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A LITERATURE REVIEW ON HYPERTENSIVE CRISIS

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ABSTRACT

Hypertension (HTN) is a leading cause of global disease, mortality, and disability. In developed countries because of increased awareness regarding the health and widespread availability of antihypertensive drug, there has been decreased in the number of patient visiting to primary physician due to increased "crisis level" of blood pressure (BP). Thus, only few patients with the history of HTN or pervious use of antihypertensive drugs can automatically developed hypertensive crisis (HC). HC are the acute medical problem seen in the clinical practice and also most misunderstood and mismanage problem. HC can be divided into hypertensive urgencies (HU) and hypertensive emergencies (HE). This classification is extremely useful in clinical practice because according to this classification, the management to the patient can be judge like, to give oral medication or parental medication, to hospitalize the patient or not, who low and how fast should we go to reduce the BP. Due to lack of knowledge most of the physician, aggressively revert the elevated blood pressure which in turn cause more harm to the patient and is associated in increasing the rate of morbidity and death. The aim of this narrative review is to summarize the basis concept, misconceptions and pitfalls of HC, to improve the public awareness, recognition the risk factor, how to diagnose, how to treat the patient of HC present in the emergency department (ED). (Pre-eclampsia and eclampsia related to pregnancy induced hypertension is not included in this review.)

KEYWORDS: Hypertension, Hypertensive Crisis, Hypertensive Emergencies, Hypertensive Urgencies, Pathophysiology, Management.

INTRODUCTION

Systemic hypertension (HTN), which is the most common chronic clinical disorder encountered by primary physician in the emergency department.[1] Globally, It is the leading cause of mortality and disability[2] and due to obesity, aging, growing population are the incidence which tends to increase in the rate of HTN.[3] HTN has been effected more the 1 billion which is about 26% worldwide, out of which 1-2% will ultimately develop HC in the life time[4] and approximately about 7.1 million died per year.[2] More than 65 million has been affected with HTN in United State.[5] The incidence of HTN has been seen more in men then in women and is also more common in older patients aged more than 65 year and black people.[6] In many poor developing countries, lack of poverty, lack of health awareness, lack of health insurance policy, lack of primary health care physician was leading cause of severe, uncontrolled HTN.[7] HTN remain the most common cause for the primary physician visit in the United States.[5]

As per the National Heart Foundation Australia, the 2016 guideline for the diagnosis and management of HTN in adult, HC was divided into HU and HE according to the presence and absence of acute target organ damage, respectively. HU are diagnosed when the blood pressure is >180/120,[8] associated with symptoms like headache without neurological deficit, dizziness, vomiting. It is not immediately life threatening. It is treated as an outpatient with oral drugs. BP should be lowered over 24-48 hours. HE are diagnosed when the blood pressure is very high often >180/120 together with acute target organ damage or dysfunction like Heart (acute pulmonary edema, heart failure, acute myocardial infarction, aortic aneurysm), the kidneys (acute renal failure), the eye (fundoscopy findings, such as hemorrhages, exudates or papilloedema), the brain (hypertensive encephalopathy, cerebral infarction, hemorrhagic stroke). It is a life threatening condition which required hospitalization usually in an intensive care unit (ICU). Initially it should be treated with parenteral medication with aiming to reduce the level of blood pressure more quickly within 1 hour. In Aortic dissection lowering of blood pressure

require more rapidly within 5-10 minute targeting SBP <120 mmHg and MAP <80 mmHg.[8,10]

It is very important for the primary physician in the ED to distinguish between HU and HE as it play an important role in the diagnosis and management of the patient with HC, which result in the rate of morbidity and mortality. Medication for the HC should be based on the history of the patient with underlying pathophysiological changes, clinical findings, mechanism of action and the potent side effect of the drugs or previous use of antihypertensive drugs.[2,11]

The aim of this narrative review is to summarize the new guideline basis concept, misconceptions and pitfalls of HTN, HC, to improve the public awareness, recognition the risk factor, how to diagnose, how to treat the patient of HC present in the ED.

