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RESEARCH ARTICLE

EFFICACY AND SAFETY OF AZILSARTAN COMPARED WITH TELMISARTAN IN HYPERTENSIVE PATIENTS.

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Key words:-

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Abstract

Objective: Angiotensive receptor blockers (ARBs) are very potent antihypertensive agents, Telmisartan being the prototype and most widely used. This study was undertaken to compare the efficacy and safety of Azilsartan a new ARB with Telmisartan.

Material and methods : This prospective study was carried out in patients attending the Department of Medicine, SCB Medical college, Cuttack. Patients with newly diagnosed with stage I-II essential hypertension of either sex within the age group of 18–65 years with blood pressure of $\geq 140/90$ mmHg were included in the study. Severe hypertension $>180/110$ mm of Hg, hypersensitivity to ARBs, secondary hypertension with any other etiology, pregnant women, history of Drug/ Alcohol abuse, cardiac arrhythmias were excluded. Patients who gave consent for the study were divided into 2 random groups 1 and 2 – the first received azilsartan and the second received telmisartan. Point of control was defined as blood pressure $<140/90$ mm of Hg after initiation of therapy.

Results : 180 patients were randomized into two groups. Out of 90 patients included in group 1 who received azilsartan, 4 lost for follow up. Out of 90 patients included in group 2 who received telmisartan, 5 lost for follow up. There was no significant difference between the two drugs in both mean systolic and diastolic blood pressure at 24hrs, 1 month and 3 months and 6 months. Mean diastolic blood pressure at 24 hrs was reduced more with telmisartan compared to azilsartan which is significant. Hypotension related adverse effects occurred in 3% of the patients in azilsartan group while it occurred in 8% of them in telmisartan group.

Conclusion: Azilsartan is an effective blood pressure lowering drug with its safety and efficacy comparable to that of telmisartan.

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Introduction:-

Hypertension is defined as either a systolic blood pressure of ≥ 140 mm Hg or a sustained diastolic blood pressure of ≥ 90 mm Hg, according to Joint National committee (JNC VIII) on hypertension.

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Although many patients may not have symptoms but chronic hypertension can lead to heart disease and stroke, the top two causes of death in the world. Hypertension is also an important risk factor in the development of chronic kidney disease.¹

Effective control of blood pressure in patients with hypertension is required to produce a maximum reduction in clinical cardiovascular events^{2,3} and expert consensus guidelines advocate BP levels <140/90 mm of Hg in patients lacking target organ involvement and <130/80 mmHg in patient with diabetes mellitus, heart disease, or kidney disease^{4,5}.

Angiotensin II appears to exert a central role in both the pathophysiology of essential hypertension and arteriosclerosis-associated hypertension⁶ and insulin resistance⁷.

Angiotensin receptor blockers are selective blockers of angiotensin receptors and are more potent than angiotensin converting enzyme (ACE) inhibitors⁸. ARBs are better tolerated with lesser side effects.

Among the angiotensin receptor blockers telmisartan has favourable pharmacokinetic profile, has longest plasma half-life and is the commonly prescribed ARB. US Food and Drug Administration (FDA) has approved azilsartan medoxomil as the 8th ARB for the treatment of hypertension⁹.

Azilsartan was discovered by modifying the tetrazole ring present in candesartan^{10,11}. Azilsartan has been shown to be effective in reducing BP when administered orally as either the ester prodrug azilsartan medoxomil or as the primary compound¹²⁻¹⁴.

The aim of this study was to compare safety and efficacy of newer ARB Azilsartan with Telmisartan.

Material And Methods:-

This Prospective, randomized open labelled parallel study was carried out in patients attending the Out-Patient and In-patient Department of Health care institute & research centre, Cuttack, Odisha.

Inclusion criteria:

Patients newly diagnosed with stage I & II essential hypertension of either sex within the age group of 18–65 years with blood pressure of $\geq 140/90$ mmHg were included in the study.

The upper limit of blood pressure in both groups was 179/109 mmHg. Only newly diagnosed hypertensive patients without prior antihypertensive treatment and without any associated diseases were included.

