The Crisis in Hypertension

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Hypertension (HT), diabetes mellitus (DM) and obesity are in the forefront of the epidemic of non-communicable diseases. Kearney PM et al estimated the global burden of hypertension as 26 percent of the world adult population.¹ In India, HT prevalence is 17 to 21 percent with marginal rural – urban difference.²

Percentage of Blood pressure (BP) goal achievers have increased from a 29 percent in 1988 to a more satisfying 50 percent in 2008.³ BP control is influenced by race and co-morbidities. Patients enrolled in health care plans have better BP control of upto 60 percent.

Does Hypertensive Crisis Develop only in Patients of Resistant Hypertension?

In an eye-opening study by Grigoryan L et al, 140 patients with uncontrolled clinic BP were analysed. Only 31 were found to have true resistant hypertension (22.1%).⁴ The SYMPATHY trial enrolled patients of resistant hypertension for renal denervation.⁵ Their blood samples were analyzed using mass spectrometry for BP lowering medications presence/levels. Poor adherence was detected in 80 percent of all patients! Overall, participants took an average of only two antihypertensive medications despite being prescribed an average of four medications.⁵

The potential danger of hypertensive crisis is omnipresent. It can develop in patients with/without pre-existing chronic hypertension. Often the diastolic BP is ≥ 120 mmHg but there is no specific threshold since it is the rapidity in rise of BP and not the absolute BP level which is more predictive (eclampsia, acute glomerulonephritis).⁶

Hypertensive crises are classified into hypertensive urgencies (HU) and hypertensive emergencies (HE). HU are conditions where a severe elevation in BP represents a potential threat to vital organs and BP should be lowered with oral drugs within 24 hrs. HE are conditions where elevated BP (typically ≥ 180/120 mmHg) represents acute threat to vital organs and patient survival with progressive end organ damage. The common presentations include dyspnoea, chest pain, headache, and neurological deficit. BP should be lowered within one hour using parenteral drugs in the ICU setting.⁷

Hypertensive emergencies are uncommon with an estimated population incidence of one to two cases per million per year. A study in US emergency departments from 2006 to 2013 (STAT registry) revealed the incidence of HE as 0.2 percent overall (0.6 percent for hypertensive patients).⁸ In the current issue, salagre et al have studied the prevalence and clinical profile of patients of hypertensive crisis in single tertiary care hospital over a one year period and observed a prevalence of 0.59% (120/ 20008).⁹ In this study, hypertensive crisis accounted for 18.04% of the ICU admissions (120/665), with almost equal proportion of HU and HE patients. This study included adults ≥ 18 years of age and excluded pregnant women. BP of ≥180/120 mm of Hg was used as cut off. An important observation from this study was that hypertensive crises occurred a decade earlier in India as compared to western population.¹⁰

The mean baseline SBP and DBP (mm Hg) values were significantly higher in the HE group as compared to HU group. The incidence of new onset hypertension was 40.8% (49/120). Even in the 71 known cases of hypertension, noncompliance to therapy was as high as 57.7% (41/71). Therefore, hypertensive crisis could be an initial presentation of undiagnosed hypertension or occur due to treatment non-compliance. A significantly higher number of patients in HE group were males, had diabetes, dyslipidemia and were alcoholics. This emphasises the association of co-morbidities with hypertensive crisis. Metabolic syndrome is a global epidemic. The above data establishes its presence in HT crisis in Indian setting. Alcohol withdrawal hypertension could be a contributory factor in the present study.

The clinical profile of HE in ICU was outlined in a two year study by Dhadke et al published in recent issue of JAPI.¹⁰ They found prevalence of 1.22% (50/4076 ICU admissions).¹⁰ 39 out of 58 patients (67.2%) of HE showed evidence of TOD in the present study. This included cardiac and cerebrovascular involvement in 67.2% each, renal involvement in 24.1% and ophthalmic in 37.9%. In Dhadke et al’s study, as regards TOD, retinopathy, cardiac and neurological involvement was

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seen in 88, 64 and 32 percent respectively. The TOD in Western studies is as follows:

1. Katz et al – The STAT registry: - 26% had cardiovascular(CVS) involvement, 14.9% neurological involvement.
2. Martin et al. – CVS-59.1%, neurological- 40.5%.

Thus, even extent of TOD tends to be higher in Indian patients.

