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COMPARATIVE STUDY TO EVALUATE QUALITY OF LIFE OF AZILSARTAN AND TELMISARTAN IN PATIENTS OF HYPERTENSION.

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Abstract
Background: Hypertension (HTN) is a major cardiovascular disease and is a major worldwide clinicalproblem. The prevalence of hypertension increases in urban and rural areas. The treatment of hypertension began in the 1960s with oral diuretics. The other modalities of treatment of hypertension are beta – blockers, calcium-channel blockers, alpha receptors blockers, ACE inhibitors and ARBs. Quality of life was assessed by SF -12 questionnaire.
Objective: To compare and evaluate the quality of life of Azilsartan and Telmisartan in patients of hypertension.
Material and Methods: In this prospective, open,parallel group, comparative study, 80 patients of hypertension attending the Cardiology Outpatient Department, Govt. Medical College & Rajindra Hospital,Patiala was recruited. This comparative study was done on 80 patients for 8 weeks.
Quality of Life: In my project of Quality of life, I had taken total 80 patients and the patients were divided into two groups and 40 patients each of Azilsartan and Telmisartan. To assess quality of life questionnaire SF-12 was administered to the patients.
Results: There was significant improvement in the quality of life with Azilsartan than Telmisartan.
Conclusion: Azilsartan was a better choice than Telmisartan because there was greater improvement in all the domains of quality of life.

Keywords: Hypertension, Quality of life, Azilsartan, Telmisartan.

INTRODUCTION

Hypertension is an iceberg disease. Hypertension is a very common and important disease related to modern civilized life and its complications pose a major health problem in populations worldwide. Its prevalence is quite high in India, and affects both rural and urban populations [1].Both randomized clinical trials and observational studies have confirmed the effect of uncontrolled hypertension on cardiovascular morbidity and mortality [2]. Early treatment can reverse and retard

the complications associated with hypertension.As a globally prevalent disease, hypertension is a major risk factor for ischemic heart disease, heart failure, stroke, atrial fibrillation, chronic kidney disease, peripheral vascular disease, and cognitive decline. It is also the leading cause of premature death [3].

With increasing prevalence of HT there has been a growing interest in understanding the health-related quality of life (HRQOL) of patients with HT. Although HT is often perceived as asymptomatic, it is associated with impaired HRQOL because of:

• Complications or comorbidities
• Diagnosis itself
• Adverse drug reactions from anti-hypertensive medications. [4]

Quality of life (QOL) is widely perceived to be an important end point in therapeutic assessment. In this study, we will ascertain whether two agents in the same general pharmacological class (i.e. the two ARBs) would exert a similar influence on QOL. In the present study, we intend to use a generic instrument SF-12 Health Survey. It is a self-evaluation instrument consisting of 12 items. This survey asks for the patients views about his health. This information helps to keep track of how the patient feels and how he is doing his usual activities. [5]

MATERIAL AND METHODS

The present study was conducted by the Department of Pharmacology, Government Medical College, Patiala, in association with Out Patient Department of Medicine of Government Medical College and Rajindra Hospital, Patiala.

Study design

In this prospective, open, parallel group, comparative study, patients of hypertension attending the Medicine Outpatient Department, Govt. Medical College & Rajindra Hospital, Patiala were recruited.

Patients were selected based on the following criteria:-

Inclusion criteria

1. New patients with Hypertension i.e not on any antihypertensive therapy.
2. Adult males and females of age 21 years or more.

Exclusion criteria

1. Patients already on anti-hypertensive's.
2. Patients with hypersensitivity to AZILSARTAN or TELMISARTAN.
3. Pregnant/ lactating women/ women planning to conceive.
4. Evidence of severe renal disorder.
5. Patients with hepatic insufficiencies.
6. Patients unwilling or unable to comply with the study proceedings.
7. Patients with severe bradycardia, cardiogenic shock, heart block, sick sinus syndrome, decompensated HF, bronchial asthma, hypothyroidism, CVA, CAD.
8. Patients with other co morbidities like hyperthyroidism, anxiety disorders.
9. Patients with refractory HT.

