described as vertigo (a sensation that the room is spinning). (26).

Nausea, vomiting or loss of appetite:

Nausea associated with severe hypertension can develop suddenly. (27).

Preeclampsia

In some cases, pregnant women with hypertension may develop preeclampsia during their pregnancy. This condition of increased blood pressure can cause kidney and other organ complications. This can result in high protein levels in the urine, problems with liver function, fluid in the lungs, or visual problems. (28).

Hypertension is generally a silent condition. Many people won't experience any symptoms and may take years or even decades for the condition to reach levels severe enough that symptoms become obvious. Even then, these symptoms may be attributed to other issues. Symptoms of severe hypertension can include:

- headaches
- shortness of breath
- nosebleeds
- flushing
- dizziness
- chest pain. (29).

CAUSES

Primary (essential) hypertension:

For most adults, there's no identifiable cause of high blood pressure. This type of high blood pressure, called primary (essential) hypertension, tends to develop gradually over many years.

Secondary hypertension:

Some people have high blood pressure caused by an underlying condition. This type of high blood pressure, called secondary hypertension, tends to appear suddenly and cause higher blood pressure than does primary hypertension. Various conditions and medications can lead to secondary hypertension, including:

- Obstructive sleep apnoea
- Kidney disease
- Adrenal gland tumours
- Thyroid problems
- Certain defects you're born with (congenital) in blood vessels
- Certain medications, such as birth control pills, cold remedies, decongestants, over-the-counter pain relievers and some prescription drugs
- Illegal drugs, such as cocaine and amphetamines. (3)

BENEFITS AND ADVERSE EFFECTS OF ANTI HYPERTENSION DRUGS

BENEFITS/RECOVERY WITH ANTI HYPERTENSIVE DRUGS

Cardiovascular benefits of antihypertensive medications

A meta-analysis of studies of the treatment of elevated BP with antihypertensive medications in the very elderly showed a reduction in CV events including stroke and heart failure but also a nonsignificant increase in all-cause mortality (86). This meta-analysis of 1670 hypertensive elderly patients aged ≥80 years included seven trials in which the first-line treatment for hypertension was either a diuretic or BB (87). The mean age of the elderly participants in the trials vari-ed from 66 to 84 years, with the proportion of women ranging from 31% to 75% in the different studies

A significant reduction in stroke incidence was observed as a primary outcome in five trials, including the Hypertension in the Very Elderly Trial (HYVET) pilot(88), Medical Research Council (MRC) trial (89)., Systolic Hypertension in the Elderly Program (SHEP) (90), Swedish Trial in Old Patients with Hypertension (STOP-H) (91),. and Systolic Hypertension in Europe (Syst-Eur) trial(92),, and as a secondary outcome in four trials, including the European Working Party on High Blood Pressure in the Elderly (EWPHE)(93),Prospective Randomized Open-label Blinded-Endpoint Assessment (PROBE) study(94),on Cognition and Prognosis in the Elderly (SCOPE)(95),and STOP-H2 post hoc analysis(96).

It has been reported that antihypertensive medications are also beneficial in reducing CV disease in the elderly, although this finding has not been consistent in all trials. The decrease in CV events was observed as a main outcome in two trials [Avoiding Cardiovascular events through Combination therapy in Patients Living with Systolic Hypertension (ACCOMPLISH) post hoc antihyps (97),and the trial by Wing et al. (98).

ADVERSE EFFECTS OF ANTI HYPERTENSIVE DRUGS

The J-curve phenomenon

The risk of CV events decreases when elevated BP is lowered, but lowering BP below a critical point is no longer beneficial and becomes potentially harmful due to impaired organ perfusion; this has been termed the J-curve phenomenon (99).This phenomenon was first reported in 1979 when, in a cohort of 169 well-matched hypertensive patients treated with antihypertensive drugs, those with DBP <90 mmHg experienced a five-fold increase ($P < 0.01$) in the occurrence of MI after 6 years of follow-up compared to those with DBP of 100–109 mmHg (100).

Antihypertensive drugs and the risk of cognitive decline and/or dementia

Hypertension is a risk factor for the development of cognitive decline and/or dementia in late-life (101-103).. However, inconsistent results have been reported regarding the use of antihypertensive drugs to reduce the risk of cognitive decline and/or dementia. Placebo-controlled clinical trials of antihypertensive drugs have failed to demonstrate an association between these drugs and cognitive impairment and/or dementia (104-105), with the exception of one trial. The only study in hypertensive elderly subjects (mean age 70 years) that demonstrated a relative risk reduction (RRR) of 50% in incident dementia (both vascular dementia and Alzheimer's disease) was the Syst-Euro trial (106).

OH in the elderly

Orthostatic hypotension is the failure of cardiovascular reflexes to maintain BP on standing from a supine or sitting position 7. In OH, assumption of the upright posture results in an abrupt translocation of thoracic blood volume to the lower body (107).Ageing is associated with a reduction in the baroreceptor reflex-mediated response to hypotensive stimuli (108,109). Although there are many different definitions of OH, it is most commonly defined as a reduction in SBP of at least 20 mmHg, or in DBP of at least 10 mmHg, in response to a change from a supine to an upright position (standing), occurring within 3 min of the change in posture

Antihypertensive drugs and the risk of falls and/or fractures

Antihypertensive medications used to treat hypertension in the elderly may cause and/or exacerbate pre-existing OH resulting in poor balance, dizziness, fatigue, weakness and even falls with subsequent injury including fractures (110).Whilst drug-induced OH may occur in the initial period of antihypertensive drug treatment (42 days)(111) , long-term antihypertensive therapy (≥1 year) may have a very different action on bone.

Antihypertensive drugs and the risk of cancer

Evidence regarding the association between antihypertensive drugs and risk of cancer has been inconsistent. The possibility of an increased risk of cancer with the use of CCBs was first raised by Pahor et al.(112),who reported a statistically significant increased risk of all cancers amongst CCB users (relative risk 2.02, 95% CI 1.16–3.54), including a nonstatistically significant increased risk of breast cancer, in an elderly cohort. A network meta-analysis examining the risk of cancer with antihypertensive drug use, including 70 RCTs regarding cancer risk or cancer-related death from 1950 to August 2010, found no statistically significant risk of cancer with the use of diuretics, ACE inhibitors, ARBs, CCBs or BBs (113).

Antihypertensive drugs and the risk of DM

The effect of different antihypertensive drugs on the incidence of DM has been reviewed in meta-analyses . As hypertension often co-exists with impaired glucose tolerance, insulin resistance and obesity, in large study populations many patients with hypertension develop DM whilst receiving placebo and antihypertensive drug treatment (114).A network meta-analysis of the effect of different antihypertensive agents on incident DM, including 22 RCTs from 1966 to September 2006, found that the association between antihypertensive drugs and new-onset DM was lowest for ARBs and ACE inhibitors followed by CCBs, placebo, BBs and diuretics (115).It is thought that thiazide diuretics may worsen glycaemic control in a dose-dependent manner by inhibiting insulin resistance and reducing peripheral insulin sensitivity (116,117).BBs inhibit both pancreatic insulin secretion via β2-receptors and peripheral glucose utilization.(118,119).

PATHOGENESIS

The pressure exerted on the wall of arteries by the strength of the Contraction of the heart is called Blood Pressure. (30).

Arterial Blood pressure that is usually indicated by an adult systolic blood pressure of 140mm Hg or greater or a diastolic blood pressure of 90 mm Hg or greater. (31).

It is chiefly of unknown aetiology but may be due to a pre-existing condition such as a renal or endocrine

Disorder, that typically results in a thickening of arterial walls and Hypertrophy of the left heart ventricle. (32).

Uncontrolled hypertension is a risk factor for various pathological conditions such as heart attack, Heart failure, stroke, kidney disease and retinal haemorrhage. (33).

The Disease has been appropriately nicknamed ‘silent-killer’ because in most patient’s hypertension does not have any symptom and usually goes unnoticed. (34).

Types of hypertensions

1.Primary hypertension (also known as Essential Hypertension) –

For almost 90% of the patients, the cause of this Hypertension is unknown. Your doctor will diagnose this Hypertension type after analysing your blood pressure after three or four visits. People who suffer from this Hypertension type show no significant symptoms. However, a few patients do show the below signs:

Frequent headaches

Fatigue

Dizziness

Nosebleeds

2.Secondary Hypertension –
This Hypertension type occurs when there is an abnormality in the arteries that supply blood to the kidneys.
Some common causes of this Hypertension include:
Abnormalities or tumours of the adrenal glands
Thyroid
Hormonal imbalances
Excessive salt or alcohol intake

3.Malignant Hypertension –
Here the blood pressure rises rather quickly and causes a medical emergency where the patient needs to be rushed to the hospital. It is typically observed in small fractions of society such as young African-American men and women with pregnancy toxaemia, to name a few.
Some common symptoms include:
Numbness in arms and legs
A headache
Chest pain
Blurry vision

4.Resistant Hypertension –
This type of Hypertension is usually observed in people who are aged, obese or are suffering from diabetes or kidney ailments. (2)

DIAGNOSIS
CLASSIFICATION OF ANTI-HYPERTENSIVE DRUGS
1. ACE INHIBITORS:
Captopril,
Enalapril,
Lisinopril,
Perindopril,
Ramipril.

2.ANGIOTENSIN ANTAGONISTS:
Losartan,
Candesartan.

3.CALCIUM CHANNEL BLOCKERS:
Verapamil,
Diltiazem,
Nifedipine,
Felodipine,
Amlodipine,
Lacidipine.

4.DIURETICS:
Thiazide=hydrochlorothiazide, chlor Amiloride thalidone. indapamide
High ceiling=furosemide,
K+ sparing=spironolactone.

5.ß - ADRENERGIC BLOCKERS:
Propranolol,
Metoprolol,

6.a+ß ADRENERGIC BLOCKERS:
Labetalol,8
Carvedilol

7.a- ADRENERGIC BLOCKERS
terazosin,
phentolamine.

8.CENTRAL SYMPATHOLYTIC:
Clonidine,
Methyldopa.

9.VASODILATORS:
Hydralazine,
minoxidil sodium

Some of the more commonly prescribed Drugs used in hypertension include:
Diuretics or water pills –

These are often the first agents used to control essential hypertension and examples include hydrochlorothiazide, thiazide, indapamide and chlorathalidone. As their name suggests, these drugs act on the kidneys to increase the amount of water expelled from the body in the urine, which lowers the blood volume inside the body and therefore the blood pressure.
In addition, some diuretics also help to dilate or relax the walls of the arteries meaning blood can flow more easily through these vessels, which also reduces blood pressure.

Beta blockers:

Examples of beta blockers include atenolol, metoprolol, nadolol, pindolol, carvedilol and labetelol. These agents block the beta receptors of the heart and lower the force the heart pumps with. Beta blockersalso for the heart rate.(4).

Calcium channel blockers:

These agents block the flow of calcium in the muscles of the blood vessels causing them to relax and dilate. This reduces the pressure against which the heart has to pump and, in turn, the blood pressure. Examples of these agents are amlodipine, nifedipine,nicardepine and verapamil.(5).

Angiotensin converting enzyme :These drugs stop the action of angiotensin II, which normally narrows blood vessels. Blocking its action dilates blood vessels and reduces blood pressure. Some examples of these agents are enalapril, captopril and Ramiprily.(6).

Angiotensin Receptor Blockers:

These drugs act by preventing the action of angiotensin II on its receptor and therefore exert similar effects to as ACE inhibitors. Examples include drugs such as losartan, candesartan, and telmesartan.(7).

Centrally acting sympatholytic:

These are substances that act on the central nervous system to induce blood vessel dilation and, in turn, blood pressure. Drugs in this class include methyldopa and clonidine. Methyldopa is suitable for pregnant women with hypertension.

Alpha blockers:

These act by blocking the alpha adrenergic receptors, which relaxes and dilates the blood vessels. This reduces the pressure against which the heart has to pump and therefore the blood pressure.(8).

Vasodilators:

Drugs of this class include hydralazine and minoxidil which relax the smooth muscle of the blood vessels causing the vessels to relax and dilate. Again, this reduces the pressure against which the heart has to pump and therefore the blood pressure.(9).

TYPES

Blood pressure measurements fall into several categories:

- **Normal blood pressure.** Your blood pressure is normal if it's below 120/80 mm Hg.
- **Elevated blood pressure.** Elevated blood pressure is a systolic pressure ranging from 120 to 129 mm Hg and a diastolic pressure below (not above) 80 mm Hg. Elevated blood pressure tends to get worse over time unless steps are taken to control blood pressure. Elevated blood pressure may also be called prehypertension.
- **Stage 1 hypertension.** Stage 1 hypertension is a systolic pressure ranging from 130 to 139 mm Hg or a diastolic pressure ranging from 80 to 89 mm Hg.
- **Stage 2 hypertension.** More-severe hypertension, stage 2 hypertension is a systolic pressure of 140 mm Hg or higher or a diastolic pressure of 90 mm Hg or higher.
- **Hypertensive crisis.** A blood pressure measurement higher than 180/120 mm Hg is an emergency situation that requires urgent medical care. If you get this result when you take your blood pressure at home, wait five minutes and retest. If your blood pressure is still this high, contact your doctor immediately. If you also have chest pain, vision problems, numbness or weakness, breathing difficulty, or any other signs and symptoms of a stroke or heart attack, call 911 or your local emergency medical number.