In the present study, the overall mortality was 15.83% (19/120). This mortality was observed only in HE group giving a mortality of 32.76% (19/58) for hypertensive emergencies. Unfavorable predictors of survival included HE, smoking, dyslipidemia, DM, cardiovascular and cerebrovascular involvement. This calls for holistic comprehensive treatment strategies of co-morbidities in HT. US data on HE from 2000 to 2007 shows a rising incidence from 50,000 to 60,000 per year with decrease in mortality from 3 to 2.5%. In the Study the Treatment of Acute Hypertension (STAT) registry, 1588 patients of HE treated with intravenous therapy were included from 25 US hospitals between January, 2007 and April, 2008. The analysis revealed a 6.9% hospital mortality and 37% 90-day readmission rate. The mortality in present study is very high as compared to the Western data. The high TOD in this study could be a possible cause. The high readmission rate in the STAT registry warrants meticulous follow-up of HT crisis after discharge with effective patient and caregiver counselling.

Do weather conditions affect BP? Circannual peaks were noted in the present study in hot and humid months of May and October. However the authors have not commented on mortality concordance for these two peaks. In Scotland, the effect of weather patterns on BP was studied by Aubiniere-Robb et al. In asymptomatic individuals, every 10°C decrease in minimum temperature was associated with 1.85 and 1.18 mm Hg increase in SBP and DBP respectively. The postulated mechanism could be activation of the sympathetic nervous system by severe cold in temperature sensitive individuals. Does a similar mechanism operate in tropical climates in heat sensitive individuals? The PAMELA study implicated climatic conditions as hitherto unknown determinants of BP variability (BPV).

As regards circadian distribution, a large peak was observed between 2 am and 6 am (27 patients) followed by 2 pm to 6 pm (26 patients). This could correlate with circadian pattern of cortisol release.

The authors need to be applauded for their exhaustive and genuine efforts to delineate and gather Indian data on both HU and HE. What are the limitations of the study? Exclusion of pregnant ladies has deprived us of the data on eclampsia as a cause of HT crisis in Indian setting. This study, being non-interventional, could have included pregnant ladies with a due institutional ethics committee approval. Secondly, the BP inclusion criterion was > 180/120 mmHg. Since it is the rapidity of rise of BP and not only the absolute BP reading which determines the occurrence of HT crisis, a lot of young patients with acute rise of BP e.g.; acute glomerulonephritis, may develop HT encephalopathy at a DBP between 100 to 110 mmHg. These patients would thus get excluded from the study giving rise to a lower prevalence rate of HT crisis. The authors have not commented on aetiology of hypertension. Certain aetiologies including serotonin syndrome and use of recreational drugs like cocaine and amphetamine have a high chance of presenting with acute severe HT. Abrupt drug withdrawal may be extremely dangerous as regards beta-blockers and clonidine.

Treatment of HT crisis could become a tight-rope walk. Kaplan makes a classic statement in this regard- “Most of the catastrophes seen in HT crises are due to overzealous reduction in blood pressure and not because of the elevated blood pressure itself.” Rapid correction of severely elevated BP below the auto regulatory range of the vascular beds can result in marked reduction in perfusion causing ischemia and infarction in brain, heart and kidney. A reasonable goal is to lower the MAP by about 25% or to reduce the DBP to 100 to 110 mm Hg. In HU, a wide variety of drugs including oral nifedipine SR, captopril, nitrates, clonidine or hydralazine have been used. Sublingual nifedipine is now contraindicated due to erratic and excessive fall in BP. In HE, the suggested goal is MAP reduction by 10 – 20 % in the first hour and by further 5 – 15% over next 23 hours. The major exceptions to this rule are:

1. Acute phase of ischemic stroke – BP not lowered unless it is ≥ 185/110 mmHg in reperfusion candidates or ≥ 220/120 mmHg otherwise.
2. Acute aortic dissection – SBP is rapidly reduced to 100-120 mmHg to be attained in 20 minutes. After 8 to 24 hours of BP control at target in ICU, oral medication is instituted and IV treatment tapered off. IV Nicardipine and IV Labetolol are most often used first line agents. IV Sodium Nitroprusside (SNP) and nitroglycerine (NTG) are still traditionally used in ICU setting. Clevidipine and Fenoldopam are the newer agents. Clevidipine is an ultra short acting third generation calcium antagonist acting by selective inhibition of L type calcium channel. The initial dose is 1 mg/hr and maximal dose is 21 mg/hr. Fenoldopam is a peripheral dopamine-1 receptor agonist given as an IV infusion. Initial dose is 0.1 mcg/kg/min and dose is titrated at 15 minute intervals depending upon the BP response. These options make
treatment of HT crisis easier in the modern era. Prompt detection of HT, refined treatment and good compliance remain key factors to prevent HT crises.

References