Study sequence

In the prospective, open, parallel group, comparative study, a total of 80 patients with hypertension were evaluated after having fulfilled the inclusion and exclusion criteria and were randomly allocated into 2 groups from time to time i.e. 40 cases in each group. The study was conducted over 8 weeks. A written informed consent was taken from patients after explaining them about study drugs. Group I patients were started on Azilsartan at a dose of 40 mg/d and subsequent titration was carried out up to maximum recommended dose of 80 mg/d depending on therapeutic response.

Group II patients were put on Telmisartan at a dose of 40mg/d and subsequent titration was carried out up to maximum dose of 80mg/d depending on therapeutic response.
BP was measured on day 0, day 4th week and then on 8th week in supine and sitting position with the same sphygmomanometer on right arm after 10 minutes rest. SBP was taken as appearance of Korotkoff sounds (phase I) and diastolic end point was at the disappearance of Korotkoff sounds (phase V).
Following base line investigations were carried out at the commencement of treatment—hemoglobin (Hb), total leucocyte count (TLC), differential leucocyte count (DLC), fasting blood sugar (FBS), Blood Urea, uric acid, Serum Creatinine, serum electrolytes, liver function test (LFT), Lipidogram, echocardiography (ECG) and urine routine examination (R/E). At the end of the treatment the investigations were repeated and compared with the previous ones. Adverse effects as reported by patients were recorded and compared.

Study parameter
Quality of life assessment: To assess QOL, SF-12 questionnaire was used. The questionnaire was administered face to face by the same interviewer to every patient and it took about 10 min to administer these questionnaires to the patient.
SF 12 is a multidimensional questionnaire, composed of 12 items, and it covers eight domains of health: physical functioning (2 items), role limitations caused by physical health problems (2 items), pain (1 item), general health perceptions (1 item), energy and/or fatigue (1 item), social functioning (1 items), role limitations caused by emotional health problems (2 items), and emotional well-being (2 items). Each question in the SF-12 is given a score that is later translated to a scale from 0 to 100, in which zero corresponds to the worst health status and 100 to the best.

Composition of domains of SF 12v2

Domains	**Questions**
Physical functioning	2,3
Role limitations due to physical health	4,5
Role limitations due to emotional health	6,7
Fatigue/ vitality	10
Emotional well being	9,11
Social functioning	12
Pain	8
General Health	1

Scoring of SF 12 items

Question	**Original response**	**Scoring**
1, 8	1	100
	2	75
	3	50
	4	25
	5	0
2, 3	1	0
	2	50
	3	100
4,5,6,7	1	0
	2	100
9,10	1	100
	2	80
	3	60
	4	40

	5	20
	6	0
11	1	0
	2	20
	3	40
	4	60
	5	80
	6	100
12	1	0
	2	25
	3	50
	4	75
	5	100

The responses were recorded on SF 12v2 questionnaire as told by the patients and later the responses were decoded as per the scoring system in the above table and analyzed.

Ethical approval
The present study was reviewed and approved by Institutional ethical committee.

Statistical analysis: The results of observations of individual patients were pooled for each group. Statistical analysis was performed using SPSS software version 22. All the analyses were performed on an intention to treat basis. For analysis of quantitative data, paired/unpaired t test was used in case of 2 groups. For categorical variables, chi square test or fisher's exact test was used for analysis. The results were finally presented in tables and graphs.

RESULTS
The table 1 shows that in Group I, mean scores (SD) for various domains of SF 12 at baseline were 30.00 (14.10) for general health, 37.50 (20.41) for physical functioning, 35.00 (32.42) for role limitation due to physical health, 36.25 (42.35) for role limitation due to emotional health, 41.00(14.29) for fatigue, 45.00 (11.08) for emotional well-being, 60.00 (15.81) for social functioning and 64.38 (14.86) for pain.
The above table shows that in Group I, mean scores (SD) for various domains of SF 12 at 8 weeks were 51.25 (7.91) for general health, 70.00 (15.15) for physical functioning, 98.75 (7.91) for role limitation due to physical health, 98.75 (7.91) for role limitation due to emotional health, 94.38 (10.57) for pain, 76.50 (12.92) for emotional well-being, 48.50 (15.01) for fatigue and 85.00 (14.76) for social functioning
On comparing the mean scores of various domains of SF 12 questionnaire in Group I between baseline and 8 weeks, there was a statistically significant improvement in all the domains at 8 weeks.