PREVENTION

LIFESTYLE MODIFICATION ADVICE IN THE GUIDELINES

The hypertension clinical guideline from the National Institute for Health and Clinical Excellence (NICE) usefully recommends regular aerobic exercise and reduction of salt, alcohol, and smoking, and advocates 'healthy, low-calorie diets' for 'overweight individuals with raised blood pressure', but gives a rather negative comment about its 'modest effect' and the unexplained variability of effect in trials. (120).

This is in stark contrast to the far more comprehensive British Hypertension Society (BHS) guidelines,(121), which largely concur with guidance from the World Health OrganiAmerican(122), European Society of Cardiology,(123),American Society of Hypertension,(124), the American Heart Association,(125) and the American MedicalOrganiAmerican(126) .These guidelines recognise the wealth of quality clinical trials showing unequivocally that diet and behavioural interventions can have a significantly beneficial effect on hypertension, which is not confined to the overweight.

BHS guidelines state that advice should be provided for prevention as well as treatment of hypertension and should be given to pre-hypertensives and those with a strong family history.

PROVEN LIFESTYLE MODIFICATIONS

The DASH diet is low in total and saturated fat, red meat, sugar, sugary drinks, and refined carbohydrates, but high in fruits, vegetables, whole grains, fish, poultry, and low-fat dairy products. The DASH diet has been found to lower weight, heart rate, risk of type 2 diabetes, C-reactive protein, apolipoprotein B, and homocysteine and is associated with a lower incidence of heart failure, all-cause mortality, and stroke. (127,128).

The Optimal Macronutrient Intake Trial to Prevent Heart Disease (or OMNI Heart trial) found that replacement of some of the DASH diet's carbohydrate intake with either protein (50% from plant sources) or unsaturated fat (mainly monounsaturated, found in olives and olive oil) could reduce blood pressure, low-density lipoprotein, homocysteine, and coronary heart disease risk even further. (129,130).

The PREMIER trial found that the DASH diet combined with alcohol and salt reduction, weight loss, and aerobic exercise achieved a reduction of 14.2/7.4 mmHg among hypertensives, while hypertension prevalence fell over a period of 6 months from 38% to 12%.alt reduction, possibly the single most important hypotensive measure, involves staying away from processed foods, regularly checking food labels for salt content, and using herbs or spices for flavour.

A recent UK study showed that hypertension management delivered by practice nurses could provide improved clinical outcomes. Where these resources are not available, a physician needs to be able to give patients the basic information in the table.

Table no 2: Diet and behavioural modifications to control hypertension.

Stop smoking
Reduce:
Total and saturated fat
Red meat
Sugar, sugary drinks
Refined carbohydrates
Salt
Alcohol (except modest amounts of red wine)
Weight
Increase:
Fruits, vegetables, whole grains
Fish and poultry
Low-fat dairy product
Olives and olive oil
Garlic
Aerobic exercise

TREATMENT

MEDICATION

ANTI HYPERTENSIVE DRUGS WIDELY OR LARGELY MARKETED IN OUR COUNTRY

According to therapeutic class, calcium channel blockers occupied the largest antihypertensive drugs market share in 2018, owing to lesser side effects exhibited by these drugs as compared to the other type of antihypertensive drugs. However, the ACE inhibitors segment is anticipated to depict fastest growth during the forecast period, due to benefits offered such as positive impact on overall health and decrease in progression of kidney diseases. (10).

Commonly used antihypertensive drugs (23 single + 15 combination preparations) manufactured by different pharmaceutical companies were analysed. (11).

Table no 3 shows percentage cost variation of 23 commonly used antihypertensive drugs used as a single drug therapy. (12).

Table No 3.

Drug	Dosage form	Minimum cost (INR)	Max cost (INR)	cost ratio
Amlodipine 2.5mg	Tablet	7.4	86	11.41
Amlodipine 5mg	Tablet	5.71	44	7.71
Clinidipine 5mg	Tablet	25	42	1.68
Nifidepine 10mg	SR-Tablet	11.33	14.2	1.25
Atenolol 50mg	Tablet	5.71	37.92	6.64
Atenolol 25mg	Tablet	4.14	27.07	6.54
Labetalol 100mg	Tablet	29.57	110	3.72
Metoprolol 25mg	Tablet	12	37	3.08
Metoprolol 50mg	Tablet	18.5	55.97	3.03
Carvedilol 12.5mg	Tablet	30	66	2.20
Metoprolol25mg	ER-Tablet	21	45.35	2.16
Metoprolol25mg	ER-Tablet	31.5	62.95	2.00
Carvedilol 25mg	Tablet	52	100	1.92
Nebivolol 5mg	Tablet	52	81.5	1.57
Ramipril 10mg	Tablet	31	179.3	5.78
Ramipril 5mg	Tablet	45	123.9	2.75
Enalapril 2.5mg	Tablet	8.8	22.6	2.57
Enalapril 5mg	Tablet	15	36.84	2.46
Lisinopril 5mg	Tablet	25.1	53.24	2.12
Drug	Dosage form	Minimum cost(INR)	Max cost(INR)	cost ratio
Lisinopril 10mg	Tablet	43.45	73.7	1.70
Telmisartan 40mg	Tablet	18	115.6	6.42
Telmisartan 80mg	Tablet	25.5	160	6.27
Losartan 25mg	Tablet	12	45.1	3.76
Losartan 50mg	Tablet	24.5	68.5	2.80
Olmesartan 20mg	Tablet	49	135	2.76
Olmesartan 40mg	Tablet	79	144.6	1.83
Valsartan 80mg	Capsule	69	85.79	1.24
Candesartan 4mg	Tablet	28.48	34.95	1.23
Chlorthalidone 12.5mg	Tablet	13.25	49	3.70

Torsemide 10mg	Tablet	19.5	55	2.82
Metolazone 5mg	Tablet	90.5	187.9	2.08
Hydrochlorothiazide 12.5mg	Tablet	6	9.53	1.59
Hydrochlorothiazide 25mg	Tablet	11	16.51	1.50
Prazosin 2.5mg	Tablet	72	99	1.38
Prazosin 5mg	Tablet	130	163.5	1.26
Methyldopa 250mg	Tablet	21.77	24.14	1.11

NEW METHODS ADOPTED BY PEOPLE TO CONTROL HYPERTENSION

Slow breathing exercises:

When you take slow, controlled breaths, you send calming signals to your nervous system, which can help with high blood pressure.

Meditation-

Transcendental meditation (TM), where you sit quietly and repeat a given phrase to yourself, can have a modest effect on lowering blood pressure. Other types of meditation may help, too, but most of the research has focused on TM.

Tai chi:

It's a slow, gentle form of exercise that comes from traditional Chinese medicine. Recent studies show that it could work as well as some high blood pressure meds or more intense exercise.(131).

Qi gong.

This method, based on traditional Chinese medicine, combines slow movement, breathing, and meditation. It doesn't work as well at lowering your blood pressure as drugs or other types of physical activity, but it can still be helpful.

Yoga.

It can be helpful for high blood pressure. Check with your doctor before you start. If you already have high blood pressure, you're pregnant, or you have conditions like glucoma and sciatica, you may want to avoid or change certain poses.(132).

The role of yogic practices in BP management is controversial. Yogic practices have been reported to reduce BP and multiple cardiovascular risk factors in many studies from India(133).From UK, Patel et al (134),reported long-term benefit of yoga in reducing coronary risk but a randomized trial of relaxation therapy and meditation in the Netherlands failed to show any benefit on ambulatory BP (135).

In a meta-analysis of lifestyle interventions to reduce raised BP data from 105 trials were included (136).Robust statistically significant benefits were observed for improved diet, aerobic exercise, alcohol and sodium restriction and fish oil supplements with BP reductions of 5.0/4.6 mm Hg.

Relaxation significantly reduced BP only when compared with non-intervention controls and the authors did not recommend this form of therapy for BP control. The American Seventh Joint National Committee (JNC-7) report or the European Society of Hypertension guidelines do not recommend stress management and yoga for hypertension control due to lack of evidence (137).

Hypnosis.

Some therapists use hypnosis, also called hypnotherapy, to help people manage stress and anxiety. When you get hypnosis, you tend to be calmer and more relaxed.

Acupuncture:

Some small studies show that it may also be helpful to lower your overall blood pressure, but more research is needed.

A new study suggests that a form of acupuncture may benefit patients with high blood pressure and lower their risk of stroke and heart disease.

The single-blind trial, conducted at the University of California-Irvine (UCI), is the first scientific confirmation that the ancient Chinese medical technique is beneficial for patients with mild to moderate hypertension.

Electroacupuncture is a form of acupuncture that applies low-intensity electrical pulses through needles inserted at specific points on the body

70% of treated patients experienced noticeable drop in blood pressure.

According to the Centres for Disease Control and Prevention (CDC), there are about 70 million American adults (29%) with high blood pressure – only about half of whom have the condition under control

Supplements and Herbs:

More research is needed to figure out the benefits of supplements to manage high blood pressure. It's always best to make changes to what you eat rather than rely on dietary supplements that are in the form of pills. For instance, you may want to add fatty fish to your diet, such as salmon or tuna, which are high in omega-3s (138)

TREATMENT BY NATURAL HERBS

Information on plants containing chemical properties or constituents for antihypertensive drugs

UNANI AND AYURVEDIC

In ancient Ayurveda texts, we cannot find a word corresponding to hypertension. Academicians have suggested different names to demonstrate the phenomenon. These names include Raktagata vata, Rakta Vikshepa, Shiragata Vata, Avrita Vata, Rakta Chapa, Rakta Sampida, Vyana Bala, Dhamani pratichaya, Dhamani Prapurnata, Rasa Bhara, Rakta Vriddh, Rudhira Mada and Raktavata.(36).

In the Management of hypertension, Ayurveda has certain limitations Especially in the emergency management for the hypertensive crisis and other vascular episodes. However, a number of studies have suggested that Ayurveda can effectively treat chronic hypertensive conditions.

This section presents the results of the study and discusses a number of medicinal plants that have been reported to be effective in the management of hypertension.

A. AJMODA

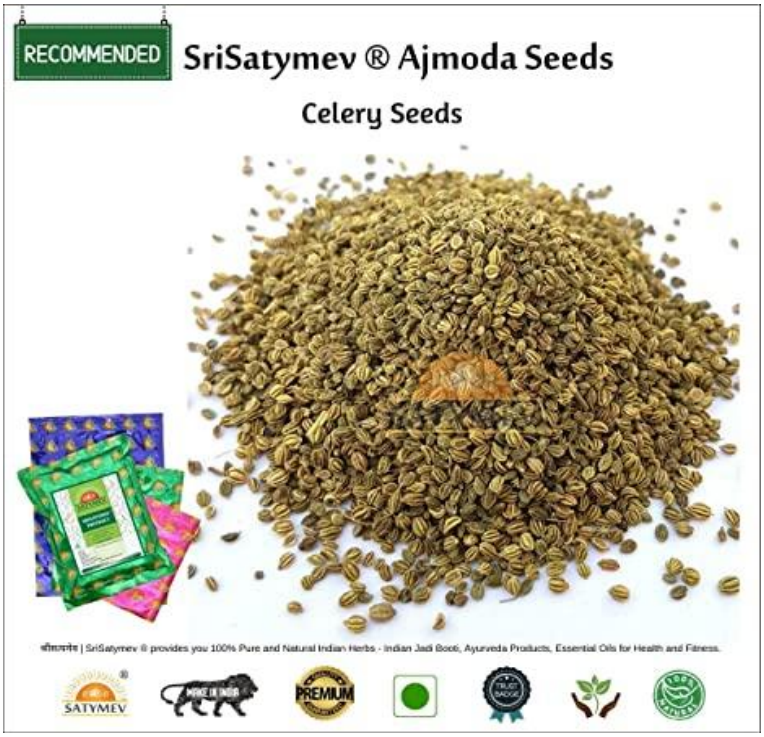

Figure no:1

Latin name: Carum roxburghianum Graib.

Family: Umbelliferae

Chemical composition: Meethers of thymol, Carvacrol, 3nB and Thymoquinol.

Parts use: Seeds

Mechanism of action: In one animal study, 3nB appears to lower blood pressure by acting as both a diuretic and vasodilator through impacting the production of prostaglandins, as well as acting in a similar manner to calcium-channel blockers.(37).
In another study 75mg per capsule of a celery seed extract was given in a dose of 1 capsule bid to mild to moderate hypertensive patients. After 3weeks of intake there was significant decrease in systolic blood pressure of 4.6 mmHg ($P<0.005$) and diastolic blood pressure of 4.5mmHg ($P<0.005$) compared to baseline. Similarly after 6 weeks of intake, the decrease in SBP and DBP compared to baseline was 8.9 and 8.5mmHg, respectively ($P<0.005$). This is statistically highly significant effect of celery seed extract in the management of hypertensionB.(38).