Epidemiology and Clinical Profile

In the retrospective study of a university-affiliated hospital of brazil during the year 2000, the prevalence of HC was 1.7% in clinical emergency unit and 0.5% of clinicosurgical emergency unit was found.. Out of 452 cases of HC, 179 (39.6%) are HE and 273 (60.4%) are HU. Patient presenting with HE were older (59.6 ± 14.8 versus 49.9 ± 18.6 year, p<0.001) and had greater diastolic BP (129.1 ± 12 versus 126.6 ± 14.4 mmHg, p < 0.05) then those with HU. Almost 18% of this patient ignored their hypertensive status prior to the study. Smoking and diabetes were the associated risk factor for the development of HC. Cerebrovascular lesion (58%) like ischemic stroke, hemorrhagic stroke and subarachnoid hemorrhage is the most common caused for the HE which is independent of sex. Cardiovascular complication like left ventricular failure, acute pulmonary edema, acute myocardial infarction, unstable angina was found in 38% of those patients to cause HE. According to this study, In clinical practice the most common sign and symptom for HE were headache and dizziness while in HE, the most common clinical manifestation were neurological defect and dyspnea together with end target-organ lesion.[12]

In a large multicenter Italian study[13] 333,407 patient were admitted in ED of 10 different Italian hospital during 2009, out of which 1546 diagnosed as HC. The incident of HE was 391 (25.3%), among which 121 (30.9) had acute pulmonary edema, 86 (22.0%) had stroke, including 60 ischemic strokes and 26 hemorrhagic strokes, 70 (17.9%) had myocardial infarction, 31 (7.9%) had acute aortic dissection, 23 (5.9%) had acute renal failure and 19 (4.9%) had hypertensive encephalopathy. HE had also occurred in 23% of patient with unknown history of hypertension (27.9% in men and 18.5% in women). Most of the patient (55.6%) with HC had reported a non-specific symptom like headache without neurological deficit, dizziness, vomits, palpitation etc even among emergencies patient (49.3%). Less common symptom like heart related (dyspnea, chest pain, arrhythmia, syncope etc) are reported by 28.3% patient This study shows that the incident of HC involved in all 5 patient out of 1000 patient admitted in ED and emergencies occur in all 1/4th of patient admitted as HC with more risk in men than in women by 34% of similar age group. The frequency of HE was high in previously unknown hypertension and also in those 10% who are diagnosed but not taking any antihypertensive medication previously.

A prospective study[14] conducted between November 2009 and April 2010, which evaluated the prevalence and clinical presentation of HC in the Emergency medical services of the Community Health Centre "Dr. Mustafa Šehović" Tuzla. There was 180 patient in total out of which 95 subject are without HC and 85 subjects with HC i.e.; the incidence of HC was 47.22%, with HU significantly more represented than emergency (16.47% vs. 83.53%, p<0.0001).The results also indicate that female were significantly over- represented compared to men (60% vs. 40 %, p=0.007). The average age of the male subjects was 55.83±11.06 years, while the female subjects' average age was 59.41±11.97 years. The most common frequent symptoms in hypertensive subjects were headache (75%), chest pain (48.33%), vertigo (44.44%), shortness of breath (38.88%) and nausea (33.89%). The most common symptoms in HC were headache (74.11%), chest pain and shortness of breath (62.35%), vertigo (49.41%), and nausea and vomiting (41.17%).

For differentiation between HU and HE, different clinical presentation with different sign and symptoms has been reported in studies.[15] Importantly, age and diastolic pressure remains the main indication and it also remain higher in HE then in HU. The most non-specific sign and symptoms for HU was headache (22%) and chest pain (27%) and in additional dyspnea (22%) in HE. Frequency for the end-organ damage for HE includes cerebral hemorrhage (24%), acute pulmonary edema (23%), and hypertensive encephalopathy (16%).

In the study of the Tertiary care center of Karachi between 2005 and 2010, 73,063 hypertensive patients were present in ED and only 1336 patients was taken for the study. Headache is the most common and frequently presenting symptom 35.7% followed by dyspnea 32.6% and chest pain 21.4%. The most common comorbidity was dyslipidemia in the patient presentation with uncontrolled hypertension in ED then diabetes mellitus 36.9%, ischemic heart disease 21.4% and 13.9% of them are smokers accordingly. Dyslipidemia was the most common comorbidity in patients presenting with uncontrolled hypertension to the ER with the prevalence of 43.2%(167) followed by diabetes mellitus, 36.9% (143), and ischemic heart disease, 21.4% (83), and 13.9% (54) of them were smokers.[16]

PATHOPHYSIOLOGY

Till now, the precise mechanism for HC is not well understood.[1] There are two main mechanisms which play a central role in the Pathophysiology of HC. These two mechanisms are different from each other but are interrelated.[2]

