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Research Article

An Observational and Comparative Study of Cardiovascular Drug: Chlorthalidone and Hydrochlorothiazide the First Line Drug Therapy of Hypertension

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Abstract

Background: Hypertension is when the pressure in blood pressure vessels is too high. The heart has to work harder to pump blood. Hypertension also known as silent killer. There are 2 types of hypertension each has a different cause. It causes complications such as heart attack or stroke heart failure, kidney problems, metabolic syndrome, etc. The risk of hypertension increases with age. Smoking and alcohol consumption also raises blood pressure.

Objective: The present investigation to observe and compare cardiovascular drug chlorthalidone versus hydrochlorothiazide the first line drug therapy of hypertension.

Methodologies: - The present observational study was conducted on 133 hypertension patients. This study was evaluated for the comparative study of two prescribed drugs that is, hydrochlorothiazide and chlorthalidone on hypertension patient the data was collected using suitable design data collection form. Patients having comorbidities conditions were excluded.

Results: Among 133 patients, 26% of total study population were females and 74% of total population were males. Majority of the patients were in the age group of 45-54 years accounting 33.83% of total study population and total 24.06% were alcoholic and chronic smoker. In this study we were included the patient on drug therapy of hydrochlorothiazide and chlorthalidone in which 61% were prescribed for hydrochlorothiazide treatment and 39% to a prescribed for chlorthalidone treatment and as per the data collected chlorthalidone lasts longer in the body than hydrochlorothiazide and it lasts up to 36 hours in the body. Chlorthalidone is 1 to 2 times as potent as hydrochlorothiazide but the quality of life of hydrochlorothiazide is better than chlorthalidone accounting with 61%

Conclusion: The present study revealed that the hypertension patients have poor quality of life and it is very important to improve their quality of life so that the patients can enjoy their day-to-day life. Experts prefer chlorthalidone and hydrochlorothiazide both works well but hydrochlorothiazide prescribe more often.

Keywords: Hypertension, blood pressure, chlorthalidone and hydrochlorothiazide.

INTRODUCTION

Blood pressure is defined as the pressure of blood pushing against the walls of arteries. Arteries carry blood from the heart to other parts of the body. Blood pressure normally increases and falls throughout the day. Blood pressure is usually measured by a Sphygmomanometer and the result shows in millimeters of mercury (mm Hg). If the measurement reads 120 systolic and 80 diastolic, it means "120/80 mmHg."¹ Hypertension is a reading of 130/80 millimeters of mercury (mm Hg) or higher.² The higher the blood pressure levels, the more risk a person has for other health problems, such as heart disease, heart attack, and stroke. The American College of Cardiology and the American Heart Association categories blood pressure into four general categories.³

- **Normal blood pressure.** Normal blood pressure ranges 120/80 mm Hg or lower.
- **Elevated blood pressure.** The upper number ranges from 120 to 129 mm Hg and the lower numbers are below, not above, 80 mm Hg.
- **Stage 1 hypertension.** The upper number ranges from 130 to 139 mm Hg or the lower numbers are between 80- and 89-mm Hg.
- **Stage 2 hypertension.** The upper number is 140 mm Hg or higher or the lower number is 90 mm Hg or higher.

Blood pressure higher than 180/120 mm Hg is considered a hypertensive emergency or crisis. Emergency medical help for those who have these blood pressure numbers.

SYMPTOMS

High blood pressure is also known as the “silent killer” because it usually has no warning signs or symptoms, and many people do not know they have it. It may take years or even decades for the condition to reach levels severe enough that symptoms become obvious. Even then, these symptoms may be attributed to other issues.

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Symptoms of severe hypertension may include:⁶

- Severe Headaches
- Chest pain
- Dizziness
- Difficulty Breathing
- Nausea & Vomiting
- Blurred vision or other vision changes
- Anxiety, Confusion
- Buzzing in the ears
- Nosebleeds
- Abnormal Heart Rhythm

Measuring your blood pressure is the only way to know whether a person has high blood pressure.

ETIOLOGY

There are two types of hypertension. Each type has a different cause.^{7,8,9}

- Primary hypertension
- Secondary hypertension

Essential (Primary) Hypertension

Essential hypertension is also called primary hypertension. This kind of hypertension develops over time. Most people have primary type of hypertension. A combination of factors typically plays an integral role in the development of essential hypertension.

- Genes
- Age
- Race
- Living with obesity
- High alcohol consumption
- Living a very sedentary lifestyle
- Living with diabetes and/or metabolic syndrome
- High sodium intake.