B. ARJUN.

Figure no:2

Latin name: Terminalia arjuna (Roxb.) W & A)
Family: Combretaceae
Chemical composition: Tannins, Triterpenoid Saponins, Flavonoids, Gallic acid, Ellagic acid, OPCs, Phytosterols, Calcium, Magnesium, Zinc and Copper
Parts use: Bark

Mechanism of action: Numerous studies have elucidated Terminalia arjuna effects on various cardiac disorders including myocardial infraction, angina pectoris, hypertension, congestive heart failure and coronary artery disease. The effect of bark powder of T. arjuna,on blood pressure, anginal frequency, body mass index, blood sugar, cholesterol and HDL cholesterol was studied in 15 stable and 5 unstable angina patients for 3months. It lowered systolic blood pressure and BMI to a significant level ($p<0.05$) and increased HDL cholesterol only slightly along with marginal improvement in left ventricular ejection fraction instable angina patients10.(39).

C. ASHWAGANDHA

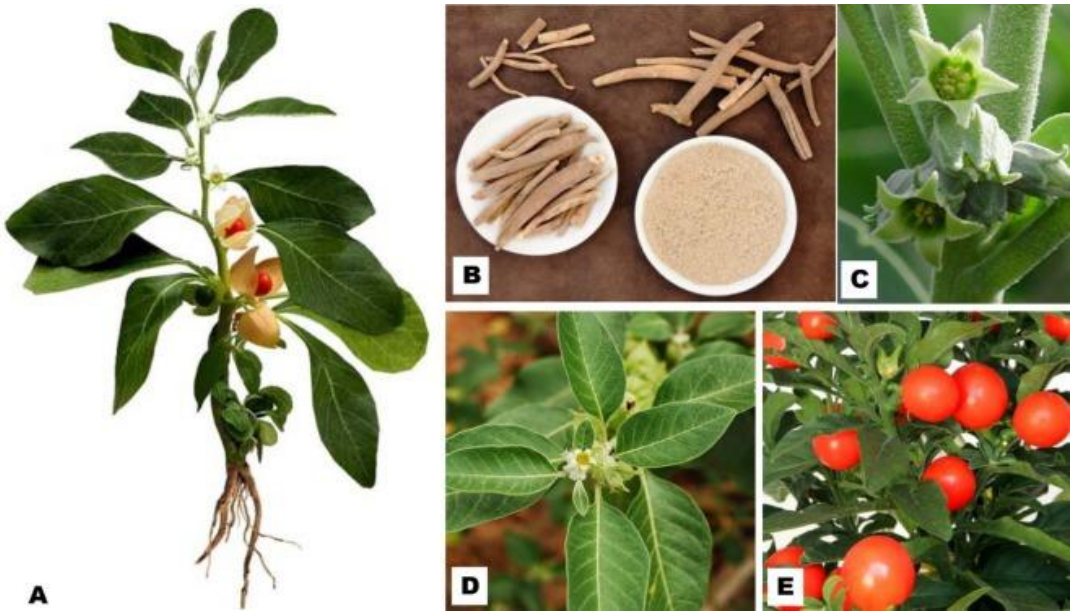

Figure no:3

Latin Name: Withania somnifera Linn.
Family: Solanaceae
Chemical composition: Cuseohygrine, Anahygrine, Anaferine, Isopellertierine, Withanolides, Withaferins, Saponins
Parts use: Root

Mechanism of action: one study was conducted to see the difference of antihypertensive effect of Ashwagandha root powder with milk and water. The blood pressure of group I and group II were compared before and after supplementation. Mean systolic blood pressure of group I and group II before supplementation was 164mmHg and 157mmHg respectively whereas after supplementation mean systolic blood pressure decreases to 158mmHg for group I and 154mmHg for group II. Mean diastolic blood pressure of group I and group II before supplementation was 100.50mmHg and 101.2mmHg respectively whereas after supplementation mean diastolic blood pressure decreased to 85mmHg for group I and 92mmHg for group II. Decrease in diastolic pressure was significant in both the group but differences were greater for patient in group I than for patient in group II. This study shows that Ashwagandha with milk is more effective in decreasing blood pressure in hypertensive patients than Ashwagandha with water. (40).

In another study the effect of Ashwagandha was studied on the cardiovascular and respiratory systems in dogs and frogs. The study found that the alkaloids had a prolonged hypotensive, bradycardia, and respiratory-stimulant action in dogs. The hypotensive effect was mainly due to autonomic ganglion blocking action and depressant action on the higher cerebral centres. (41).

D. GOKSHURA

Figure no:4.

Latin name: Tribulus terrestris Linn.
Family: Zygophyllaceae
Chemical composition: Protodioscin, Beta- carbolinea alkaloids
Harman and norharman.
Parts use: whole plant and fruits

Mechanism of action: A study was conducted with 75 patients of either sex, different age groups having non-complicated, mild to moderate essential hypertension with the symptoms of headache, giddiness, insomnia etc. The test drug i.e whole plant and fruits of Gokshura in the form of ghanasatwa (solid water extract) was given orally to the Group A&B respectively, at the dose of 3gm/day in three divided doses for four weeks and assessment was made at the end of every week. The results of both subjective and objective parameters of the study reveals that both the whole plant and fruits of Gokshura had a significant action in reduction of clinical symptoms, systolic and diastolic blood pressure without any side effects on the patients of mild to moderate essential hypertension. Therefore, this plant diuretic can be safely recommended for a longer period to the patients of mild to moderate hypertension.(42).

E. JATAMAMSI

Figure no:5.

Latin name: Nordostachys jatamansi DC.
Family: Valerianaceaea.
Chemical composition: Jatamansika, Jatamansine
Parts use: Rhizome

Mechanism of action: In an open clinical trial 20 patients of grade-I and grade-II uncomplicated essential hypertension of either sex aged between 25-70years, were given Jatamamsi Churna in a dose of 10grams per day in two equal divided doses. After 60days of therapy mean systolic blood pressure which was 148.9mm of Hg before treatment was reduced to 132.6mm of Hg and mean diastolic blood pressure was reduced to 97.1mm of Hg to 86mm of Hg. Reduction in both systolic and diastolic blood pressure was statistically highly significant ($P<0.001$). Pharmacological studies have also revealed its central depressant action and vascular smooth muscle relaxation properties. So probably Anti-hypertensive action of Jatamamsi is mediated partly through reduction in cardiac output and partly through reduction in peripheral resistance.(43).

F. JEERA (BLACK CUMIN)

Figure no:6.

Latin Name: Nigella sativa
Family: Ranunculaceae
Chemical composition: Thymoquinone, Dithymoquinone, Thymohydroquinone, Thymol 32, Carvacrol, t- anethole and 4-terpineol. Hypotensive action of Nigella is mainly due to its volatile oils.
Parts use: Seeds

Mechanism of action: In an animal study, an oral dose of Nigella sativa extract (0.6ml/kg/day) and furosemide (5 mg/kg/day) increased significantly the diuresis by 16 and 30% respectively after 15days of treatment; urinary excretion of Cl-, Na+, K+ and urea is also increased. In the same study the mean arterial pressure decreased respectively by 22 and 18% in the Nigella sativa treated rat and nifédipine treated rat (0.5mg/kg/day). In conclusion, the diuretic activity observed in the SHR rat treated with Nigella sativa seeds may be partially responsible for its diuretic action and antihypertensive action; it seems that other pathways may also be involved in their cardiovascular effects.(44).

G. KESAR (SAFFRON)

Figure no:7.

Latin name: Crocas sativus
Family: Iridaceae
Chemical composition: Crocin, Picrocrocin and Safranal
Parts use: Stigmas, petals

Mechanism of action: In one animal study, researcher investigated the effects of Crocus sativus petals extract on blood pressure in anaesthetised rats and also on responses of the isolated rat vas deferens and guinea-pig ileum induced by electrical field stimulation (EFS). Aqueous and ethanol extracts of C. sativus petals reduced the blood pressure in a dose-dependent manner. Administration of 50mg/100g of aqueous extract changed the blood pressure from 133.5+/-3.9 to 117+/-2.1 (mmHg). EFS of the isolated rat vas deferens and guinea-pig ileum evoked contractions were decreased by aqueous and ethanol extracts of C. sativus petals. The aqueous extract (560mg/ml) significantly reduced the contractile responses of vas deferens to epinephrine (1microM) without any change in contraction induced by KCl (300mM). This results may suggest that the relaxatory action of C. sativus petals extract on contraction induced by EFS in the rat isolated vas deferens is a postsynaptic effect.(45).

H. LASUN (GARLIC)

Figure no:8.

Latin name: Allium sativum L.
Family: Amaryllidaceae
Chemical composition: S- allyl-cysteine sulfoxides, Ajoene, Allicin,
Alliin, Allixin, Methyl allyldisulfide
Parts use: Rhizome

Mechanism of action: In one animal study, it was found that intravenous infusion of garlic extract reduces blood pressure and heart rates in both hypertensive and normotensive rats. This study also provides evidence that garlic reduces blood pressure in a dose dependent manner by a mechanism not involving acetylcholine. As a part of safety evaluation, this study was performed to verify the effects of garlic in hemodynamic parameters, particularly in relation to its effects on blood pressure and heart rate. The results showed that garlic at higher doses (15 and 20mg/kg) induced marked hypotension and bradycardia when injected intravenously whereas at a lower dose (5 and 10mg/kg) it produced only a slight and insignificant fall in mean arterial pressure. Various mechanisms for antihypertensive effect of garlic have been reported to include vasorelaxation through H2S production, inhibition of angiotensin-converting enzyme in vitro endothelium and beta-adrenoceptor blocking action. (46).

MAKANDI (FORSKOLIN)

Figure no:9.

Latin Name: Coleus forskolin / Plectra thus barbatus
Family: Lamiaceae
Chemical composition: coleonol
Parts Use: Root

Mechanism of action: Forskolin has been used in Ayurvedic medicine for many years. In 1974, the Indian Central Drug Research Institute discovered that forskolin, a component of this plant, has hypotensive and antispasmodic action. Forskolin's blood pressure lowering effects appear to be due to relaxation of arterial vascular smooth muscle. In a study with isolated heart tissue, Forskolin activated membranebound adenylatecyclase and cytoplasmic cAMP-dependent protein kinase. The researchers postulated the positive inotropic effect was via an enhanced calcium uptake by the heart muscle cell. Another constituent from Coleus, ditermene coleonol, has been found to lower blood pressure in both rat and cat models.(47).

J. MANDUKPARNI

Figure no:10.

Latin name: Centella asiatica (L) Urban
Family: Apiaceae
Chemical composition: Pentacyclic triterpenoids, Asiaticoside, Quercetin, Brahmoside, Asiatic acid, Brahmic acid, Centellose, Centelloside and Madecassoside.
Parts use: Whole Plant

Mechanism of action: In one animal study, researcher assessed effects of Centella asiatica extract on blood pressure and heart rate (HR) of N-nitro-L-arginine methyl ester (L-NAME) induced hypertensive rats. Male Wistar rats were anesthetized with sodium pentobarbital (50mg/kg, i.p.) and their left carotid arteries were cannulated for invasive blood pressure measurement. Mean arterial blood pressure (MABP),systolic blood pressure (SBP), diastolic blood pressure (DBP), and HR were recorded continuously throughout the experiment using PowerLab system. A single intragastric administration of Centella asiatica extract (4, 8 and 32g/20 ml/kg) did not cause changes in MABP, SBP and DDBP.(48).

At 90 min after administration, Centella asiatica extract (16 g/20ml/kg) significantly decreased the elevated MABP and DBP.19In another animal study, Long-term quercetin, a flavonoid found in Centella asiatica administration induced a progressive reduction in SBP in SHR and this effect reached statistical significance after the first week of treatment while no changes were observed in WKY rats. At the end of the 5 weeks of treatment, direct measurements of blood pressure in conscious rats showed that quercetin induced a significant reduction in systolic (-18%), diastolic (-23%) and mean (-21%) arterial blood pressure in SHR. Heart rate was also significantly reduced by quercetin in SHR (-12%).This antihypertensive effect was may be due to direct vasodilator action of quercetin and related bioflavonoids.(49).

K. PUNARNAVA

Figure no:11.

Latin name: Boerhavia diffusa Linn.
Family: Nyctaginaceae
Chemical composition: Lirridodendrin & Hypoxanthine.
Parts use: Whole plant, root

Mechanism of action: In one clinical trial, 250mg of Punarnava extract was given orally in a dose of 2 capsules twice in a day with water for six weeks. It has shown statistically significant reduction of mean Systolic and diastolic BP. Before treatment mean SBP was 151.48±5.75 and it reduced to 137.33±5.23, similarly before treatment mean diastolic BP was 95.41±2.06 which reduced to 87.11±4.75. It is due to Liridodendrin, Hypoxanthine and boeravinones which are active antihypertensive agents of Punarnava which acts as Ca+2 channel antagonist. It also acts as diuretic by increasing renal blood flow by relaxing the smooth muscles of the arterial wall.(50).

L. RUDRAKSHYA

Figure no:12.

Latin name: Elaeocarpus ganitrus
Family: Elaeocarpaceae
Chemical composition: Elaeocarpidine, Isoelaeocarpine, Rudarakine,
Flavonoids, Gallic acid, Quercetin
Parts use: Fruit and Bark

Mechanism of action: An aqueous extract of E.ganitrus seeds given intravenously in hypertensive rats at the dose levels of 25, 50 and 100mg/kg. It shows significant ($p<0.05$) decreased in the elevated blood pressure in dose dependent manner. The antihypertensive activity of aqueous extract of E. ganitrus may be due to the action on rennin-angiotensin system.(51).

M. SAHACHAR

Figure no:13.

