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A SHORT SURVEY ON THE CLINICAL PRESENTATION AND MANAGEMENT OF HYPERTENSIVE CRISIS AMONG INDIA PHYSICIANS

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ABSTRACT

Hypertension is a chronic disorder whose burden is being carried by millions of patients around the world. Approximately 1% of patients with hypertension will develop hypertensive crises at some point during their lifetime. The agent of choice in any particular situation will depend on the clinical presentation. The preferred agents include IV, Nitroglycerine, IV labetalol, IV Enalaprilat, IV Sodium Nitroprusside, Sublingual nifedipine, etc. Hypertensive crisis relatively rare type of clinical presentation out of the surveyed doctors 66.67% of the doctors say they see only less than 10 cases per month presented with hypertensive emergency, and it is commonly seen among the elderly patients aged between 51-60 year of age. Hypertensive emergency associated with cardiological complications, these include Heart failure with or without Left ventricular hypertension, Myocardial infarction, and Accelerated hypertension. Among the surveyed doctors 91% of the doctors have used enalaprilat IV in the management of hypertensive crisis with a starting dose of 1.25 mg as a 5 minute slow infusion. According to doctors opinion enalaprilat is a fast, safe and effective treatment option in the management of hypertensive crisis.

KEYWORDS: Hypertension, Hypertnsive crisis, Enalaprila IV.

INTRODUCTION

Hypertension is a chronic disorder whose burden is being carried by millions of patients around the world. Hypertension till recent past was considered to be a rich man's disease, but today its prevalence is in an exponential phase, the epidemiological studies published in 2000

have estimated a total 972 million adults live with hypertension, and it is projected to increase by about 60% to a whopping total of 1.56 billion by 2025.[1] The scenario is similar in developing nations like India.

Approximately 1% of patients with hypertension will experience hypertensive crises at some point during their lifetime.[2] Hypertensive crisis is defined as a sudden rise in systolic blood pressure of over 200 mm Hg and diastolic of over 120 mm Hg with or without end organ damage.[3] The management of hypertensive crisis requires urgent reduction of blood pressure (BP).

The aim the treatment should by rapid blood pressure reduction and preserving the organ function with minimum side effects. In the management of hypertensive crisis there are several rapid acting intravenous antihypertensives are available, which will control the blood pressure to reasonable levels and prevent fatal complications.[4] The agent of choice in any particular situation will depend on the clinical presentation. The preferred agents include IV, Nitroglycerine, IV labetalol, IV Enalaprilat, IV Sodium Nitroprusside, Sublingual nifedipine, etc.

Eighth Joint National Committee (JNC 8), 2014 Evidence-Based Guideline for the Management of High Blood Pressur and 2013 ESH/ESC Guidelines for the management of arterial hypertension do not really provide guidance on the management of hypertensive crisis.[5] The recent ESH/ESC Guidelines for the management of arterial hypertension define, Hypertensive emergencies as a large elevations in SBP or DBP (>180 mmHg or >120 mmHg, respectively) associated with imminent or progressive organ damage, such as major neurological changes, hypertensive encephalopathy, cerebral infarction, intracranial haemorrhage, acute LV failure, acute pulmonary oedema, aortic dissection, renal failure, or eclampsia. Were as hypertensive urgencies are isolated large BP elevations without acute organ damage and is often associated with treatment discontinuation or reduction as well as with anxiety.[6]

Still there are many ambiguities about hypertensive crisis, like the cut of BP, definition varies guidelines to guidelines and there is no robust clinical management algorithm about the management of hypertensive crisis. So we have conducted a physician survey to quantitatively establish a physician perspective on hypertensive crisis diagnosis and management. The aim of the survey was to establish the clinical perspective of physician on

hypertensive crisis and its management. The study could give an insight into the current management which may help in developing new treatment algorithms.

METHOD

This was a cross-sectional survey conducted from January to April 2014, among physicians who regularly treat hypertension and attend hypertensive crisis cases. Physicians from major cities around India (Bangalore, Mumbai, New Delhi, Chandigarh, Surat) was randomly selected, a questionnaire was developed to obtain information from the recruited doctors. The questionnaire contained precise questions related to the diagnosis, patient assessment and treatment option in the management of hypertensive crisis. A prior consent from the doctor was taken before filling the survey questionnaire. The statistical analysis was done using Microsoft Excel for Windows.