Secondary Hypertension

Secondary hypertension usually occurs quickly and can become more severe than primary hypertension. There are several conditions that may cause secondary hypertension include:

- kidney disease

- obstructive sleep apnea
- congenital heart defects
- side effects of medications
- chronic consumption of alcohol
- adrenal gland problems
- certain endocrine tumors

COMPLICATIONS

The excessive pressure on the artery walls caused by high blood pressure can damage blood vessels and body organs. The higher the blood pressure and the longer it goes uncontrolled, the greater the damage. Uncontrolled high blood pressure can lead to complications including:¹⁰

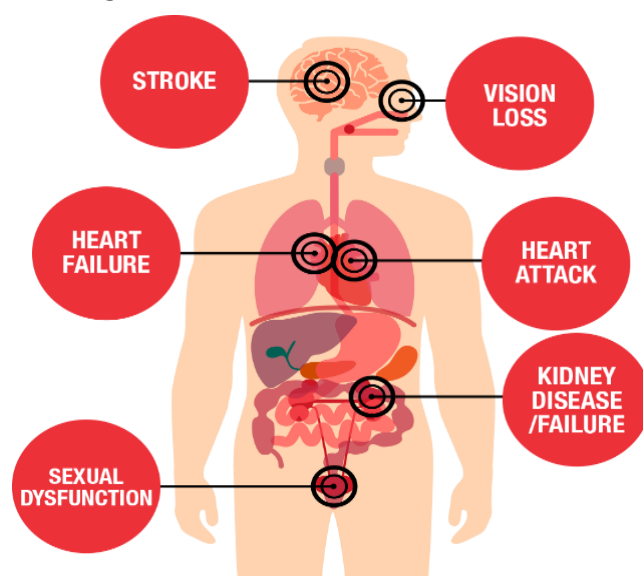


Fig 1: Complications associated with Hypertension.

DIAGNOSIS

Hypertension (high blood pressure) is diagnosed when two or more blood pressure readings measure above 129 mmHg systolic or above 79 mmHg diastolic. Blood pressure is measured using a blood pressure cuff and digital or manual sphygmomanometer. This non-invasive device detects the pressure inside your arteries. Healthcare providers may also use lab tests or imaging tests to diagnose some of the causes or complications of hypertension.

The cuff is placed around upper arm and inflated, causing it to become tight and restrict arterial blood flow. The air is then released from the cuff and a sensor or stethoscope measures the pressure at its highest and lowest points. Healthcare providers may take two or blood pressure readings at least five minutes apart. Readings may be taken on both arms.

If the readings vary by more than 5 mmHg, further readings may be done until closer readings are obtained. The purpose is to get a consistent reading, not to average widely ranging measures.

A diagnosis of hypertension usually requires two or more elevated blood pressure readings taken at separate times.

How to get an accurate reading?

Blood pressure fluctuates from minute to minute during the course of the day. To get the accurate reading, blood pressure should be taken in a quiet, warm environment. Sit quietly with feet supported for at least five minutes before taking reading. This is known as a resting blood pressure reading, which is considered the most accurate.¹⁴

Before the test

Avoid the following for at least 30 minutes prior to taking the test:

- Drinking coffee or other caffeinated beverages.
- Exercising or being active such as taking the stairs.
- Smoking cigarettes or using other tobacco or nicotine products.

During the test

To ensure an accurate reading during the test following can help:¹²

- ♦ Do not talk.
- ♦ Keep feet flat on the floor and do not cross legs or ankles.
- ♦ Rest the arm on a table and keep it relaxed.
- ♦ Take slow deep breaths.

Make sure the blood pressure cuff fits correctly. A cuff that is too big or too small could cause an inaccurate reading.

Home Blood Pressure Monitoring (HBPM)

Blood pressure measured at home; a process is referred to as home blood pressure monitoring (HBPM). HBPM has become much easier and more accurate in recent times.¹⁵

Ambulatory Blood Pressure Monitoring (ABPM)

An ambulatory blood pressure monitoring device consists of a blood pressure cuff that is worn on the arm and attached to a recording device, which can be worn on a belt.¹⁵

TREATMENT

- Pharmacological treatment
- Non-pharmacological treatment

Pharmacological Treatment

There are five effective classes of medication for treating high blood pressure:

- Diuretics
- ACE inhibitors
- Angiotensin II Receptor blockers
- Beta blockers

- Calcium channel blockers

Diuretics

These are also referred to as “water pills” because they help rid the body of salt and fluid via urine production. There are three classes of diuretics:

- Thiazide diuretics
- Loop diuretics
- Potassium sparing diuretics.

