The Current Practice of Hypertensive Crises Treatment and the Underestimated Role of Clinical Pharmacists in Ambo Hospital Medical Ward, Ethiopia

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Abstract
Background: Hypertension is an extremely common clinical problem, affecting approximately 1 billion individuals worldwide. An estimated 1% to 2% of patients with chronic hypertension will at some time develop hypertensive crises (Hypertensive urgency and emergency). Hypertensive urgency and emergency are differentiated by the absence or presence of acute end-organ damage, respectively. The blood pressure of patients with hypertensive emergencies should be reduced rapidly during the treatment. It should not be reduced to the normal value, but by approximately 20-30% of the baseline value. The reason for a stepwise reduction in blood pressure is the fact that patients with chronic hypertension have an altered auto regulation curve.

Case presentation: A 60 year old male patient, who has been a known hypertensive patient admitted due to sudden onset of body weakness, difficulty of speech, diverted lips towards the left side, difficulties in eating, moving, coughing and inability to move right side of his extremities since one day. On P/E the pt. was severely sick looking, and unconscious.

Conclusion: A number of both parenteral and oral antihypertensive drugs can be used in these patients. Treatment of hypertensive crises in patients with hypertensive encephalopathy, intracranial haemorrhage, subarachnoid haemorrhage, and thrombotic stroke has been recommended to be initiated with nicardipine, fenoldopam, nimodipine, flunarizine or labetalol.

Keywords: Malignant hypertension; Hypertensive crises; Accelerated hypertension; Hypertensive urgency; Hypertensive emergency

Acronyms and Abbreviations: BP: Blood Pressure; C/C: Chief Complaints; FH: Family History; Hx: History; INC VII: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure; P/E: Physical Examination; PMH: Past Medical History; SH: Social History

Introduction
Hypertension is an extremely common clinical problem, affecting approximately 1 billion individuals worldwide [1]. The incidence and prevalence of hypertensive crises have been little addressed in the literature. However, over the last decade increasing numbers of young patients with different forms of the disease have been observed in emergency departments [2]. An estimated 1% to 2% of patients with chronic hypertension will at some time develop hypertensive crises. According to recent data from the National Health and Nutrition Examination Survey (NHANES) 1999 to 2010, the prevalence of hypertension has remained stable at 30.5% among men and 28.5% among women in the United States; however, 74% of the hypertensive population is unaware of having this condition [3]. Furthermore, the prevalence of hypertension increases with age, affecting 75% of people over the age of 70 [4].

According, to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-VII Report) and American Heart Association blood pressure in adults has generally been classified as normal (90-119/60-79 mmHg), pre-hypertension (120-139 mmHg/80-89 mmHg), stage one hypertension (140-159 mmHg / 90-99 mmHg), stage two hypertension (160-179/100-109 mmHg) and hypertension crisis (≥180/110 mmHg) [5-7].

The terms malignant hypertension, hypertensive crises, and accelerated hypertension have been replaced by hypertensive urgency or Hypertensive Emergency. Hypertensive urgency and emergency are differentiated by the absence or presence of acute end-organ damage, respectively [3,8] and its classification and management have been recently reviewed in the context of both European and American guidelines. The key points for proper blood pressure control in severe arterial hypertension are: Distinction between urgent intervention and emergencies, Choice of the best drug(s), and Choice of the correct route of administration [9]. The most important causes of hypertensive crises are non-compliance (reduction or interruption of therapy), inadequate therapy, endocrine disease, renal (vessel) disease, pregnancy and intoxication (drugs) [10]. Severe hypertension is often seen in the setting of acute strokes. The elevation in BP could be from the stress of the stroke, a physiologic response to hypoxia, or the result of the body’s attempt to increase response to hypoxia, or the result of the body’s attempt to increase channel perfusion in the setting of an ischemic stroke. Alternatively, severe hypertension may have caused the acute stroke [11]. Overall a wide range of therapeutic options are available however its management in hospitals of developing countries is haltered by a number of factors. Therefore, the aim of this case presentation is to review the current knowledge and treatment trends in Ambo hospital.

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Ethiopia; and to compare its trend with the standardize diagnosis and treatment approaches.

Case Presentation

Case summary

Patient's Name: I.S, Age: 60 year, Sex: M, Address: Ambo, Ethiopia, Date of admission: 17/03/14.

C/C

Sudden onset of body weakness, Difficulty of speech, Inability to move right side of his extremities since one day, His lips were diverted towards the left side, had difficulties in eating, moving and coughing. FH

Divorced, father of five children (2 males and 3 females, all are married). He was imprisoned before 5 years, currently lives alone.

PMH

He has been known hypertensive patient.