Latin name: Barleria prionitis
Family: Acanthaceae
Chemical composition: Alkaloids, Flavonoids, Methanolic,
Saponins, Tannin and Phenolic compounds
Parts use: Whole plant

Mechanism of action: In vivo anti-hypertensive study using DOCA salt induced hypertensive rats, methanolic extracts of Barleria prionitis possessed profound antihypertensive activity in dose of 200mg/body weight and 400mg/body weight.(52).

N. SARPAGANDHA

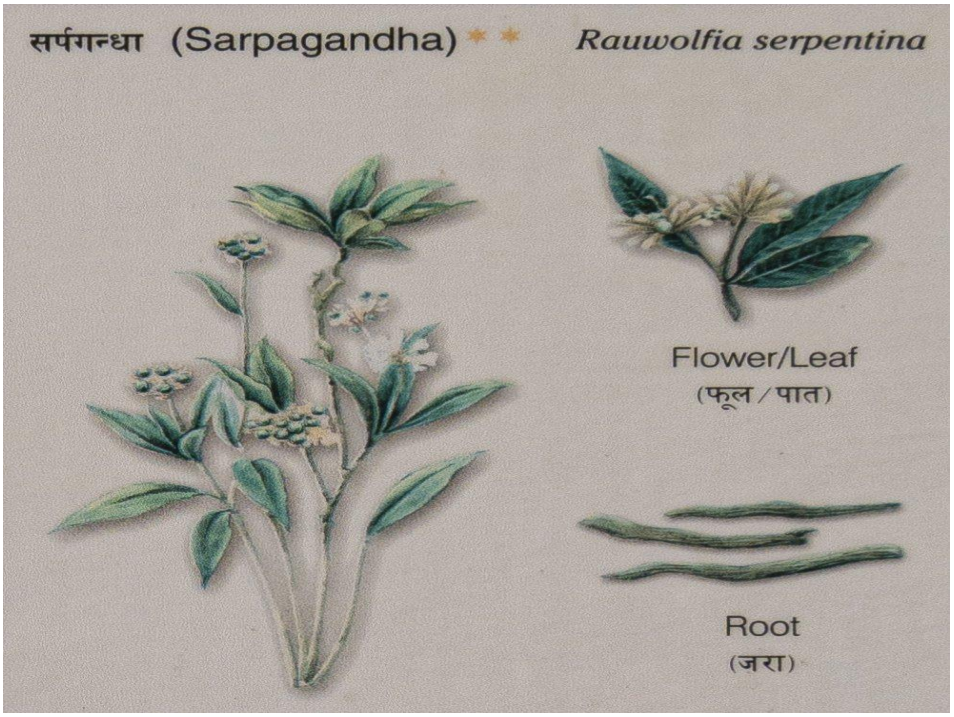

Figure no:14.

Latin name: Rauwolfia serpentina Benth ex. Kurz
Family: Apocynaceae
Chemical composition: Ajmalidine, Ajmaline, Ajmalinine, Ajmalicine, Rauwolfinine, Recanescine, Rescinnamine, Reserpiline, Reserpine, Reserpinine, Sarpagine, Serpentine, Serpentinine, Thebaine, Vohimbinine.
Parts use: Root

Mechanism of action: In a clinical trial of Rauwolfia serpentina in essential hypertension, researcher treated 50 patients with initial blood pressures greater than 160/95mm Hg. Tablets of the dried root of R. serpentine was prescribed in optimum doses. Within a week of treatment, 77 percent cases showed a drop of systolic blood pressure ranging from 2 to 38mm. with an average drop of 13mm. A drop of 10mm. or over was noted in 40 per cent of cases. In the case of the diastolic blood pressure, 73 percent of cases displayed a drop ranging from 2 to 18mm. with an average drop of 6mm. a diastolic response of 5mm. or over was noted in 35 percent. In 73 percent of cases, there was a drop of both systolic and diastolic blood pressure after one week of therapy. After four weeks of treatment, 85 per cent of cases displayed a drop of systolic blood pressure varying from 2 to 54 mm. with an average of 21mm. A systolic drop of 10mm. or over was noted in as many as 74 percent of cases. In 81 per cent of cases, the diastolic pressure showed a drop of 4 to 34mm. with an average of 11mm. A diastolic fall of 5mm. or over was noted in 72 per cent. In 62 per cent of cases there was a significant drop of both systolic and diastolic pressure levels. The hypotensive action of the drug was perceptible at 2weeks after stopping the drug in 91% of patients and at 4 weeks after discontinuing the drug in 75% of patients. No serious adverse side effects were noted.(53).

Another study was conducted to evaluate various effects of oral reserpine on a group of hypertensive patient in an outpatient clinic. Reserpine from CIBA Pharmaceuticals was given to fifteen patient who had initial blood pressures between 160/98 and 240/150mm Hg in a dosage of 20mg twice a day. The result shows systolic blood pressure reduced an average of 30.7mm Hg and diastolic blood pressure reduced an average of 19mm Hg. Some patients reported transient nausea, fainting, and dyspnoea. The researchers concluded that the drug was a useful and potent agent in some patients with severe as well as mild hypertension (54).

O. VACHA

Figure no:15.

Latin Name: Acorus calamus L.
Family: Acoraceae
Chemical composition: Beta- Asarone, Beta- Gurjunene, Asarone.
Sequesterpenes, Beta- Daucosterol, Xylose, D- Galacturonic Acid.
Parts use: Rhizome

Mechanism of action: In normotensive rats under anaesthesia, intravenous administration of crude extract of A. calamus causeda fall in mean arterial pressure. The percent fall in MAP at the respective doses of 10, 30, and 50mg/kg was 18.86± 6 0.48, 27.50 ±6 0.97, and 42.25±6 1.0 and was statistically different ($P<0.05$) at doses of 30 and 50mg/kg in comparison to 10mg/kg. This show that crude extract possesses a combination of effects, We effects mediated possibly through Ca+2 antagonism in addition to a nitric oxide pathway. Calcium channel antagonist prevents the intracellular inflow of calcium resulting in smooth muscle relaxation and decrease in heart rate, which eventually contributes for lowering the blood pressure. Similarly, nitric oxide is responsible for vasodilation that is essential for controlling blood pressure.(55).

P. VISNUKRANTHA (BLUE SANKHAPUSPI)

Figure no:16.

Latin name: Volvulus alsinoides Linn.
Family: Convolvulaceae
Chemical composition: Scopoletin, Umbelliferone, Scopolin etc.
Parts use: Root, Whole plant

Mechanism of action: In vivo anti-hypertensive study using DOCA salt induced hypertensive rats, methanolic extract of Evolvulus alsinoides shows significant antihypertensive effect. SBP, DBP, MABP and PP were significantly decreased in MEEA treated rats as compared to disease control group enalapril ($p<0.001$/ $p<0.01$/ $p<0.05$). The antihypertensive effect may be due to ACE inhibitor mechanism of Evolvulus alsinoides herb extract because the extract lowers the blood pressure as similar to enalapril which is an ACE enzyme inhibitor Q.(56).

Q. YARROW

Figure no:17.

Latin name: Achillea millefolium L.
Family: Asteraceae
Chemical composition: Flavonoids and Sesquiterpene lactone
Parts use: Leaves with flowering shoots, Flowers and Steam

Mechanism of action: A double-blind, placebo-controlled trial was conducted to see the antihyperlipidemic and antihypertensive effects of Achillea. Levels of HDL-cholesterol were significantly increased after six months treatment. Similarly, it shows significant reduced in systolic and diastolic blood pressure after two and six months respectively($p<0.05$).(57).

PALLIATIVE CARE

New Techniques Adopted To Treat Hypertension

Baroreflex Activation Therapy

Knowledge of baroreflex regulation of BP goes back to ancient times. The arteries of the neck were named karotides, based on the Greek rout karos (heavy sleep) and karoun (to choke, to stupefy) because pressing on these arteries produced sedation. In the 20th century, the role of the carotid baroreflex was demonstrated for short-term BP regulation, but it was assumed to play no role in long-term BP control.

However, based on several important studies in animals, interest in the role of the carotid sinus baroreceptor on long-term BP control has returned,[164–166] and a surgical implantable device has been developed to administer BAT via electrical stimulation of the carotid baroreceptors.(139).

The prospective nonrandomized DEBut-HT trial was a multicenter European feasibility trial for the early-generation device (Rheos System; CVRx Inc., Minneapolis, MN) performed in 45 patients with TRH (systolic BP ≥160/90 mm Hg, despite ≥3 antihypertensive drugs, including a diuretic).

In this proof-of-concept study, there was a reduction of 21±4/12±2 mm Hg (n=37) in office BP at 3 months, with further decreases of 30±6/20±4 (n=26) at 1 year and 33±48/22±26 mm Hg (n=17) at 2 years (all P=<0.005), respectively. There was also a statistically significant reduction in 24-h ABP at 1 year follow-up. In contrast, no BP change was observed in 10 control patients who declined device implantation.(140).

In total, 8 serious adverse events (7 procedure-related and 1 device-related) were reported, a number comparable to published complication rates with carotid surgery.(141,142). A substudy of 12 patients from the DEBut-HT trial demonstrated that muscle sympathetic nerve activity and BP were decreased after activation of BAT and increased without activation, providing evidence that reduction of sympathetic outflow is the primary mechanism for BP reduction with BAT.(143).

The double-blind, randomized, parallel-design Rheos Pivotal trial enrolled 256 patients with TRH. One month after Rheos device implantation, patients were randomized in a 2:1 manner to immediate BAT (device on) or delayed BAT (device remained off for 6 months).

The prespecified acute primary efficacy end point (proportion of patients achieving BP reduction of ≥10 mm Hg after 6 months with a superiority margin of 20%) was not met, and the secondary efficacy end point (mean change in systolic BP after 6 months) failed statistical significance (group A [device on]: −16±29 versus group B [device off]: −9±29 mm Hg; P=0.08).

There was an unexpected difference in systolic BP between preimplant (−1 month) and immediately postimplant (month 0) time points, prompting an additional post hoc analysis of the data. BP reductions from preimplant levels to 6 months postimplant were 26±30 mm Hg in the device on group versus 17±29 mm Hg (P=0.03) in the device off group.

The sustained primary efficacy end point, defined as BP reduction of ≥10 mm Hg from months 0 to 12, with ≥50% of BP reduction seen at month 6 (primary end point) was reached.

The procedural primary safety end point was not met, mainly because of surgical complications (4.8%) and transient (4.4%) or residual (4.8%) nerve injuries, but the prespecified criteria of both BAT and device safety were met.(141).

After completion of the Rheos Pivotal Trial, participants continued in an open-label, nonrandomized follow-up for an average of 28±9 months. A mean BP reduction of 36/16 mm Hg (P<0.001) was observed in the selected group of long-term responders (n=245, 76%), defined by achieved systolic BP ≤140 mm Hg (≤130 mm Hg for diabetic or renal disease patients) or systolic BP reduction of ≥20 mm Hg from device activation.(145).

Second-generation system of BAT

A second-generation system of BAT (Barostim neo™) has been designed to address shortcomings of the original device. A single (instead of 5) electrode is implanted at one carotid site, thus reducing the operating field (and hence possible complications). Moreover, the battery is smaller, with an extended life span (≈3 years).

In a single-arm open-label study enrolling 30 patients with TRH (based on systolic BP ≥140mm Hg although on ≥3 antihypertensive drugs, including a diuretic), a BP reduction of 26.0±4.4/12.4±2.5 mm Hg was observed after 6 months and 3 perioperative and 1 long-term procedure-related complications occurred.(146). Upcoming studies (eg, Barostim Hypertension Pivotal Trial, NCT01679132) will clarify the future of this approach to BP reduction.

Animal studies indicate that BAT directly affects autonomic regulation of the heart. Analysis of data from 34 patients pooled from different studies that used BAT demonstrated improvement in left atrial and ventricular structure and function (assessed by echocardiography). Left atrial dimensions and left ventricular mass, wall thickness, and stroke work were reduced, although left ventricular ejection fraction increased.(147). The effects of BAT on metabolic parameters (eg, glucose metabolism) and hypertensive organ damage have not yet been examined.

Carotid Body Ablation

Studies in animal models(148),and human subjects(149),have revealed enhanced carotid body (CB) sensitivity in hypertension, but the mechanisms of this abnormality are not known. CB hypersensitivity has been shown to precede the development of hypertension in SHR(150),and in patients with white-coat hypertension.(151).

In a small, randomized, crossover, placebo-controlled study, deactivation of CB chemoreceptors by hyperoxia (respiration with 100% oxygen) attenuated the enhanced muscle sympathetic nerve activity in untreated hypertensive men, but no change was observed in controls.(152). It has also been shown that hyperoxia decreases BP acutely in patients with hypertension, but not in normotensive controls.(154).

These data point to a potential pathogenetic role of tonic chemoreceptor drive in the development of sympathetic overactivity in hypertension.(153).

Surgical removal of the CB has been performed in humans for reasons other than hypertension (eg, bronchial asthma and chronic obstructive pulmonary disease [COPD]). A BP fall from 170 to 130 mm Hg was observed 5 days postop and sustained for 6 months after bilateral CB surgery in hypertensive patients, whereas no BP lowering effect was seen in normotensive patients, and a rise in BP was documented in hypotensive patients after bilateral CB resection.(151,156). To date, no study addressing the effect of uni- or bilateral CB resection for hypertension in humans has been completed, but first-in-man studies are ongoing.