Thiazide and thiazide-like diuretics are usually the first line of treatment for hypertension. Thiazide diuretics can be used as the first-line treatment for hypertension (either alone or in combination with other antihypertensives) in all age groups regardless of race unless the patient has evidence of chronic kidney disease where angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker is indicated.^{17,18}

Medications include Hydrochlorothiazide, Chlorthalidone, Indapamide, Metolazone.

Loop diuretics are more effective than thiazides in patients with a low estimated glomerular filtration rate of less than 30 mL/min. They have been approved to treat peripheral Edema associated with congestive heart failure and other noncardiac causes of Edema, as in liver and kidney diseases.²⁹ Loop diuretics are not the first-line agents for HTN treatment.

Medications include Furosemide, Bumetanide, Torsemide.

Potassium Sparing Diuretics: "Mineralocorticoid receptor antagonists" are not usually used as first-line treatment. Spironolactone and eplerenone are considered good in hypertension treatment when added to other antihypertensive medications.^{30,31,32}

Medications include Amiloride Hydrochloride, Spironolactone, Triamterene, Eplerenone.

Calcium channel blockers (CCBs)

Medications include: Amlodipine, Diltiazem, Felodipine, Isradipine, Nicardipine, Nifedipine LA, Nisoldipine, Verapamil

ACE inhibitors and Angiotensin II Receptor blockers (ARBs)

ACE Inhibitor medications include: Benazepril, Captopril, Enalapril, Fosinopril, Lisinopril, Moexipril, Perindopril, Lramipril, Quinapril, Trandolapril.

Angiotensin II receptor blockers (ARBs) medications include: Azilsartan, Candesartan, Eprosartan, Irbesartan, Losartan, Olmesartan, Telmisartan, Valsartan.

Beta blockers

Medications include: Acebutolol, Atenolol, Betaxolol, Bisoprolol, Carvedilol, Metoprolol Tartrate, Metoprolol Succinate, Nadolol, Propranolol IR, Timolol maleate, Carvedilol Phosphate.

MECHANISM OF ACTION

Thiazide and Thiazide like diuretics: mechanism of action for thiazide-type diuretics is not fully understood. Thiazides inhibit sodium transport in the distal tubule by blocking the Na/Cl channels.³² Thiazides can have a small effect on the proximal tube by impairing sodium transport, but the main action is on the distal tubule. Thiazides cause initial volume depletion associated with decreased cardiac output, which recovers within 6 to 8 weeks of starting the treatment in a reverse autoregulation mechanism while the blood pressure remains controlled; thiazide diuretics can acutely activate the renin-angiotensin system and cause systemic vascular resistance, which prevents a good response to the diuretic treatment, this increase in renin-angiotensin activity may resolve with chronic thiazide treatment, the addition of an ACE inhibitor or ARB can enhance the blood pressure control. Also, the thiazide-type diuretics have a modest vasodilation effect, although the mechanism is still unclear.

AIM:

An Observational and Comparative study of Cardiovascular Drug: Chlorthalidone Vs Hydrochlorothiazide the first line drug therapy of Hypertension.

OBJECTIVES:

- To assess the demographic profile of the hypertension patients.
- To compare the impact of longer effect of Hydrochlorothiazide and Chlorthalidone in the body of hypertension patients.
- To assess the quality of life after taking Hydrochlorothiazide and Chlorthalidone in hypertension patients.

STUDY DESIGN AND METHODOLOGY

Study Design: A prospective observational study was conducted to study the comparison of Cardiovascular drug: Chlorthalidone and Hydrochlorothiazide the first line drug therapy of hypertension. This study was conducted among 133 patients which were diagnosed with hypertension. The patients participated in this study where of all age group. The data is collected through retail chain pharmacies (Blue-Medix) from selected demographic area.

Study Site: The data was collected from retails in pharmacy through randomise selected demographic area of Patna, Bihar. The pharmacies are located in Chakmusallahpur, Langartoli, Bhootnath, Rukanpura in Patna, Bihar.

Study Criteria:

Inclusion criteria:

- Patient of all age.
- Patient of either gender.
- Patients willing to participate.

Exclusion criteria:

- Patient having comorbidities condition.
- Patient who refuses to take part in this study.
- Pregnant and lactation period were excluded.