RESULTS

Clinical Presentation

Hypertensive crisis relatively rare type of clinical presentation out of the surveyed doctors 66.67% of the doctors say they see only less than 10 cases per month presented with hypertensive emergency, and it is commonly seen among the elderly patients aged between 51-60 year of age (68.33%) followed by age group 40-50 years of age (23.33%). The interesting outcome from the survey was 83.33% of the physicians plan the treatment after carefully considering a difference in hypertensive emergency and hypertensive urgency but 10% of the physicians said they did not consider any differentiation in hypertensive emergency and urgency, rest 6.77% of the doctor did not respond to the question.

Type of Clinical Presentation

During the survey most of the physicians doctors reported that the most common type of clinical presentation are hypertensive emergency associated with cardiological complications, these include Heart failure with or without Left ventricular hypertension, Myocardial infarction, and Accelerated hypertension. Out of the surveyed physicians 84% reported that most of the patients with hypertensive emergency are presented with cardiac complication, followed by neurological and renal hypertensive emergency cases. Hypertensive crisis aroused from catacholamine excess and obstetric cases (4.5% and 2%) are extremely rarely presented (Figure 1). The common signs and symptoms include headache (84.09%), Nausea & Vomiting (52.27%), Chest pain (27.27%).

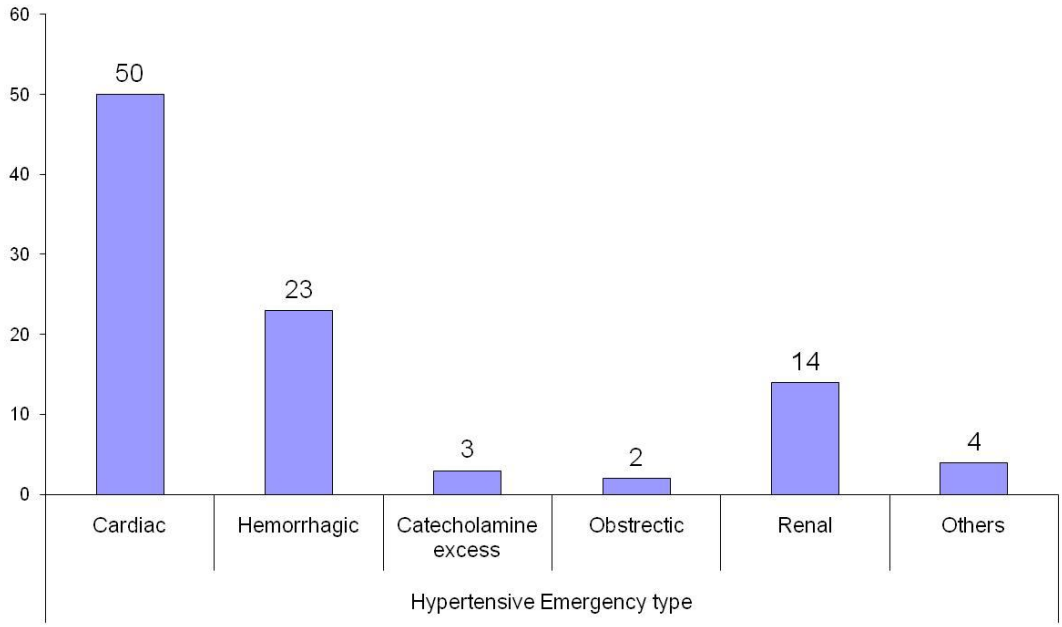

Figure 1: Type of hypertensive cases clinically presented

Treatment of Hypertensive emergency

The gold standard in the management of Hypertensive crisis is still IV nitroglycerine almost 63.64% of the physicians agreed to this. Other agents used in the management were IV Enalaprilat, IV Labetolol, rarely IV Sodium nitroprusside and Nifedipine is used. The most preferred property of the drug is it should have a faster onset of action with desirable safety and efficacy some doctors agree to the fact that the drug should have minimum interaction with co administered drugs.

Among the surveyed doctors 91% of the doctors have used enalaprilat IV in the management of hypertensive crisis with a starting dose of 1.25 mg as a 5 minute slow infusion (figure 2).

