

Original Research Article**A Comparative Study of Effectiveness and Tolerability of Indapamide SR (1.5 mg) and Hydrochlorothiazide (25 mg) in the Treatment of Mild Hypertension****Sangita Kumari<sup>1</sup>, Keshav Kumar Sinha<sup>2\*</sup>, Vijayendra Prasad<sup>3</sup>, Naresh Kumar<sup>4</sup>**<sup>1</sup>Tutor, Department of Pharmacology, Patna Medical College, Patna Bihar, India.<sup>2</sup>Associate Professor, Department of Pharmacology, Patna Medical College, Patna Bihar, India.<sup>3</sup>Associate Professor, Department of Anesthesia, Vardhman Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India<sup>4</sup>Assistant Professor, Department of Pharmacology, Patna Medical College, Patna, Bihar

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**Abstract**

**Introduction:** Hypertension is a major Cause of Premature death World Wide. Globally, at least 1 billion people have hypertension and a projected figure of 1.5 billion is expected by 2025. Systemic hypertension is the leading cause of global cardiovascular mortality and morbidity. Uncontrolled hypertension promotes target organ damage and Significantly increases disease burden on the Community Control of Hypertension is mandatory to preserve and protect Public health worldwide. Now a days for mild Hypertension Indapamide is drug of Choice It is a thiazide like diuretics. Indapamide is more effective than Hydrochlorothiazide for (thiazide type diuretic) control of hypertension.

**Objective:** The Study was undertaken to compare the efficacy and tolerability of Indapamide in one group and Hydrochlorothiazide in the other group in the therapeutic treatment of mild Hypertensive Patients.

**Materials and Methods:** It was an observational study on 40 Patients each in Indapamide group and Hydrochlorothiazide group. The Study was conducted in the 80 cases and the effects were evaluated at 8 weeks. For monitoring the effects of the drug two parameters were evaluated for 8 weeks They included Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) in the two groups.

**Results:** The Change in systolic blood Pressure (SBP) in Group – A was from  $155.37 \pm 2.49$  to  $133.55 \pm 2.32$  mm Hg and in Group – B from  $154.55 \pm 2.73$  to  $140.40 \pm 2.70$  mm Hg. The Change in Diastolic Blood Pressure (DBP) in Group – A was from  $96.92 \pm 3.20$  to  $80.10 \pm 1.42$  mm Hg and in Group – B from  $95.02 \pm 1.79$  to  $88.20 \pm 1.32$  mmHg.

Changes in both the groups were statistically Significant with P-value < 0.001.

The difference between Group – A and Group – B for reduction in Blood Pressure (for both systolic and diastolic) showed Group A to have Significantly higher reduction than Group B (  $P < 0.001$  )

**Conclusion:** The Present Study Clearly indicates Indapamide 1.5mg to be more effective than Hydrochlorothiazide 25 mg in control of mild hypertension with better tolerability.

**Keywords:** Hypertension, Indapamide, Hydrochlorothiazide

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## Introduction

Hypertension (HTN) is one of the most prevalent health problems worldwide, associated with high morbidity and mortality. The trend of global Prevalence of hypertension has been dramatically increasing for the past two decades. Globally, at least 1 billion people have hypertension and a projected figure of 1.5 billion is expected by 2025[1].

Hypertension is defined as Systolic Blood Pressure (SBP)  $\geq 140$  mmHg and / or Diastolic Blood Pressure (DBP)  $\geq 90$  mmHg[2].

It Can be divided into two types.

1. Primary Hypertension – When the Cause for rise in Blood Pressure is not Known .

2. Secondary hypertension when the hypertension is Secondary to a known organic disease Such as Pheochromocytoma, Renovascular disease, Coarctation of aorta, Cushing disease etc. About 90% of the Cases of HTN have Unknown aetiology[3].

The Prevalence of hypertension increases with age, and it is more common in Black than in White Population[4].