Exclusion criteria :

Severe hypertension $\geq 180/110$ mm of Hg, hypersensitivity to ARBs, secondary hypertension with any other etiology, history of Drug/Alcohol abuse, cardiac arrhythmias (atrial flutter, atrial fibrillation, ventricular tachycardia), Patients with sinus bradycardia, Sick sinus syndrome, Prinzmetal's angina, Heart block, Chronic heart failure, Myocardial infarction, Peripheral vascular disease, pregnant and lactating women, patients with impaired kidney function test confirmed by serum creatinine level >2 mg/dl, patients with impaired liver function test such as SGPT or SGOT >2 times than normal limit, patients with asthma.

180 patients who were willing to participate and give informed consent and fulfilled inclusion and exclusion criteria were enrolled in the study. Patients were randomly divided into 2 groups by computer generated numbers. Group 1 received AZILSARTAN 40 mg to 80 mg daily and Group 2 received TELMISARTAN 40 mg to 80 mg daily depending on the initial blood pressure.

Standard Conventional sphygmomanometer was used for BP measurement and the pressure at which the korotokoff sounds were first heard was taken as the systolic pressure and the pressure at which the sounds disappeared was taken as the diastolic pressure. Two recordings of blood pressure were taken at an interval of 15 min in sitting position. After initial screening, the demographic data, past medical history, family history, findings of physical examination, and clinical examination were recorded in the case report form and following investigations were done. ECG, X-ray chest PA view, CBC, Blood urea, creatin, LFT, FBS, 2 hr PPBS, Serum electrolytes, urine RM & micral exam.

Selection of patients was restricted to those who had a BP of $\geq 140/90$ mm of Hg to $< 180/110$ mm of Hg (stage I and stage II hypertension).

Telmisartan was started at a dose of 40 mg to 80 daily while Azilsartan was started at a dose of 40 to 80 mg daily depending on the blood pressure.

Point of control was defined as blood pressure $< 140/90$ mm of Hg after initiation of therapy. They were followed up at the end of 1, 3 & 6 month.

Adverse Drug reaction(ADR) monitoring :

The ADRs related to Azilsartan and Telmisartan were monitored and documented in suitably designed ADR documentation form after initial notification of the suspected ADR by physicians.

Causality of the ADRs were assessed by using Naranjo's Algorithm.

Statistical analyses:-

The primary end point for assessing efficacy was the change from baseline in mean systolic and diastolic BP after 8 weeks of treatment.

Data were entered in MS excel 2007, same were exported into STATA (version 10). For normally distributed continuous data, comparison for significance of difference were done by using 1) Student's paired t test for within group before and after treatment. 2) Student's unpaired t test was used for comparison of normally distributed continuous data between the two treatment groups. P value < 0.05 was considered statistically significant.

Results:-

This study was carried in the 180 patients were randomized and divided into two groups of 90 each. Group 1 received 40 to 80 mg of Azilsartan and Group 2 received 40 to 80mg of Telmisartan (figure 1).