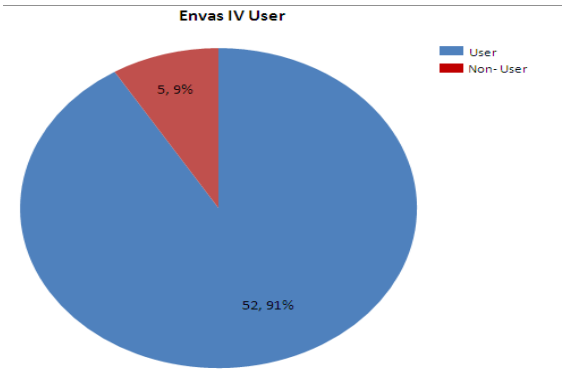

Figure 2: Enalaprilat users

Enalaprilat IV in the management of hypertension

Inhibition of the renin-angiotensin system by blockade of angiotensin-converting enzyme with either parenteral or oral enalapril has been successful in lowering BP both in severe hypertension and associated heart diseases.[7] The survey has shown has shown that enalaprilat is effective in the management of heart failure, Myocardial infarction, stroke, hypertensive encephalopathy, pulmonary edema, etc.

Enalapril, is an oral angiotensin-converting enzyme inhibitor that contains no sulfhydryl group, has been approved by US FDA and DCGI, India in the treatment of hypertension.[8] Enalapril is converted to the biologically enalaprilat in the liver. When administered intravenously, enalaprilat has been found to reduce blood pressure.[7] The recommended dosing schedule for enalaprilat IV is 1.25 mg every 6 hours administered intravenously over at least 5 minutes. For patients on diuretic therapy or patients with creatinine clearance >30 mL/min [>0.50 mL/s] (serum creatinine of up to approximately 3 mg/dL [265.2 µmol/L]) the recommended starting dose for hypertension is 0.625 mg administered intravenously over at least five minutes.[8] Majority of the doctors prefer to start with a standard dosing (70.18%), some doctors prefer to start with a low dose of 0.625 mg (19.3%). Likewise some doctors prefer a high dose of 2.5 mg which is not recommended by the standard dosing algorithm.

When asked for the most desirable feature of enalaprilat IV majority of the doctor responded that “efficacy” by 31.4% and “onset of action” by 37.19% of doctors followed by 29.75% saying “safety” and other 1.65 responded “others” like safety as the key feature of enalaprilat IV in the management of hypertensive emergency (figure 4). The molecule is especially effective in patients with hypertension or Heart failure with or without diabetes. Most of the surveyed doctors believe enalaprilat is contraindicated in obstrectic and renal cases (figure 3).

Table 1: Characteristics of Hypertensive emergency and urgency

	Hypertensive emergency	**Hypertensive urgency**
Significant elevation ib BP	Yes	Yes
BP >180/>120	Yes	No
Target organ damage	Yes	No
Associated condition	Heart attack, aortic bleeding, optic swelling, hypertensive encephalopathy, excess circulatory fluid	Nose bleed, scleroderma