The first mechanism which results in HC is the failure in auto-regulation system which plays a vital role in the vascular system. Auto-regulation is the key factor which is defines as the ability of the organs like brain, heart, kidney, eye etc to maintain a stable blood flow irrespective of alteration of perfusion pressure.[2] Due to some disease or ischemia in the organ (brain, heart, kidney or eye) the perfusion pressure drop resulting in decrease blood flow which is only for some few minutes as it is maintain by auto- regulation ability of those respective organ.[2] In the case when auto-regulation ability is disturbed, the perfusion pressure decrease thus blood flow will decrease. This all result due to increased vascular resistance due to vasoconstriction leading to mechanical stress and endothelial damage and dysfunction. Finally cause HC.[17,18]

The second most accepted mechanism is the activation of the renin-angiotensin-aldosterone system. When more amount of rennin is produced by the kidney, it stimulates in the over production of angiotensin II. Angiotensin II is a potent vasoconstrictor. Thus both peripheral vascular resistance and BP will increase leading to vascular injury, tissue ischemia.[18] Beside these two most accepted mechanisms, prothrombotic state or platelet activation also plays a key role in causing HC. It is caused by sP-selectin which is found in higher amount in the patient with HC then in normotensive patient regardless of retinopathy.[2]

PATHOPHYSIOLOGY OF HYPERTENSIVE CRISIS

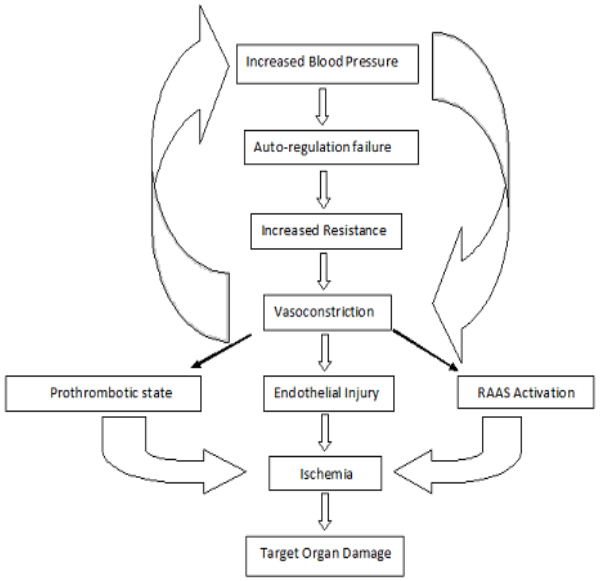

FIGURE 1

Diagnosis

The evaluation and diagnosis of the HC include physical examination, living lifestyle of the patient with detailed past medical history (duration of HTN, duration of uncontrolled BP, history of taking drugs e.g. non-steroid anti-inflammatory drugs) laboratory analysis, and other diagnostic imaging procedures. Physician should be able to evaluate the cause of HC to assess the presence or absence of target organ damage.[19]

Physical examination of the patient include i) The proper measurement of the blood pressure in a quiet and peaceful environment at room temperature with appropriate measuring device (mercury sphygmomanometer with the cuff dimensions 34.3x11x25.3 cm) in both arm on sitting position after taking rest for several minutes.[20] ii) The proper heart auscultation to identify the presence of abnormal heart sound/murmur (aortic coarctation), raised jugular venous pressure, and examination of abdominal aortic murmur/abdominal aortic aneurysm.[2,21] iii) Assessment of neurological sign and symptom like headache, vomiting, focal cerebral infarction, cerebral ischemia, intracerebral hemorrhage.[22] iv) Assessment of the eye (grade III micro vascular changes, soft exudates/flame-shaped hemorrhages, micro aneurysms changes, blot/hard exudates, and hemorrhage and grade IV papilloedema) with fundoscopy to know the presence and severity.[2,23,24] v) Assessment of the vital sign like BP, heart rate, oxygen saturation, respiratory rate, body temperature, pulse.[2] In one study, it has been shown that heart rate is an important factor to distinguished between HE and HU as tachycardia which is caused by over activation of sympathetic nervous system is associated with left ventricular heart failure in HE.[25,26]

A complete laboratory analysis includes i) CBC count and peripheral blood smear to known about microangiopathic hemolytic anemia. ii) Electrolytes. iii) Renal function test. iv)Urinalysis for proteinuria, red blood cell, and cellular casts metanephrines in pheochromocytoma. V) Plain chest radiography to know pulmonary edema or cardiomegaly. Vi) Computed Tomography (CT) of brain to know neurological deficit, and of chest. Vii) Transesophageal echocardiography to know left ventricular function and ejection fraction (EF), hypokinesia, aortic dissection.[27] Speckle-tracking echocardiography may also used to evaluate the function of left ventricle in HC but it is difficult to implement in the setting of ED.[28]

Treatment

Patient with HC either with HU or HE should receive treatment mostly in a heterogeneous or empirical way. Nowadays, there are many different kinds of drugs available for the treatment of HC in ED of every hospital.