TABLE-1: SF 12 SCORES OF GROUP I (AZILSARTAN) AT BASELINE AND 8 WEEKS

Domains	Time Interval	N	Mean	SD	Std. Error Mean	t-test	p value
General Health	Baseline	40	30.00	14.10	2.23	8.640	0.001 (HS)
	8th Week	40	51.25	7.91	1.25		
Physical Functioning	Baseline	40	37.50	20.41	3.23	9.635	0.001 (HS)
	8th Week	40	70.00	15.19	2.4		
Role Limitations Due to Physical Health	Baseline	40	35.00	32.42	5.13	12.599	0.001 (HS)
	8th Week	40	98.75	7.91	1.25		
Role Limitations Due to Emotional Health	Baseline	40	36.25	42.35	6.69	9.415	0.001 (HS)
	8th Week	40	98.75	7.91	1.25		
Pain	Baseline	40	64.38	14.86	2.35	10.014	0.001

	8th Week	40	94.38	10.57	1.67		(HS)
Emotional Well-Being	Baseline	40	57.25	8.47	1.34	8.258	0.001
	8th Week	40	76.50	12.92	2.04		(HS)
Fatigue/Vitality	Baseline	40	41.00	14.29	2.26	2.152	0.038
	8th Week	40	48.50	19.16	3.03		(S)
Social Functioning	Baseline	40	60.00	15.81	2.5	8.421	0.001
	8th Week	40	85.00	14.76	2.33		(HS)

The table 2 shows that in Group II, mean scores (SD) for various domains of SF 12 at baseline were 32.50 (16.21) for general health, 36.25 (23.99) for physical functioning, 33.75 (41.81) for role limitation due to physical health, 33.13 (41.37) for role limitation due to emotional health, 66.25 (20.06) for pain, 59.75 (16.72) for emotional well-being, 39.00 (20.73) for fatigue and 59.38 (14.64) for social functioning.

The above table shows that in group II, mean scores (SD) for various domains of SF 12 at 8 weeks were 43.75 (15.76) for general health, 60.00 (17.72) for physical functioning, 91.88 (16.40) for role limitation due to physical health, 90.94 (16.50) for role limitation due to emotional health, 87.50 (16.98) for pain, 68.50 (15.78) for emotional well-being, 59.00 (20.23) for fatigue and 69.38 (14.42) for social functioning.

On comparing the mean scores of various domains of SF 12 questionnaire in Group II between baseline and 8 weeks, there was a statistically significant improvement in all the domains at 8 weeks.

TABLE-2: SF 12 SCORES OF GROUP II (TELMISARTAN) AT BASELINE AND 8 WEEKS

Domains	Time Interval	N	Mean	SD	Std. Error Mean	t-test	p value
General Health	Baseline	40	32.50	16.21	2.56	3.636	0.001
	8th Week	40	43.75	15.76	2.49		(HS)
Physical Functioning	Baseline	40	36.25	23.99	3.79	7.104	0.001
	8th Week	40	60.00	17.72	2.80		(HS)
Role Limitations Due to Physical Health	Baseline	40	33.75	41.81	6.61	7.910	0.001
	8th Week	40	91.88	16.40	2.59		(HS)
Role Limitations Due to Emotional Health	Baseline	40	33.13	41.37	6.54	8.224	0.001
	8th Week	40	90.94	16.50	2.61		(HS)
Pain	Baseline	40	66.25	20.06	3.17	6.449	0.001
	8th Week	40	87.50	16.98	2.69		(HS)
Emotional Well-Being	Baseline	40	59.75	16.72	2.64	3.320	0.002
	8th Week	40	68.50	15.78	2.49		(S)
Fatigue/Vitality	Baseline	40	39.00	20.73	3.28	5.186	0.001
	8th Week	40	59.00	20.23	3.20		(HS)
Social Functioning	Baseline	40	59.38	14.64	2.31	5.099	0.001
	8th Week	40	69.38	14.42	2.28		(HS)

The table 3 shows comparison of in mean scores of various domains of SF 12 at baseline between Group I (Azilsartan) and Group II (Telmisartan).

