ARBS STUDIES' EFFECTIVENESS AND SAFETY IN DECREASING BLOOD PRESSURE WITH NO SIGNIFICANT CHANGES IN OTHER CLINICAL AND BIOCHEMICAL PARAMETERS

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ABSTRACT:
This study is for evaluation of efficacy and safety of ARBs in stage 1 Hypertensive patients (JNC 8).

INTRODUCTION
Hypertension, simply put, is high blood pressure. It's called "Silent Killer". It is defined as a persistent elevation of the systolic blood pressure at a level of 140mm Hg and of diastolic blood pressure of 90 mm Hg or higher. The Joint national committee 8 reports document some disturbing current trends. It is one of the important risk Factors for cardiovascular disease accounting for 20-30% of all adults. In the 1970, in most of the developed countries, 50% of the general population of hypertensive patients were aware of the problem. Among them only half of them were treated. If this is the situation with highly developed medical services, then it's difficult to imagine scenario of patients in other developing countries.The International Society on Hypertension and National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure have recommended certain lifestyle changes to lower BP, enhance antihypertensive drug efficacy and reduce CV risk, therapeutic lifestyle changes include a diet modification, physical activity, weigh management, limiting alcohol consumption and no tobacco use. However, evidence suggests that patients have difficulty to follow certain lifestyle changes

Angiotensin receptor blockers (ARBs) are included in Antihypertensive drugs in JNC8. It is evident now that most patients with hypertension will not be able to maintain blood pressure in normal range with only 1 medication. Choice of drug in absence of compelling indications are still unresolved issue except thiazide diuretics which is recommended in most of hypertensive patients. ARBs are good add on drugs

Or can be effective monotherapy in stage 1 hypertension or in the presence of contraindications to thiazide diuretics.ARBs achieve all characteristics that should be present in an ideal antihypertensive agent. Ideal antihypertensive medication should have following features:

1. Effective as single medication in & 50% of patients.
2. continuous blood pressure controls during activities.
3. Hemodynamically logical and effective.
4. Lack of tolerance and pseudo tolerance.
5. Favourable biochemical and metabolic effects.
6. Reduces end organ damage.
7. Negligible side effects and better quality of life.
8. Best compliance.

METHODOLOGY
Study Design
We studied 100 patients of age more than 40 years having stage 1 hypertension as outdoor and indoor of Tertiary care Hospital during year March 2023- March 2024.

SELECTION OF PATIENTS
Inclusion criteria:
Age- 40 to 60 years.
Patients should have stage 1 hypertension as defined by JNC 8 recommendations which are as follows:

Blood Pressure Classification	Systolic mmHg	Diastolic mmHg
Normal	<120	*and*<80
Prehypertension	120–139	*or* 80–89
Stage 1 hypertension	140–159	*or* 90–99
Stage 2 hypertension	>160	*or*>100
Isolated systolic hypertension	>140	*and*<90

Exclusion criteria
Age below 40 years and above 60 years.
Women of child bearing age and pregnant women.
Patients having manifestations of malignant hypertension.
Patients with essential hypertension with other concomitant conditions like angina, previous myocardial infarction, heart failure were excluded from study as these are compelling indications for ACE inhibitors or beta blockers or use of both according to Joint national committee 8.
Patients with hypersensitivity to ARBs.
Patients having manifestations of secondary hypertension like Reno vascular hypertension (renal artery stenosis or abdominal bruit).
Renal parenchymal hypertension (altered renal function test).
Hyperkalemia
Patients on long term steroid therapy and having concomitant hypertension.

EVALUATION CRITERIA:
Patients' blood pressure was measured with appropriate cuff size in sitting position (seated blood pressure). At least 2 readings were recorded at different times as per the guidelines of JNC 8 for diagnosis of hypertension. Patients' renal function tests and serum potassium are measured at baseline, 7 days after initial dose, as and when needed and after 3 months of therapy. CT scan brain was done in patients with complaint of unilateral limb weakness. All other biochemical parameters like serum electrolytes, random blood sugar, lipid profile is investigated at the base line and at the end of study. Patients are inquired and examined at every visit for evidence of adverse effects and counselled to report them as soon as any new symptom occurs. Required investigations are done to

detect any adverse effect of drug as and when needed. Response is considered as achievement of blood pressure below 140 mm Hg systolic and below 90 mm Hg diastolic.