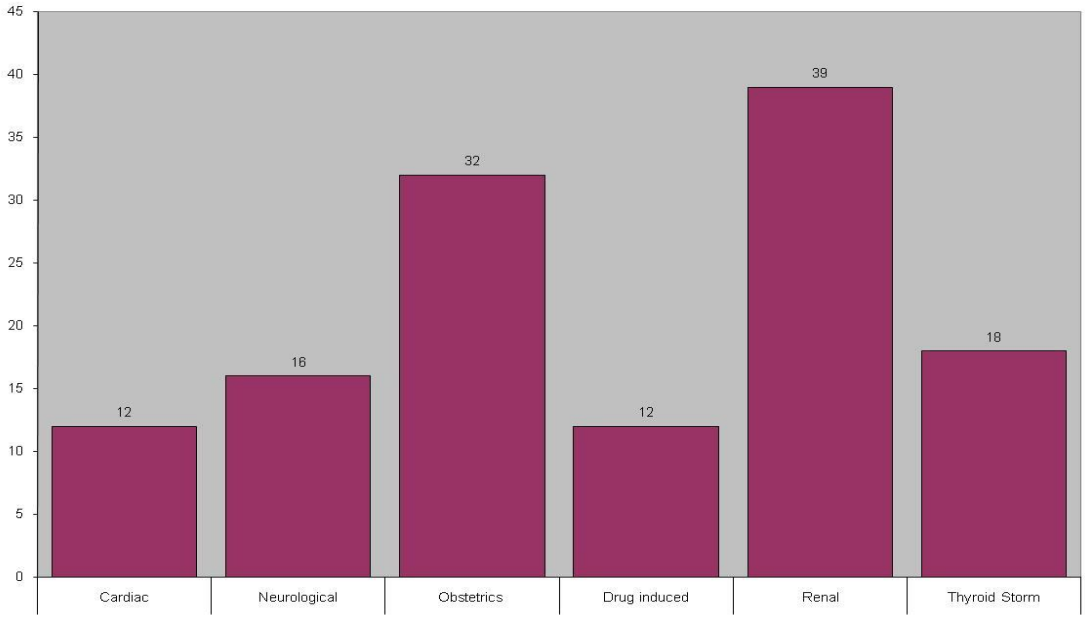

Figure 3: Cases were enalaprilat is contraindicated

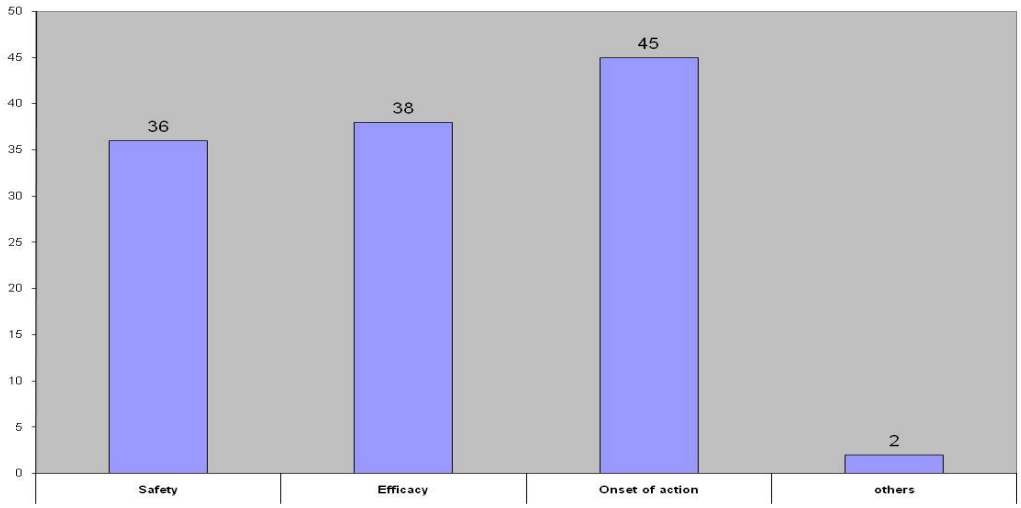

Figure 4: Clinical features of enalaprilat injection.

DISCUSSION

The factors that lead to the severe and rapid elevation of blood pressure in patients with malignant hypertension are poorly understood. The release of humoral vasoconstrictor substances from the stressed vessel wall is thought to be responsible for the initiation and perpetuation of the hypertensive crisis. Increased blood pressure results in endothelial damage, with local intravascular activation of the clotting cascade, fibrinoid necrosis of small blood vessels, and release of vasoconstrictor substances. This leads to a vicious cycle of further vascular injury, tissue ischemia, and release of vasoconstrictor substances. The volume depletion that results from pressure natriuresis further simulates the release of

vasoconstrictor substances from the kidney. The release of vasoconstrictor substances from the kidney has long been postulated to play a central role in the pathophysiology of malignant hypertension. Activation of the renin–angiotensin system has been strongly implicated in the initiation and perpetuation of the vascular injury associated with malignant hypertension. In addition to activation of the renin–angiotensin system vasopressin, endothelin and catecholamines are postulated to play important roles in the pathophysiology of hypertensive emergencies.[2]

The present survey estimate the clinical symptom, incidence and management of hypertensive crisis which is clinical phenomenon presented with a sudden elevation in blood pressure and seen in less than 1% of chronic hypertensive patients will experience a hypertensive crisis, which generally occurs at an average age of 50 years.[9] Hypertensive crisis affects almost 3,686,260 Indians or approximately 1% of hypertensive adults.[10] Nearly 3.2% of patients presenting to the emergency room have a hypertensive crisis. The survey has shown the majority of the patients with hypertensive crisis are elderly (51-60 Years), so treatment plan should be more comprehensive care with extra caution.