On comparison there was no statistically significant difference between the two groups at baseline.

TABLE 3: COMPARISON OF MEAN SCORES OF SF 12 OF GROUP I (Azilsartan) VERSUS GROUP II (Telmisartan). AT BASELINE

Domains	Groups	N	Mean	SD	Std. Error Mean	t-test	p value
General Health	Group 1	40	30.00	14.10	2.23	0.736	0.464
	Group 2	40	32.50	16.21	2.56		(NS)
Physical Functioning	Group 1	40	37.50	20.41	3.23	0.251	0.802
	Group 2	40	36.25	23.99	3.79		(NS)
Role Limitations Due to Physical Health	Group 1	40	35.00	32.42	5.13	0.149	0.882
	Group 2	40	33.75	41.81	6.61		(NS)

Role Limitations Due to Emotional Health	Group 1	40	36.25	42.35	6.70	0.334	0.739 (NS)
	Group 2	40	33.13	41.37	6.54		
Pain	Group 1	40	64.38	14.86	2.35	0.475	0.636 (NS)
	Group 2	40	66.25	20.06	3.17		
Emotional Well-Being	Group 1	40	57.25	8.47	1.34	0.844	0.401 (NS)
	Group 2	40	59.75	16.72	2.64		
Fatigue/Vitality	Group 1	40	41.00	14.29	2.26	0.502	0.617 (NS)
	Group 2	40	39.00	20.73	3.28		
Social Functioning	Group 1	40	60.00	15.81	2.50	0.183	0.855 (NS)
	Group 2	40	59.38	14.64	2.31		

The table 4 shows comparison of in mean scores of various domains of SF 12 at 8 weeks between group I (AZILSARTAN) and group II (Telmisartan).
On comparison there was a statistically significant difference between the two groups at 8 weeks, where group I (AZILSARTAN) shows more improvement in all the domains of SF 12 questionnaire as compared to group II (Telmisartan), except for Fatigue/ Vitality domain, where there was more improvement in group II (Telmisartan).

TABLE-4: COMPARISON OF MEAN SCORES OF SF12 OF GROUP I VERSUS GROUP II AT 8 WEEKS

Domains	Groups	N	Mean	SD	Std. Error Mean	t-test	p value
General Health	Group 1	40	51.25	7.91	1.25	2.690	0.009 (S)
	Group 2	40	43.75	15.76	2.49		
Physical Functioning	Group 1	40	70.00	15.19	2.40	2.709	0.008 (S)
	Group 2	40	60.00	17.72	2.80		
Role Limitations Due to Physical Health	Group 1	40	98.75	7.91	1.25	2.389	0.019 (S)
	Group 2	40	91.88	16.40	2.59		
Role Limitations Due to Emotional Health	Group 1	40	98.75	7.91	1.25	2.700	0.008 (S)
	Group 2	40	90.94	16.50	2.61		
Pain	Group 1	40	94.38	10.57	1.67	2.173	0.033(S)
	Group 2	40	87.50	16.98	2.69		
Emotional Well-Being	Group 1	40	76.50	12.92	2.04	2.481	0.015 (S)
	Group 2	40	68.50	15.78	2.49		
Fatigue/Vitality	Group 1	40	48.50	19.16	3.03	2.384	0.020 (S)
	Group 2	40	59.00	20.23	3.20		
Social Functioning	Group 1	40	85.00	14.76	2.33	4.789	0.001 (HS)
	Group 2	40	69.38	14.42	2.28		

