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Contents

EDITORIAL

Hypertension and Stroke

Bhupendra Chaudhary, Binay Karak.....5

ORIGINAL ARTICLE

Congestive Heart Failure with Hypotension: A Misdiagnosis

Priyanka Pandey, Abhishek Singhai, RK Jha.....9

Epidemiologic Surveillance of Indian Hypertensive Patients after Treatment with a Single Tablet, Fixed Dose Combinations of Indapamide SR 1.5 mg and Incremental Strengths of Amlodipine

Hemant Thacker, Rahul Patil, Pankaj Rastogi, Amitabh Gautam, K Satish 11

Epicardial Adipose Tissue Thickness:**A Novel Cardiometabolic Risk in Hypertensive Obese Adults**

Arvind Mittal, Pranay Bajpai, Dolly Joseph, RK Jha 16

Prevalence of Diabetes, Hypertension and Cardiovascular Disease in COPD

Deepika Patel, A Singhai, R Doshi, S Motiwale, RK Jha 18

REVIEW ARTICLE

Home Blood Pressure Monitoring

Nihar Mehta, Vishal Vanani..... 20

Clinical Diagnosis and Management of Hypertensive Crises

Santosh B Salagre, Shobha M Itollikar 25

CASE REPORTS

Rare Cause of Uncontrolled Hypertension

Ishita Shah, Falguni Parikh, Dheeraj Kapoor, TB Yuvraja 36

Biochemical Silent Pheochromocytoma Presented as New Onset Resistant Hypertension

Hozefa Runderawala, Iqbal Bagasrawala, Siddharth Shah..... 39

Hypertension Abstracts of APICON 2017 42

ANNOUNCEMENTS

2nd International Conference on Hypertension & Health Care..... 15**The 4th Latin America Congress on Controversies to Consensus in Diabetes, Obesity and Hypertension (CODHy 2017)** 17**Nephrology 2017**..... 24**National Annual Conference of Hypertension Society of India**..... 35



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Hypertension and Stroke

Bhupendra Chaudhary¹, Binay Karak²

Hypertension, an enigmatic disease, remains one of the most important preventable contributors to disease and death. It is very common but commonly untreated, or remains uncontrolled. Even after many decades of its clinical significance, still 90% of hypertensives are primary (idiopathic or essential). In addition to this enigma, guidelines recently published add confusion with their discordant suggestions. All these guidelines unanimously accept that the treatment of hypertension starts from lifestyle modification.

Several observations have demonstrated spontaneous elevation of blood pressure in the first 24-48 h after stroke onset with a significant spontaneous decline after a few days. Several mechanisms may be responsible for the increased blood pressure including stress, pain, urinary retention, Cushing effect due to increased intra cranial pressure and the activation of the sympathetic, renin-angiotensin and ACTH-cortisol pathways. Despite of increased prevalence of hypertension following stroke, optimal management has not been yet established. Several arguments speak for lowering the elevated BP: risks of hemorrhagic transformation, cerebral edema, recurrence of stroke and hypertensive encephalopathy. On the other hand, it may

be important to maintain the hypertensive state due to the damaged autoregulation in the Ischemic brain and the risk of cerebral hypoperfusion exacerbated by the lowered systemic blood pressure.

Hypertension is the most important modifiable risk factor for stroke. It is estimated that 25% or more of strokes may be attributable to hypertension. Because many patients with stroke have mild hypertension or prehypertension, we have shifted our focus and now think of stroke on a continuum of risk based on blood pressure (BP) level rather than on a threshold effect. Because high BP may not exist in isolation, a wider definition of hypertension has been proposed that also takes into account the absolute risk of cardiovascular events and associated metabolic factors or early disease markers.

Lowering BP reduces the risk of stroke. Epidemiological studies have shown that for each 10 mm Hg lower systolic blood pressure (SBP), there is a decrease in risk of stroke of approximately one third in persons aged 60 to 79 years. This association is continuous down to levels of at least 115/75 mm Hg and is consistent across sexes, regions, stroke subtypes, and for fatal and nonfatal events. Lowering diastolic blood pressure (DBP) was once the main target to achieve stroke and other cardiovascular event reduction, but SBP has now become the target. As recently

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shown, even the elderly with sustained SBP elevation may gain from BP reduction in relation to less fatal or nonfatal stroke, death, and heart failure.

Although the role of longer-term BP control to improve outcomes in patients with stroke is undisputed, BP management immediately after a stroke remains controversial.

BLOOD PRESSURE MANAGEMENT AFTER ACUTE ISCHEMIC STROKE

Although hypertension in the immediate post-stroke period is frequently observed, BP tends to spontaneously fall within the first hours and days following the acute event, with the pattern of blood pressure change varying with stroke subtype. Precipitous falls in BP have, however, been associated with poor outcome and should be avoided. A 'U-shaped' association between admission BP and stroke outcome has been identified, with very high and very low BP being associated with poor post-stroke outcome. Early recurrent stroke has been suggested as one possible mechanism by which elevated BP may be associated with poor outcome. Cerebral perfusion becomes dependent upon systemic arterial BP following stroke due to impairment of cerebral autoregulation, and therefore changes in systemic BP can directly influence cerebral perfusion. Hypertension may sustain cerebral perfusion to the ischemic penumbra, with BP having been shown to fall spontaneously in response to successful recanalization of cerebral vessels following thrombolytic treatment, perhaps suggesting the restoration of cerebral autoregulation. High pre-thrombolysis BP has also been shown to be associated with poor recanalization and sustained hypertension may contribute to worsening cerebral edema and hemorrhagic transformation following acute ischemic stroke. Cardiovascular complications as well as early stroke recurrence in patients with elevated post-stroke BPs have been proposed as possible mechanisms for poor outcome.

DILEMMA ON BP MANAGEMENT IMMEDIATELY AFTER AN ACUTE ISCHEMIC STROKE

Apart from managing the ischemic penumbra, the management of other parameters like hyperglycemia, hyperthermia, raised ICP and the accelerated HT are of paramount importance, of which the high blood pressure leads the situation.

SHOULD BLOOD PRESSURE BE LOWERED IN PATIENTS WITH ELEVATED BP AFTER AN ISCHEMIC STROKE?

As per the AHA/ASA guidelines, it is recommended that before intravenous thrombolytic treatment, BP should be lowered if >185 mm Hg systolic or >110 mm Hg diastolic. After thrombolytic treatment, SBP should be kept <180 mm Hg and DBP <105 mm Hg. Intravenous labetalol, nitroglycerin, nicardipine infusion, and, if BP remains elevated, sodium nitroprusside are the recommended agents. Despite the absence of supporting evidence, these recommendations are often applied to patients receiving other forms of reperfusion therapy (e.g., intra-arterial thrombolysis, clot retrieval, and so on). Patients with other indications for BP-lowering such as acute heart failure, aortic dissection, and so on should have the BP lowered. One should be cautious about abruptly lowering BP in other patients due to the risk of worsening cerebral ischemia. Guidelines suggest withholding antihypertensive agents in these patients unless the DBP is >120 mm Hg or the SBP is >220 mm Hg and limiting the drop in BP during the first 24 hours by approximately 15%.

Should Blood Pressure Be Elevated to Improve Cerebral Perfusion in Patients With Ischemic Stroke?

A few small case series have shown neurological improvement with induced hypertensive therapy. Studies are underway to

assess the usefulness of this form of therapy in patients with a diffusion-perfusion mismatch on MRI. In the meantime, it is reasonable to try volume expansion and/or vasopressors in patients with hypotensive stroke or in patients who have had a worsening of the neurological deficit in association with a drop in BP.

Should Patients on Antihypertensive Agents Have Their Medications Held or Continued?

The AHA/ASA guidelines recommend restarting antihypertensives at 24 hours in previously hypertensive neurologically stable patients unless contraindicated.

BLOOD PRESSURE MANAGEMENT AFTER INTRACEREBRAL HEMORRHAGE

Patients with intracerebral hemorrhage (ICH) often have elevated BP. Approximately one third of all patients with ICH presenting within 3 hours of symptom onset have a significant expansion of the hematoma over the next 20 hours. Initial hematoma volume and hematoma expansion are powerful predictors of mortality after ICH. Some studies have suggested an association between high BP and hematoma expansion and BP is often lowered under the assumption that high BP promotes hematoma expansion.

Nonetheless, there may be other reasons to lower BP. Hypertensive patients with ICH may have heart failure or elevated cardiac troponin in which lowering BP might be helpful.

The argument against lowering BP in acute ICH is based on the possible existence of a perihematomal ischemic zone. Recent studies, however, indicate that low blood flow around the hematoma may be a consequence of reduced cerebral metabolism in this area rather than a primary reduction of blood flow. In addition, chronic hypertensives (due to a shift in the autoregulatory curve) and patients with increased intracranial pressure (ICP; due to lowered cerebral perfusion

pressure) may develop cerebral ischemia if BP is acutely lowered.

DILEMMA ABOUT BLOOD PRESSURE MANAGEMENT AFTER ACUTE INTRACEREBRAL HEMORRHAGE

While treating the patient of acute intracerebral hemorrhage the question of controlling the blood pressure in domain of when, how and how much always remains in mind of internist. Despite of vast experience in treating such situation many times one find himself in a difficult way to deal such an emergency situation so.

WHAT BLOOD PRESSURE LEVEL IS CONSIDERED TO BE TOO HIGH AND REQUIRING IMMEDIATE REDUCTION?

Despite absence of definitive supportive evidence, some experts believe that a SBP of >180 mm Hg or a mean arterial pressure (MAP) of >130 mm Hg would warrant immediate lowering. In the presence of conditions such as acute heart failure, hypertensive encephalopathy, active cardiac ischemia, and so on, lower BP targets may be appropriate.

WHAT IS THE APPROPRIATE TARGET BLOOD PRESSURE IN PATIENTS WITH ICH?

Immediately after an ICH, it is perhaps more appropriate to tailor the target BP to each patient rather than using a “one size fits all” approach. The possibility of increased ICP and a history of chronic untreated hypertension should be considered while choosing the target. Recognizing the absence of definitive data, the American Heart Association/American Stroke Association (AHA/ASA) guidelines suggest maintaining a cerebral perfusion pressure of 60 to 80 mm Hg in patients with possible increased ICP and a BP of 160/90 or a MAP of 110 mm Hg in other patients.

HOW FAST SHOULD BLOOD PRESSURE BE LOWERED?

Results of small studies suggest that rapidly lowering MAP by approximately 15% does not lower cerebral blood flow, whereas reductions of >20% can do so. Therefore, if BP-lowering is considered, current guidelines suggest cautious lowering of BP by no more than 20% in the first 24 hours.

WHAT ANTIHYPERTENSIVE AGENTS ARE APPROPRIATE FOR USE IN THE ACUTE SETTING?

Short and rapidly acting intravenous antihypertensive agents are preferred. In the United States, labetalol, hydralazine, esmolol, nicardipine, enalapril, nitroglycerin, and nitroprusside have been recommended. Intravenous urapidil is also used in Europe. Large studies comparing various antihypertensives are not available. Sodium nitroprusside and nitroglycerin should be used with caution because these agents can potentially increase ICP. It is the target of BP lowering which is more important than the agent used.

At the end, the optimum post-stroke BP, and how to achieve it, is yet to be identified. Current clinical guidelines do not advocate the active reduction of hypertension in the immediate post-stroke period unless there is a concurrent indication to do so. If elevated

BP is to be lowered in the acute post-stroke period, the reduction should be cautious.

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Congestive Heart Failure with Hypotension: A Misdiagnosis

Priyanka Pandey, Abhishek Singhai, RK Jha

INTRODUCTION

Bilateral subclavian artery stenosis or occlusion is a rare clinical finding.¹⁻³ Subclavian artery stenosis and occlusion leads to erroneously low blood pressure values when measured at the brachial artery on the ipsilateral side. Widespread clinical reliance on a sole brachial measurement of blood pressure, particularly in the emergency department setting, may result in inappropriate clinical management in patients with conditions that alter brachial blood pressure. A case of an apparently hypotensive patient with frequent emergency department visits for symptoms of heart failure exacerbation is presented.

CASE PRESENTATION

A 60-year-old woman with history of congestive heart failure (CHF) presented to the emergency department with exacerbation of CHF and a decreased level of consciousness. Brachial blood pressure (BP) was measured at 55/40 mmHg. The patient had four recent admissions with exacerbation of CHF. Recent echocardiography had revealed moderate concentric left ventricular hypertrophy with diastolic dysfunction, and mild to moderate

mitral regurgitation. Cardiac catheterization in a recent admission demonstrated 50% stenosis in the second diagonal artery, with mild diffuse disease in the other coronary arteries. Previous BP values were also low; systolic BP was between 60 mmHg and 65 mmHg, and diastolic BP was between 40 mmHg and 45 mmHg.

Following intubation, dopamine was started for hypotension management and was later replaced with noradrenaline. The patient developed atrial flutter but successfully converted to sinus rhythm with two direct current cardioversion. On admission, BP was measured at 56/36 mmHg in the left arm but was not detectable in the right arm. An arterial line was inserted via the femoral artery, and BP was measured at 191/92 mmHg. BP values were consistently higher through the femoral arterial line than the cuff on the arms, and was higher in the left arm than in the right arm. To investigate the inconsistency between brachial and femoral BP values, a computed tomography (CT) scan of the thorax was obtained using 1.25 mm slices, both before and after intravenous contrast injection with sagittal and coronal planar reformatting of maximum-intensity projection images. Analysis of the initial unenhanced CT images showed densely calcified plaque or thrombus

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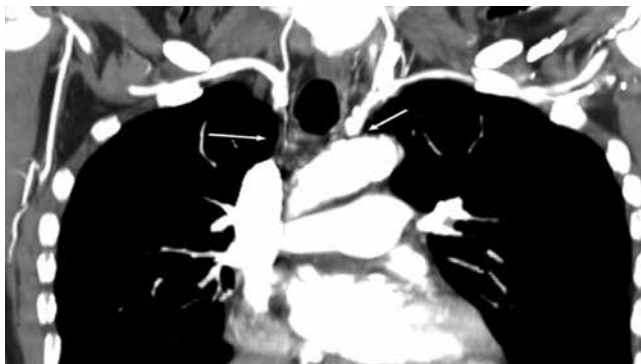


Fig. 1: Coronal image from a contrast-enhanced computed tomography scan of the thorax. Arrows indicate absence of flow in the right subclavian artery, a very tight stenosis at the origin of the left subclavian artery

at the origins of both subclavian arteries and the right common carotid artery. The CT angiogram showed absence of flow in the right subclavian artery, a very tight stenosis at the origin of the left subclavian artery and a tight stenosis at the origin of the right common carotid artery. Both vertebral arteries showed normal calibre and flow (Figure 1).