SH

He's a history of using alcohol in daily base (2-4 pint beer at least 3X a week), uses salty diet and drinks coffee regularly (1 cup/day), smokes cigarettes (10-20 cigarettes/day).

Investigations

P/E

General appearance: severely sick looking, unconscious. HEENT: Pupil Dilated, Facial Palsy, Chest: Clear Sound, S1 and S2 Well Heard. Abdomen: Not Moving with Respiration. GUS: NAD. EXT: Loss of Pain Pupil Dilated, Facial Palsy. Chest: Clear Sound, S1 and S2 Well Heard.

Differential Diagnosis

Metabolic toxicity, Head injury, epilepsy, Anxiety disorders, cardiomyopathy, Cocaine toxicity, hypertrophic cardiomyopathy, Congestive Heart Failure and Pulmonary Edema, Hyperaldosteronism, Primary Hyperthyroidism, Thyroid Storm, and Graves' Disease, and Myocardial Infarction, all of which were ruled out. Exclusion was done based on physical examination, clinical pictures and laboratory diagnosis.

Treatment

Non pharmacologic treatment

Counselling and health education was provided to patient family on the use of the medication, the adherence problem the patient have and on how to live a better healthier life by the ward assigned clinical pharmacists. The points of the discussions include: The definition of what modified life style mean, why to restrict Salt and fat in the diet, the need of avoiding alcohols, smoking and cigarettes, etc.

- Patient was admitted & maintenance fluid secured.
- Position change was ordered to be done every 2 hours.
- Patient was catheterized and physiotherapy was ordered.
- Monitoring Vital signs especially the BP, Q 6 hours.
- NG tube feeding.

Pharmacologic treatment

Clinical questions

- Was the patient treatment approaches according to the current major guidelines and standard books?
- What was the major drug therapy problems (DTPs) identified?
- Was the role of clinical pharmacists' significantly affected in management approaches?
- What was the role of the role of endothelial function and of carotid artery abnormalities in the overall cerebral lesions in hypertensive patients?

Discussion

Current management approaches of hypertensive emergencies

The blood pressure of patients with hypertensive emergencies should be reduced rapidly during the treatment. It should not be reduced to the normal value, but by approximately 20-30% of the baseline value. The reason for a stepwise reduction in blood pressure is the fact that patients with chronic hypertension have an altered auto regulation curve. Acute normotension would lead to hypoperfusion in these patients. Therefore, Immediate but careful reduction in blood pressure is indicated in hypertensive emergencies settings [10]. An excessive hypotensive response is potentially dangerous, possibly leading to ischemic complications such as stroke, myocardial infarction or blindness in some cases. Thus, in patients who are severely hypertensive but asymptomatic, slower reductions in blood pressure should be provided with oral agents [12]. Those without end-organ damage need to adjust or reinstate their regimens, but do not need immediate aggressive treatment [13].

A number of both parenteral and oral antihypertensive drugs can be used in these patients. For a rapid BP reduction parenteral

| Date       | BP mmHg (time) | PR beat/min | RR breath/min. | Tem. c° |
|------------|----------------|-------------|----------------|---------|
| 17/03/14   | 190/110 (6 pm) | 98          | 32             | 38      |
| 18/03/14   | 190/100 (6 am) | 100         | 32             | 38      |
| 19/03/14   | 220/110 (10 pm)| 104         | 30             | 37.5    |
| 20/03/14   | 170/100 (6 am) | 100         | 30             | 38      |
| 21/03/14   | 160/90 (6 am)  | 98          | 32             | 38.6    |
| 22/03/14   | 140/90 (6 am)  | 90          | 30             | 37.8    |

Table 1: Vital sign chart of I.S. Ambo hospital medical ward, Ambo, Ethiopia 2014.

| Date       | BP mmHg (time) | PR beat/min | RR breath/min. | Tem. c° |
|------------|----------------|-------------|----------------|---------|
| 17/03/14   |                |             |                |         |
| 18/03/14   |                |             |                |         |
| 19/03/14   |                |             |                |         |
| 20/03/14   |                |             |                |         |
| 21/03/14   |                |             |                |         |
| 22/03/14   |                |             |                |         |

Table 2: Laboratory chart of I.S. Ambo hospital medical ward, Ambo, Ethiopia.
Nitroprusside, Diazoxide

Nitroprusside is the drug of choice for acute hypertensive emergencies. Parenteral hydralazine is an intermediate treatment between oral agents and more aggressive therapies such as antihypertensive medications such as diazoxide, esmolol, enalaprilat, fenoldopam, hydralazine, labetalol, nicardipine, nitroglycerin, nitroprusside, or trimethaphan and for a slower BP reduction which takes several hours to days, rapid-acting oral therapy is acceptable using captopril, clonidine, prazosin, labetalol, or minoxidil [14] (Tables 4-6).
nitroprusside or diazoxide [14,15]. However, treatment of hypertensive crises in patients with hypertensive encephalopathy, intracranial hemorrhage, subarachnoid hemorrhage, and thrombotic stroke has been recommended to be initiated with nicardipine, fenoldopam, nimodipine, flunarizine or labetalol. Whereas, the use of drugs such as nitroprusside, nitroglycerin, enalaprilat, or hydralazine should be avoided. Hence, such management will result in vasodilation effects without compromised Cerebral Blood Flow (CBF) induced by nitroprusside and nitroglycerin [14].