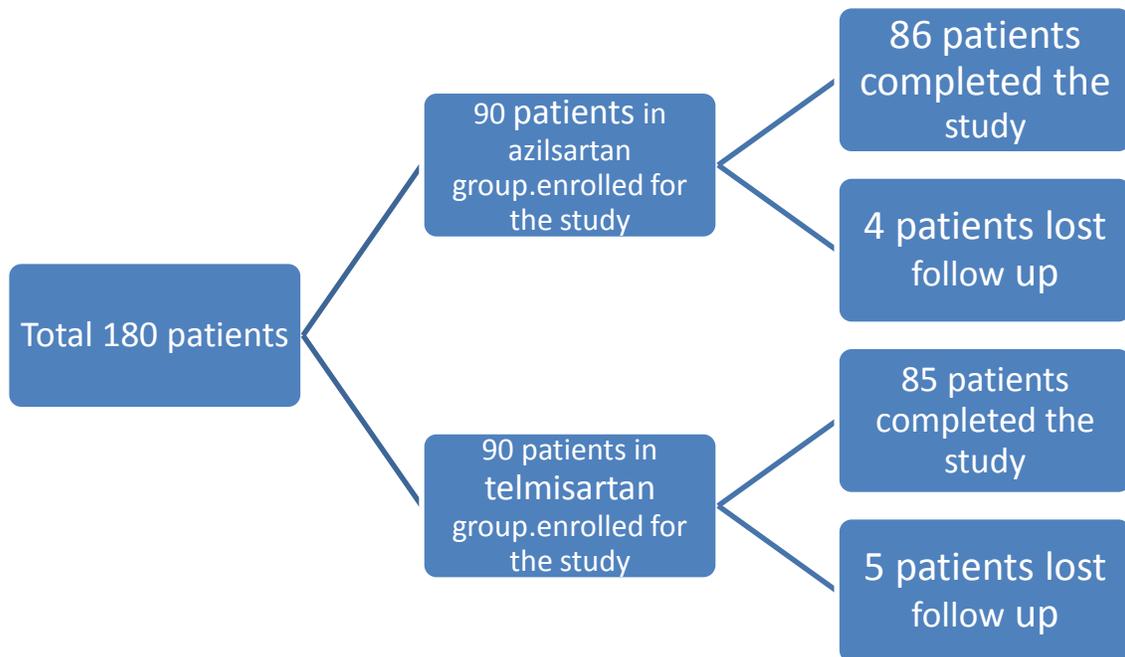


Figure 1:-Number of patients in both groups

Effect of Telmisartan on blood pressure

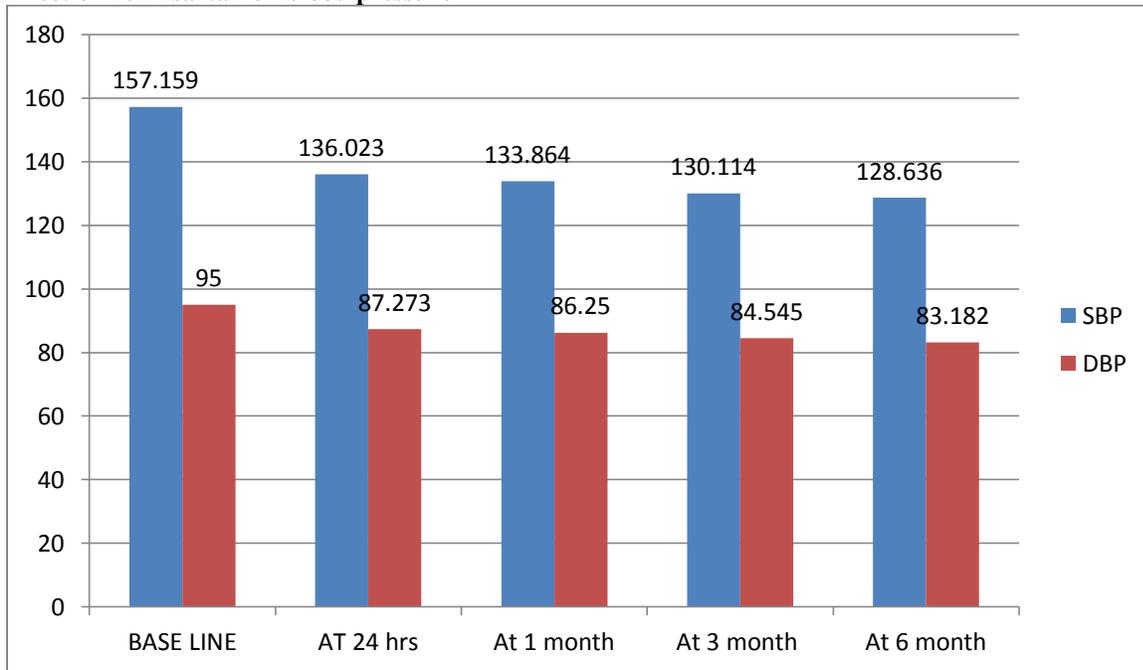


Figure 2:-Effect of Telmisartan on blood pressure

Effect of Azilsartan on blood pressure

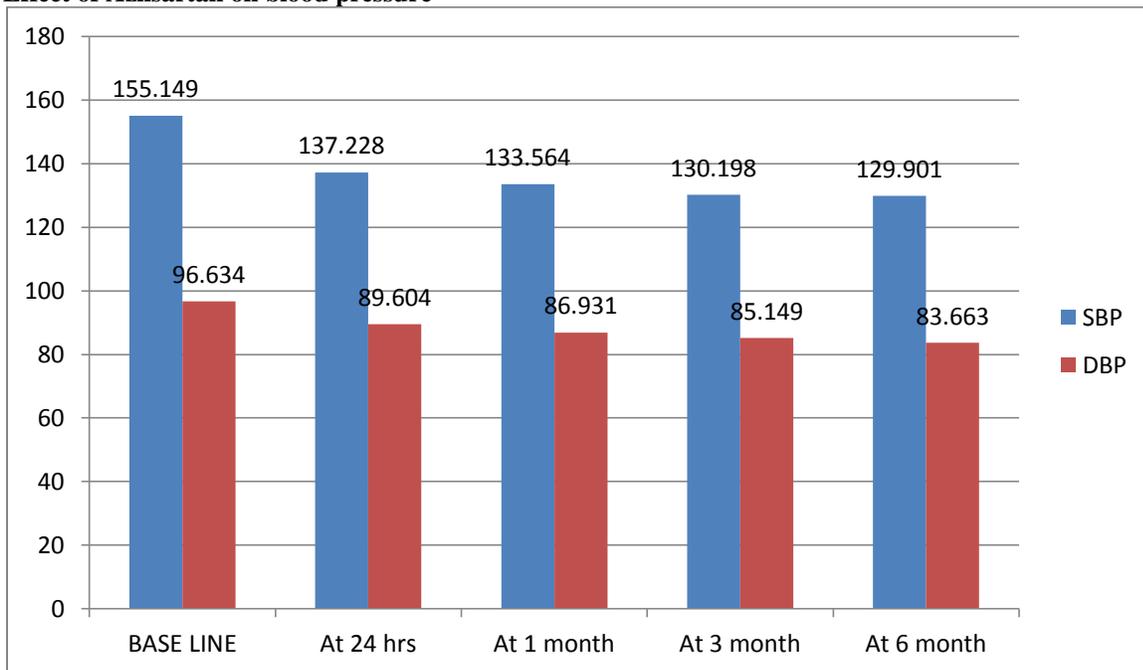


Figure 3:-Effect of Azilsartan on blood pressure

Comparison between the two drugs

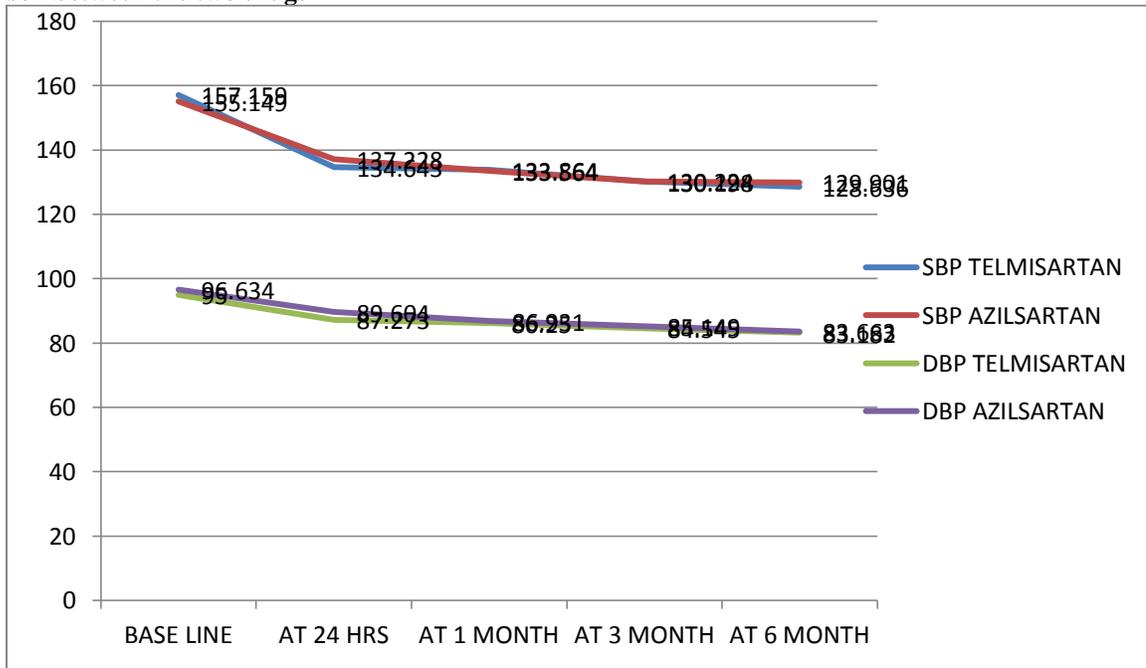


Figure 4:-Comparison between the two drugs

In Telmisartan group, at baseline mean systolic blood pressure was 161.72 ± 12.35 , and at the end of the study mean systolic blood pressure was 132.36 ± 9.41 (systolic blood pressure was reduced by 29.36 ± 4.12 mm of Hg). Mean diastolic blood pressure was decreased from 99.3 ± 9.42 to 87.06 ± 8.59 (diastolic blood pressure was reduced by 11.11 ± 2.058 mm of Hg). There was a significant reduction in both systolic and diastolic blood pressure (P value < 0.001) (figure 2).

In Azilsartan group, mean systolic blood pressure at baseline was 160.54 ± 11.37 , and at the end of the study mean systolic blood pressure was 134.57 ± 8.22 (systolic blood pressure was decreased by 25.97 ± 3.92 mm of Hg). Mean diastolic blood pressure at baseline was 96.68 ± 8.67 and mean diastolic blood pressure at the end of the study was 86.62 ± 5.52 (diastolic blood pressure decreased by 10.06). There was a significant reduction in blood pressure (P value < 0.001) (figure-3).