Further management following the insertion of the femoral arterial line was based on femoral BP readings with diuretics and BP-lowering agents. The patient was eventually discharged in stable condition.

DISCUSSION

The existence of rare bilateral occlusion and severe stenosis of subclavian arteries in the present patient was masked by the concomitant presence of CHF, which was the most plausible cause of low BP values. In retrospect, it appears to be clear that the low brachial BP values were indeed due to subclavian artery occlusion and stenosis, and did not accurately

reflect the systemic BP. Low brachial BP readings in the previous admissions also precluded administration of antihypertensive agents, a crucial component in the optimal management of CHF. Untreated hypertension, which was the real ongoing issue, resulting in multiple further admissions until it was diagnosed and properly managed.

CONCLUSION

The present case demonstrates how a rare clinical entity can be easily masked by a much more common, better-recognized, concomitant clinical diagnosis. It also emphatically underscores the importance of BP measurement in all extremities, especially when brachial BP values and the clinical picture do not match well. Unfortunately, however, common clinical practice relies much more frequently on BP measurement from upper extremities only, and even then, brachial BP is quite often measured on one side. Finally, the paramount role of medical imaging techniques in complicated clinical presentations is, once again, exemplified in the present brief clinical case report.

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Epidemiologic Surveillance of Indian Hypertensive Patients after Treatment with a Single Tablet, Fixed Dose Combinations of Indapamide SR 1.5 mg and Incremental Strengths of Amlodipine

Hemant Thacker¹, Rahul Patil², Pankaj Rastogi³, Amitabh Gautam⁴, K Satish⁵

Abstract

Background: *The combination of indapamide and amlodipine has been recommended for initiating treatment of stage 2 hypertension. Recently, a single tablet fixed dose combination (FDC) of these drugs, in a range of three dosage strengths, was introduced in India.*

Objective: *To assess the initial blood pressure lowering efficacy, blood pressure control, and patient acceptability of the single tablet FDCs of indapamide SR 1.5mg and incremental strengths of amlodipine among untreated Indian patients in day to day general practice.*

Methods: *In a multi centre epidemiologic surveillance protocol, patients with untreated hypertension who were prospectively prescribed the single tablet FDCs of indapamide SR 1.5mg and incremental strengths of amlodipine during the course of daily practice were studied. Primary data on demographic and clinical characteristics, together with blood pressure response, and adverse events during a 60 day follow up was extracted for analysis from the case records of patients kept with the investigators.*

Results: *On an intention to treat analysis of 1056 patients, the number (% , 95% CI) of patients who achieved blood pressure control was 520 (49.2, 46.2 to 52.3). Mean (95% CI) SBP / DBP mmHg, decreased from baseline by 30.8 (29.8 to 31.8) / 12.7 (12.0 to 13.4). The treatments were well tolerated.*

Conclusion: *The fixed dose single tablet formulations of indapamide SR 1.5mg and incremental strengths of amlodipine, were effective in controlling BP in a large proportion of patients, with few adverse effects.*

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INTRODUCTION

Even though hypertension is a major risk factor of cardiovascular mortality and morbidity¹ and treating it reduces such risk,²

only one in five patients in India have their blood pressure under control.³

One reason is that two or more drugs are frequently required to achieve control.⁴ In this regard, it has been demonstrated that initiating treatment with a fixed dose combination (FDC) of two hypotensive agents, is significantly more effective and quicker, in controlling blood pressure than the same two agents used in a sequential drug step wise titration strategy.⁵

In recognition of these issues, the recent AHA/ACC/CDC science advisory on the treatment of hypertension⁶ recommends treatment with a fixed dose combination (FDC) of a thiazide diuretic plus a calcium channel blocker (CCB), together with life style modification in patients with hypertension.

Recently, a single tablet FDC range of indapamide SR 1.5mg and incremental strengths of amlodipine for once daily administration was introduced in India.

Indapamide, a thiazide like diuretic, and amlodipine, a calcium channel blocker (CCB) act by causing direct peripheral vasodilation, but by separate mechanisms.^{7,8} This synergy of action may explain the strong hypotensive effect when the two drugs are used in combination,⁹ and ameliorate the principal adverse event of oedema associated with amlodipine.¹⁰ Additionally, indapamide and amlodipine have been shown separately to reduce cardiovascular risk in hypertension.^{11,12}

The aim of this multi centre prospective epidemiological surveillance protocol was to assess the initial blood pressure lowering efficacy, blood pressure control, and patient acceptability of the single tablet FDCs of indapamide SR 1.5 mg and incremental strengths of amlodipine among Indian patients in day to day general practice.

PATIENTS AND METHODS

Selection of study investigators

Primary care physicians known to the authors and interested in the management of hyper-

tension were identified. Of these, those who agreed to maintain surveillance on selected hypertensive patients under their care were invited to participate as investigators of the study.

Selection of patients

Any patient with a diagnosis of hypertension who was prospectively prescribed the FDC combination of either indapamide SR 1.5mg and amlodipine 2.5mg, indapamide SR 1.5mg and amlodipine 5mg, or indapamide SR 1.5mg and amlodipine 10mg by the investigator during the course of daily practice, was selected.

Surveillance

Primary data on demographic and clinical characteristics, together with blood pressure response, and adverse events after the 30th and 60th day of treatment was extracted for analysis from the case records of selected patients kept by the investigators.

Statistical analysis

The primary outcomes were the number of patients achieving blood pressure control (SBP < 140 and DBP < 90 mmHg) on an intention to treat basis, mean change in blood pressure from baseline, and frequency of side effects, after receiving treatment. Categorical data were expressed as percentages with their 95% confidence intervals (CI). Changes in continuous variables were expressed as the mean with its 95% confidence intervals (CI).

RESULTS

Thirty seven investigators maintained epidemiologic surveillance for 60 days on 1056 patients between October 2013 and June 2016 (Table 1). Patients' mean (SD) age was 56.8(±10.0) years, and systolic blood pressure (SBP) / diastolic blood pressure (DBP), 167.1(±17.5) / 92.8(±11.8) mmHg. The number of females was 427 (40.4%); stage 1 hypertension, 315(29.8%); stage 2 hypertension, 547(51.8%); stage 3 hypertension, 194(18.4%); diabetes, 334(31.6%); obesity, 251(23.8%); and

Table 1: Surveillance flow

1056 patients received treatment		
Day 30		
BP at target 245	BP above target 799	Lost to follow up 12
Day 60		
BP at target 520	BP above target 443	Lost to follow up 81

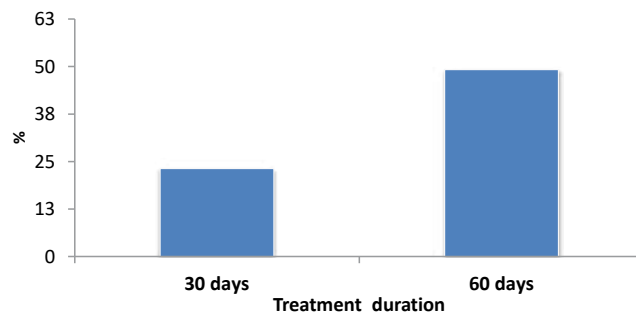
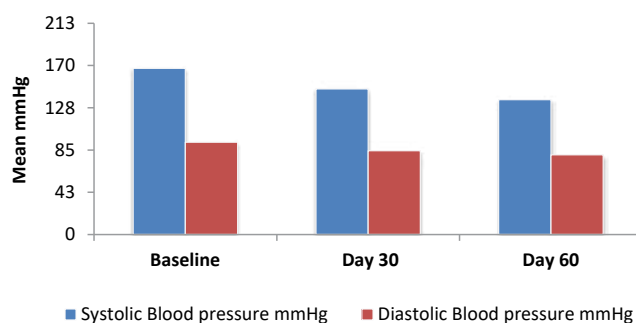
Table 2: Baseline characteristics of hypertensive patients selected for surveillance on receiving treatment with the single tablet FDCs of indapamide SR 1.5mg and incremental strengths of amlodipine

	N= 1056
Mean age, years	56.8 ± 10.0
Female sex	427(40.4%)
Cardiovascular risk	
Diabetes	334(31.6%)
Obesity	251(23.8%)
Dyslipidemia	205(19.4%)
Left ventricular hypertrophy	36(3.4%)
Previous MI	39(3.7%)
History of stroke	30 (2.8%)
Chronic kidney disease	11(1.0%)
Systolic blood pressure mmHg	167.1 ± 17.5
Diastolic blood pressure mmHg	92.8 ± 11.8
Grade 1 hypertension	315(29.8%)
Grade 2 hypertension	547(51.8%)
Grade 3 hypertension	194(18.4%)
Indapamide SR 1.5mg and amlodipine 2.5mg	143(13.5%)
Indapamide SR 1.5mg and amlodipine 5mg	802(75.9%)
Indapamide SR 1.5mg and amlodipine 10mg	111(10.5%)

Plus minus values are means ± standard deviation. All other values are numbers of patients followed by percentages of the group in parenthesis

dyslipidemia, 205(19.4%). Few patients had previous myocardial infarction, stroke, or chronic renal disease (Table 2).

On an intention to treat analysis, the number (% , 95% CI) of patients who achieved blood

**Fig. 1: Blood pressure control in patients treated with the single tablet FDCs of indapamide SR 1.5mg and incremental strengths of amlodipine****Fig. 2: Blood pressure response to treatment with the single tablet FDCs of indapamide SR 1.5mg and incremental strengths of amlodipine**

pressure control was, after 30 days treatment, 245(23.2%, 20.8 to 25.8); and after 60 days treatment, 520 (49.2%, 46.2 to 52.3) (Figure 1).

Mean (95% CI) SBP / DBP mmHg, decreased from baseline, after 30 days treatment by 20.9 (19.0 to 21.9)/12.7(8.3 to 9.3); and after 60 days treatment by 30.8 (29.8 to 31.8) / 12.7 (12.0 to 13.4) (Figure 2).

Headache was reported by 2, and giddiness by one patient.

DISCUSSION

The hypertensive patients selected for surveillance were in their early 6th decade of life and of either sex. About a third was diabetic and a quarter obese, but few had chronic kidney disease or prior history of myocardial infarction, TIA, or stroke. Most had Stage 2 hypertension. Treatment with either indapamide SR 1.5mg and amlodipine

2.5mg, indapamide SR 1.5mg and amlodipine 5mg, or indapamide SR 1.5mg and amlodipine 10mg for 60 days, resulted in clinically useful benefits. About half the patients achieved blood pressure control with a decrease in SBP/DBP of about 30/13 mmHg.

The treatment was well accepted. Few patients reported or discontinued treatment due to side effects. There was no instance of pedal edema.

In comparison to these results, the FDC of losartan 50mg + HCZ 12.5mg, reduced SBP/DBP by 18/12.7 mmHg over a 2 month period.¹³ The ACCOMPLISH study showed that over the long term, the FDC of benazepril and amlodipine, reduced SBP/DBP by 13.7/6.8 mmHg, while the FDC of Benazepril plus hydrochlorothiazide, reduced SBP/DBP by 12.5/5.6 mmHg. Both treatments controlled about 70% of patients.¹⁴ The EFFICIENT study demonstrated that the FDC of indapamide SR 1.5mg and amlodipine over a period of 2 months, decreased SBP/DBP by 42/23 mmHg, that controlled blood pressure in 66% of patients.⁹

Indapamide and amlodipine have individually been shown to reduce cardiovascular risk in the HYVET study on elderly hypertensive patients¹¹ and in the ASCOT study on high risk hypertensive patients.¹²

The strong hypotensive efficacy and lack of side effects, particularly pedal edema, may be related to the synergistic actions of indapamide and amlodipine. Indapamide is a thiazide like diuretic, which at a low dose of 1.5mg, does not cause clinical diuresis but directly lowers peripheral resistance by reducing the contractile sensitivity of vascular smooth muscle cells to plasma noradrenaline.⁷ This action may be synergistic with the inhibition of inward calcium current in vascular smooth muscle cells by amlodipine.⁸

In the ACCOMPLISH trial, about one third of patients developed pedal edema after receiving amlodipine in combination with an ACEI.¹⁴ In contrast, as observed in this study,

amlodipine in combination with indapamide did not cause pedal edema.

The survey has limitations. Data on the use of other antihypertensive drugs and their dose that could have influenced the result was not considered. The treatment was over the short term, and limited in scope to initial blood pressure response. However, patients received treatment under conditions reflective of usual clinical practice.

These results suggest that in patients requiring combination antihypertensive treatment, the FDCs of indapamide SR 1.5mg and incremental strengths of amlodipine reduced blood pressure effectively, resulting in high rates of blood pressure control over the short term, with a low frequency of side effects including pedal edema.