Sources of Data:

- Verbal communication with patients.
- Prescription written by Medical Practitioners.
- Patient history record by verbal communication.

Statical Analysis: Statical Analysis was conducted descriptively by using Microsoft Office Excel Worksheet 365.

Duration of Study: The study was conducted for period of 6 month.

Collection of Data: The data was collected using suitable designed data collection form.

Sample size: This sample size of the data is 106. Which was calculated by using Raosoft Software. At confidence level 95.

RESULTS

The study was conducted on 133 patients for observational and comparative study on hydrochlorothiazide and chlorthalidone the first line drug therapy of hypertension. The data was collected, analysed and evaluated to get an accurate reading.

1. Gender Categorization

According to the data collected in study, among 133 patients 98 were males and 35 were females accounting 74% and 26% respectively as shown in table 1 and figure1.

Table 1: Gender distribution of the patients

Gender	Number of patients	Percentage %
Male	98	74%
Female	35	26%
Total	133	100%

Gender categorization

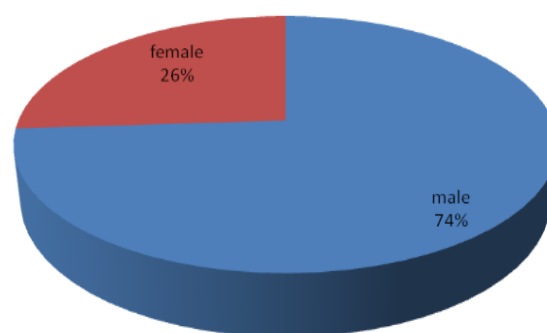


Figure 1. Representing the gender distribution of the patients

2. Age Group Categorization

Out of 133 patients, 6 patients were in age group of below 25, 11 patients were in age group of 25-34, 29 patients were in age group of 35-44, 45 patients were in age group of 45-54, 30 patients were in age group or 55-64 and 12 patients wherein age group of 65 or above years shown in table 2 and figure 2.

Table 2: Age classification in different categories

Age	Number of patients	Percentage %
Below 25	6	4.5%
25-34	11	8.27%
35-44	29	21.80%
45-54	45	33.83%
55-64	30	22.55%
65 and above	12	9.02%

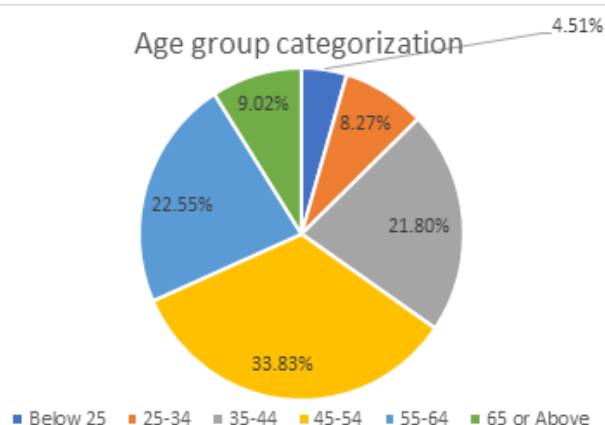


Figure 2 Representing the age group classification

3. Socio Economic Parameters

It was observed that out of 133 patients, 5 patients below income level of ₹5000 (Lower class) and accounting 6.77% of total population involved in the study, 13 patients were between the income level of 5000-10,000 (middle class), accounting 14.29% of total study population, 66 patients were between the income level of 10,000-20,000 (upper middle class), accounting 49.62% of total population involved in the study and 39 patients were above the income level of 20,000 (higher class), accounting 29.32% of total study population as shown in table 3 and figure 3.

Table 3- Socio economic parameters

Income level (Rs.)	No. of patients	Percentage
<5000	5	6.77%
5000-10000	13	14.29%
10000-20000	66	49.62%
>20000	39	29.32%

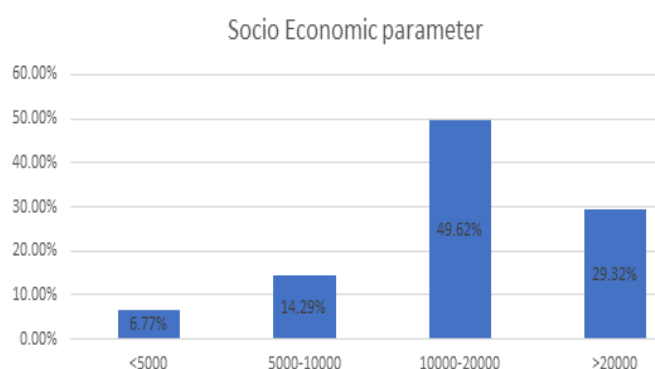


Figure 3 Representing socio economic parameters

4. Social History

In total number of 133 patients, 29 (21.80%) patients were smokers, 26 (19.55%) patients were consumed alcohol, 32 (24.06%) patients smoke and consumed alcohol and 46 (34.59%) patients did not smoke nor consumed alcohol as shown in table 4 and figure 4.