Hypertension is a progressive chronic disease, so the chances of having a hypertensive crisis attach is very high among hypertensive patients. Medication noncompliance or the inadequate treatment of stage 1 or stage 2 hypertension may lead to the development of hypertensive urgency.[11, 12] Clinical studies have founded out that only 58% of individuals with coronary heart disease and 50% of individuals who had a stroke did not receive any of the effective drug types (Antihypertensives, statin, Antiplatelet); these rates were highest in the low-income countries.[13] Likewise non-compliance to medication is also major issue, Overall, 25% of patients were totally or partially non-adherent to antihypertensive treatment (total non-adherence 10.1%, partial non-adherence 14.9%).[14]

The incidence of Hypertensive crisis is predetermined by various etiopathological factors like old age, diabetes, non-compliance. Our study have revealed that the incidence of hypertensive crisis is higher in between the age of 51 to 60 years, the prevalence of diabetes is also higher in between the age 50 – 70 years, the prevention of hypertensive crisis need a holistic approach by addressing the etiological factors thus the incidence of hypertensive crisis can be largely decreased.

Nitroglycerin is a venodilator and acts as an arteriolar dilator only in high doses. It reduces the blood pressure by decreasing the preload and after load at higher doses. Similar to nitroprusside, it can compromise cerebral perfusion and hence is not used in hypertensive encephalopathy.[15] Development of tolerance is another issue with use of Nitroglycerine.

Labetalol is a combined alpha adrenergic and nonselective beta-adrenergic receptor blocker. A potential side effect could be bradycardia because of the beta blocking effect.[16] Bolus injections of 1–2 mg/kg have been reported to produce precipitous falls in blood pressure and should therefore be avoided.[17] By the virtue of its class properties it is has limitation in used in acute heart failure and patients with bronchial asthma and COPD.

The management of hypertensive crisis requires a fast, safe and effective treatment option; there are many treatment options currently available with certain limitations for each individual drug. Enalaprilat is a safe and effective option with relatively faster onset of action in the management of hypertensive crisis. Enalaprilat is the only available ACE inhibitor that can be administered intravenously. Enalaprilat rapidly lowers BP within minutes in patients with severe hypertension, without causing excessive hypotension or adverse reactions. The initial recommended dose for enalaprilat is 0.625 to 1.25mg administered over 5 minutes. The maximal single dose should not exceed 5mg for patients receiving diuretics and 1.25 mg for patients with renal impairment.

Enalaprilat doctor opinion survey showed similar results as stated above with majority of doctors using a starting dose of 1.25 mg as slow infusion for 5 minutes showing a reliable safe and effective faster onset of action with relative faster onset of action. According to the doctors opinion enalaprilat is a safe in diabetes, this is a desirable feature as the a majority (70%) of patients with diabetic are hypertensive.[2] The survey has also clearly revels the distinct advantage of enalaprilat in the management of heart failure with or without LV dysfunction, MI, Stroke, etc. Enalaprilat has shown to decrease mean blood pressure, who were given 1.25 mg intravenous enalaprilat. Reduction in their blood pressure started at 5 min with peak reduction noted at 4 hours among Indian patients with grade III essential hypertension.[18]

There are certain limitation of this is cross sectional survey, in terms of sample size without clinical outcome data etc. Nonetheless it does provide the trends and perspectives of physicians in the management of hypertensive crisis. This data would of significant relevance

in developing a proper randomized blinded clinical trial to establish the above findings in future.

CONCLUSION

The survey reveals that injectable enalaprilat is one of the commonly used therapeutic agent in the management of hypertensive emergencies with heart failure with/without LV failure. The clinically reliable safety, efficacy and onset of action of enalaprilat injection make as effective tool in hypertensive crisis management.

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