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Epicardial Adipose Tissue Thickness: A Novel Cardiometabolic Risk in Hypertensive Obese Adults

Arvind Mittal, Pranay Bajpai, Dolly Joseph, RK Jha

INTRODUCTION

The global epidemic of overweight and obesity is rapidly becoming a major public health problem in many parts of the world. Obesity is now becoming an independent risk factor for many chronic vascular diseases like hypertension, coronary artery disease, arrhythmias, stroke, atherosclerosis¹

Echocardiographic evaluation of Epicardial Adipose Tissue (EAT) thickness is a new cardiometabolic risk factor as it secretes various inflammatory cytokines & chemokines which plays significant role in the pathogenesis of coronary atherosclerosis & cardiomyopathy.^{2,3}



Fig. 1 : Epicardial Adipose Tissue

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AIM/OBJECTIVE

To Study Epicardial Adipose Tissue (EAT) as an independent prognostic marker in hypertensive obese adult as recent cardiovascular risk marker and its comparison with body mass index (BMI).

METHODS

100 hypertensive obese adults patient attending the Medicine department between Sept. 2012-May 14 were enrolled in the study and 100 normal adults were enrolled as control group. Anthropometric data was collected to calculate BMI. Epicardial Adipose Tissue was measured by M-mode 2D-echocardiography as recommended by American Society of echocardiography (ASE). EAT was identified as an echo-free space in the pericardial layers on 2-dimensional echo and its thickness measured perpendicularly on the free wall of the right ventricle at end diastole for three cardiac cycles and mean values were taken (Figure 1).

RESULT & DISCUSSION

The BMI was found higher in the study group with mean value 42.48 (± 7.35) than control group 21.69 (± 3.32). Body surface area (BSA) was also significantly higher in study group with mean value 2.19 (± 0.22) than control

MEAN EAT IN BOTH THE GROUPS

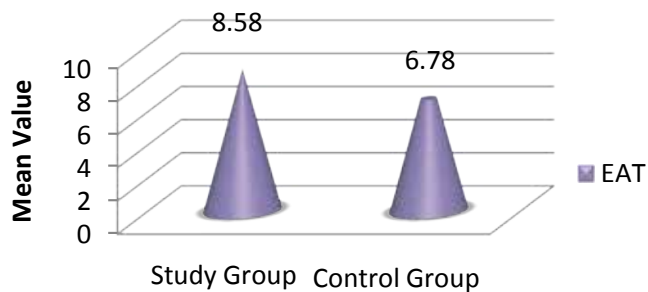


Fig. 2: Epicardial adipose tissue thickness in study group and control group

group $1.68 (\pm 0.23)$ (z test 16.02 & p value 0.001) & waist hip ratio (WHR) was also significantly higher in study group with mean value $0.97 (\pm 0.13)$ than control group $0.92 (\pm 0.07)$ (z test 3.39 & p value 0.001). EAT were significantly higher in study group with mean value $8.58 (\pm 1.26)$ than control group $6.78 (\pm 1.12)$ (z test 10.68 & p value 0.001) (Figure 2). Among the three parameters of anthropometry highest correlation of EAT was seen with BMI ($r=0.544$) ($p<0.001$) in males & ($r=0.402$) ($p<0.001$) in females. *Okpara IC et al* found the strongest correlation was noted between

BMI and LVM ($r=0.708$, $p<0.001$) in males & ($r=0.799$, $p<0.001$) in females".⁴

CONCLUSION

Higher values of EAT in both the genders shows positive correlation with BMI and BSA & shows no correlation with WHR. EAT is an indirect evidence of visceral adiposities and has a strong correlation with obesity. Thus reduction in BMI, marker of obesity will lead to improvement of epicardial adipose tissue thickness and will likely to prevent further cardiovascular morbidity and mortality"

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Prevalence of Diabetes, Hypertension and Cardiovascular Disease in COPD

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is an important cause of morbidity and mortality in the India and around the world.¹ An important factor in both the prognosis and functional capabilities of COPD patients is the role of comorbid disease. The disease processes most closely linked to COPD include lung cancer, depression, congestive heart failure and ischemic heart disease. However, there are several other diseases potentially linked to respiratory disease or its treatment with a weaker association, i.e. osteoporosis, cataracts, hypertension and diabetes mellitus.² The aim of the present study was to determine the relationship between COPD and the common, chronic comorbid conditions of cardiovascular disease, hypertension and diabetes mellitus.

METHODS

The present study analysed data from 245 subjects aged 35-65 yrs. The sample was stratified based on baseline lung function data, according to modified Global Initiative for Obstructive Lung Disease (GOLD) criteria. All subjects underwent pulmonary function testing during a baseline clinical examination,

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fasting and postprandial blood sugar level, electrocardiogram, echocardiography and provided information on history of respiratory symptoms and diagnoses, body mass index (BMI), smoking history and medical history. Comorbid diseases were then searched for.

RESULTS

The demographics of the studied subjects are shown in Table 1. Overall, GOLD stage 3 or 4 COPD was present in 82 (33.5%) subjects, GOLD Stage 2 COPD in 79 (32.2%) and restriction on spirometry was present in 64 (25%) subjects. Diabetes, hypertension and cardiovascular disease were present in 25 (10.2%), 74 (30.2%) and 24 (9.79%) subjects, respectively. Analyses showed that increasing age, a higher BMI and male sex were associated with a higher risk of diabetes, hypertension and cardiovascular disease. GOLD stage 3 or 4 COPD was associated with a higher risk of diabetes (19.79%), hypertension (44.8%) and cardiovascular disease (15.8%).

DISCUSSION

The association between respiratory disease and cardiovascular disease is an area of research that has received a great deal of attention in recent years. The reasons for this association are unclear, but may be related to systemic inflammation, chronic infections,

Table 1: Demographics of Studied Subjects

Age group yrs	Subjects (Number)	Diabetes Mellitus %	Hypertension %	Cardiovascular Diseases %
35-45	78	07%	28.3%	09.8%
46-55	70	11.2%	30.3%	8.9%
56-65	97	12.4%	32.1%	12.1%
Sex				
Female	90	10.3%	28.8%	08.3%
Male	155	10.1%	31.4%	12.1%
Smoking Status	218	13.3%	34.3%	13.3%
Body Mass Index (> 25)	88	40.5%	44.5%	43.2%

Table 2: Gold Stage COPD with Diabetes and Hypertension

Age group yrs	Subjects (Number)	Diabetes Mellitus %	Hypertension %	Cardiovascular Diseases %
GOLD Category				
3 or 4	82	19.7%	44.8%	15.8%
2	79	15.6%	39.2%	14.45%
1	64	08.7%	21.1%	08.9%
0	99	5.0%	14.9%	1.4%

shared risk factors (such as smoking) or other undefined factors.³

A novel finding in the analysis was a modest association of subjects with GOLD stage 2 COPD or higher and those with GOLD stage 0 COPD with diabetes (Table 2). This relationship is interesting and merits further investigation, with the potential to reveal new information on the development of both COPD and diabetes. Potential mechanisms explaining the relationship between respiratory impairment and diabetes might be an increased BMI and altered respiratory compliance, weakness of the respiratory muscles, neuropathies or other undefined factors. In addition, the analysis found an association between GOLD stage 2 COPD and higher and restriction on spirometry and the presence of hypertension. Hypertension is an early manifestation of cardiovascular disease so a possible explanation of the association is that the same factors explaining the link between respiratory and cardiovascular disease are important here.

The present data support this concept and also provide data suggesting that additive comorbid conditions affect outcomes in

COPD. These findings raise the possibility that interventions in early COPD may best target the inflammatory and systemic component of the disease, rather than the lung disease per se.

CONCLUSIONS

These findings suggest that the presence of respiratory impairment could provide a rationale to look for other comorbid disease and, conversely, that the presence of diabetes, hypertension or cardiovascular disease might be the basis for the evaluation of patients regarding respiratory impairment.

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Home Blood Pressure Monitoring

Nihar Mehta¹, Vishal Vanani²

DEFINITION

HBPM is defined as the regular measurement of blood pressure by the patient *outside the clinical setting*, either at home or elsewhere. It is the proven strategy to reduce the risk of disability or death due to high blood pressure in hypertensive patients.¹ It is also called Self-Measured Blood Pressure Monitoring (SMBP).

WHY IS HOME MONITORING IMPORTANT?

It is important to know the amount of pressure load being faced by various organs in the body of a hypertensive person. As the blood pressure is varying throughout the day and can be temporarily influenced by factors such as emotions, diet and medication, one measurement taken at the physician's chamber acts like a snapshot. It only shows a one-time blood pressure at that moment. Since there are no consistent symptoms for high blood pressure and no way to sense fluctuations in blood pressure, measuring is the only way to get the facts. A record of readings taken over time can provide a clearer picture of a patient's blood pressure.

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WHO SHOULD MONITOR BLOOD PRESSURE AT HOME?

Home monitoring may be especially useful for:

- Patients starting hypertension treatment to determine its effectiveness
- Patients requiring closer monitoring than intermittent office visits provide, especially individuals with coronary artery disease, diabetes and/or kidney disease
- Pregnant women, for early detection of pregnancy-induced hypertension/preeclampsia
- People who have some high readings at the doctor's office, to rule out White-coat Hypertension and confirm true hypertension
- Elderly patients, because the white-coat effect increases progressively with age
- People suspected of having masked hypertension (normal clinic BP but high ambulatory BP reading)

WHO SHOULD NOT USE A HOME MONITOR?

People with atrial fibrillation or other arrhythmias may not be good candidates for home monitoring because oscillometric-method monitoring devices recommended for

use at home may not be able to give accurate measurements for people with these conditions.

HOW CAN IT IMPROVE BP CONTROL?

HBPM *Correlates More Closely* with the results of Ambulatory BP monitoring than Clinic BP readings, hence HBPM is more *Predictive Of Adverse Outcomes* (eg, stroke, end-stage renal disease [ESRD]) than Clinic BP.^{2,3}

- In a meta-analysis⁴ of 52 trials, patients were randomly allocated to HBPM or Clinic-based monitoring. It showed greater decrease in BP by 3.9/2.4 mmHg at 6 months when HBPM was compared with usual care and greater decrease in BP by 8.3/4.4 mmHg at 12 months when HBPM with additional supportive interventions was compared with usual care.
- DALLAS HEART STUDY⁵ including 3097 subjects showed prevalence rate of White Coat Hypertension (WCH) of 3.3% and that of Masked Hypertension was 17.8%. It also showed that both WCH and MH were independently associated with Increased Aortic Stiffness, Renal Injury and Incident Cardiovascular Events compared with normotensive group. It concluded that MH being more common and associated with an adverse cardiovascular profile, HBPM should be routinely performed by hypertensive adults.
- In another meta-analysis⁶ of 25 eligible randomized controlled trials, office systolic BP (20 RCTs, 21 comparisons, 5,898 patients) and diastolic BP (23 RCTs, 25 comparisons, 6,038 patients) were found to be significantly reduced in those who self-monitored compared to usual care (weighted mean difference (WMD) systolic -3.82 mmHg (95% confidence interval -5.61 to -2.03), diastolic -1.45 mmHg (-1.95 to -0.94)). Self-monitoring increased the chance of meeting office BP targets (12 RCTs, 13 comparisons, 2,260 patients, relative risk = 1.09 (1.02 to 1.16)).

EQUIPMENT

- Fully automated monitors that use the Brachial Artery (Arm) for measurements are the most reliable.
- Wrist monitors are not recommended
- Oscillometric devices may not work well with patients who have Atrial Fibrillation or other Arrhythmias.
- Patients monitor should be calibrated against mercury sphygmomanometer every 6 – 12 months

CUFF SIZE

- Most off-the-shelf monitors are stocked with a regular adult size cuff. This size may not be appropriate for everyone
- The accurate cuff size for an individual patient should be measured using a tape measure. The distance from the acromion to the olecranon process is measured and at the midpoint the ‘Mid Arm Circumference’ is measured.
- The cuff size actually refers to the size of the bladder inside. The cuff width should equal 40% of the mid arm circumference and the cuff length should equal to 80% of the mid arm circumference.
- If cuff used is too small, it causes overestimation of BP

If cuff used is too wide, it causes underestimation of BP

Cuff Name	Bladder Width	Bladder Length	Mid Arm Circumference
Child	8	21	16 to <22cm
Small arm	10	24	22 to <27cm
Average arm	13	30	27 to <33cm
Large arm	16	38	33 to <41cm
Extra Large	17	43	41 to <52cm

METHOD OF HOME BLOOD PRESSURE MONITORING

- Patient should sit calmly with back support, feet flat on floor for 5 minutes

before taking a reading. Should not cross the legs.

- Caffeine, smoking, alcohol, bathing and exercise should be avoided for at least 30 minutes before the reading is taken.
- Upper arm should be bare.
- When taking a reading the arm with cuff should be supported on a firm surface (table or arm-rest) at heart level.
- The Cuff should fit snugly on the arm, about ½ -1 inch above the elbow crease.

SCHEDULE OF BP READINGS

- Readings should be routinely taken in the morning before medication & at night before bed.
- Each time, patients should take at least two readings separated by one to two minutes between readings. (Four readings each day)
- Readings should be taken twice every day for 7 consecutive days.
- One should record all the readings.
- Readings of the first day to be discarded.
- This gives a total of at least 12 readings. Home BP is defined as the average of these readings.
- In patients with stable BP, this process of 12-14 measurements over 1 week should be repeated every 3 months to ensure adequate BP control.
- Proper documentation of the date, time & blood pressure readings is essential.