Monotherapy with azilsartan 40mg, to 80mg daily has been compared with telmisartan 40mg to 80mg daily. There was no significant difference between the two drugs in both mean systolic and diastolic blood pressure at 1 month, 3 month and 6 month. Mean diastolic blood pressure at 24 hrs was reduced more with telmisartan compared to azilsartan (P value = 0.011) which was statistically significant (figure-4).

The most common adverse effects occurring in 3% of the patients in the Azilsartan group were rashes, and in 3% were hypotension related events (dizziness, dizziness postural, syncope, vertigo and vertigo positional), whereas in telmisartan group dizziness, postural syncope and vertigo were observed in nearly 8%.

Discussion:-

Azilsartan a newer angiotensin receptor blocker has shown cardiovascular benefits of lowering blood pressure in preclinical as well as clinical trials. These benefits are due to its property of high affinity to and slow dissociation from AT1R. In clinical trials, antihypertensive therapy has been associated with reductions in (1) stroke incidence, averaging 35-40%; (2) myocardial infarction (MI), averaging 20-25%; and (3) HF, averaging $> 50\%$ ¹⁵.

Azilsartan in clinically approved doses as azilsartan medoxomil has demonstrated to lower 24-hour BP in hypertensive patients significantly more than the maximum approved dose of olmesartan medoxomil, the later being considered by some to be one of the most potent ARBs for lowering BP¹⁶⁻¹⁸.

In the present study we observed that Monotherapy with azilsartan is equally efficacious to telmisartan given once daily in reducing mean blood pressure, by using mean systolic BP and mean diastolic BP monitoring at 8 weeks as primary efficacy end point. Telmisartan has shown slightly greater reduction in diastolic blood pressure at 24 hours.

Other studies have demonstrated superior efficacy and safety of azilsartan over routinely used ARBs but we observed patients who complained of rashes(3%) required discontinuation of azilsartan.

There were no remarkable findings of clinical concern in laboratory test results, vital signs, body weight and 12-lead electrocardiogram findings.

Conclusion:-

Azilsartan, a newer angiotensin receptor blocker is an effective and safe blood pressure lowering drug. Its efficacy is comparable to that of telmisartan with additional benefit of lesser side effects and hence can be safely used in all the patients.

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