DISCUSSION

Quality of life: In the present study QOL was assessed using SF 12 questionnaire. Previous studies have shown that the questionnaire is valid, reproducible and responsive to changes in QOL.
QOL is a multifactorial variable and its measurement requires valid, repeatable and sensitive tools. It has been reported in a number of studies that hypertensive patients have a poor QOL as compared to normotensive populations and effective antihypertensive treatment has been linked to positive impact on many domains of QOL [6, 7].
It has also been observed that adverse drug reactions of antihypertensive drugs may interfere with certain domains of QOL and may be one of the reasons for poor compliance to therapy [8, 9].
Beyond safety and tolerability, experiences with QOL also contribute to patient adherence [10].
SF 12v2 scores: In the present study, there was a significant improvement in mean scores of various domains of SF 12 from baseline to 8 weeks in both group I and group II. On comparison of group I and group II, there was no significant difference in SF 12 scores for various domains at baseline ($p>0.05$) which shows that the two groups were comparable at baseline. However, at 8 weeks, there was a statistically significant difference ($p<0.05$) between group I and group II in all the domains, where group I (AZILSARTAN) shows more improvement as compared to group II (Telmisartan) except in fatigue/vitality group where there was more improvement in group II (Telmisartan).

Yamamoto (2003) did an open labeled study to evaluate the effects of switching treatment from CCBs to ARB therapy on the QOL of hypertensive patients. One hundred patients with mild to moderate HT, being treated with CCBs, were randomly selected to receive candesartan cilexetil (8-12 mg once a day). The patients were followed for 3 months, while BP, side-effects and QOL were monitored. BP was equally well controlled before and after the change of antihypertensive therapy. The candesartan cilexetil-treated patients exhibited improvement of several aspects of QOL, including general symptoms, physical symptoms and well-being, work and satisfaction and sleep scale. Emotional state and cognitive function also improved. Changing treatment from CCBs to ARB therapy achieved equal BP control with a lower drug dose. Moreover, the change to cadesartan cilexetil had a positive impact on the QOL [11, 12].

Varis J (2013) did a study to see the effect of candesartan alone or combined with hydrochlorothiazide and felodipine on the QOL of Finnish hypertensive patients. There were total 98 hypertensive patients, out of which 42 were men and 56 were women. The only statistically significant change in QOL was a reduction in QOL among the patients on candesartan monotherapy throughout the study. Their physical functioning, total physical and mental health and total SF-36 score decreased significantly. Non-significant increases in QOL were recorded among patients who had a reduction in their systolic blood pressure, who were older and who had a high systolic blood pressure in the beginning of the study. This study suggests that an adequate antihypertensive effect is an important predictor of QOL for patients being treated for high blood pressure. Candesartan alone without an adequate blood pressure decrease does not improve QOL [13].

Maladkar et al (2012) did a study where they found that triple drug combinations including telmisartan, amlodipine and hydrochlorothiazide had improved quality of life of patients from baseline [14].Fujiwara N (2017) did a study to assess the effects of switching from a conventional angiotensin II receptor blocker (ARB) to Azilsartan on blood pressure (BP) and health-related quality of life (HR-QOL) in patients with uncontrolled hypertension. Switching ARB therapy to Azilsartan improved several HR-QOL scores independently from the degree of BP lowering in patients whose HRQOL at baseline were relatively low [15].

Weber MA (2003) found that least improvement in quality of life was observed in those patients who were switched to telmisartan from other angiotensin receptor blockers, confirming the validity of the differences between telmisartan and the other antihypertensive drug classes [16].

Tanaka and Node (2018) did a study and found that besides sufficient BP-lowering, intensive anti-hypertensive treatment with Azilsartan have a favourable impact on the short term health related quality of life in the specific patients with uncontrolled hypertension [17].

CONCLUSION

Both Azilsartan and Telmisartan belong to the same antihypertensive drug class i.e. ARBs and effectively reduce SBP and DBP but Azilsartan is a better choice as compared to Telmisartan in my study because it caused more statistically significant decrease in BP and there was greater improvement in all the domains of QOL, except for fatigue/vitality domain where there was more improvement in group II (Telmisartan). So, prevents future cardiovascular complications and patients have better QOL. However, the antihypertensive effects of Azilsartan in hypertensive patients with serious co-morbidities remain to be determined, as we have excluded patients having any co-morbidities. Another limitation of this study is its limited sample size and short duration, as well as the follow ups could have more to look for the long term adverse effects of Azilsartan as not much studies have been done on it.

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