INTERPRETATION

- The upper limit of normal for home blood pressure is **135/85 mmHg**.
- This corresponds to a clinic BP of **140/90 mmHg**.
- **Threshold levels of BP for diagnosis of hypertension**

	SBP (mmHg)	DBP (mmHg)
Office	>140	>90

	SBP (mmHg)	DBP (mmHg)
Self/home BP Monitoring	>135	>85
Ambulatory BP Monitoring Day	>140	>90
Ambulatory BP Monitoring Night	>125	>75
Ambulatory 24 hr BP Monitoring	>135	>85

- Patient should be educated to understand the readings.
- Only 60% of the HBPM readings are within 5 mmHg of the actual BP, therefore multiple readings are necessary.⁷
- A single high reading of BP is not an immediate cause for alarm. If the patient gets a single high reading, one should take BP several more times and consult the physician. When blood pressure reaches a systolic >180 mmHg or diastolic >110 mmHg, he/she should immediately alert the physician

HBPM IN SPECIAL POPULATIONS

- **Elderly:** BP variability tends to be high, and white coat hypertension is common.
- **Diabetics:** Tight BP control is important and home monitoring may help achieve this.
- **Pregnancy:** The early detection of pre-eclampsia might be facilitated by HBPM.
- **Chronic Kidney Disease:** BP may fluctuate a lot and home monitors help with management.
- **Children:** White coat hypertension occurs in children, and there are some data on normal home BP levels at different ages.

RECOMMENDATIONS BY AMERICAN HEART ASSOCIATION²

1. It is recommended that HBPM should become a routine component of BP measurement in the majority of patients

with known or suspected hypertension;

2. Patients should be advised to purchase oscillometric monitors that measure BP on the upper arm with an appropriate cuff size and that have been shown to be accurate according to standard international protocols. They should be shown how to use them by their healthcare providers;
3. Two to 3 readings should be taken while the subject is resting in the seated position, both in the morning and at night, over a period of 1 week. A total of ≥ 12 readings are recommended for making clinical decisions;
4. HBPM is indicated in patients with newly diagnosed or suspected hypertension, in whom it may distinguish between white-coat and sustained hypertension. If the results are equivocal, ambulatory BP monitoring may help to establish the diagnosis;
5. In patients with prehypertension, HBPM may be useful for detecting masked hypertension;
6. HBPM is recommended for evaluating the response to any type of antihypertensive treatment and may improve adherence;
7. The target HBPM goal for treatment is $<135/85$ mm Hg or $<130/80$ mm Hg in high-risk patients;
8. HBPM is useful in the elderly, in whom both BP variability and the white-coat effect are increased;
9. HBPM is of value in patients with diabetes, in whom tight BP control is of paramount importance;
10. Other populations in whom HBPM may be beneficial include pregnant women, children, and patients with kidney disease.

SUMMARY

- HBPM is easy to use, more reproducible, more accurate and has higher prediction of target organ damage than clinic BP. (Class IIa, LOE B)

- It differentiates between White Coat HT and Sustained HT.
- In patients with pre-hypertension, it detects Masked HT.
- It is used to determine Response to Treatment
- Improves adherence to antihypertensive medications. (Patients who use HBPM are more likely to take medications regularly).
- Improves quality of treatment while reducing cost.
- It is recommended that HBPM should become a routine component of BP measurement in the majority of patients with known or suspected hypertension;
- Patients should be advised to purchase oscillometric monitors that measure BP on the upper arm with an appropriate cuff size and that have been educated regarding the standard international protocols.
- HBPM has minimal cost, enhances self-care and compliance.⁸

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Clinical Diagnosis and Management of Hypertensive Crises

Santosh B Salagre¹, Shobha M Itollikar²

ABSTRACT

Hypertension is a major contributor to cardiovascular disease and death in India as well as the world over. Severe elevations in blood pressure i.e. hypertensive crises can be seen in both essential and secondary forms of hypertension. It is frequently encountered in untreated or noncompliant patients suffering from systemic hypertension.

Hypertensive urgency (i.e. without target organ damage) can usually be managed by oral anti-hypertensive agents for gradual reduction of blood pressure under close scrutiny. On the other hand, hypertensive emergency (i.e. with target organ damage) warrants aggressive management in the form of urgent BP control with intravenous medications. Such prompt treatment initiation is often justified over the time consuming diagnostic work-up that is employed in search for an etiological factor before treatment initiation. The treatment decisions in either case are dictated not merely by absolute blood pressure values but also by factors like co-morbid diseases and type of end organ affliction.

In the absence of large clinical trials and specific guidelines about this important medical emergency, we thought it necessary to review the available literature in order to shed more light on the diagnostic and therapeutic aspects of hypertensive crises.

INTRODUCTION

It is not without reason that hypertension is known as 'the silent killer'. In spite of recent advances in medical science, improved access to healthcare facilities, and availability of well-researched management guidelines on hypertension, issues related to awareness,

diagnosis, compliance and control of hypertension abound; thus creating an enormous cardiovascular burden globally. Little wonder then, that the emergency physician is not new to cases that present with severely elevated blood pressure along with disabling vital organ damage. Hence, we cannot undermine the importance of prompt diagnosis and expeditious management of this medical emergency.

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Table 1: Risk factors for hypertensive crises.

1. Poor compliance to antihypertensive medications.
2. Long-standing hypertension.
3. Sudden withdrawal of drugs like β -blockers, clonidine, methyldopa or interaction with MAO inhibitors (tranylcypromine, phenelzine and selegiline).
4. Drug abuse: steroids, cocaine, amphetamine and phencyclidine.
5. Associated disorders causing secondary hypertension:
 - a. Renal parenchymal diseases
 - b. Reno vascular disease
 - c. Renal Artery Stenosis
 - d. Systemic Lupus Erythematosus
 - e. Systemic Sclerosis/ Scleroderma renal crisis
 - f. Wegener's granulomatosis
 - g. Polyarteritis nodosa
 - h. Eclampsia/ severe pre-eclampsia
 - i. Pheochromocytoma
 - j. Primary aldosteronism
 - k. Glucocorticoid excess
 - l. Renin secreting tumors
 - m. Hemolytic uremic syndrome
 - n. Thrombotic thrombocytopenic purpura
 - o. Thyrotoxicosis

DEFINITIONS

Hypertensive crises are a heterogeneous group of disorders characterized by severe hypertension with or without evidence of target organ damage to the brain, heart, kidney, retina or blood vessels. Typically, blood pressure (BP) values are 180/120 mm Hg or higher.¹

Hypertensive Emergency denotes a state of severely high blood pressure in which the patient shows evidence of one or more target organ damage. The rapidity with which such high BP levels are reached is more important than the absolute BP reading.

In contrast, *hypertensive urgency* indicates a state of uncontrolled hypertension with symptoms attributable to elevated blood pressure; these patients do not show any evidence of target organ damage.

Hypertensive emergency warrants rapid reduction in blood pressure with parenteral medications in an intensive care setup under close observation whereas, in hypertensive urgency, blood pressure is lowered over a period of 24 to 48 hours in a carefully followed-up out-patient setting.

In a patient with chronic hypertension, commonly due to medication compliance issues, blood pressure may be 180/110 mm Hg or higher without any symptoms or acute target organ damage, and such cases are labeled as *severe hypertension*. These patients can be treated with titration of oral antihypertensive medications after laying emphasis on drug compliance.

PATHOPHYSIOLOGY OF HYPERTENSIVE CRISIS

Hypertensive emergency constitutes 1% of emergency room admissions. Various risk factors (Table 1) may be responsible for severe elevations in blood pressure. Increased systemic vascular resistance associated with the rapid rise in blood pressure leads to a stretch on the vessel wall causing activation of renin-angiotensin-aldosterone system. The resultant endothelial damage increases the endothelial permeability. Furthermore, platelet and fibrin deposition leads to fibrinoid necrosis and intimal proliferation. The increased vascular resistance also triggers spontaneous natriuresis which causes a decrease in vasodilators and increase in vasoconstrictors resulting in further rise in blood pressure (Figure 1).

PRESENTING FEATURES

Hypertensive emergency patient may with one or more of the manifestations enlisted in Table 2.

Hypertensive urgency may be associated with some clinical scenarios like:

1. Accelerated / malignant hypertension
2. Severe hypertension associated with coronary artery disease
3. Severe hypertension in the organ trans-

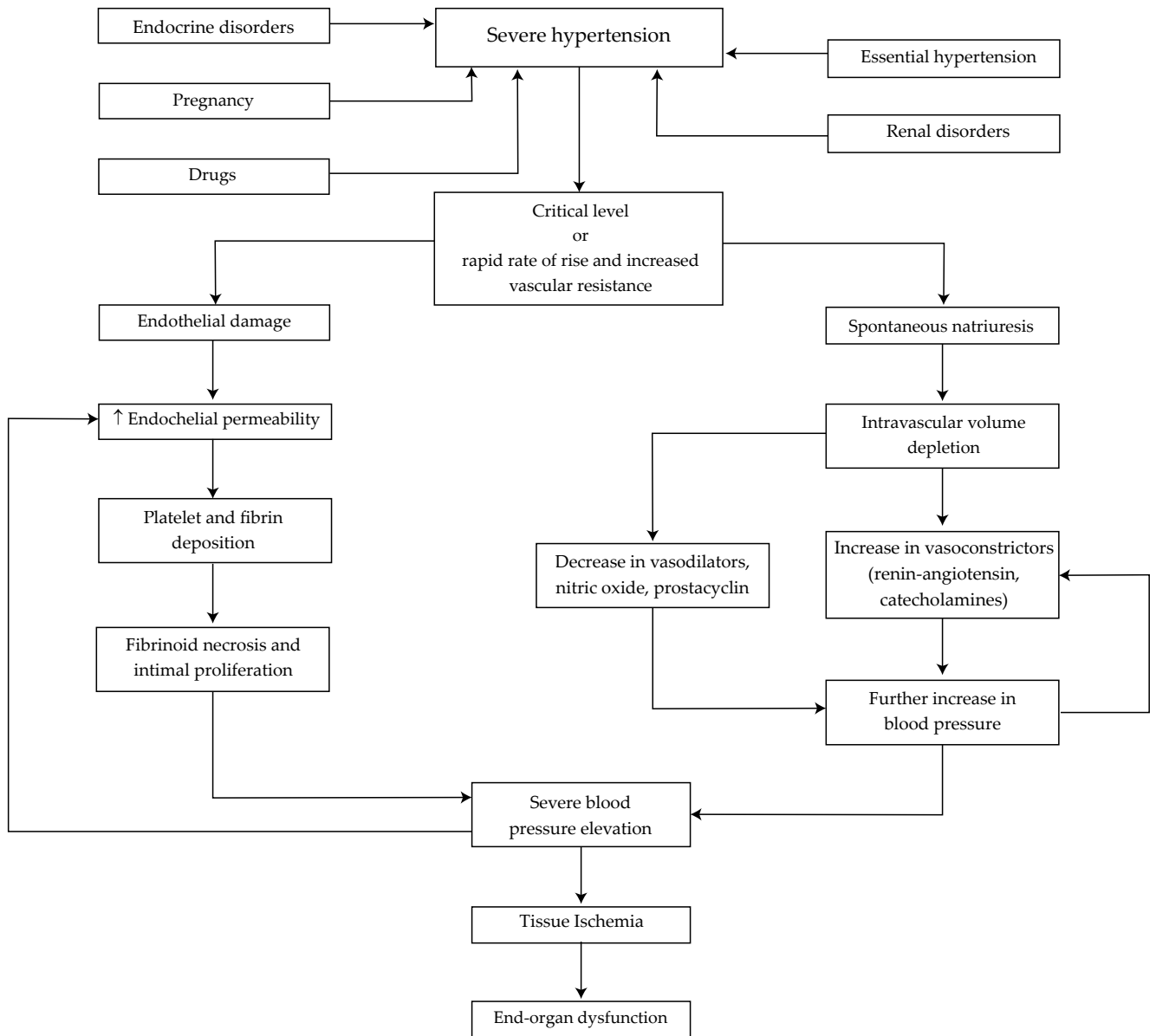


Fig. 1: Pathophysiology of end-organ affliction hypertensive crisis

- plant patient
- 4. Preoperative hypertension
- 5. Hypertension in burns patients and head injury

APPROACH TO A PATIENT WITH HYPERTENSIVE CRISES

Distinction between episodes of hypertensive emergency versus urgency is the most crucial step in effective management of these conditions, as treatment paradigms differ in both. An accurate history and a meticulous

clinical examination become pertinent not only to determine the severity of acute organ involvement but also to figure out the contributory etiological factors.

Clinical assessment

Emergency room history-taking should address factors related to duration of hypertension, baseline blood pressure readings, current medications, noncompliance or abrupt discontinuation of treatment, smoking and tobacco consumption, use of over-the-

counter/recreational/alternative medications , previous episodes of hypertensive crises and past history of stroke, myocardial infarction and renal disease. Symptoms of acute severe pain should not be neglected in patients of hypertensive crises. In female patients, a detailed menstrual history, history of contraceptive pill use or hormone replacement therapy as well as history of thyrotoxicosis

Table 2: The manifestations of hypertensive Emergencies

<i>CNS:</i>	a. Hypertensive encephalopathy b. Intracranial hemorrhage c. Subarachnoid hemorrhage d. Acute Ischemic Stroke
<i>Cardiac:</i>	a. Acute decompensated heart failure b. Acute myocardial infarction/ unstable angina c. Aortic dissection
<i>Renal</i>	a. Acute renal failure b. Renovascular hypertension c. Renal artery stenosis
<i>Obstetrics</i>	Eclampsia/ preeclampsia
<i>Miscellaneous</i>	Microangiopathic hemolytic anemia Pheochromocytoma crisis Perioperative

and collagen vascular disorders should be sought.