CONCOMITANT USE OF OTHER DRUGS:

Concomitantly any other antihypertensive was not used. Also, the drugs which can blunt antihypertensive effect of ARBs like NSAIDs were not used. Any other vasoactive drug was not used during the study.

METHOD:

We selected 3 ARBs – Losartan, telmisartan, Olmesartan. Other ARBS in this group were not taken in study due to higher cost and less easily availability in selected population. We started losartan (50 mg/day) or Telmisartan (40 mg/day) or Olmesartan (20 mg/day) as a monotherapy for stage 1 hypertension on random basis to avoid any bias for drugs. Then patients were followed every 15 days for BP measurement, to check compliance, to observe any adverse effects. Aspirin and atorvastatin therapy were also started along with ARBs when needed in cerebrovascular accident patients. If there was no expected response in BP reduction at the end of 2 weeks, dose of ARBs was increased to maximum daily dose. All relevant information were recorded in pre-tested proforma.

Study End point:

If patient had not responded or had inadequate response to this maximum dose after 4 weeks, patient was declared Non responder and shifted to other antihypertensive therapy.

RESULTS

Here we tabulated the various observation of our study below.

Table1. SYSTOLIC B.P. REDUCTION AFTER ARBs TREATMENT

SYSTOLIC B.P.	AFTER 15 DAYS	AFTER 1 MONTH	AFTER 2 MONTHS	AFTER 3 MONTHS
150-159	43	25	8	6
140-149	34	28	38	42
130-139	18	34	42	14
120-129	5	13	12	38
TOTAL	100	100	100	100

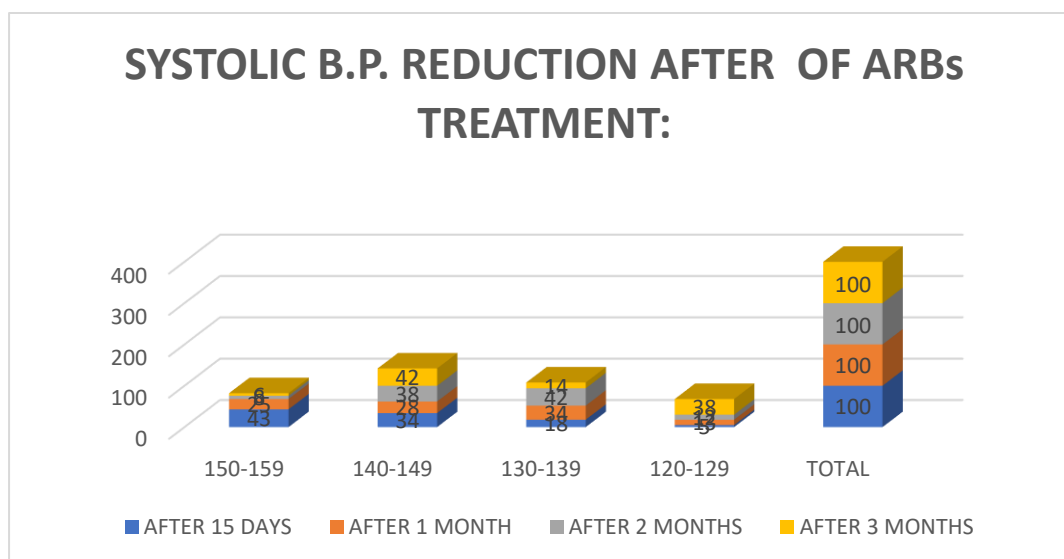SYSTOLIC B.P. REDUCTION AFTER OF ARBs TREATMENT:

Table 2. DIASTOLIC B.P. REDUCTION AFTER 15 DAYS OF ARBs TREATMENT:

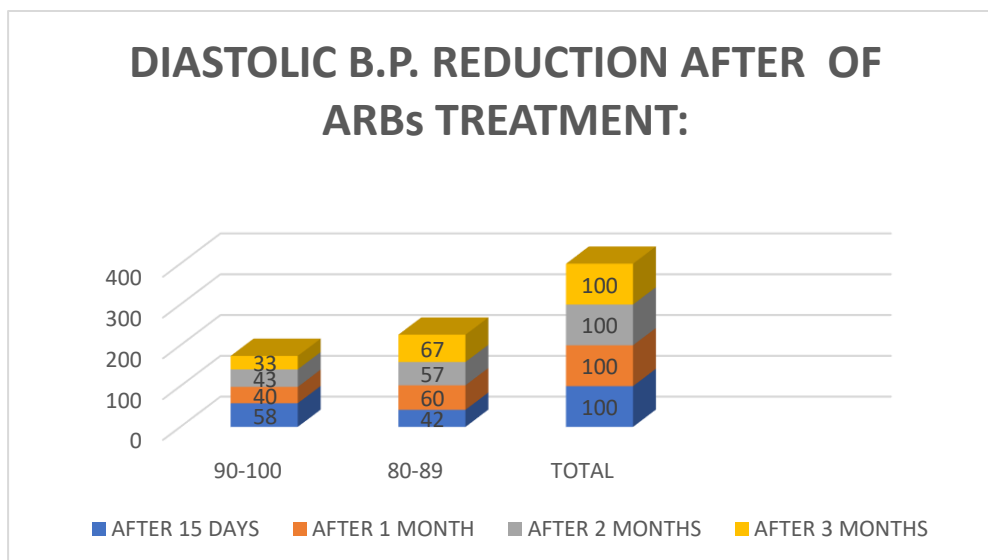| DIASTOLIC B.P.	After 15 days	After 1 month	After 2 months	After 3 months
90-100	58	40	43	33
80-89	42	60	57	67
TOTAL	100	100	60	100

DIASTOLIC B.P. REDUCTION AFTER OF ARBs TREATMENT:

Table 3. ADVERSE EFFECTS OBSERVED DURING FOLLOW UP OF PATIENTS ON ARBs:

Adverse Effects	Losartan	Telmisartan	Olmesartan
Headache	0	0	1
Nausea/Vomiting	0	0	0
Giddiness/Dizziness	0	0	0
Cough	0	0	0
Fatigue	0	0	0
Diarrhea	0	0	0
Hypotension	0	0	0
Pruritus	0	0	0
Angioneurotic enema	0	0	0
Rash	0	0	0
Oliguria	0	0	0
Syncope	0	0	0
TOTAL	0	0	1

Table 4. EFFECT ON PULSE RATE:

PRE-TREATMENT MEAN PULSE RATE (per minute)	POST TREATMENT MEAN PULSE RATE (per minute)	DIFFERENCE
78.5	79.7	1.2

.Table 5. EFFECT ON PLASMA LIPID PROFILE:

LIPID PROFILE	MEAN PRE-TREATMENT READING (mg/dL)	MEAN POST TREATMENT READING (mg/dL)	MEAN REDUCTION (mg/dL)
HDL	41.13	40.43	0.7
LDL	131.18	130.50	0.6
Triglyceride	170.38	169.90	0.4
Cholesterol	210.88	210.12	0.7

Thus, during ARBs therapy, there is no significant change in pre-treatment and post treatment levels of HDL, LDL, Triglycerides and cholesterol at 3 months of therapy.

Many of patients were on atorvastatin therapy, so effect of ARBs as alone drug on lipid profile cannot be evaluated.

Table 6. EFFECT ON OTHER BIOCHEMICAL PARAMETERS:

PARAMETER	MEAN PRE-TREATMENT READING	MEAN POST TREATMENT READING	MEAN REDUCTION
Blood urea (mg %)	31.0	30.6	0.4
S. creatinine mg %%)	0.9	0.87	0.03
S. potassium (mEq/L)	4.1	4.2	0.1
S. sodium (mEq/L)	139	139	1.0
S.G.P.T.(Unit)	27.9	28.5	0.6
RBS (mg %)	109.2	107.5	1.7

Thus, pre-treatment and post treatment mean values of blood urea, serum creatinine, SGPT, blood sugar, serum sodium and serum potassium do not differ significantly.

DISCUSSION

The final target of antihypertensive medication is to decrease atherosclerotic cardiovascular, cerebrovascular and renal morbidity and mortality[1]. In clinical trials, antihypertensive medication has been associated with ~30-35% mean reduction in stroke incidence, 20 to 25% mean reduction in cardiac disease, and >50% mean reduction in heart failure incidence[1].

I have studied 100 patients to evaluate efficacy and safety of ARBs instage 1 hypertension.

AGE:

The present study included patients between 40 to 60 years of age. All ARBs were found to be effective in control of hypertension in all age groups in this study. These results are comparable with Fasce and Wage man et al[22], LaCour ice et al[24] study, Lieu et al study[25].