In HU, the entire patients are treated as an outpatient with oral antihypertensive medication so that the

pressure should be lowered over 24-48 hours. Oral labetalol is the drugs used to treat HU. It is the combination of non-selective β blocker and postsynaptic α-1 blocking agent in the ratio of 3:1.[2,29,31]

In HE, all patient need ICU admission[32] and required parenteral antihypertensive drugs to reduce BP within a minutes to an hour by about 20-25% and then up to 160/110-100 mmHg in next 2-6 hour.[33,34] We should not lower the BP to normal as lowering of BP to normal may lead to ischemia in brain due to abnormal cerebral flow auto-regulation.[34] But exception exist in Aortic dissection in which we should lower the BP within 5-10 min targeting SBP and MAP up to < 120 mmHg and < 80 mmHg respectively mainly by using parenteral β-blocker like Esmolol,[2,34] There are many other parenteral drugs available for the treatment of HE.

Sodium nitroprusside, an excellent first choice having low price and safe agent for lowering BP in HE,[2,35] it is a potent venous and arterial dilator[36] and work with in a seconds after IV admistration.[2] but it cause thiocyanate toxicity.[37] It has also a narrow therapeutic window.[36] It should be avoided in the patient with hepatic and renal dysfunction and should not be used for more then 48-72 hours.[38]

Nitroglycerin is also commonly used for the treatment HC specially HE. It mainly reduces the demand of oxygen for myocardium by reducing preload, systolic wall stress, and afterload. It also impairs the aggregation of platelet. It is also often use in acute pulmonary edema and acute myocardial infarction in combination with some other antihypertensive drugs.[2,39,40]

Labetalol is also available in parental form in the ration of 6.9:1.[2] Centrally acting oral drugs like clonidine which is a α-2 agonist is also used to treat HU.[41,42]

Nicardipine (dihydropyridine calcium channel blocker) is a parental drugs also used in the treatment of HC.[43] It has high arterial vascular selectivity. It results in increased coronary and cerebral blood flow by dilating coronary and cerebral arteries. It is titratable with dosing that is independent of body weight. Nicardipine has high arterial vascular selectivity, with strong coronary and cerebral vasodilator effect that results in increased coronary and cerebral blood flow.[44]

Clevidipine is a new dihydropyridine calcium channel blocker used in HC with extreme short half-life. It is ultra-short onset of action. It is selective arteriolar dilator and lack venous capacitance.[45]

Parenteral ACEI like Enalapril, frequently used Angiotensin Converting Enzyme Inhibitor seems to be effective in the treatment of HC. Usually it is used as sublingually or parentally in HC.[46] It is more effective and act quickly as a vasodilator in the patients of heart failure, mitral regurgitation, Left Ventricular Diastolic dysfunction and coronary blood flow in hypertrophic obstructive cardiomyopathy.[47,48] but in the case of HC with kidney failure, it is not recommended as it's metabolite enalaprilat fail to excreted by the kidney and increase its accumulation in body.[49]

There are other alternative drugs that are easy to administer in HC like Fenoldopam[50] because it acts as selective short acting peripheral dopamine-1 receptor agonist to cause vasodilatation, as diuresis and natriuresis in chronic kidney diseases.[51,53]

Nowadays, Diuretics are not used more frequently except in acute pulmonary edema with dyspnea for the treatment of HC, because it lead to the excess loss of sodium and plasma volume reduction which may result in the raise of blood pressure again and again by several mechanism, making difficult to control hypertension.[54]

CONCLUSION

In the world population, the prevalence of the HC is in increasing trend with potential to damage end-organ. So, it is important for all the primary physician in ED to understand the basic concept for the diagnosis and management of the HC, when and how quickly blood pressure should be reverted, by which regimens in order to avoid further deterioration and damage of end-organ.

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