Suspicion of target organ damage should arise when symptoms such as headache, nausea, and vomiting, sweating, chest pain, shortness of breath, blurred vision, diplopia, confusion, decreased cognition, convulsion, focal neurological deficit, hematuria or oliguria are present.²

A brisk, yet attentive physical examination will give important clues as to the possible etiology. Peripheral pulses examination and accurate recording of three limb blood pressure with an appropriate sized cuff, along with a detailed systemic examination will add valuable information. General examination should be done specifically to look for palor, edema as well as signs of endocrine or collagen vascular disorders. Chest auscultation should be done with an aim to detect abnormal cardiac rhythm, gallop, murmurs, rales and wheezes. Neurological examination should include assessment of mental status, coma scale, possibility of convulsion and focal neurological deficit. The fundus should be examined to screen for papilledema and retinopathy. The abdomen should be examined for flank tenderness and bruit over abdomen.³

Table 3: Interpretation of investigations in hypertensive emergency

Investigation	Laboratory Finding	Significance in hypertensive emergency
CBC with peripheral smear	Anemia Schistocytes	Renal failure Microangiopathic hemolytic anemia
Urine	Significant proteinuria RBCs or cellular casts	Renal parenchymal disease
Serum Potassium	Hypokalemia	Hyperaldosteronism
Renal function tests	Raised serum creatinine	Renal failure
EKG	LVH , ST-T changes	Coronary ischemia
ECHO	Systolic / diastolic dysfunction	Myocardial infarction
X-ray chest	Hilar shadows / Cardiomegaly Mediastinal widening	Pulmonary edema Aortic dissection
Abdominal ultrasound & renal Doppler	Unequal sized kidneys	Renal Artery Stenosis
Neuroimaging (CT/MRI)	Hypo/ hyper densities	Cerebrovascular ischemia Cerebral hemorrhage

Diagnostic Tests

Emergency investigations such as hemogram, urinalysis, kidney function tests, chest radiograph and electrocardiogram are sufficient for preliminary evaluation (Table 3). Precious time should not be spent in the pursuit of an etiology. It should be borne in mind that prompt initiation of therapy should supersede the time-consuming diagnostic studies. If dissection of aorta is suspected, a CTAortogram should be planned or if pheochromocytoma is suspected, relevant investigations should be ordered simultaneously. An urgent imaging of brain becomes imperative in patients presenting with altered mentation. An urgent bedside 2D Echocardiography might give valuable hints in patients presenting with pulmonary edema or myocardial ischemia. In those patients whose clinical examination yields clues towards endocrinological cause of hypertensive crises, specialized investigations such as estimation of vanillyl mandelic acid, peripheral renin and plasma aldosterone might have to be planned.

GENERAL GUIDELINES FOR MANAGEMENT OF HYPERTENSIVE CRISES^{4,5}

Patients presenting in hypertensive emergency should be promptly hospitalized, while those with hypertensive urgency may not always require hospitalization. The decision related to the choice of antihypertensive agent needs to be individualized depending upon patient's clinical condition, specific target organ involvement, associated co-morbidities, and availability and ease of administration of the drug.

Treatment goals: The goal of emergency care should be not only to lower the BP quickly, but also to prevent, halt and reverse the target organ damage. The aim of therapy should be to achieve a decrease in mean arterial pressure (MAP) by 20 % over a period of few minutes to an hour^{6,7} and to around 160/110 mm Hg over the next 6 hours in case of hypertensive emergency; preferably with the use of intravenous drug. Oral agents are preferred

in hypertensive urgency where it might be acceptable to reduce the blood pressure levels gradually over 24 hours. Further decrease in blood pressure should be done judiciously to avoid hypo perfusion of vital organs; more so in the elderly who are likely to have atherosclerotic peripheral vascular, cardiovascular or neurovascular disease. In addition, cerebral auto regulation might be altered in these patients and too rapid BP reduction might lead to cerebral hypo perfusion, further aggravating the neurological damage. It is noteworthy that acute aortic dissection is a rare clinical condition where aggressive reduction in blood pressure to less than 120 mm Hg within 20 minutes becomes necessary.

Emergency management should comprise of the following:

- Assessment of circulatory and airway status.
- Monitoring of vital parameters.
- Symptomatic treatment for presenting features such as chest pain, headache.
- Injectable Furosemide: Diuretics have a limited role in the management of hypertensive emergencies but they help by potentiating the therapeutic response of non-diuretic antihypertensive drugs. In heart failure, they have a definite role to play. Routine use of diuretics in hypertensive crises should be discouraged since such patients could be in volume depleted states and use of diuretic might cause more harm than good.
- BP reduction with continuous infusion of a fast acting, parenteral anti-hypertensive agent under close scrutiny in the intensive care in case of hypertensive emergency.

Oral Drugs for management of hypertensive urgency:

Clinical experience has shown that antihypertensive drugs given orally in either single or multiple doses can lower the BP immediately in patients with severe hypertension. Patients with hypertensive urgency are ideal candidates for such oral therapy. The preferred agents are enlisted in detail in Table 4.

Table 4: Oral agents for the treatment of hypertensive urgency

Drug	Mechanism of action	Dosage	Onset / Duration of Action	Precautions
Captopril	ACE inhibitor	PO 25 mg; repeat as needed SL 25 mg	15-30 min/6-8 hrs 10-20 min/2-6 hrs	Hypotension, renal failure, C I : Bilateral Renal Artery Stenosis
Clonidine	Centrally acting alpha 2 adrenergic agonist	0.1-0.2 mg , repeat hourly to maximum of 0.6 mg	30-60 min/8-16 hrs	Hypotension, drowsiness, dry mouth
Labetalol	Alpha- beta adrenergic blocker	200-400 mg repeat every 2-3 hrs	1-2 hr/ 2-12hrs	Bronchoconstriction heart block, orthostatic hypotension
Minoxidil	Direct vasodilator	2.5- 10mg every 4-6 hourly	2-4 hrs	Reflex tachycardia
Amlodipine	Calcium channel blocker	5-10 mg	1-2 hrs/12-18 hrs	Tachycardia, Hypotension

Table 5: Parenteral drugs used for hypertensive emergencies.⁹

Drug	Mechanism of Action	Dose	Onset of action	Duration of Action	Adverse Effects/ Precautions
Sodium nitroprusside	Nitric oxide compound, direct arterial and venous vasodilator	0.25-10 microgm/kg/min IV infusion	Immediate	3-4 min after stopping infusion	Hypotension, nausea, vomiting, muscle twitching, thiocyanate and cyanide intoxication Increased intracranial pressure Methemoglobinemia/ delivery system must be light resistant
Nitroglycerin	Nitric oxide compound, direct arterial and venodilator	5-200 microgm/ min IV infusion	2-5 min	5-10 min	Headache , tachycardia, flushing, Methemoglobinemia/ require special delivery system due to drug binding to tubings
Labetalol	alpha- beta adrenergic blocker	20-80 mg IV bolus every 10 min; 0.5-2.0 mg/ min IV infusion	5-10 min	2-4 hrs after stopping infusion	Bronchoconstriction, heart block, vomiting, scalp tingling, orthostatic hypotension, heart failure exacerbation
Enalaprilat	ACE inhibitor	1.25-5 mg every 6 hr IV	within 30 min	6-24 hrs	Acute renal failure in patients with bilateral renal artery stenosis Prolonged half life

Contd...

Table 5: Parenteral drugs used for hypertensive emergencies⁹ (Contd...)

Drug	Mechanism of Action	Dose	Onset of action	Duration of Action	Adverse Effects/Precautions
Hydralazine	Direct vasodilatation of arterioles with little effect on veins	10-20 mg IV or 10-40 mg IM ; repeat every 4-6 hrs	IV-10-20 min IM-20-30 min	4-12 hrs	Reflex tachycardia, flushing, headache, Sodium and water retention, increased intracranial pressure, aggravation of angina
Nicardipine	Dihydropyridine Calcium channel blocker, vasodilator	5-15 mg /hr IV infusion	5-15 min	15-30 min , may exceed 4 hrs	Reflex tachycardia, flushing, headache, local phlebitis, aggravation of angina
Esmolol	beta adrenergic blocker	500microgm/kg bolus IV or 50-300 microgm/kg/min by infusion	1-2 min	10-30 min	Hypotension, nausea, asthma, second or third degree AV block, heart failure
Phentolamine	alpha-beta adrenergic receptor blocker	1-5 mg IV bolus	1-2 min	3-5 min	Reflex tachycardia, flushing, headache
Fenoldopam	Dopamine-1 receptor agonist	0.1-1.6 microgm/kg/min infusion	< 5 min	30 min – 1 hour after stopping infusion	Headache, flushing, reflex tachycardia, local phlebitis, hypokalemia, non-specific T wave changes, ventricular extra systole, sulfite allergy
Clevidipine	Ultra-short acting Dihydropyridine Ca channel blocker	2-16 microgm/kg/min	1-5 minutes	5 minutes after stopping	allergy, heart failure

One should avoid drugs like sublingual nifedipine as , although it is cheap, easily available and rapidly acting, it is found to be associated with dangerous, at times life threatening events. An abrupt fall in BP induced by nifedipine can cause symptomatic hypotension, tachycardia and ischemic events. Hence, use of nifedipine should be discouraged in clinical practice in management of hypertensive crises.⁸

PARENTERAL DRUGS FOR TREATMENT OF HYPERTENSIVE EMERGENCY

Table 5 summarizes the recommended paren-

teral drugs for treatment of hypertensive crises.⁹ Table 6 summarizes treatment recommendations for hypertensive crises as per affected organ system.

Special Situations: The ensuing discussion will describe the treatment modalities concerning specific organ affliction.

- a. *Hypertensive crisis with Advanced Retinopathy:* Patients with severely high blood pressure (> 180/120 mm Hg) may have Keith-Wagener-Barker grade 3 or 4 hypertensive retinopathy. They may also have headache, visual disturbances, nausea/vomiting, heart failure, encephalopathy, ECG evidence of LVH

Table 6: Recommended Treatment of Hypertensive Emergencies by End Organ Involved

Type of Emergency	Timeline, Target BP	First-line Therapy	Alternative Therapy
Hypertensive crisis with retinopathy, microangiopathy, or acute renal failure	Several hours, MAP- 20-25%	Labetalol	Nitroprusside Nicardipine
Hypertensive encephalopathy	Immediate, MAP- 20-25%	Labetalol	Nicardipine Nitroprusside
Acute aortic dissection	Immediate, SBP < 110 mm Hg	Nitroprusside + Metoprolol	Labetalol
Acute pulmonary edema	Immediate, MAP 60-100 mm Hg	Nitroprusside with loop diuretic	Nitroglycerin
Acute coronary syndrome	Immediate, MAP 60-100 mm Hg	Nitroglycerin	Labetalol
Acute ischemic stroke and BP > 220/120 mm Hg	1 hour, MAP- 15%	Labetalol	Nicardipine Nitroprusside
Cerebral hemorrhage and SBP >180 mm Hg or MAP>130 mm Hg	1 hour, SBP < 180 mm Hg or MAP < 130 mm Hg	Labetalol	Nicardipine Nitroprusside
Acute ischemic stroke with indication for thrombolytic therapy and BP > 185/110 mm Hg	1 hour, MAP less than 15%	Labetalol	Nicardipine Nitroprusside
Pheochromocytoma crisis	Immediate	Phentolamine	Nitroprusside
Perioperative hypertension during or after CABG	Immediate	Nicardipine	Nitroglycerin
During or after craniotomy	Immediate	Nicardipine	Labetalol
Severe preeclampsia/ eclampsia	Immediate	Labetalol (plus magnesium sulfate and oral antihypertensives)	Nicardipine
Cocaine intoxication	Several hours, SBP<140mm Hg	Phentolamine (after benzodiazepines)	Nitroprusside

Abbreviations: MAP –Mean Arterial Pressure. SBP - Systolic Blood Pressure.

and microangiopathic hemolytic anemia; a condition referred to as Malignant Hypertension. First-line drug options are intravenous Labetalol, Nitroprusside or Nicardipine. A multicenter, randomized, trial comparing Urapidil (a central sympatholytic that acts on central serotonergic pathways and also selectively blocks peripheral alpha-adrenergic receptors) versus Nitroglycerin (NTG) in multifactor heart failure in the elderly proved that Urapidil demonstrated better efficacy than NTG on lowering and stabilizing systolic BP, attenuating cardiac afterload, and improving cardiac function.¹⁰ Both NTG and Urapidil significantly reduced fasting glucose levels in multifactor heart failure

patients with Diabetes Mellitus. Urapidil is a therapeutic option for the multifactor heart failure patients complicated with hypertension and DM.

- b. *Hypertensive crisis with Encephalopathy:* Hypertensive encephalopathy is characterized by altered sensorium, delirium, agitation, stupor, convulsions or cortical blindness in the setting of acute severely raised blood pressure. Hypertensive encephalopathy is a cause of reversible posterior leucoencephalopathy syndrome. Neuroimaging findings showing areas of cerebral edema confirms the diagnosis of encephalopathy. The areas of brain edema will resolve with timely treatment of the hypertensive crisis.

The treatment of hypertensive encephalopathy is always with an intravenous antihypertensive drug, preferably Labetalol to lower blood pressure in a controlled manner which avoids cerebral hypoperfusion and irreversible brain damage. It is advisable to lower the elevated arterial pressure by 10 % in the first hour and by additional 15% during the next 12 hours to a BP of no less than 160/110 mm Hg and then further reduction over the next 48 hours.

- c. *Acute Ischemic Stroke:* In acute ischemic stroke, blood pressure should be lowered with caution to avoid ischemic insult to the potentially salvageable tissue i.e. the ischemic penumbra. The AHA/American Stroke Association 2013 guidelines¹¹ recommend that (1) if the stroke cannot be treated with thrombolytic therapy, BP should be treated if it remains higher than 220/120 mm Hg and initially lowered by no more than 15% of the systolic blood pressure, and (2) if the stroke can be treated with thrombolytic therapy, BP needs to be lowered to less than 185/110 mm Hg. The first-line drug recommended for this condition is intravenous labetalol. Alternatively, Nicardipine or Nitroprusside can be used.

Hemorrhagic Stroke: Recent results of INTERACT2 (Intensive BP Reduction in Acute Hemorrhagic Trial 2) showed improved functional outcome without more adverse events in patients with acute hemorrhagic stroke randomly assigned to intensive treatment to lower SBP to less than 140 mm Hg than to the conservative guideline-recommended goal of less than 180 mm Hg.¹² The agent of choice to lower BP in hemorrhagic stroke includes labetalol. Nitroprusside and hydralazine should be avoided in this setting.