Table 4 Social history

Patients with alcohol and smoking habits	No. of patients	percentage
Smoking	29	21.80%
alcohol	26	19.55%
Smoking and alcohol	32	24.06%
None	46	34.59%

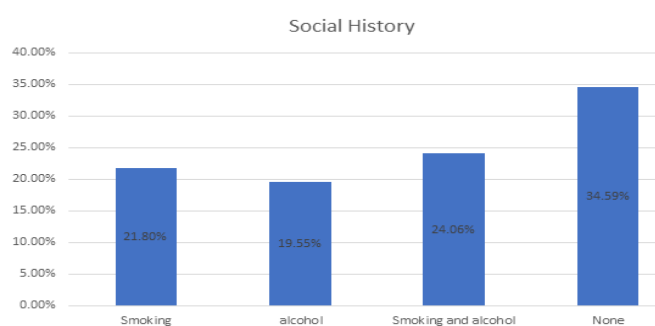


Figure 4 Representing social history of hypertension patients

5. Assessment of Most Prescribed Drug

Among 133 patients, 81 patients were prescribed for HCTZ treatment while 52 other patients were prescribed for CTD treatment as shown in table 5 and figure 5.

Table 5: Assessment of most prescribed drug

Drug	No. of patients	Percentage %
HCTZ	81	61%
CTD	52	39%

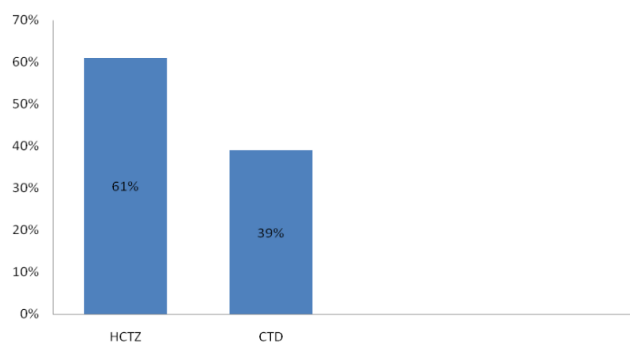


Figure 5 Representing the assessment of most prescribed drug

6. As Per Longer Effect in the Body Categorization

According to the data collected, CTD lasts longer in the body than HCTZ. CTD starts working within 2 to 3 hours, and its effects last up to 36 hours. HCTZ, on the other hand, starts working within 2 hours and lasts for 12 hours shown in table 6 and figure 6.

Table 6: Comparison as per longer effect in the body categorization

Drug	Onset of action	Duration of action
Chlorthalidone	2-3 hours	36 hours
Hydrochlorothiazide	2 hours	12 hours

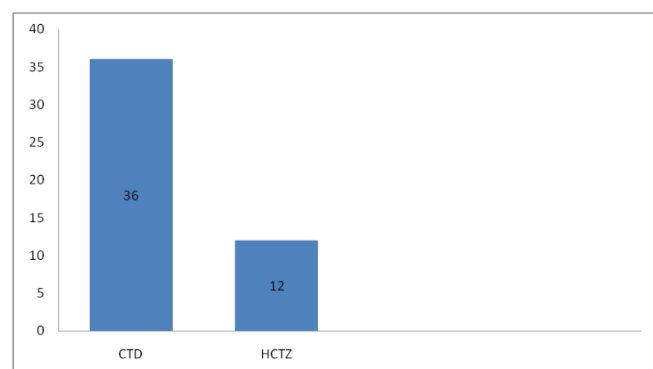


Figure 6 Representing the longer effect of drug in the body.

7. Quality of Life After Taking Hydrochlorothiazide and Chlorthalidone

According to the study, the quality of life of HCTZ is better than CTD. Kidney problems and low potassium (hypokalemia) were more common in adults after taking CTD compared to those taking HCTZ shown in table 7 and figure 7.