Arteriovenous Fistula

A novel mechanistic approach to BP reduction is used by the ROX coupler system (ROX Medical Inc., San Clemente, CA). This self-expanding device creates a 4 mm arteriovenous fistula (AVF) between the iliac artery and vein, generating a sustained calibrated shunt volume (≈ 800 mL/min) within a short period of time (≈1 h). Detailed technical information about deployment of the device is given elsewhere.(157). Several mechanisms are hypothesized to cause BP reduction after creation of an AVF.(158).

Reduction in total systemic vascular resistance, despite an increment in cardiac output, is considered to be the key mechanism. Enhanced tissue oxygen delivery caused by increased arterial oxygen content may reduce peripheral and renal chemoreceptor activation and thus decrease sympathetic activity.

Reductions in systemic vascular compliance and effective arterial volume may also improve arterial compliance, contributing to a reduced cardiac workload, despite increased cardiac output.[182] Expected adverse effects are induction of venous stenosis and thrombosis and potential worsening/development of right ventricular failure.

The Rox coupler system was originally developed for the treatment of patients with COPD. Early positive results extended the indication to patients with concomitant arterial hypertension.

A subset of 24 COPD patients (NCT00832611 and NCT00992680) with an office systolic BP ≥130 mm Hg when on antihypertensive treatment was retrospectively analyzed after the ROX coupler procedure was performed.

Compared with baseline (145±12/86±13 mm Hg), systolic and diastolic BP were significantly reduced after 6 (130±18/71±13 mm Hg, P<0.01) and 12 months (132±18/67±13 mm Hg, P<0.01), respectively.(159).

No clinical meaningful BP reduction was seen in normotensive COPD patients after creation of an AVF using the ROX coupler.

Based on this first evidence of efficacy of AVF in patients with COPD and coexisting arterial hypertension, the concept was further tested in a small prospective, nonrandomized study enrolling 8 patients with TRH, but without COPD.

Compared with baseline, both office BP (175±19/87±14 versus 158±26/74±19 mm Hg) and 24-h ABP (152±17/82±15 versus 142±18/69±14 mm Hg) decreased at 6 months post creation of AVF. Subsequently, the European prospective, open-label, multi-center ROX CONTROL-HTN (NCT01642498) study was initiated to evaluate the ROX Coupler used along with standard drug therapy in 100 patients with TRH without COPD.

In the ROX coupler group, office BP decreased by 26.3/20.1 mm Hg (control group 3.7/2.44 mm Hg) and ambulatory BP by 13.5/13.5 mm Hg (control group 0.5/0.1 mm Hg) after 6 months. Reductions were of similar magnitude in those with previous renal denervation.(160). Procedural complications related to arteriovenous coupler placement occurred in N=13 (31%) with venous stenosis occurring in N=12 (29%) of the 42 patients treated.(161).

In relation to worsening of hypertension, 5 hospital admissions for hypertensive crisis were reported in 3 (8%) of the 39 control patients, compared with none in the arteriovenous coupler group (P=0.0225

Neurovascular Decompression

Animal studies have shown that pulsatile compression of the rostral ventrolateral medulla at the root-entry zone of cranial nerves IX and X increases both BP and sympathetic outflow, (162,163), and clinical data suggest that neurosurgical decompression of the rostral ventrolateral medulla (used for neurological disorders) leads to BP reduction.(164).

A relationship between relief of hypertension and neurovascular decompression was demonstrated by Geiger et al, who observed improvement in BP control (7 out of 8 patients) 3 months after neurovascular decompression.(165).

Sympathetic nerve activity was significantly reduced after microvascular decompression in parallel with the BP decrement. Long-term effects were less promising, however, because hypertension relapsed, and 18 months post intervention, sympathetic nerve activity had increased to preoperative levels.(166,167).

Because no long-term clinically significant BP reduction has been demonstrated in a randomized controlled study and special postprocessing software for the analysis of MRI images of the rostral ventrolateral medulla (that are not commonly available) are required to qualify a patient for the procedure, microvascular decompression for treatment of TRH is restricted to compassionate use in patients with severe TRH and proven neurovascular compression using advanced imaging techniques.(168).

Renal Artery Stenting (Revascularization)

Clinical indications for percutaneous transluminal angioplasty with stenting for renal artery stenosis are controversial. Recent clinical findings from large prospective randomized controlled trials revealed little or no benefit for BP control, preservation of kidney function, or prevention of cardiovascular or renal events, calling into question broad use of renal artery stenting in hypertensive patients with renal artery stenosis.(169-171).

In the ASTRAL trial, renal arterial revascularization did not result in a clinically relevant reduction in BP, but did cause a high incidence (17%) of adverse procedure-related complications.(172). However, methodological questions have been raised regarding the inclusion criteria. To enroll a patient in the trial, physicians had to be uncertain whether the patient would profit from the intervention, thus excluding those patients with a clear indication for renal artery stenting and creating a selection bias.

For example, 40% of the enrolled patients had <70% narrowing of the renal artery.

The STAR trial showed that the primary end point, ≥20% decrement of estimated creatinine clearance, did not differ between medical therapy alone and medical therapy combined with revascularization.(172).

However, ≈30% of patients allocated to combined therapy did not undergo revascularization because at the time of angiography, the degree of stenosis was <50%..(173).In the CORAL study of patients with atherosclerotic renal artery stenosis, hypertension, and chronic kidney disease,(174), reduction in systolic BP over time was greater (−2.3 mm Hg; 95% confidence interval, −4.4 to −0.2; P=0.03) in the revascularization group, but this did not result in prevention of cardiovascular or renal events over a median follow-up of 43 months.

All of the studies of renal artery revascularization have been criticized on grounds that they did not critically evaluate the hemodynamic relevance of the renal artery stenosis.(175,176). With the exception of subtotal occlusion of the renal artery, the angiographic degree of renal artery stenosis is a poor reflection of hemodynamic relevance.(176).

Hemodynamic relevance (to be suspected if stenosis is >80%) can be assessed by intraarterial pressure measurement or duplex sonography. A diminished resistance index in the cortical tissue reveals hemodynamic relevance, but measurement of blood flow velocity alone is not valid.(176,177). In the CORAL study, translesional renal artery pressure gradients were obtained, but are not yet published.(177).

The ongoing controversy about the utility of renal revascularization is portrayed in many publications of pooled data, meta-analyses, and long-term follow-up data. In the absence of more convincing evidence of benefit (Figure 6),(178), t may be wise not to stent as a primary therapeutic option in patients with atherosclerotic renal artery stenosis unless hemodynamic relevance can be demonstrated or rapid deterioration in kidney function or worsening BP is evident.(178).

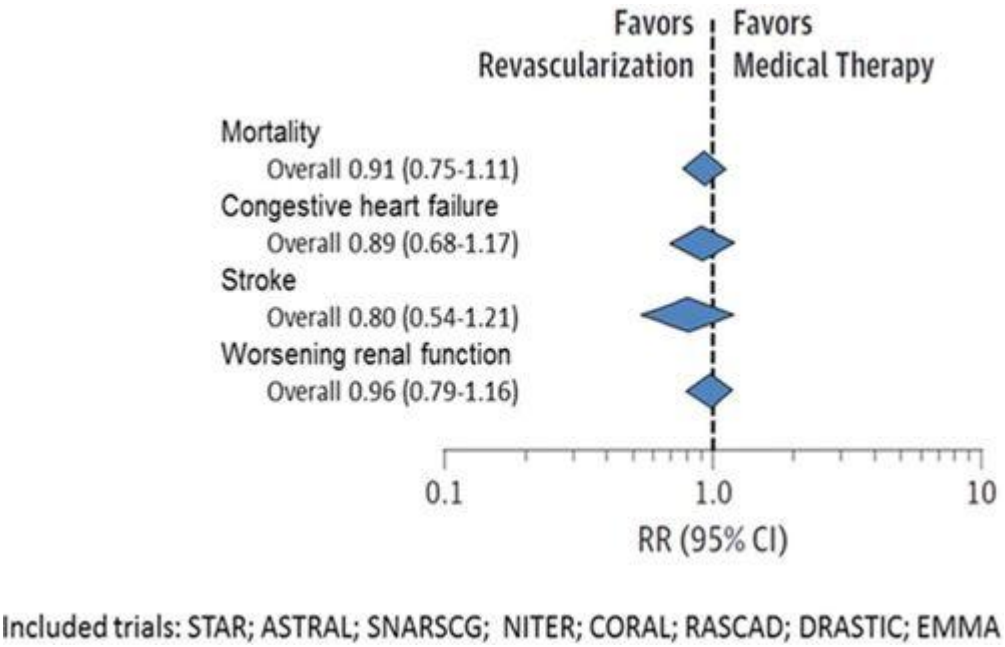

Figure no:18 Renal Artery Stenting (Revascularization) INCLUDED TRIALS.

In contrast to atherosclerotic renal artery stenosis, a systematic review and meta-analysis of patients with fibromuscular dysplasia as cause of renal artery stenosis revealed that percutaneous transluminal angioplasty alone (without stenting) improves BP control or even cures hypertension.(179). Further, BP outcome was inversely associated with age.

Hence, the European consensus on the diagnosis and management of fibromuscular dysplasia proposes revascularization for hypertension because of fibromuscular dysplasia, especially in patients with recent onset hypertension or TRH.(180).

Novel device technologies for treatment of hypertension.

Table no 4.

Technology	Mode of action	Stage of development	Limitations
Renal sympathetic denervation Ablation catheters and generators available from several manufacturers including Medtronic, St Jude Medical, Boston Scientific, Terumo, and Verve Medical	Sympathomodulatory—results in destruction of renal afferent and efferent sympathetic nerves and BP reduction through mechanisms that remain unclear in human hypertension	CE Mark approval for hypertension for most catheters A variety of catheters/platforms now available includes: Radiofrequency ablation, ultrasound ablation, chemical ablation, and cryoablation using balloon/non-balloon and irrigated catheters	Lack of markers of procedural success Inability to screen for increased renal nerve signalling prevents identification of best responders Damage to renal artery from endovascular approach using thermal energy
Baroreflex activation therapy Barostim neo™ (CVRx Inc, Minneapolis, MN, USA)	Sympathomodulatory: unilateral electrical field stimulation of the carotid sinus stimulates the baroreflex and down-regulates sympathetic outflow while increasing parasympathetic tone	CE Mark approval for hypertension Pivotal study published with the first-generation device Small proof of concept study with the second-generation device	Open loop system lacks feedback mechanism Exceedingly high cost Implantable generator must be replaced at end of battery life (currently 3 years)
Baroreceptor amplification therapy Mobius HD™ (Vascular Dynamics, Mountain View, CA, USA)	Sympathomodulatory: dramatic increase in carotid bulb strain causes durable amplification of baroreceptor feedback and BP reduction	European and US studies now enrolling Case report and early report from first-in-man study published	Concerns over instrumentation of the carotid artery, risks of distal embolization Open loop system with no feedback mechanism
Central iliac AV anastomosis ROX AV coupler™ (ROX Medical, San Clemente, CA, USA)	Targets mechanical aspects of the circulation Lowers BP through reduction in effective arterial volume and systemic vascular resistance	CE Mark approval for hypertension Small randomized controlled study in resistant hypertension publishedand US IDE study with sham control is planned to start enrolling in 2016	30% incidence of ipsilateral venous stenosis Risk of high output cardiac states not known No long-term safety data
Carotid body ablation Cibiem Carotid Body Modulation System™ (Cibiem, Los Altos, CA, USA)	Sympathomodulatory: unilateral carotid body ablation reduces sympathetic vasomotor tone without affecting respiratory drive	Proof of concept study using unilateral surgical excision in resistant hypertension Endovascular ablation planned using novel catheter-based system	Only appears effective in those with high carotid body tone. Screening for this will be essential Endovascular approach is complicated by the difficulty of accessing the target and risks to important adjacent structures
Deep brain stimulation Activa Neurostimulator, (Medtronic Inc.,	Sympathomodulatory: electrical field stimulation of the dorsal and ventrolateral periaqueductal grey	The technology was primarily developed for management of movement disorders and	Limited efficacy/safety data High costs of therapy

Technology	Mode of action	Stage of development	Limitations
Minneapolis, MN, USA) Vercise™ DBS System (Boston Scientific, Marlborough, MA, USA)	region within the midbrain reduces BP through mechanisms that are not clearly defined in human hypertension	chronic pain syndromes. Isolated reports of BP-lowering independent of pain control	Open loop system Frequent generator recharging required
Vagal nerve stimulation CardioFIT™ Systems (BioControl Medical, Yehud, Israel) Precision™ System, (GUIDANT Europe/Boston Scientific)	Sympathomodulatory—unilateral vagal nerve stimulation restores vagal tone and improves sympathovagal balance	Under investigation for use in heart failure and hypertension. Animal data only for hypertension indication	Inability to selectively target nerve fibres to avoid bradycardia and bradypnoea
Median nerve stimulation Subcutaneous Neuromodulation System (Valencia Technologies, Valencia, CA, USA)	Sympathomodulatory—subcutaneous unilateral implantation of a coin-sized device (in a 20-min office procedure) causing electrical stimulation of the median nerve and subsequent down-regulation of sympathetic outflow	A double-blinded study in 29 patients has shown reduction in ambulatory BP at 3 (9.2 mmHg) and 6 (18.9 mmHg) months	No published randomized controlled data

Renal sympathetic denervation:

Renal sympathetic nerves are important in the initiation of hypertension, and maintenance of the hypertensive state and interventions in animal models to abrogate renal sympathetic signalling prevent both the development of hypertension and lower BP. Increased renal sympathetic outflow, demonstrated in human hypertension, suggests that renal sympathetic nerves, conveniently located in a peri-arterial distribution, might be an attractive target for the treatment of hypertension.(181,182,183).