- d. *Acute coronary syndrome:* In patients with severely high BP with acute coronary syndrome, BP should be lowered with intravenous nitroglycerin after administration of a beta blocker such as

Metoprolol or Esmolol so as to prevent reflex tachycardia. There are fewer studies with labetalol or Urapidil. Nitroprusside should be avoided since it can cause coronary steal. A careful monitoring of patient in intensive care set-up should be instituted in order to prevent hypotension which can trigger infarct extension.

- e. *Acute Pulmonary Edema:* Myocardial oxygen requirement increases in acute LVF due to increased end-diastolic fiber length and high left ventricular volume. IV Nitroprusside and IV Nitroglycerine are drugs of choice for hypertensive crisis with acute heart failure. Initial use of injectable loop diuretic such as furosemide helps in lowering the BP effectively and also decreases the pulmonary congestion. Rapid reduction of blood pressure by 20% in the first hour followed by slower further reduction is advisable.

In patients with bilateral renal artery stenosis, recurrent flash pulmonary edema and even refractory heart failure can occur. These patients develop refractory fluid retention related to impaired renal perfusion. This may simply reflect sodium avidity resulting from reduced renal perfusion pressure or, in some cases, acute decompensation of left ventricle related to abrupt rises in arterial pressure during volume expansion. In such cases, clinical improvement occurs after successful renal revascularization.

- f. *Acute Aortic Dissection:* Thoracic Aortic Dissection is a life threatening situation, warranting prompt intervention. Pharmacotherapy is used as a bridge to more definitive surgical treatment. Patients presents with acute chest or back pain, unequal upper and lower limb pulses/ blood pressure and widened mediastinum on chest X-ray. Rapid reduction in blood pressure with beta blocker like labetalol is necessary.
- g. *Acute Kidney Injury:*¹³ Acute kidney injury presents with proteinuria, microscopic hematuria, oliguria and/or Anuria. It is

important to note that acute kidney injury can be a cause or effect of hypertensive emergency. IV labetalol is commonly used and safe drug in this emergency. IV Fenoldopam, if available is recommended, as it improves natriuresis, diuresis and creatinine clearance. While using IV Nitroprusside, care should be taken for prevention of cyanide toxicity.

h. Hypertensive emergency during pregnancy: Severely high blood pressure in a pregnant female can present as eclampsia or preeclampsia. Assisted delivery is the mainstay in this setting, and decision related to obstetric intervention needs to be individualized as per clinical findings. Although other antihypertensive drugs may be effective in reducing the BP, the agent of choice for rapid control of severe hypertension is Hydralazine, which has a long record of safety.¹⁴ For seizure prophylaxis, the drug of choice is magnesium sulphate. The injectable antihypertensive drugs that are recommended during pregnancy are labetalol or Nicardipine. For hypertensive urgency situations, oral hydralazine, retard preparations of nifedipine are preferred with alpha methyl dopa.

*i. Adrenergic Crises:*¹⁵ Conditions associated with catecholamine excess are Pheochromocytoma, MAO inhibitor crisis and cocaine abuse. Treatment should be always initiated with alpha-blockade and beta blockers should be added later. Initial treatment with beta blockers will lead to unopposed alpha receptor stimulation and rapid rise of blood pressure. Pheochromocytoma crisis should be treated acutely with Phentolamine followed by administration of a beta blocker. Effective alternatives are Nitroprusside and Urapidil. Clonidine withdrawal can be corrected by reintroduction of this agent. Cocaine-induced hypertension should be treated with intravenous benzodiazepines followed by Phentolamine.

CONCLUSION

Prompt diagnosis and swift treatment of hypertensive crises are fundamental to achieve a good clinical outcome in a hypertensive crisis. Rather than generalizing the treatment protocol, it will be pragmatic to individualize the treatment as per the emergency clinical scenario, the extent and type of organ involvement and logistics involving the drugs and diagnostic tests. Close monitoring in intensive care helps to decrease morbidity and mortality in this life-threatening, yet treatable condition.

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Rare Cause of Uncontrolled Hypertension

Ishita Shah, Falguni Parikh, Dheeraj Kapoor, TB Yuvraja

ABSTRACT

Secondary Hypertension accounts for 15-20% of patients with hypertension.

We report a case of young female with uncontrolled hypertension due to Paraganglioma (extra adrenal pheochromocytoma) who underwent surgical treatment, which resulted in fair control of blood pressure with a single drug.

INTRODUCTION

Hypertension is one of the leading causes of the global burden of cardiovascular disease. It doubles the risk of cardiac events, ischemic and hemorrhagic stroke, renal failure and peripheral arterial disease. Primary hypertension comprises of 80-95% of hypertensive patients. In the remaining 5-20% of patients a specific underlying disorder causing the elevation of blood pressure can be identified.

In individuals with secondary hypertension a specific mechanism for blood pressure elevation is more apparent. It is important to identify secondary cause of hypertension especially while evaluating younger patients with hypertension, since surgical treatment of such cases can be corrective and appropriate intervention results in amelioration or substantial improvement of the hypertension.

CASE REPORT

A 37-year-old female, known hypertensive on medical management since last 13years

(2003) diagnosed post pregnancy, came with complaints of sweating and palpitations on and off since last one year. She required increasing doses of blood pressure lowering medications for control. She was on Telmisartan 40mg, Cilnidipine 10mg, Chlorthalidone 6.25mg, Nebivolol 5mg and Prazosin 5mg daily when she visited as an outpatient at our hospital. There was no family history of hypertension. There was no history of seizures.

On examination she was afebrile, Pulse-78/min regular, no bruit, all peripheral pulses well felt, BP-160/100mmHg in all four limbs, Respiratory rate -18/min, no goitre, no hirsutism, no Cushingoid features and no neurocutaneous markers. Systemic examination including the heart, lungs, central nervous system and gastrointestinal system was normal. There was no renal bruit heard over the abdomen.

On Investigations, complete blood count, liver function test, renal function test, thyroid function test, urine examination and renal Doppler were normal. Two-dimensional Echocardiography showed concentric Left ventricular hypertrophy with 60% Ejection

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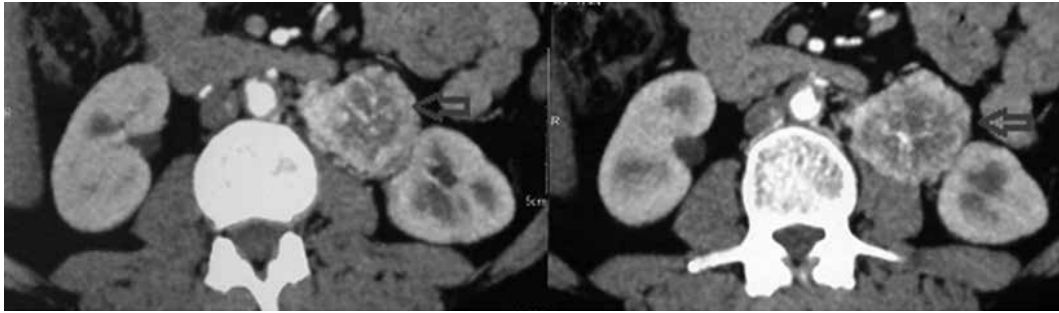


Fig. 1: Post contrast arterial phase demonstrating juxtarenal mass lesion showing intense peripheral enhancement and with relative minimally enhancing central component.



Fig. 2: Normal renal artery

Fraction. Ultrasonography of Abdomen showed neoplastic mass lesion involving left paraaortic and paraspinal region. Specific blood investigations showed Plasma Metanephrine 30.7pg/ml (normal<100pg/ml), Plasma normetanephrine 3099pg/ml(normal 18-111pg/ml) and Chromogranin A 124ng/ml(normal<36.4). Computed Tomography of whole abdomen showed well defined multilobulated enhancing lesion in left mid para aortic region, left renal hilar region with fat stranding encasing ureter and gonadal vein suggesting Paraganglioma (Figures 1, 2) She was started on Phenoxybenzamine which was titrated until normalization of blood pressure. Once target blood pressure was achieved she was started on Atenolol. After this preparation, she underwent left D-J stenting and laproscopic excision of left retroperitoneal mass under general anesthesia. Intra and postoperative period was uneventful. Histopathology revealed a circumscribed tumour measuring 4x2.5x2.5cm with pinkish brown cut surface, without necrotic areas. Microscopy showed thinly capsulated

tumour arranged in zellballen pattern with nests and trabeculae separated by thin fibrovascular septae. The cells showed abundant granular to vacuolated cytoplasm with mildly pleomorphic nuclei. The tumour cells were positive for synaptophysin and chromogranin A. S-100 was focally positive in sustentacular cells. These are neuroendocrine markers for pheochromocytoma on immunohistochemistry. Post operatively her antihypertensive drug requirements came down drastically and she required Tablet Amlodepin 2.5mg/day.

DISCUSSION

Paraganglioma (extra adrenal pheochromocytoma) is a rare neoplasm originating from extra-adrenal pheochromocytes of the sympathetic and parasympathetic nervous system.¹ Usually located within the abdomen in association with celiac, superior mesenteric and inferior mesenteric ganglia and organ of zuckerkanndl (chromaffin body derived from neural crest located at the bifurcation of the aorta or at the origin of the inferior mesenteric artery).² Though they mimic pheochromocytoma clinically differentiation is required as it has increased incidence of metastases compared to adrenal pheochromocytoma. Traditional 10% rule which noted that 10% of all pheochromocytomas are extraadrenal may actually be an underestimation. A review of literature suggests that extra adrenal pheochromocytomas constitute 15% of adult pheochromocytomas.³

The clinical presentation of these tumours can be either due to mass effect or due to excess catecholamine secretion. The signs and

symptoms vary from headache, hypertension, palpitations and sweating to fatigue, nausea, weight loss, fever. Patient may present with myocardial infarction, arrhythmia, stroke or other vascular manifestations and therefore it is referred as the "great mimic".⁴ The diagnosis is based on high suspicion, physical examination, biochemical testing, imaging modalities as in our patient and molecular genetic testing.

In any case of a sustained, paroxysmal hypertension or paradoxical hypertension despite the antihypertensive therapy, the diagnosis of pheochromocytoma has to be kept in mind and it has to be ruled out. Other forms of secondary hypertension such as renal artery stenosis, hyperaldosteronism or hypercortisolism should be kept as differential diagnosis.

To date germ line mutations in five genes have been described, which lead to several familial disorders which are associated with pheochromocytomas. An activating mutation of RET Protooncogene leads to Multiple Endocrine Neoplasia(MEN).⁵ An abnormal VHL gene is responsible for Von Hippel Lindau. Mutations of the neurofibromatosis type 1 gene cause Von Recklinghausen's disease and the hereditary pheochromocytoma paragangliomas syndrome is associated with the mutation in succinate dehydrogenase subunit genes SDHB and SDHD. The pheochromocytomas associated with Multiple Endocrine Neoplasia, Von Hippel Lindau and Neurofibromatosis 1 are more likely to be benign and bilateral.⁶

CONCLUSION

Our patient was already on treatment for hypertension post pregnancy. She however

was not investigated at that time for any secondary causes. Increasing requirement of antihypertensives should alert a physician to seek for presence of secondary cause. All young patients with hypertension should undergo workup for secondary hypertension. Paraganglioma accounts for hypertension in 0.05% patients. It is gratifying to diagnose it as once the tumour is removed the antihypertensive drug requirement comes down and occasionally patient is rendered normotensive.

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Biochemical Silent Pheochromocytoma Presented as New Onset Resistant Hypertension

Hozefa Runderawala*, Iqbal Bagasrawala**, Charu Jani***, Siddharth Shah****

ABSTRACT

Pheochromocytoma is a rare tumor mainly of adrenal medulla. It is presented with varied symptoms like flushing, palpitation, paroxysmal or sustained hypertension. The symptoms are principally due to catecholamines secreted by chromaffin cells within the tumor. Recent onset hypertension is not always essential hypertension and needs further evaluation. We report a case of 42-year-old female presented with new onset of hypertension resistant to standard antihypertensive treatment, diagnosed as a biochemical silent pheochromocytoma of right adrenal gland confirmed histologically.

CASE REPORT

42-year-old female, married, no previous co morbidities except recently diagnosed hypertension since 6 months presented with complaints of diffuse abdominal pain since 2 months. She gives no h/o nausea, vomiting, headache or fever.

Patient was recently diagnosed with hypertension 6 months back for which she was started on anti-hypertensive (ACEi) and was advised for regular BP monitoring. In spite of adequate doses and compliance of ACEi, her BP remained high and was advised admission.

On admission, she was afebrile, P-98/min,

BP-160/100mm hg, RR-20/min, mild pallor, mild pedal edema.

Her menstrual cycle was normal, systemic examination was essentially normal.

She was started on beta blocker for high blood pressure and also a diuretic was added.

With standard antihypertensive treatment with adequate dose, her BP was uncontrolled and hence decided to investigate for secondary hypertension.

Her complete haemogram, Renal function test and Liver function test was normal.

24-hour urine fractionated metanephrine was 325mcg/24 hours which is normal, normetanephrine was 654mcg/24 hours which was also normal.

Computed Tomography of Abdomen and pelvis was done s/o right adrenal mass

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measuring 2.8X1.7X1.3 cm with marked enhancement with intravenous contrast medium.

Patient underwent right laparoscopic adrenalectomy, adrenal mass weighed 19 grams, histopathologically proved to be pheochromocytoma (Figures 1, 2) with immunohistochemistry marker S100 (Figure 3), Synaptophysin (Figure 4) and Chromogranin (Figure 5) strongly positive (3+).

DISCUSSION

Secondary hypertension is defined as increased systemic blood pressure (BP) due to an identifiable cause. Only 5-10% of patients suffering from hypertension have a secondary form, rest majority of them has essential (idiopathic) hypertension. The prevalence of secondary hypertension depends mostly on age and clinical characteristics of the screened population.