Table 7: quality of life in hypertension patients after CTD and HCTZ treatment

Drug prescribed	Percentage %
Chlorthalidone	39%
Hydrochlorothiazide	61%

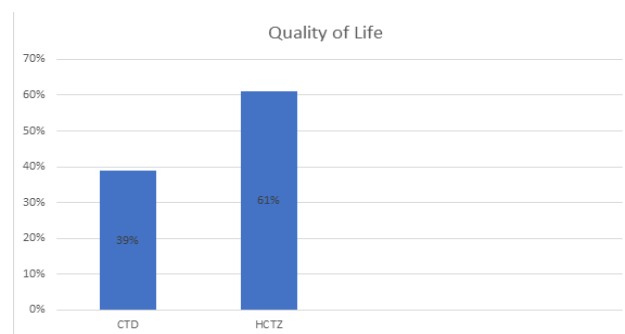


Figure 7 Quality of life in hypertension patients after taking CTD and HCTZ

DISCUSSIONS

Hypertension (high blood pressure) is when the pressure in blood vessels is too high, the heart has to work harder to pump blood. In general, hypertension is a blood pressure reading of 130/80 millimetres of mercury (mmHg) or higher. There are two main types of hypertension i.e., primary hypertension and secondary hypertension. In primary hypertension for most adults, there's no identifiable cause of high blood pressure. It tends to develop gradually over many years. In secondary hypertension, it tends to appear suddenly and cause higher blood pressure than primary hypertension. Uncontrolled high blood pressure can lead to complications including heart attack or stroke, aneurysm, congestive heart failure, kidney problems, eye problems, metabolic syndrome, changes with memory or understanding, dementia, etc. Blood pressure is measured using a blood pressure cuff and digital or manual sphygmomanometer.

The study was conducted to compare the first line therapy Hydrochlorothiazide and Chlorthalidone of hypertension and assess the most prescribed drug for it. Total 133 hypertension cases were studied. Patients who have hypertension have these symptoms such as fainting, dizziness, irregular heartbeat, nose bleeds, fatigue, nausea, vomiting.

According to the study, hypertension affects men more compared to women. The age group of 45-54 years (45 patients, 33.83%) are at more risk of hypertension.

Anti-hypertensive agents are the medications used to treat hypertension. Thiazide and Thiazide like diuretics are one of the preferred pharmacological treatments for hypertension. Hydrochlorothiazide and Chlorthalidone have been the 2 most commonly used diuretics. They used to treat high blood pressure and remove extra fluid from the body.

Chlorthalidone is approximately 1.5 to 2.0 times as potent as Hydrochlorothiazide. Chlorthalidone has much longer duration of action. Chlorthalidone is the first choice for older patients with osteoporosis, as it was associated with lower evidence of pelvic fractures. Chlorthalidone lowers the risk of cardiovascular events about 18% more than Hydrochlorothiazide at the same achieved blood pressure. Experts prefer Chlorthalidone but it may be more likely to cause kidney or electrolyte problems. Hydrochlorothiazide works well and is

usually prescribed more often. Hydrochlorothiazide has better quality of life than Chlorthalidone.

CONCLUSION

In the present study, patients of hypertension were investigated to find out the better first line drug therapy and the most prescribed drug. Chlorthalidone and Hydrochlorothiazide are both diuretics used to treat high blood pressure. Chlorthalidone and Hydrochlorothiazide work in a similar way to remove extra salt and water from the body but their chemical structures are slightly different because of this, HCTZ is considered as thiazide diuretics and CTD is considered as thiazide like diuretics.

Total 133 cases were investigated. The evidence presented in the study shows that the age group of 45-54 years are at higher risk of hypertension. Chlorthalidone is 1 to 2 times as powerful as Hydrochlorothiazide. Chlorthalidone lasts longer in the body, but it may have a higher risk of kidney and electrolyte problems. Chlorthalidone is the first choice for older patients with osteoporosis, but the patients had poor quality of life. Experts recommend Chlorthalidone as the preferred diuretic for high blood pressure. But in practice, Hydrochlorothiazide is prescribed much frequently. It is very important to improve the quality of life so that the hypertension patients can enjoy their day-to-day life.

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Conflicts of interest: The authors declare no conflicts of interest.

Authors Contributions: Ishika Roy designed the study, conducted field sampling and collection and drafted the manuscript. Abhishek Prasad supervised the study, provided scientific guidance, reviewed the manuscript, and coordinated the overall research activities. All authors read and approved the final version of the manuscript.

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