### Drug Therapy Problems (DTPs)

Recent studies provided evidence that Simvastatin 40 mg/day can reduce stroke risk in high-risk individuals (including patients with prior stroke) by 25%, even in patients with LDL concentrations of less than 116 mg/dl [15,16]. However, the use of simvastatin in I.S. was not rational because no lipid profile data was obtained and no CT scan was done (unavailable at the study place). However, the clinical pictures and patient history indicate high possibility of hemorrhagic stroke rather than ischemic stroke. So, an initial management approach of I.S. has to be targeting urgent reduction of BP. Beside these facts, the dose of Simvastatin prescribed for I.S. was lower than the standard books [16].

Different stroke trials showed that, the use of ASAab resulted in a significant increase in hemorrhagic transformation of the infarction [17,18]. Hence, the use of ASA in I.S. was a safety concern (Table 7).

### I.S: I.S has hypertensive crises with a BP of 190/110 mmHg. Plus, he was manifesting typical of stroke symptoms such as sudden onset of body weakness, difficulty of speech, inability to move his extremities, facial palsy; and difficulties in eating, moving and coughing. Therefore, I.S. should have been treated with intravenous antihypertensive agents such as nicardipine, fenoldopam, and nimodipine to reduce blood pressure by 25% within the first hour [4].

When nifedipine was given orally, as previously recommended, as a rapid-acting alternative to parenteral therapy in the acute management of hypertension; the dose should have to be titrated to 30-90 mg in three divided doses. However, the use of nifedipine in such patients was not a reasonable option considering its life-threatening adverse events of ischemia, MI, and stroke [14,19].

### Role of Clinical Pharmacists

Clinical pharmacists are an integral part of the health care system and seek to improve quality of pharmaceutical care by providing supportive services to health professionals and patients’ alike. In a hypertension clinic, pharmacists can be a cost-effective alternative to physicians in management of patients, and they can improve clinical outcomes and patient satisfaction [20]. Studies also showed that Patients randomized to collaborative primary care-pharmacist hypertension management achieved significantly better blood pressure control compared to usual care [21]. In this specific case the clinical pharmacists tried their best to save the patient life until the last minutes.

**The major contribution made were:**

- ASA was discontinued
- Parenteral antihypertensive agents such as nicardipine, fenoldopam, and nimodipine were recommended rather than the oral use nifedipine. The patient did not receive the recommended medications because of drugs unavailability and patient's unaffordability to buy the medications from private pharmacies.

### The Role of Endothelial Function and of Carotid Artery Abnormalities

Endothelial dysfunction is a well-established response to cardiovascular risk factors and precedes the development of atherosclerosis [22] and its understanding has advanced greatly in the past decade [23]. However, the relationship between blood pressure and arterial stiffness is more difficult to ascertain because blood pressure is a major covariate in the various measurements of stiffness [23]. Endothelium-dependent vasodilation can be assessed in the coronary and peripheral circulations [22] and further it can be managed by pharmaceutical agents that decrease arterial stiffness include nitroglycerin, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers, and calcium channel blockers [23,24].

In our case the association between endothelial dysfunction and hypertension cannot be confirmed because it requires further biomarker study and a single patient result can also not be used to extrapolate and discuss risk factor association.

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| Sr. No | Major DTPs | Specific DTPs | Responsible agents for Specific DTPs |
|-------|------------|--------------|-------------------------------------|
| I     | Indication | Unnecessary drug therapy | Simvastatin ASA |
|       |            | Needs additional drug therapy | IV antihypertensive agents |
| II    | Effectiveness | Ineffective drug | HCT |
|       |            | Dosage too low | nifedipine simvastatin |
| III   | Safety problems | Adverse drug reaction | nifedipine |
|       |            | Dosage too high | None |
| IV    | Compliance problems | non compliance | The patient was not adherent to his medication and had history of social drug use. |

Table 7: Major DTPs identified in patient case I.S. Ambo hospital medical ward, Ambo, Ethiopia; 2014.

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