Most common causes of secondary hypertension:

1. Obstructive Sleep Apnea
2. Renal Parenchymal disease
3. Renovascular disease
4. Primary Aldosteronism
5. Cushing's syndrome
6. Pheochromocytoma
7. Coarctation of the Aorta.

The evaluation of secondary hypertension requires extensive laboratory testing, hence all cases should not be undergone for such extensive investigation. Patients who have clinical clues suggesting possible presence of secondary hypertension should undergo a more extensive evaluation. The goal of identification of secondary causes of hypertension is to treat the cause which is reversible and curable and hence blood pressure can be normalized in such patients.

There are general clinical clues which should raise the suspicion of secondary hypertension.

1. Severe or resistant hypertension: Resistant hypertension is defined as the persistence

of hypertension despite concurrent use of adequate dose of three antihypertensive agents from different classes, including a diuretic.

2. An acute rise in blood pressure developing in a patient with previously stable values.
3. Age less than 30 years in non-obese patient with negative family history of hypertension and no other risk factors for hypertension.
4. Malignant or accelerated hypertension (severe hypertension with end organ damage).
5. Proven age of onset before puberty.

Clinical clues for specific causes of secondary hypertension:

1. Renovascular Disease
 - a. An acute elevation in serum creatinine of at least 30% after administration of ACEi or ARB
 - b. Moderate to severe hypertension in a patient with diffuse atherosclerosis, a unilateral small kidney or asymmetry in renal size of more than 1.5cm that cannot be explained by another reason.
 - c. Moderate to severe hypertension in patients with recurrent episodes of acute pulmonary edema.
 - d. Systolic or diastolic abdominal bruit.
2. Primary renal disease
 - a. Elevated serum creatinine concentration
 - b. Abnormal Urinalysis.
3. Pheochromocytoma:
 - a. Paroxysmal elevations in blood pressure,
 - b. Triad of headache, palpitations, and sweating.
4. Cushing's syndrome:
 - a. Cushingoid facies, central obesity,

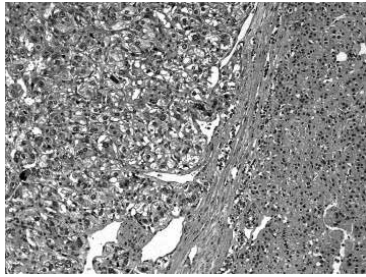


Fig. 1: HP Low resolution

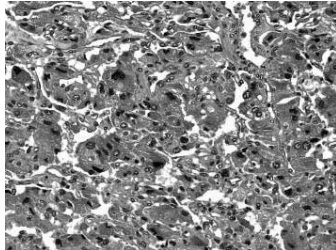


Fig. 2: HP High resolution

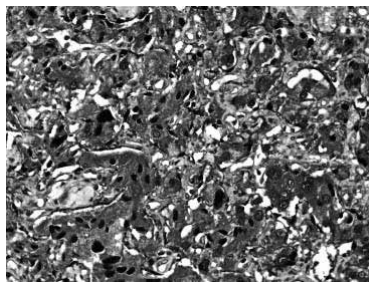


Fig. 3: S100 positive

proximal muscle weakness, ecchymoses

b. History of glucocorticoid use.

5. Sleep apnea syndrome:

a. Obese individual who snore loudly while asleep

b. Daytime somnolence, fatigue and morning confusion.

6. Coarctation of aorta: Difference in blood pressure between upper and lower extremity.

DIAGNOSIS

After initial work up of hypertension with routine investigation, evaluation for pheochromocytoma should be done.

- 24 hour urine fractionated metanephrines and catecholamines, or

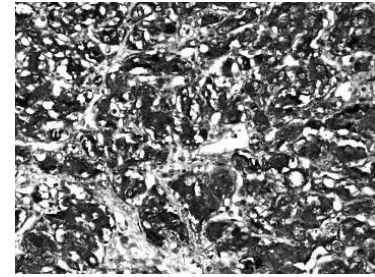


Fig. 4: Synaptophysin positive

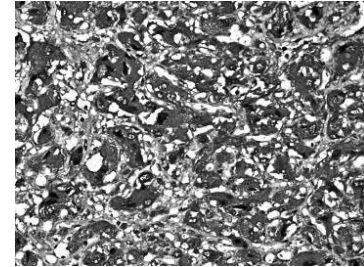


Fig. 5: Chromogranin A positive

- Plasma fractionated metanephrines levels. If normal, then recheck during spells of pheochromocytoma.

If twofold elevation above upper limit of normal in urine catecholamines or increase urine metanephrines (Normetanephrines > 900mcg per 24 hours or Metanephrine > 400mcg per 24 hours) or significant rise in fractionated plasma metanephrines, then

Localize the tumor by abdominal MRI or CT, Typical adrenal or para-aortic mass, consider genetic testing, preoperative alpha and beta adrenergic blockade and surgical resection if feasible.

If negative abdominal imaging, then do whole body MRI scan or PET, tumor found, then do the genetic testing, preoperative alpha and beta adrenergic blockade and surgical resection if feasible.

TREATMENT

The treatment of choice of Pheochromocytoma is surgical resection. Resecting a pheochromocytoma is a high risk surgical procedure and an experienced surgeon s required. Cardiovascular and hemodynamic variables must be monitored closely. It requires preoperative medical therapy which is aimed at controlling hypertension (preventing hyper-

tension crisis during surgery) and volume expansion.

Combined alpha and beta adrenergic blockade is one approach to control blood pressure and prevent intraoperative hypertensive crises.

An alpha adrenergic blocker is given 10-14 days preoperatively to normalize blood pressure and expand the contracted blood volume. Phenoxybenzamine is the preferred drug. The initial dose is 10mg od or bid and can be increased by 10 or 20 mg in divided doses every two to three days.

After adequate alpha adrenergic blockade has been achieved, beta adrenergic blockade is initiated, generally 2-3 days preoperatively. The laparoscopic approach to the adrenal gland is the procedure of choice for solitary intra adrenal pheochromocytoma that are less than 8cm in diameter and have no malignant radiologic features.

In our case, laparoscopic adrenalectomy was done as the pheochromocytoma was localized to adrenal gland and it was confirmed by histopathology with features of Zell ballen pattern and pleomorphic hyperchromatic nuclei (Figures 1 and 2) and also supported by immunohistochemistry markers S100 (+++) (Figure 3), Synaptophysin (+++) (Figure 4), Chromogranin A (+++) (Figure 5).

CONCLUSION

Pheochromocytoma is one of the rare cause of secondary hypertension. For new onset resistant hypertension, reversible secondary cause to be looked for and if treatable, then the cause of hypertension to be removed. Pheochromocytoma is a treatable cause and in our case laparoscopic adrenalectomy was the treatment of choice.

Hypertension Abstracts of APICON 2017

Clinical Study of Hypertensive Crisis in Medicine Ward

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Introduction: In India, prevalence of hypertension increased from 5% in 1960s to nearly 12% in 1990s, to more than 30% in 2008. It is estimated that approximately 1% of patients with hypertension develop a hypertensive crisis at some point. Although chronic hypertension is an established risk factor for cardiovascular, cerebrovascular, and renal disease, even acute elevations in BP can result in acute end-organ damage with significant morbidity. This study aimed to analyze the risk factors, modes of presentations and spectrum of end organ damage in HC.

Material: This study were done on patients with SBP \geq 180 mmhg or DBP \geq 120 mmhg admitted in medicine ward, SGMH, Rewa from march 2015 to may 2016 (200 patients). On admission detailed history, complete clinical examination, and necessary investigations like (blood and urine chemistry, ECG, CXR, fundoscopy, etc) were done know the end organ damage.

Observations : In our study of 200 patients of hypertensive crisis (HC), 144 individuals (72%) met the criteria for hypertensive emergency (HE) and 56 (28%) met the criteria for hypertensive urgency (HE). Patients with HE were older ($P < 0.001$), more sedentary ($P = 0.037$), more smoker ($p = 0.0073$) and more non adherence to anti hypertensive medications ($p = 0.049$) than those with HU. Furthermore, fewer HE patients than HU patients had known history of hypertension ($P = 0.0029$). The groups did not differ regarding BP levels, gender, obesity, alcohol, known history of diabetes and family history of hypertension. Neurological deficit (47.22%), Dyspnea (37.5%) and Chest pain (25%) were common presentation in those with HE. Meanwhile, in the group with HU, we most frequently found Headache (44.64%), Giddiness (42.86%), followed by Epistaxis (37.5%). Retinopathy (66%), Ischemic stroke (23%), Hemorrhagic stroke (16%), Acute heart failure (18%) and Acute coronary syndrome (16%) were target-organ damage in HE. Mortality among all cases of hypertensive crisis was 9%.

Conclusions: The prevalence of hypertensive crisis in the patients admitted to the ICU is approximately 1.76%. This study highlights the importance of knowing the associated risk factors, clinical profile and the most frequent types of target-organ damage in individuals who present with HC.

The early detection of end organ damage and appropriate treatment are key determinants to avoid this severe complication of hypertension.

The Study of Blood Pressure Variability and Effect of Antihypertensive Treatment on Outcome in Intracerebral Hemorrhage

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Introduction: Stroke is the 2nd leading cause of death worldwide, after ischemic heart disease. Although the hemorrhagic stroke is less common (15%) than ischemic stroke, this stroke is associated with higher mortality rates than is ischemic stroke. The treatment of acute hypertension in subjects with ICH is highly controversial as the effect of pharmacological reduction of mean arterial pressure (MAP) on cerebral blood flow (CBF) is unclear. There is strong evidence to suggest that one third of the subjects presenting with ICH continue to demonstrate lesion expansion in the next few hours after the initial ictus. This situation can lead to clinical deterioration and death. Persistently elevated BP may predispose the subject to hematoma expansion.

Aim:

1. To study the time course of elevated blood pressure in intracerebral hemorrhage.
2. To study the effect of antihypertensive treatment on outcome in intracerebral hemorrhage.

Materials and Method: The present study was carried out in 96 patients of intracerebral hemorrhage presented to us within 24hrs and with BP >140/90, proven by CT scan, admitted in Medical wards of Gandhi Memorial and Associated Hospitals, King George's Medical University, Lucknow.

Exclusion Criteria

- Traumatic intracerebral hemorrhage.
- Patients with very low general condition [GCS <4].
- Patients with severe systemic illness or neoplasm.
- Patients with renal failure [serum Creatinine >3].
- Patients with chronic liver disease.
- Patients with bleeding diathesis.
- Unwilling or uncooperative patients.

CT scan of the selected patient was done at the time of admission.

Evaluation of all the patients was carried out as follows:

Detailed history including Mode of onset of neurological manifestation was carefully checked. History of hypertension, diabetes, smoking or alcohol, Nature of treatment and adequacy of treatment was asked. Detailed

physical examination was carried out. Blood pressure; was recorded every 6 hour for first 48 hour then 12 hourly. Cardiovascular system Examination; in all cases. Central nervous system Examination; in all cases; the following has been specially recorded.

CT SCAN AND MRI brain was done.

Assessment and improvement monitored by:

1. Level of consciousness according to Glasgow coma scale (GCS).
2. Extent and severity of focal neurological deficit on MRS scale and NIHSS score.

Observations: Both the groups were matched for

Age, sex. Blood pressure at the time of admission. Risk factors viz. diabetes mellitus, hypertension, smoking, alcohol intake. Severity of disability viz. GCS, MRS, NIHSS at presentation. CT scan findings viz. volume, midline shift, intraventricular extension.

In the Group1, out of 44 patients, 24(54.5%) and in Group2 out of 52 patients 23(44.23) were hypertensive. Hence, nearly half of the patients were known hypertensive.

The survival rate at 30 days in Group1 was 81.6% and in Group2 was 84.6%, difference was statistically non-significant ($p>0.05$).

The MRS at 7th day in Group1 (4.47 ± 0.61) and in Group2 (3.67 ± 1.23), NIHSS at 7th day in Group1 (21.47 ± 4.56) and in Group2 (18.04 ± 6.87), the decrease in MRS and NIHSS was statistically significant ($p<0.001$) in Group2 but not in Group1.

The MRS at 30 day in Group1 (3.94 ± 0.73) and in Group2 (3.30 ± 1.08), NIHSS at 30 day in group1 (20.17 ± 4.58) and in group2 (16.05 ± 4.48), the decrease in MRS from day of presentation was statistically significant in both group ($p<0.001$), but the decrease in NIHSS was statistically insignificant ($p>0.5$) in Group1 and significant in Group2 ($p<0.001$).

The findings of small size sluggish reacting pupil at presentation doesn't significantly alter the outcome ($p<0.5$). The patients of GCS ≤ 8 at presentation results in poor outcome. As in Group1, only 2 out of 8 survived (25%), in group2, only 5 of 9 survived (55.5%).

The SBP higher (>200 mm Hg), DBP (>110 mm Hg) and MAP (>130 mmHg) at presentation results in poor outcome ($p<0.05$) in both groups.

On CT Scan finding, the volume of hemorrhage of >30 ml resulted in poor outcome in both groups($p<0.05$).similarly, the midline shift of >5 mm and presence of intraventricular extension resulted in poor outcome in both groups($p<0.05$)

The mean NIHSS score at presentation of expired patient were higher than improved one in both group, but difference was found statistically insignificant ($p0.05$)and significant ($p<0.05$) in group2 and the association of final outcome(expired/improved) MRS at presentation was found statistically insignificant($p>0.05$) in both group.

Conclusion:

Blood Pressure: The mean SBP, DBP and MAP decrease significantly ($p < 0.001$) in both groups, except that in Group2 it started decreasing from day1. The mean SBP, DBP and MAP of two groups were found similar ($p > 0.05$) at all periods; though at final evaluation, the mean decrease in SBP, DBP and MAP of Group2 was 3-5% higher as compared to Group1.