Evidence to date

Selective endovascular renal sympathectomy has been available for the past 5 years using catheter-based renal ablation with radiofrequency (RF) energy. The Symplicity HTN-1 feasibility study ignited interest in the field after demonstrating substantial and safe office BP reduction of 27/17 mmHg in patients with resistant hypertension (RHTN) after 12 months of follow-up.

The subsequent open label randomized non-sham-controlled Symplicity HTN-2 study also generated enormous publicity in the medical and lay press after demonstrating striking office BP reduction of 33/11 mmHg in RHTN patients treated with renal denervation (RDN) compared with control patients ($P < 0.001$).

However, ambulatory BP monitoring, performed in only half the patients, showed less impressive reduction than office BP in the RDN group (11/7 mmHg).

Heterogeneity of response to RDN was beginning to emerge in these earliest studies and continued to be a feature of numerous small, uncontrolled studies of RDN thereafter. Criticisms of the accumulating RDN dataset iterated several common themes including sub-optimal work up for secondary hypertension, study bias due to lack of blinded BP endpoints, lack of sham-controlled procedure and inadequacy of follow-up. To address these and other valid issues, the Symplicity HTN-3 study was undertaken in the USA and published its report in early 2014 to the surprise of many clinicians and those in the medical device industry.

This study, the largest of RDN to date, failed to demonstrate a difference in office and ambulatory BP lowering between patients treated with RDN and the sham (renal angiogram)-controlled group and thus failed its primary and secondary efficacy endpoints, although crucially the RDN procedure was deemed to be safe. Substantial limitations of this study have been subsequently identified by the investigators and have been the subject of extensive commentary.

These include important differences in baseline medication usage between the groups, unstable medications at baseline and 40% medication changes in both groups throughout the study. Most worryingly, only 19 of 364 patients (5%) treated with RDN actually received bilateral ablation in all four quadrants of the renal artery.

Not surprisingly, those that did receive per-protocol ablation therapy exhibited the greatest reductions in office, home, and ambulatory systolic BP (−24.3, −9.0, and −10.3 mmHg, respectively).

Prior to Symplicity HTN-3 several thousand patients had been treated worldwide, mostly using the first-generation single-electrode Symplicity catheter. Most of these patients were treated as a standard of care rather than in clinical trials, although data for some was captured in the Global Symplicity Registry. The first report from this dataset indicates that RDN is a safe and effective treatment for RHTN: 6 months following RDN, the reductions in office and 24-h systolic BPs were 12 and 7 mmHg, respectively, for all 998 patients (baseline office BP 164 mmHg) and 20 and 9 mmHg for 323 patients with severe hypertension (baseline office BP 179 mmHg), respectively ($P < 0.001$ for all responses).187

Similarly, the UK Renal Denervation Affiliation has reported large reductions in office and ambulatory BP (22/9 and 12/7 mmHg, respectively, P < 0.001 for both) in 253 patients with severe hypertension (baseline office BP 185/102 mmHg) treated according to strict criteria with five different RDN catheters and suggests that real world application of RDN is successful when done per protocol.

Despite the widespread adoption of RDN soon after the initial studies were published, there is a striking paucity of randomized controlled trial (RCT) data for RDN and the majority of the studies that exist are small in size with only 180 patients actively treated with RDN (excluding flawed Simplicity HTN-3), substantially less than the registries described earlier. A recent meta-analysis of these studies indicates that among all 588 patients treated with RDN in RCTs, there were heterogeneous effects for office and ambulatory BP which were not significantly reduced compared with control(25)

Randomized controlled trials of renal denervation SBP, systolic BP; ABP, ambulatory BP. Image supplied courtesy of Dr K Chan.(181,182,183).

Current technologies

Current approaches to RDN increasingly make use of multi-electrode catheters for RF ablation and irrigated balloon catheters for ultrasound (US) ablation. A separate class of catheters makes us of microinjection of neurotoxin (e.g. alcohol) to chemically ablate renal nerves and has the potential advantage of facilitating deeper nerve injury whilst avoiding endothelial damage. Separately, a non-vascular catheter-based technology deploys a transurethral approach to ablate the renal pelvis which is richly innervated with afferent fibres and could be an alternative for patients with bleeding disorders or renal artery anatomy that is unsuitable for current endovascular ablation catheters. A wholly non-invasive US platform (Surround Sound™, Kona Medical) that targets the distal renal artery and bifurcation using advanced Doppler imaging is currently in clinical trials in Europe with a US pivotal study planned to start recruiting in 2016.(181,182,183).

Future directions

Experts are in joint agreement over the need for the field of RDN therapy to build a new clinical basis with additional RCTs, although there is debate over the requirement for sham control. Three strategies to further identify ideal patients, enhance technical success, and optimize patient and investigator blinding have evolved:

Experimenting in drug naïve patients to eliminate the confounding effects of occult changes in pharmaceutical compliance on outcomes.

Development of tools to identify patients with significant contribution of renal sympathetic nerves to hypertension, and which enable documentation of procedural and technical success.

Requiring the use of ambulatory BP as an endpoint to eliminate the potential contribution of physician measurement bias on the outcome.

At this time, there is no obvious solution to nullify the impact of patient awareness of home BP on their pharmaceutical compliance and clinical behaviours.(181,182,183).

Central iliac arteriovenous anastomosis
Rationale and mechanism of action:

Drug	Launching	Degree of therapeutic Innovation*	Approved indications	Alternatives (cost/DDD)
Cefditoren	Sep-04	No therapeutic innovation	Pneumonia, exacerbation of chronic bronchitis, pharyngitis, tonsillitis, skin infections	Amoxicillin-clavulanate (€0.68) Cefuroxime axetil 2.27)
Duloxetine	Dec-05	No therapeutic innovation	Neuropathic pain, depresión, generalised anxiety disorder (from jul-08	Amitriptyline (€0.11) Fluoxetine (€0.24) Paroxetine (€0.79)
Etoricoxib	Jul-04	No therapeutic innovation	Osteoarthritis, rheumatoid artritis, acute gouty artritis, ankylosing spondylitis (from sep-08)	Ibuprofen (€0.24) Diclofenac (€0.17) Naproxen (€0.38)
Ezetimibe	Mar-04	Insufficient evidence	Primary hypercholesterolaemia, homozygous familial hypercholesterolaemia, homozygous sitosterolaemia	
Levocetirizine	Apr-03	No therapeutic innovation	Allergic rhinitis, chronic idiopathic urticaria	Cetirizine (€0.29)
Olmesartan	May-04	No therapeutic innovation	Hypertension	Losartan (€0.92) Enalapril (€0.13)
Pregabalin	Jan-05	No therapeutic innovation	Neuropathic pain, epilepsy, generalised anxiety disorder (from mar-06)	Gabapentin (€0.19) Amitriptyline (€0.11)

This novel approach is thought to principally address mechanical aspects of the circulation as opposed to primarily targeting the SNS. The central iliac arteriovenous (AV) anastomosis creates a fixed calibre conduit between the proximal arterial and low resistance venous circulation, which helps to restore the Windkessel function of the central circulation and thus providing a unique opportunity for improving proximal vascular compliance.

The anastomosis causes an immediate, significant reduction of BP, and systemic vascular resistance. The mechanism is related to the immediate reduction of effective arterial volume, vascular resistance, and buffering the contribution of reflected wave forms. Some sympathomodulatory effects are likely: by increasing venous oxygenation and right heart stretch through increased pre-load. (181,182,183).

Procedure

A 4-mm AV anastomosis between the external iliac artery and vein is created using a nitinol stent-like device (ROX AV coupler) in a 40-min catheterization laboratory procedure under fluoroscopic guidance.

In contrast to an RDN procedure, AV coupler deployment is verifiable and reversible if required, resulting in the diversion of a calibrated amount of arterial blood (0.8–1 L/min) into the proximal large capacitance venous circuit (. The immediate reduction in both systolic and diastolic BP obviates any contribution from placebo/Hawthorne effects.(181,182,183).

NEW DRUGS ADOPTED FOR TREATMENT OF HYPERTENSION

From the drugs marketed between 2003 and 2007, eight drugs with different indications were chosen **(Table no 5**). All of them are suitable for use both at primary and at secondary care levels and were indicated in common disorders in clinical practice.

HYPERTENSION IN PEDIATRICS AND GERIATRICS :

Hypertension in The Elders

The elderly is the most rapidly growing population group in the world. Data collected over a 30- year period have demonstrated the increasing prevalence of hypertension with age. The risk of coronary artery disease, stroke, congestive heart disease, chronic kidney insufficiency and dementia is also increased in this subgroup of hypertensive. Hypertension in the elderly patients represents a management dilemma to cardiovascular specialists and other practitioner.

During the last years and before the findings of the Systolic Hypertension in Europe Trial were published, the general medical opinion considered not to decrease blood pressure values similarly to other younger patients, in order to avoid possible ischemic events and poor oxygenation of the organs (brain, heart, kidney).

The aim of this review article is to highlight the importance of treating hypertension in aged population in order to improve their quality of life and lower the incidence of the cardiovascular complications.(58).

Hypertension is an important risk factor for cardiovascular morbidity and mortality, particularly in the elderly. It is a significant and often chronic disease, which requires optimal control and persistent adherence to prescribed medication to reduce the risks of cardiovascular, cerebrovascular and renal disease (59).

According to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-7), hypertension occurs in more than two thirds of individuals after age of 65 .(60).

Data from the Framingham Heart Study, in men and women free of hypertension at 55 years of age indicate that the remaining lifetime risks for development of hypertension through 80 years are 93% and 91% respectively.(61).

In other words, more than 90% of individuals who are free of hypertension at 55 years of age will develop it during their remaining lifespan.(62).

Hypertension prevalence is less in women than in men until 45 years of age, is similar in both sexes from 45 to 64 and is much higher in women than men over 65 years of age (63).

The severity of hypertension increases markedly with advancing age in women as well. After the age of 60 years, the majority of women (age 60-79 years: 48.8%; age ≥ 80 years: 63%) has stage 2 hypertension (BP ≥ 160/100 mmHg) or receives antihypertensive therapy.(64).

BP control is difficult to achieve in elderly women. Endothelial dysfunction, increased arterial stiffness, obesity, genetic factors, elevated total cholesterol and low high-density lipoprotein cholesterol levels have been implicated in menopause-related BP elevation rather than ovarian failure.(65).

Hypertension among blacks is earlier in onset, more severe and uncontrolled and contributes to the highest coronary artery disease (CAD) mortality rates in the USA in addition to the highest morbidity and mortality attributable to stroke, left ventricular hypertrophy (LVH),heart failure (HF)and chronic kidney disease.

Compared with whites, blacks are more likely to have hypertension more likely to be aware of it and more likely to be pharmacologically treated, but less likely to achieve BP control. (66).

Hypertension is an important factor in the disproportionate decreased life expectancy for blacks: African-American men 70.0 years' vs 75.9 years for white men and African- American women 76.8 years' vs 80.8 years for white women.(67).

Table no 6. Classification of blood pressure for adults according to JNC-7.

Classification	SBP (mmHg)	DBP (mmHg)
Normal	≤ 120	And ≤ 80
Prehypertension	120-139	Or 80-89
Stage 1 hypertension	140-159	Or 90-99
Stage 2 hypertension	≥ 160	Or ≥ 100

Preeclampsia happens when a woman who previously had normal blood.

pressure suddenly develops high blood pressure* and protein in her urine or other problems after 20 weeks of pregnancy. Women who have chronic hypertension can also get preeclampsia. Preeclampsia happens in about 1 in 25 pregnancies in the United States.(68).

High blood pressure during pregnancy poses risks, including: Decreased blood flow to placenta .

Hypertension in Paediatrics

In children and adolescents, the normal range of BP is determined by body size and age. BP standards that are based on sex, age, and height provide a more precise classification of BP according to body size. This approach avoids misclassifying children who are very tall or very short. (69).

If the child's BP (systolic or diastolic) is at or above the 95th percentile, the child may be hypertensive, and the measurement must be repeated on at least two additional occasions to confirm the diagnosis.

On repeated measurement, hypertensive children may have BP levels that are only a few mmHg above the 95th percentile; these children would be managed differently from hypertensive children who have BP levels that are 15–20 mmHg above the 95th percentile. An important clinical decision is to determine which hypertensive ■ BP standards based on sex, age, and height provide a precise classification of BP according to body size. ■ The revised BP tables now include the 50th, 90th, 95th, and 99th percentiles (with standard deviations) by sex, age, and height. children require more immediate attention for elevated BP. (70).

The difference between the 95th and 99th percentiles is only 7–10 mmHg and is not large enough, particularly in view of the variability in BP measurements, to adequately distinguish mild hypertension—where limited evaluation is most appropriate—from more severe hypertension where more immediate and extensive intervention is indicated. (71-73).