Data from the Framingham Cohort study indicate that blood pressure bears a linear relationship with cardiovascular risk significantly increases after a Systolic blood pressure of 155 mmHg; based on these data, it has been suggested that individuals with blood pressure of 120 – 139 / 80 89 mmHg

should be categorized as having pre hypertension[5].

An estimated 77.9 million Americans have elevated blood pressure (Systolic blood pressure  $\geq 140$  mmHg or Diastolic blood pressure  $\geq 90$  mmHg) of these, 78% are aware of their diagnosis but only 68% are receiving treatment and only 64% of those treated are under Control[6].

Paul Muntner, PhD, et al, Suggests the 2017 ACC / AHA Hypertension guideline has potential to increase hypertension awareness, encourage life style modification and focus anti hypertensive medication initiation and intensification on US adults with High CVD risk[7].

Uncontrolled hypertension promotes target organ damage and significantly decreases disease burden on the community. Therefore aggressive control of Hypertension is mandatory to preserve and protect public health in India and worldwide. Now a days for mild Hypertension Indapamide is the drug of choice. Its intrinsic mechanisms are related to the antioxidant properties and also its action on calcium channels, when compared with Hydrochlorothiazide. Indapamide has no adverse effects on both the lipid metabolism and on the renal function. Indapamide is a thiazide – like diuretic superior to thiazide – type diuretic Hydrochlorothiazide in reducing blood pressure without increasing the incidence of hypokalemia, hyponatraemia and

any change of blood glucose and serum total cholesterol levels. The primary objective is to compare the effectiveness of Indapamide (Sustained release) with Hydrochlorothiazide in the treatment of mild hypertension and Secondary objective is to compare the tolerability profile.

### Aim and Objective

Earlier many studies have been done with different drugs for their comparative safety and efficacy in the management of Hypertension. Through our study we aim to compare the efficacy and tolerability of Indapamide (SR) and Hydrochlorothiazide in the therapeutic treatment of mild Hypertensive patients.

### Materials and Methods

This prospective, randomized, open, comparative observational study was conducted in department of Pharmacology PMCH Patna. This was 8 weeks study between 2 March 2021 to 27 April 2021 in 80 mild Hypertensive patients of age ranging between 30-65 years in patients visiting outdoor, Medicine Department, Patna Medical College and Hospital (PMCH), Patna.

The following categories of Patients were enrolled in the study.

### Inclusion Criteria

1. Mild Hypertensive Patients without any Co-morbid condition.
2. Written and informed consent form was taken from each patient before the start of study.

The following Categories of Patients were excluded from the study.

### Exclusion Criteria

1. Patients having any Co-morbid condition.
2. Patients with moderate to severe hypertension.
3. Patients with Secondary hypertension.
4. Hypertension in Pregnancy or lactating mother.

Patients were randomly distributed into two groups each of 40 patients.

Group A- Comprised of patients receiving Indapamide SR (1.5 mg orally daily)

Group B- Comprised of patients receiving Hydrochlorothiazide (25 mg orally daily)

Baseline Systolic Blood Pressure (SBP) and Diastolic Blood pressure (DBP) were measured. Follow up was done at 8 weeks of therapy. At 8 weeks Systolic Blood pressure (SBP) and Diastolic Blood Pressure (DBP) were measured and safety of drugs were noted.

### Results

**Table 1: Age and Gender distribution of patients in the 2 groups**

Characteristics	Group A	Group B
Age (years, mean)	50.9	51.1
Gender (numbers)		
Male	25	24
Female	15	16

**Table 2: Change in average Systolic Blood Pressure (SBP) Values in The two groups.**

Group	Baseline, SBPmmHg (mean±SD)	8Weeks, SBPmmHg (mean ±SD)	Reduction in SBPmmHg (means± SD)	P - value
Group A Indapamide SR 1.5mg n = 40	155.37±2.49	133.55±2.32	21.82±0.17	<0.0001
Group B Hydrochlorothiazide 25 mg n = 40	154.55±2.73	140.40±2.70	14.15±0.03	<0.0001

The Change in systolic Blood pressure in Group A is from  $155.37 \pm 2.49$  to  $133.55 \pm 2.32$  mmHg and in Group B from  $154.55 \pm 2.73$  to  $140.40 \pm 2.70$  mmHg. Changes in both the groups are statistically significant with P – value < 0.0001.