A. Outcome measures

1. After 1 month of follow up, similar proportion of outcomes between the two groups (18/4 vs. 44/8, $\chi^2 = 0.09$; $p = 0.765$) though the favorable outcome (discharged) was 2.8% higher in group1 as compared to group2.
2. The overall survivals (6 months) of two groups was found similar.
3. The volume, midline shift, GCS score, SBP, DBP, MAP, MRS score and NIHSS score significantly associated with final outcomes.

B. Morbidity parameters: In both groups, the mean GCS, NIHSS, MRS scores increase (improve) linearly after the treatments. The improvement was higher in Group2 than Group 1.

Evaluation of Serum Uric Acid levels in Essential Hypertension

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Introduction: Elevated levels of uric acid have been identified as an independent predictor of hypertension severity and progression in various epidemiological studies. Also there is a growing body of data that suggests a role of hyperuricemia in pathogenesis of atherosclerosis and cardiovascular diseases (CVD) especially in patients with hypertension and type 2 diabetes mellitus. We conducted a study to evaluate serum uric acid levels in essential hypertension and its relation with severity and duration of essential hypertension.

Materials and Methods: A cross sectional study was conducted at Rajindra Hospital/Govt. Medical College, Patiala in which 100 patients of essential hypertension were included according to JNC VII criteria. Patients were further divided into categories based on severity (stage 1 and 2) and duration of hypertension since when the patient was first diagnosed as hypertensive (<5 years and >5 years). Serum uric acid levels were measured in the patients under study using Uricase-PAP test.

Observations: Mean serum uric acid (SUA) value was 6.04 mg% and prevalence of hyperuricemia was 35% using cut-off value of 6.8 mg% in patients under study. It was observed that mean SUA value in stage 2 category was 6.45 mg% against 5.21 mg% in stage 1 which was statistically significant ($p < 0.001$). It was also observed that

in patients with duration of <5 years mean SUA value was 5.22 mg% and in those with >5 years mean SUA value was 6.96 mg% which was significantly higher than the former statistically ($p < 0.001$).

Conclusion: In view of our observations SUA can be used as a biomarker to determine the severity and duration of hypertension which in turn quantifies the CVD risk.

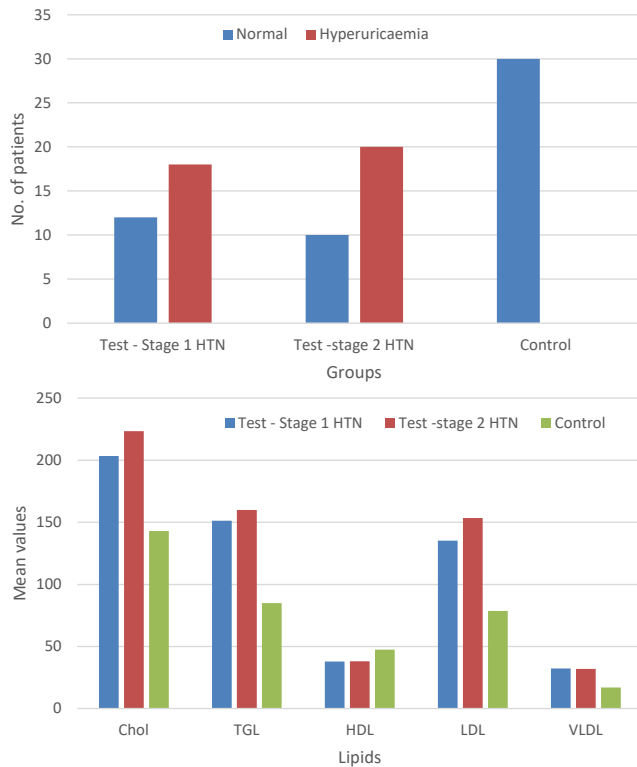
Estimation of Serum Uric Acid Levels in Drug Naive Young Adult Subjects with Hypertension and its Relation with Serum Lipid Levels in a Tertiary Care Hospital Mysuru

Chaitra CS, Shekar
Mysore Medical College

Introduction: Hypertension is common global lifestyle disorder. Clinically, it is defined as that level of blood pressure at which the institution of therapy reduces blood pressure related morbidity and mortality. Elevated blood pressure is defined as systolic blood pressure >140 mm hg and diastolic blood pressure >90 mm hg. About ~80-95% of hypertensives fall in the category of essential or primary hypertension. Primary hypertension tends to be familial and is likely to be the consequence of an interaction between environmental and genetic factors. Prevalence of primary hypertension increases with age, and individuals with relatively high blood pressures at younger ages are at increased risk for the subsequent developmental of hypertension. Uric acid is the end product of purine metabolism in human beings. Human beings convert the major purine nucleosides-adenosine and guanosine to uric acid through intermediates. Overproduction of uric acid causes gout, renal insufficiency. The association of hyperuricemia with hypertension is associated with decreased renal blood flow and decreased tubular secretion of uric acid. Many studies support this association. Disorders of lipoprotein metabolism are collectively referred as Dyslipidemias. They are characterized clinically by increased plasma levels of cholesterol, triglycerides, or both and accompanied by reduced levels of HDL cholesterol. Studies show direct correlation between increase in weight and increase in blood pressure over time. Dyslipidemia is more common in untreated hypertensives than normotensives and lipid levels increase as blood pressure increases.

Material: A clinico-biochemical study included subjects aged between 18-40 yrs who were drug naïve young adults with stage 1 hypertension ie, systolic BP of 140-159 mm of hg and diastolic BP of 90-99 mm of hg of 30 sample size and stage 2 hypertension ie, systolic BP of >160 mm of hg and diastolic BP of >100 mm of hg of 30 sample size with 30 age matched normotensives ie, systolic BP of <120 mm of hg and diastolic BP <80 mm of hg as controls. The study period was from August 2015 to August 2016. They were excluded if they were having any other known cause of raised uric acid levels and secondary hypertension.

Observations: Study showed that serum uric acid was raised in 18 out of 30 subjects with stage 1 drug naïve hypertensives and 20 out of 30 subjects with stage 2 hypertension in comparison to normotensives. Also 17 out of 30 stage 1 hypertensives and 24 out of 30 stage 2 hypertensives had hypercholesterolemia, 20 out of 30 stage 1 hypertensives and 27 out of 30 stage 2 hypertensives had hypertriglyceridemia, 13 out of 30 stage 1 hypertensives and 14 out of 30 stage 2 hypertensives had low HDL. Also all subjects who had hyperuricemia had dyslipidemia in both stage 1 hypertensives and stage 2 hypertensives. But the difference is much higher in stage 2 hypertension.



Conclusions: Since essential hypertension remains a major modifiable risk factor for cardiovascular disease despite important advances in our understanding of its pathophysiology and the availability of effective treatment strategies. Also there is strong positive and continuous correlation between blood pressure and the risk of cardiovascular disease, hence independent risk factors for hypertension like serum uric acid, serum lipid levels have an additive effect in diagnosing future hypertensives in young age. By above study as there is both hyperuricemia and dyslipidaemia in both stage 1 and stage 2 hypertensives drug naïve young adults subjects aged between 18-40 years though it is much significant in stage 2 hypertensives.

We conclude that measuring serum uric acid and serum lipid levels is a useful test for the clinician, as it carries important prognostic information in predicting future hypertension.

Study of Pro-Inflammatory Markers (Tnf-alpha and IL6) and Oxidative Stress in Hypertensive Patients

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Introduction & Background: Hypertension is one of the major global health problems. The global prevalence of the hypertension has been predicted to increase to 1.56 billion by 2025. Experimental evidences supporting direct role for endogenous proinflammatory markers and oxidative stress in mediating some of the chronic hypertensive response. We conducted a study to look into the status of inflammatory markers and oxidative stress in hypertensive patients.

Patient Material and Methods: Study included 40 hypertensive patients as cases and 20 normotensive non-diabetics as controls. Levels of Interleukin -6 (IL-6) and Tumour necrosis factor- α (TNF- α), oxidants (Malondialdehyde, Protein carbonyl) and antioxidant (vitamin C, Superoxide Dismutase) along was measured using the standardised ELISA kits and protocol.

Observation: Serum levels of TNF-alpha and IL-6 and oxidants (Malondialdehyde, Protein carbonyl) were significantly higher in patients with essential hypertension than those in normotensive control group while level of antioxidants (vitamin C, Superoxide Dismutase) were decreased.

Compressive lab characteristic of study Population

Parameters	Case	Control	p-value
MDA ($\mu\text{mol/L}$)	0.047 \pm 0.041	0.0042 \pm 0.0067	<0.002
Protein carbonyl ($\eta\text{mole/ml}$)	15.61 \pm 2.11	7.60 \pm 0.92	<0.0001
SOD (U/L)	1.79 \pm 0.91	3.57 \pm 1.20	<0.0001
IL-6 (pg/ml)	13.28 \pm 3.079	6.285 \pm 4.0084	<0.0001
TNF-a (pg/ml)	21.29 \pm 4.35	6.645 \pm 2.9584	<0.0001
Vitamin C (mg/L)	0.1255 \pm .03789	0.1546 \pm . 04673	<0.019

Conclusions: From our study, it is clear that there is an apparent increase in the levels of oxidants, proinflammatory markers (TNF-alpha and IL-6) and decrease in the levels of antioxidants in the cases of hypertension. Whereas in the controls, there is lower levels of oxidants, proinflammatory markers and higher levels of antioxidants. In future therapies targeting these inflammatory mediators could prove effective in the treatment or even prevention of this modern day epidemic patients.

Comparison of Oxidative Stress and Telomere Dysfunction in Hypertensive Patients (A Case Controle Study)

Prashanth BV, Subhash Giri, GS Ranga, Ashish Goel, Rajarshikar UCMS and GTBH

Background/Objective: Oxidative stress is the unifying patho-physiological mechanism responsible for ageing

and age related diseases like diabetes, hypertension, atherosclerosis etc. Oxidative stress is defined as increase in the intracellular concentration of reactive oxygen species. Telomeres are specialized DNA-protein structures located at the ends of eukaryotic chromosomes whose length is progressively reduced in most somatic cells during ageing. Insulin resistance and oxidative stress are associated with accelerated telomere attrition, implicated in the biology of ageing/in-ageing related disorders including hypertension. We hypothesized, higher oxidative stress, measured by Malondialdehyde(MDA) and Glutathione-S transferase(GST) associated with telomere dysfunction in hypertensive patients. So, a case control study was undertaken, to study the dysfunction of telomere in these patients.

Methods: The study was conducted at a tertiary care hospital in Delhi, India, includes 40 hypertensive male patients(aged -45- 65 years) and equal number of age matched healthy controls. We performed biophysical parameters and routine and special investigations, measurement of MDA levels (Ohkawa method), GST levels (Mozer method). In all subjects, telomere length was measured by real time PCR from the DNA isolated from leucocytes (Cawthon's method) and telomerase activity was measured by measuring hTERT mRNA expression by RT-PCR, Taqman methodology from leucocytes.

Results: It was observed that the mean MDA level in cases and controls were 0.90 ± 0.30 , and 0.65 ± 0.18 respectively ($p, 0.01$). The mean GST level in cases and controls were found to be 0.68 ± 0.17 and 1.02 ± 0.32 $\mu\text{mol/ml/min}$ respectively ($p, 0.001$). We also found that mean telomere length was found to be shorter in hypertensive patients (8.17 ± 1.26 kb) as compared to controls (10.47 ± 1.79 kb) respectively ($p < 0.001$). The expression of hTERT (mean Δct ratio) of cases (-0.18) was higher as compared to control (16.17).

Conclusion: It was observed that there was a significant shortening of telomere length with higher oxidative stress in hypertensive patients as compared to healthy control.

Clustering of Cardiovascular Risk Factors in Subjects with Prehypertension

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Background: Hypertension is a risk factor for cardiovascular diseases including coronary artery disease.

Recently, even prehypertension has been associated with metabolic and atherosclerotic alterations. This category was suggested due to evidence indicating that overall cardiovascular risk and end-organ damage were already elevated in individuals with prehypertension, when compared with those with a BP less than 120/80 mmHg. However, there is no specific study from India on prevalence of various cardiovascular risk factors in adult subjects with prehypertension.

Aims: The present study aimed to study the prevalence of various cardiovascular risk factors in prehypertensive individuals aged ≥ 18 years

Methodology: One hundred subjects in the prehypertension group formed the study population. Cardiovascular risk factors were studied viz. Obesity (BMI), Central obesity (Waist circumference), Dysglycemia, Dyslipidemia, Smoking, Alcohol intake, Family history of hypertension, Lifestyle/ physical activities and Stress/ mental health status. Clustering of risk factors was defined as presence of two or more cardiovascular risk factors in any single individual.

Results: Elevated waist circumference was observed in 79% of prehypertensive subjects. Prehypertensive subjects had prevalence of 75% of overweight/obesity, dyslipidemia (55%), dysglycemia (57%), sedentary lifestyle (46%), family history of hypertension (16%) and smoking (17%) and mental stress (35%). Implying that prehypertensive group is prone to cardiovascular disease. Low HDL-cholesterol (High density lipoprotein) was the most common lipid fraction derangement witnessed in the prehypertensive (48%). 99% in the prehypertensive group had at least one deranged cardiovascular risk factor. Clustering of ≥ 3 risk factors was seen in 83% of prehypertensive individuals.

Conclusion: Waist circumference and body mass index are significantly elevated in prehypertensive population as compared to normotensive population. Notably, all components of metabolic syndrome viz. dysglycemia, dyslipidemia, obesity and central obesity seem to be clustered in prehypertensive population suggesting the presence of a spectrum of metabolic abnormalities concentrating in prehypertensive subjects of the present study. The presence of multiple risk factors in prehypertension subjects stresses on the need for early detection of these patients. Preventive strategies should be targeted at this population subset so that progression to hypertension can be prevented and cardiovascular risk mitigated.