Therefore, Stage 1 hypertension is the designation for BP levels that range from the 95th percentile to 5 mmHg above the 99th percentile. Stage 2 hypertension is the designation for BP levels that are higher than 5 mmHg above the 99th percentile. Once confirmed on repeated measures, Stage 1 hypertension allows time for evaluation before initiating treatment unless the patient is symptomatic. Patients with Stage 2 hypertension may need more prompt evaluation and pharmacologic therapy. (74-77).

Factors responsible for hypertension in children:

The risk factors for developing primary hypertension include: Being overweight or obese. Having a family history of high blood pressure. Having type 2 diabetes or a high fasting blood sugar level pheochromocytoma.

Renal disease is the most common cause of secondary hypertension in children. 23–25 Other causes include endocrine disease (e.g., hyperthyroidism) and pharmaceuticals (e.g., oral contraceptives, sympathomimetic, some over-the-counter preparations, dietary. (78).

Classification of Hypertension in Children and Adolescents.

Table no:7 With Measurement Frequency and Therapy Recommendations.

	SBP or DBP Percentile*	Frequency of BP Measurement	Therapeutic Lifestyle Changes	Pharmacologic Therapy
Normal	<90th	Recheck at next scheduled physical examination.	Encourage healthy diet, sleep, and physical activity.	—
Prehypertension	90th to <95th or if BP exceeds 120/80 mmHg even if below 90th percentile up to <95th percentile†	Recheck in 6 months.	Weight-management counseling if overweight, introduce physical activity and diet management.‡	None unless compelling indications such as CKD, diabetes mellitus, heart failure, or LVH exist
Stage 1 hypertension	95th percentile to the 99th percentile plus 5 mmHg	Recheck in 1–2 weeks or sooner if the patient is symptomatic; if persistently elevated on two additional occasions, evaluate or refer to source of care within 1 month.	Weight-management counseling if overweight, introduce physical activity and diet management.‡	Initiate therapy based on indications in Table 6 or if compelling indications as above.
Stage 2 hypertension	>99th percentile plus 5 mmHg	Evaluate or refer to source of care within 1 week or immediately if the patient is symptomatic.	Weight-management counseling if overweight, introduce physical activity and diet management.‡	Initiate therapy.§

OBJECTIVES

GENERAL OBJECTIVE:

To assess the prescribing habits of cardiologist.

SPECIFIC OBJECTIVES:

1. to promote rational use of drugs.
2. to promote cause effective features of drugs.
3. to minimize anticipated interactions .
4. to minimize hospital stay.
5. to provide feedback.

METHODOLOGY

PHASES AND STEPS INVOLVED IN CONDUCTING A DRUG USE EVALUATION

PHASE 1 -PLANNING

STEP 1- IDENTIFY THE DRUGS WHICH ARE MOSTLY PRESCRIBED

Identify drugs of therapeutic use practice for possible inclusion in the program. It is not possible and also unnecessary to examine every drug that is used in the population . Hence, the drug utilisation review (DUR) committee must identify priority drugs to practice where improvement in use will result in the latest clinical impart. These areas can be identified through various sources of information such as medication error , adverse drug reaction reports, feedback from prescriber or clinical pharmacist and pharmaceutical literature .

STEP 2- DESIGN OF SURVEY

A variety of research methods have been used in DUR survey. Observational research methods are most commonly used than experimental methods such as randomised controlled trials , cross sectional survey, where drugs use is examined at single point in time are useful for proper identification .

The proposed design where drug use is examined before and after intervention to improve prescribing another commonly used observational method .

DUR studies may also be described as prospective ,concurrent or retrospective depending on timing of data collection.

STEP 3- DEFINE CRITERIA AND STANDARDS

After the DUR target has been selected, it is important to conduct a comprehensive literature review. The extent of work involved in thus step depends on what has been done previously or what is already available. ed. Local, reliable and authoritative guidelines or previous DUR criteria.

Criteria are those predetermined statements describing optimal drug as compared. standards are professionals developed expressions of the range of acceptable variations from a criterion. Criterion should be scientifically based and be supposed by clinical or research literature. They must be valid. Unambiguous. realistic, easily measured and outcome oriented.

STEP 4 – DESIGN AND DATA COLLECTION FORM

Just as it is impossible to monitor and evaluate all dugs used in the population .it is also impossible to address all aspects od use for each individual drugs.

Your Name: _____

Patient Study ID # _____

Date _____

Patient Survey About High Blood Pressure and Its Treatment - 1

Thank you for participating in this survey. The following questions ask about your health history, beliefs about high blood pressure, use of services, and background information. If you have a question, you may circle the question number and leave it blank. A researcher will check the survey, clarify any questions, and give you the gift card before you leave.

Thank you for your help!

A. HEALTH HISTORY

1. Have you ever been told by a doctor or other health professional that you had...

	Yes	No		Yes	No
a. Diabetes or sugar diabetes?	1☐	2☐	i. Weak or failing kidneys?	1☐	2☐
b. A heart attack?	1☐	2☐	j. Kidney dialysis?	1☐	2☐
c. Congestive heart failure?	1☐	2☐	k. Narrowing of the arteries?	1☐	2☐
d. Enlarged heart?	1☐	2☐	l. Speech difficulty?	1☐	2☐
e. Angina (chest pain)?	1☐	2☐	m. Weakness on one side?	1☐	2☐
f. A coronary bypass?	1☐	2☐	n. Slurred speech?	1☐	2☐
g. A stroke?	1☐	2☐	o. Loss of balance?	1☐	2☐
h. High cholesterol?	1☐	2☐	p. Fainting or losing consciousness?	1☐	2☐

2. Did your mother die from or suffer a heart attack or stroke before she was 65 years old?

1☐ Yes
2☐ No
8☐ Don't know/Not applicable

3. Did your father die from or suffer a heart attack or stroke before he was 55 years old?

1☐ Yes
2☐ No
8☐ Don't know/Not applicable

4. Do you now take diabetic pills or insulin for diabetes?

1☐ Yes
2☐ No
8☐ Don't know

5. Within the past 30 days, have you had the following problems?

	Yes	No		Yes	No
a. Dizziness	1☐	2☐	m. Numbness, tingling of hands	1☐	2☐
b. Headaches	1☐	2☐	n. Leg pain or swelling	1☐	2☐
c. Shortness of breath	1☐	2☐	o. Leg cramps	1☐	2☐
d. Feeling tired	1☐	2☐	p. Cold hands or feet	1☐	2☐
e. Thumping or racing heart	1☐	2☐	q. Difficulty breathing	1☐	2☐
f. Feeling weak when I stand up	1☐	2☐	r. Dry, hacking cough	1☐	2☐
g. Feeling depressed or blue	1☐	2☐	s. Decreased interest in sex	1☐	2☐
h. Frequent thirst	1☐	2☐	t. Unable to get an erection	1☐	2☐
i. Frequent urination	1☐	2☐	u. Difficulty sleeping	1☐	2☐
j. Dry mouth	1☐	2☐	v. Rash or hives	1☐	2☐
k. Loss of taste	1☐	2☐	w. Constipation or diarrhea	1☐	2☐
l. Blurry vision	1☐	2☐	x. Other → SPECIFY: _____	1☐	2☐

B. YOUR HIGH BLOOD PRESSURE & LIFESTYLE

6. How long have you been taking medication for high blood pressure

1☐ Less than one year
2☐ 1–2 years
3☐ More than 2 years
8☐ Don't know

7. Has your doctor or health care provider ever told you what your blood pressure GOAL should be?

1☐ Yes, he/she told me my blood pressure numbers should be: ____/_____ or lower.
2☐ Yes, he/she gave me a blood pressure goal, but I do not remember the numbers.
3☐ No, he/she has never told me what my blood pressure numbers should be.
8☐ I don't remember.

8. What do you think your blood pressure numbers should be?

1☐ I think my blood pressure numbers should be: ____/_____ or lower.
8☐ I don't know what my blood pressure numbers should be.

9. What do you think about your blood pressure level today? Do you think it was...

1☐ High
2☐ Borderline high
3☐ Normal/OK
4☐ Low
8☐ Don't know

10. How often can you tell by the way you feel that your blood pressure is too high?

1☐ Never
2☐ Rarely
3☐ Sometimes
4☐ Usually
5☐ Always

11.. How concerned are you about your blood pressure level at this time?

1☐ Very concerned
2☐ Somewhat concerned
3☐ A little concerned
4☐ Not at all concerned

12. Following are some medical guidelines for lowering blood pressure. In columns I and II, please check how **hard** and how **helpful** you think it would be for you to follow each guideline, **even if you have not tried to follow this guideline.**

	I. How hard do you think it would be for you to follow this guideline?	II. How helpful do you think it would be for you to follow this guideline?
a. Reduce the salt or sodium in your diet if needed	1☐ Very hard 2☐ Moderately hard 3☐ Not at all hard	1☐ Very helpful 2☐ Moderately helpful 3☐ Not at all helpful
b. Walk or exercise 30 minutes per day 5 days a week	1☐ Very hard 2☐ Moderately hard 3☐ Not at all hard	1☐ Very helpful 2☐ Moderately helpful 3☐ Not at all helpful
c. Eat 5 or more servings of vegetables and fruit a day	1☐ Very hard 2☐ Moderately hard 3☐ Not at all hard	1☐ Very helpful 2☐ Moderately helpful 3☐ Not at all helpful
d. Maintain normal weight or lose weight if needed	1☐ Very hard 2☐ Moderately hard 3☐ Not at all hard	1☐ Very helpful 2☐ Moderately helpful 3☐ Not at all helpful
e. Use alcohol in moderation (no more than 1-2 drinks per day)	1☐ Very hard 2☐ Moderately hard 3☐ Not at all hard	1☐ Very helpful 2☐ Moderately helpful 3☐ Not at all helpful
f. Take blood pressure medication every day	1☐ Very hard 2☐ Moderately hard 3☐ Not at all hard	1☐ Very helpful 2☐ Moderately helpful 3☐ Not at all helpful

13. Do you currently use the following methods for remembering your blood pressure medication?

	Yes	No		Yes	No
a. I use a 7-day pill box	1☐	2☐	e. I take pills before or after a daily routine (e.g., brushing teeth, eating, going to bed)	1☐	2☐
b. I use another type of box	1☐	2☐	f. I keep my pills where I can see them	1☐	2☐
c. I carry my pills with me	1☐	2☐	g. I use a watch with alarm(s)	1☐	2☐
d. I take my pills at the same time(s) each day	1☐	2☐	h. Other → SPECIFY: _____	1☐	2☐

14. Do you currently use the following methods for monitoring your health and lifestyle?

	Yes	No
a. I use a blood pressure monitor to check my blood pressure at home	1☐	2☐
b. I use a special card to keep track of my blood pressure readings	1☐	2☐
c. I check food labels to help control or reduce the salt or sodium in my diet	1☐	2☐
d. I use a pedometer or step-counter to help stay active or monitor my walking	1☐	2☐

15. Think about the time you spent walking in the last 7 days. This includes at work and at home, walking to work and other places, and any other walking you do for recreation, sport, exercise, or leisure.

In the last 7 days, about how many days did you walk at least 30 minutes per day? (IF NONE, WRITE '0' ON THE LINE.)

____ Days

16. Next, think about the time you spent doing other aerobic physical activities in the last 7 days. This includes any activity that takes physical effort and makes you breathe harder than normal (e.g., bicycling, water aerobics, basketball, dancing fast, washing floors, heavy lifting).

In the last 7 days, about how many days did you do other aerobic physical activities at least 30 minutes per day? (IF NONE, WRITE '0' ON THE LINE.)

____ Days

17. How many servings of fruit do you eat in a typical day? A serving includes: 1 medium fruit, ½ cup fresh, frozen, or canned fruit, ¼ cup dried fruit, or 6 ounces fruit juice. (IF NONE, WRITE '0' ON THE LINE.)

____ Fruit servings per day

18. How many servings of vegetables do you eat in a typical day? A serving includes 1 cup raw leafy vegetables, ½ cup cooked or cut-up vegetable, or 6 ounces vegetable juice. (IF NONE, WRITE '0' ON THE LINE.)

____ Vegetable servings per day

19. During the last 30 days, about how many days did you drink any type of alcoholic beverage? (IF NONE, PLEASE WRITE '0' ON THE LINE.)

____ Days

20. If you drank any alcoholic beverage during the last 30 days, how many drinks did you usually have **per day**? (One drink equals one 5 oz. glass of wine, one 12 oz. can/bottle of beer, or one shot of whiskey/hard liquor.)

0☐ None (never drank alcohol during last 30 days)
1☐ 1 drink/shot
2☐ 2 drinks/shots
3☐ 3 drinks/shots
4☐ 4 drinks/shots
5☐ 5 drinks/shots
6☐ 6 drinks/shots
7☐ More than 6 drinks/shots

C. DEMOGRAPHIC INFORMATION

21. Are you male or female?

1☐ Male
2☐ Female

22. What is your birth date?

Month:_____ Day: _____ Year: _____

23. What is your race/ethnicity? (CHECK ALL THAT APPLY.)

1☐ African American or Black
2☐ American Indian or Alaskan Native
3☐ Asian
4☐ Hispanic or Latino/Latina
5☐ Native Hawaiian/Other Pacific Islander
6☐ White

24. What is the highest level of formal education you have received?

1☐ Less than high school
2☐ Some high school
3☐ Completed high school or G.E.D.
4☐ Some college or technical school
5☐ Completed technical school/associate's degree
6☐ Completed B.A. or B.S. degree
7☐ Graduate study/advanced degree(s)

25. What is your current employment status?

1☐ Employed full-time (35 hours a week or more)
2☐ Employed part-time (less than 35 hours a week)
3☐ Not currently employed

Thank you!