SEX DIFFERENCE:

In present study, there was no any significant difference on effect of ARBs on male or female patients after 3 months. These results are comparable with Levy D et al[23] and Nishimura et al study[26].

PULSE RATE:

In present study, there was no significant change in mean pulse rate. Mean baseline pulse rate was 80.3 per minute and mean pulse rate at the end of study was 80.5 per minute without major changes. In a study done by Parker et al, he did not find any significant change in heart rate with therapy[36].

Losartan (100 mg/day) effect after 12 weeks of treatment:

Blood pressure reduction (mean)	Present study	Fasce and Wagemann study[22]	Liau et al study[25]	Stumpe and Ludwig study[32]
Systolic	20 mm Hg	28 mm Hg	14 mm Hg	12 mm Hg
Diastolic	12 mm Hg	12 mm Hg	11 mm Hg	9 mm Hg

Thus, our study results are comparable with other studies done in the past and this study shows that average reduction in SBP is 20 mm Hg and in DBP is 12 mm Hg at maximum and tolerable dose.

Telmisartan (80 mg/day) effect after 12 weeks of treatment:

Blood pressure reduction (mean)	Present study	Lacuorciere et al study[24]	Nishimura et al study[26]	Nalbantgil et al study[29]
Systolic	26 mm Hg	17 mm Hg	25 mm Hg	28 mm Hg
Diastolic	12 mm Hg	11 mm Hg	15 mm Hg	12 mm Hg

Thus, our study results are comparable with other studies done in the past and this study shows that average reduction in SBP is 26 mm Hg and in DBP is 12 mm Hg at maximum and tolerable dose.

Olmesartan (40 mg/day) effect after 12 weeks of treatment:

Blood pressure reduction (mean)	Present study	Lieu et al study[25]	Giles et al study[30]
Systolic	30 mm Hg	19 mm Hg	16 mm Hg
Diastolic	16 mm Hg	15 mm Hg	13 mm Hg

Thus, our study results are comparable with other studies done in the past and this study shows that average reduction in SBP is 30 mm Hg and in DBP is 16 mm Hg at maximum and tolerable dose.

BIOCHEMICAL PARAMETERS:
In present study, biochemical parameters like random blood sugar, serum lipid, renal functions and serum electrolytes were not affected by ARBs therapy.

In a study done by Koulouris et al, ARBs showed no effect on glucose or lipid profile, although in type 2 diabetic patients, it caused significant decrease in c reactive protein and oxidized low density lipoprotein cholesterol levels[35].

TOLERANCE:
In present study, ARBs have proven to have excellent tolerability. Only one patient had headache after treatment with Olmesartan which was mild and subsided by giving Paracetamol tablets orally. No other side effects like cough, hypotension, and angioneurotic oedema were recorded.

COMPLIANCE:
In present study, compliance with ARBs was excellent and no patient was found to have been lost in follow up or have missed taking drug or have discontinued therapy due to side effects.
In ESPIRIT study done by Sharma et al, a compliance rate of >97% was recorded[36].

CONCLUSIONS
In this study, we included 100 patients from outdoor and indoor both coming to Tertiary care hospital. Following are the conclusions from our study.

Maximum number of patients in our study is between 50-60 years.

The number of male patients [n=60] was slightly more than female patients [n=40].

Headache mainly in the occipital region was the most common presenting complaint of the patients we studied.

All ARBs were found to reduce Blood pressure efficiently, but Olmesartan (40 mg/day) showed the results in decreasing blood pressure (Both SBP and DBP) as compared to other ARBs.

Average Dose required for blood pressure control is 100mg/day for losartan, 80 mg/day for telmisartan, and 40mg/day for Olmesartan.

There was no significant effect on pulse rate and electrocardiogram of patients after 3 months of ARBs therapy.

There was no significant effect on other biochemical parameters like lipid, RBS, RFT, SGPT, electrolytes.

These drugs were found well tolerated. No major side effects were found after starting ARBs except one patient developed mild headache after treatment with Olmesartan which was subsided by giving Paracetamol tablets orally

These drugs proved to have 100% compliance rate and no patient required discontinuation of drugs due to adverse effects or non-compliance.

ARBs studied here have effectiveness and safety in decreasing blood pressure with no significant changes in other clinical and biochemical parameters.

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