**Table 3: Change in average Diastolic Blood Pressure (DBP) values in the 2 groups.**

Group	Baseline, DBPmmHg (mean±SD)	8 Weeks, DBPmmHg (mean± SD)	Reduction in DBP mmHg (means± SD)	P - value
Group A Indapamide SR 1.5 mg n = 40	96.92±3.20	80.10±1.42	16.82±1.78	<0.0001
Group B Hydrochlorothiazide 25 mg n = 40	95.02±1.79	88.20±1.32	6.82±0.47	<0.0001

The Change in Diastolic Blood pressure in Group A is from  $96.92 \pm 3.20$  to  $80.10 \pm 1.42$  mmHg and in Group B from  $95.02 \pm 1.79$  to  $88.20 \pm 1.32$  mmHg. Change in both the groups are statistically significant with P – value <0.0001

### Discussion

This study was to compare the effectiveness and tolerability of Indapamide SR (1.5mg) with Hydrochlorothiazide (25mg) in the treatment of mild Hypertension.

Both Systolic Blood Pressure and Diastolic Blood Pressure reduction in the two groups were statistically significant.

The aim of this study was to evaluate the effects of Indapamide SR 1.5 mg on Blood Pressure as compared to Hydrochlorothiazide 25mg in patients with mild Hypertension.

New European and American guidelines recommend a target Blood pressure of less than 130/80 mmHg. Indeed, it was Shown by the Hypertension optimal treatment Study (HOT study) that reducing Diastolic Blood pressure to 81 mmHg instead of 84 mmHg , the number of major Cardiovascular events is reduced by 51 %. However, Only 25 % of the patients with hypertension reach the target of 130/80 mmHg in routine clinical practice[8].

Diuretic based therapy for Hypertension has been reaffirmed in International Guidelines as effective first line therapy especially in the elderly and patients with LVH. Indapamide SR 1.5 mg Shows an improved efficacy tolerability profile, with impressive, 24 – hour effects on Blood pressure, and important ancillary properties with regard to LVH and cardiovascular protection.

In Random effects meta – analysis, Indapamide lowered systolic Blood pressure more than Hydrochlorothiazide -5.1 mmHg (95 % confidence interval, - 8.7 to 1.6 ) P = 0.004 and -3.6 mmHg (95% confidence interval, -7.3 to 0.0) P = 0.052, respectively.)[9]

Indapamide lowers SBP more than Hydrochlorothiazide without evidence for greater adverse effects. Indapamide lowered SBP by 54 % more than Hydrochlorothiazide. The advantage in antihypertensive potency of Indapamide compared with Hydrochlorothiazide has been probably underestimated.

Indapamide has reduced left ventricular mass index by 17 % (p < 0.001), whereas Hydrochlorothiazide had no significant effect on this end – organ process compared with Hydrochlorothiazide[10]. Indapamide is more effective in Scavenging oxygen radicals and in inhibiting platelet aggregation

Although Hydrochlorothiazide has less than a 24 – hour duration of diuretic and antihypertensive action[11]. The duration of antihypertensive action for Indapamide immediate release and Indapamide sustained release are estimated as 24<sup>+</sup> hours and 32<sup>+</sup> hours respectively[12]. This is important because targeting night time BP may reduce cardiovascular events more than targeting daytime BP[13]. The findings of the present study are consistent with the other studies.

### Conclusion

Significant reduction in both Systolic Blood Pressure and Diastolic Blood pressures was seen in both the groups in the present study. It may be concluded that Indapamide SR 1.5 mg was more effective than Hydrochlorothiazide 25 mg for Control of mild Hypertension with better tolerability.

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