Please return this form to a researcher.

Figure no:19 DATA COLLECTION FORM.

PHASE 2- DATA COLLECTION

STEP 5- COLLECTION DATA

Data collectors should be choosing carefully and should be familiar with the new information is arranged in the patients care notes. knowledge of dugs names, strength and the way order are written is also important. depending upon the availability, physicians, pharmacist and nurses make ideal data collectors .

Participants

The target population comprised non-compliant hypertensive patients who were diagnosed with and receiving treatment for hypertension. (79) . Inclusion criteria were: anyone between the ages of 18 and 80 years, being treated with antihypertensives for >3 months, being non-compliant and having sufficiently good physical and mental health to participate. Detailed information about the type of antihypertensive or duration of treatment could not be collected.

In order to determine whether or not the patient was compliant, an online survey was first conducted among 50 hypertensive patients, who were either the relatives of the surveyor's WhatsApp contact list or the persons of the WhatsApp contact list.

A total of 50 patients, 26 men and 24 women, participated where conventional consent and confidentiality procedures were followed. A questionnaire was forwarded in two separate WhatsApp groups of males and females in order to get the answers for it .We felt that our participants might be diffident in discussing issues related to their health in the presence of the opposite sex and therefore decided to have separate male and female groups.

The focus group interview

In order to elicit information on the patient's perspective of their condition, their treatment and the relationship with the provider, pre-determined, open-ended questions were arranged by way of a guided interview questionnaire .

Factors identified as influencing treatment compliance fell into three categories: beliefs and attitudes about antihypertensive drugs; beliefs and attitudes about hypertension; and clinical encounters.

At first glance, the results indicated negative feelings towards medicines, low awareness about the condition and dissatisfaction with clinical encounters as barriers with regard to following treatment advice. Some of these factors were similar to those found in other studies on compliance in hypertension. (82,83,84,85).

Beliefs and attitudes towards antihypertensive drugs

Fears were expressed about the long-term use of antihypertensive medication and the possibility of being stuck with it for the rest of one's life. Negative feelings were elicited in many cases, as antihypertensives were perceived as being damaging and not good for the body.

"I was afraid of the medication, because I was told that once I started to take it I would have to take it all my life". (Participant 2; focus group 2)

"I think that has to be damaging to some part of my body". (Participant 6; focus group 7)

"I don't like them (medicines), they have lots of side effects, they can make you sick. I think that I might get worse instead of better". (Participant 1; focus group 2

Beliefs and attitudes about hypertension

The fact of having high blood pressure did not seem worrisome for patients and was often associated with certain well-recognized familiar symptoms, as if the absence of them meant that blood pressure was controlled.

"The doctor told me 'your blood pressure's a bit high, 16–17'. but I didn't think that was important.". (Participant 6; focus group 3)

"I have to feel sick, or have a sore neck and then I'll have my blood pressure taken". (Participant 3; focus group 1)

"Anything I know about blood pressure I've read in books, the doctor tells me absolutely nothing. I want him to tell me where high blood pressure comes from". (Participant 4; focus group 1)

Clinical encounters

The majority of patients complained about the length of the consultation. They claimed that little time was spent with regard to informing; indeed most of the consultation time was used just to get the prescription.

"You only get to see the doctor for five minutes". (Participant 3; focus group 1)

"There's not really any conversation, you're there explaining what's wrong with you and he doesn't even look at you, he's just taking notes … He sends you away with a few words 'here is your prescription' and that's it". (Participant 7; focus group 6)

PHASE 3 -EVALUATION

STEP 6-COLLECT DATA AND EVALUATE RESULTS

Data collection is one of the most critical steps in DUR. The data obtained should be collected using available resources such as spread sheets, data bases, and word processing. the next step is to summarize the major categories of results and to identify where exact the data shows deviation from guidelines and usage criteria that are previously identified..

Clinical Evaluation.

Table no:8.

Study or Procedure	Purpose	Target Population
Evaluation for identifiable causes		
History, including sleep history, family history, risk factors, diet, and habits such as smoking and drinking alcohol; physical examination	History and physical examination help focus subsequent evaluation	All children with persistent BP ≥95th percentile
BUN, creatinine, electrolytes, urinalysis, and urine culture	R/O renal disease and chronic pyelonephritis	All children with persistent BP ≥95th percentile
CBC	R/O anemia, consistent with chronic renal disease	All children with persistent BP ≥95th percentile
Renal U/S	R/O renal scar, congenital anomaly, or disparate renal size	All children with persistent BP ≥95th percentile
Evaluation for comorbidity		
Fasting lipid panel, fasting glucose	Identify hyperlipidemia, identify metabolic abnormalities	Overweight patients with BP at 90th–94th percentile; all patients with BP ≥95th percentile. Family history of hypertension or cardiovascular disease. Child with chronic renal disease
Drug screen	Identify substances that might cause hypertension	History suggestive of possible contribution by substances or drugs
Polysomnography	Identify sleep disorder in association with hypertension	History of loud, frequent snoring
Evaluation for target-organ damage		
Echocardiogram	Identify LVH and other indications of cardiac involvement	Patients with comorbid risk factors* and BP 90th–94th percentile; all patients with BP ≥95th percentile
Retinal exam	Identify retinal vascular changes	Patients with comorbid risk factors* and BP 90th–94th percentile; all patients with BP ≥95th percentile
Further evaluation as indicated		
Ambulatory BP monitoring	Identify white-coat hypertension, abnormal diurnal BP pattern, BP load	Patients in whom white-coat hypertension is suspected, and when other information on BP pattern is needed
Plasma renin determination	Identify low renin, suggesting mineralo- corticoid-related disease	Young children with Stage 1 hypertension and any child or adolescent with Stage 2 hypertension Positive family history of severe hypertension
Renovascular imaging Isotopic scintigraphy (renal scan) Magnetic resonance angiography Duplex Doppler flow studies 3-Dimensional CT Arteriography: DSA or classic	Identify renovascular disease	Young children with Stage 1 hypertension and any child or adolescent with Stage 2 hypertension
Plasma and urine steroid levels	Identify steroid-mediated hypertension	Young children with Stage 1 hypertension and any child or adolescent with Stage 2 hypertension
Plasma and urine catecholamines	Identify catecholamine-mediated hypertension	Young children with Stage 1 hypertension and any child or adolescent with Stage 2 hypertension

PHASE 4- FEEDBACK OF RESULTS

STEP 7-FEEDBACK RESULTS TO CLINICIOUS HOSPITAL STAFF

The success of any DUR strategy depends upon feedback of the results to prescriber.

This study was conducted through web. Many patients in and around Telangana were surveyed, it was conducted online and about 50 patients was surveyed, their questionnaire was studied in detail. The survey includes treatment for geriatrics and paediatrics also. Wee focussed o different parameters like various class of drugs given to the patients, gender, age etc.

DISCUSSION AND RESULT

At first glance, the results indicated negative feelings towards medicines, low awareness about the condition and dissatisfaction with clinical encounters as barriers with regard to following treatment advice. Some of these factors were similar to those found in other studies on compliance in hypertension.[7,8,12,13] In the main, these factors can be summarized in two categories: patient and physician context related. Most of them do have clear implications for patient management, as the predominant view that emerges is that there is plenty of room for improvement in the patient–physician communication. First, it is, arguably, surprising to discover that patients with a chronic condition, such as hypertension, lack basic background knowledge about it, such as its potential risks and why it is important to follow the prescribed treatment even in the absence of symptoms. So it does not seem odd that they also have lay knowledge and beliefs on medication that can, consequently, reduce compliance. These must be addressed by the physician and, if this is the case, adequate information should be provided to reduce the fear and anxiety derived from the use of medicines, and hence this will improve compliance. Even so, this study shows that, in the ordinary clinical situation, patients often fail to understand what they are told and, what is more, without this primary basis the patient cannot build up a rationale for the therapy.[14] This aspect of the doctor–patient relationship has been visited previously, where it was argued that doctors offer simple instructions on several occasions and yet the patient, due largely to anxiety, does not receive such information.[15] This puts the physician in a unique position of responsibility and opportunity to act not only as diagnostician but also as a qualified patient educator. In this respect, participants in the focus groups put the highest emphasis on physician's empathetic qualities, in being interested.

All of this led to the conclusion that knowing patients' priorities regarding the most important aspects of care that have high potential for low compliance may be helpful in improvement of the quality in the care of the hypertensive patient.

Hypertension in the elderly when untreated is associated with increased morbidity and mortality due to long-term complications that include cardiovascular, cerebrovascular and chronic kidney disease and possibly also cognitive decline and/or dementia. However, elderly patients are often frail and have multiple age-related comorbidities that are not associated with chronic hypertension. Clinicians must balance the benefits and risks of using pharmacological treatment in hypertensive elderly patients with comorbidities in view of current evidence of the use of antihypertensive drugs in this population. Currently, there is no consensus regarding guidelines for the SBP and/or DBP target(s) for initiation of drug therapy or for optimal treatment of hypertension in elderly and very elderly patients.

ROLE OF PHARMACIST IN THIS SCENARIO {HYPERTENSION}

Pharmacists can be key players in controlling hypertension, given their medication knowledge and patient counselling skills, yet they remain an underutilized resource in the management of chronic disease states. Various models exist that allow pharmacists to provide direct patient-centred care but practices differ from state to state since pharmacists are not recognized nationally as healthcare providers.

Pharmacists can contribute to HTN management in a variety of ways, including assisting with out-of-office monitoring, providing education, identifying and resolving nonadherence, and titrating antihypertensive therapy to achieve BP control.

If a patient's BP is confirmed to be persistently above the agreed treatment targets, the patient can be seen by the practice pharmacist to optimise BP control. Pharmacists can also take into account any abnormal blood test results, and refer to the GP where necessary. If patients have low BP readings and/or are experiencing hypotensive symptoms, they could also be referred to the practice pharmacist for a possible dose reduction, or complete stoppage, of oral antihypertensive medication with continual monitoring.[12]

Practice pharmacists may also titrate (up to the maximum tolerated doses) and monitor oral antihypertensive medications started in secondary care such as beta-blockers or ACE inhibitors for patients who may have had an acute coronary syndrome (ACS).[17]

Patients may become motivated to make lifestyle changes and they may want to reduce or stop using antihypertensive drugs. If the patient is at low cardiovascular risk and their BP has been well controlled for a number of years, they should be offered a trial reduction or withdrawal of therapy with appropriate guidance and be followed up for 6 months at 4-weekly intervals, then 2–3 times annually, to ensure any recurrence is detected.[12] Patients vary in their attitudes to their hypertension and their experience of treatment. It may be worth discussing exercise referral with the patient if clinically appropriate and the patient fits the relevant criteria.

CONCLUSION

In conclusion the use of anti-hypertensive drugs in the treatment of hypertension was almost found to be rational. In this survey many different drugs were prescribed which were from national list of essential drugs. Rational use of drugs minimizes polypharmacy, drug interactions in turn it minimizes the surgery and hospital stay.

The prescribing habits are appropriate and are in accordance with the WHO guidelines. pharmacist is the key person for better management of therapy based on condition and age of patient. Working as a pharmacist is an image for pharmacist to be considered in a healthcare team to fight against hypertension.

The ability of the pharmacist to recognize condition as a critical factor in hypertension therapy is important as well as when working through the financial concerns.

Thus, the pharmacist is a DRUG EXPERT who carries out valuable, knowledgeable duties and serves the community in a very dutiful manner.

We also compared the use of drugs in patients of different ages and different gender.

It has been a sincere effort by us, to minimize the anticipated untoward events in our dissertation.

It is believed to use the rational in the coming future.

FIGURE NO:20 HYPERTENSION PATIENT JOURNEY.

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ABBREVIATIONS

1.	ABG	Arterial blood gases
2.	ACE	Angiotensin converting enzyme
3.	ACL	Anterior cruciate ligament
4.	ADHD	Attention deficit hyperactivity disorder
5.	AFIB	Atrial fibrillation
6.	BP	Blood pressure
7.	CABG	Coronary artery bypass graft
8.	CAD	Coronary artery disease
9.	CAT	Computerized axial tomography
10.	CBC	Complete blood count
11.	CHD	Congenital heart disease
12.	CHF	Congestive heart failure
13.	DVT	Deep-vein thrombosis
14.	DX	Diagnosis
15.	ECG, EKG	Electrocardiogram
16.	ECHO	Echocardiogram
17.	HCT	Hematocrit
18.	ICU	Intensive care unit
19.	IDDM	Insulin-dependent diabetes mellitus
20.	MI	Myocardial infarction
21.	NSAID	Non-steroidal anti-inflammatory drug
22.	OCD	Obsessive-compulsive disorder
23.	PAD	Peripheral arterial disease
24.	RBC	Red blood cell
25.	SOB	Shortness of Breath
26.	TIBC	Total iron binding capacity
27.	XRT	Radiotherapy
28.	WBC	White blood cell

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