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A Study of Effect of Telmisartan and Telmisartan in combination with Hydrochlorthiazide on Serum Uric acid and Serum Potassium levels in patients of Essential Hypertension

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Abstract: ***Background-*** *The objectives of the present study were to determine and compare the changes in serum uric acid and potassium level among patients treated with telmisartan and telmisartan with hydrochlorothiazide and to measure and compare the change in blood pressure among the two groups.*
Methodology- *Prospective cohort of patients attending outpatient and inpatient departments in General Medicine Department of People's Hospital for a period of 18 months from November 2016 to April 2018 in the age range of 20-70 years with essential hypertension were recruited. A total of 184 patients were examined and followed up using a questionnaire. The data collected was entered and analysed in SPSS version 22.0.*
Results- *Among 184 patients, 92 were on Group 1 (Telmisartan 40 mg (T)), 75 were on Group 2 - Telmisartan/Hydrochlorthiazide40/12.5&17 were on Group 3 - Telmisartan/Hydrochlorthiazide - 80/12.5.In group 2, at base line the mean S. Uric acid was 4.16 ± 0.97 mg/dl which on follow up rose to 4.40 ± 1.09 mg/dl. The mean elevation in S. Uric acid was 0.23 mg/dl, which is statistically significant (p>0.05) and in group 3, the mean S. Uric acid at base line 4.35 ± 0.94 mg/dl. On follow up it was 4.64 ± 1.16 mg/dl. The mean elevation in S. Uric acid was 0.29 mg/dl which is statistically significant (p<0.05).*
Conclusion- *In Telmisartan monotherapy there was no significant change in S. Uric acid and S. potassium. Telmisartan 40 mg in combination with hydrochlorothiazide12.5mg did not show a significant change in S. potassium but there was significant increase in S. Uric acid. Telmisartan 80 mg in combination with hydrochlorothiazide 12.5mg showed a significant increase in S. Uric acid.*
Keywords: *Essential hypertension, Telmisartan, Hydrochlorthiazide, uric acid, serum electrolyte.*

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I. Background

Hypertension is a public health epidemic and is one of the largest risk factor for disease burden all over the globe. In India, Hypertension has emerged as a leading risk factor for mortality.[1] It also ranks number one as a risk factor for non-communicable diseases related disability adjusted life years (DALYS).

As per the reports indicate there were nearly 1 billion adults had hypertension in 2000, and this is predicted to increase to 1.56 billion by 2025 and the cause of 50% of stroke, heart disease and heart failure.[2]

The prevalence of hypertension is rising in India.[3- 5] Kearney *et al* predicted the burden of hypertension in India is expected to almost double from 118 million in 2000 to 213.5 million by 2025.[6] Hypertension is responsible for 57% of deaths due to stroke and 24% of deaths due to coronary heart disease in India.[7]

As the prevalence of hypertension is rising in developing countries like India, control of high blood pressure by increased awareness and treatment, are critical for the reduction of cardiovascular disease risk and prevention of the associated burden of illness.[8]

Numerous prospective, double-blind, randomized, placebo-controlled studies have shown that antihypertensive drug therapy reduces the development of new coronary events, stroke, and CHF used. [9]

URIC ACID

Uric acid is the end-product of purine metabolism. It is generated primarily in the liver by the action of xanthine oxidase, a molybdenum metalloenzyme.[10,11] Most circulating uric acid is freely filtered in the kidney, About 90% of the filtered UA normally reabsorbed along the nephron.Renal excretion of uric acid represents approximately 60–70% of total uric acid excretion from the body. A smaller proportion of uric acid is secreted in the intestine.[12]

Uric acid and hypertension

A number of epidemiological studies have shown that increased uric acid concentrations are associated with increased risk for developing hypertension and identified hyperuricemia as an independent risk factor for hypertension.[13, 14]

Various studies have shown how uric acid metabolism influences blood pressure through various mechanisms. Uric acid inhibit's endothelial function by suppressing endothelial nitric oxide synthase (NOS),[15] directly influence proliferation and migration of vascular smooth muscle cells,[16] activate the renin–angiotensin system in the kidney.[17]

Uric acid and cardiovascular disease[18]

According to the Rotterdam and NHANES I ,the association between high levels of uric acid and myocardial and cerebral infarctions, and cardiovascular death is persisted. In contrast, the Framingham Heart Study and NIPPON DATA 80 indicated that hyperuricemia is not an independent risk factor for cardiovascular disease or death, but is only a marker of pathological conditions.

Hyperuricemia in a healthy individual without the risk of cardiovascular disease is considered as an independent risk factor for hypertension. Hyperuricemia in patients with cardiovascular risks such as hypertension is considered as a risk factor for cardiovascular disease.

Potassium

Potassium (K +) is the major intracellular cation, with 98% of the total is intracullar at a concentration of 140–150 mmol/l, and only 2% in the extracellular fluid, ranges between 3.5 and 5 mmol/l. A fine regulation of the intracellular-extracellular gradient is crucial for life, acute changes of K + plasma levels may have fatal consequences.

The main determinant of K + homeostasis is kidney. Potassium is freely filtered by the glomerulus. The 90% of filtered K1 is reabsorbed in the PCT and loop of Henle and 10% of the filtered load reaches the distal nephron. K1 secretion starts in the early DCT and progressively Increases up to the cortical CD under the influence of Aldosterone. [19]

Potassium and hypertension

A population study conducted by Khaw et al. (1982) in St. Lucia, West Indies suggested an increase in potassium by 20–30 mmol/day , resulted in a 2 to 3 mmHg reduction in SBP.[38] The INTERSALT study reveals, the Yanomami Indians of Brazil consumed a low sodium, high potassium diet and had low average BP, lack of BP rise with age.[20]

The antihypertensive effect of increased potassium is associated with endothelium dependent vasodilation. A short term K1 restriction in healthy humans and patients with essential hypertension induces Na^+, Cl^- retention and hypertension. Correction of hyokalemia is important in hypertensive patients treated with diuretics.[21]

TELMISARTAN[22]

Telmisartan is an angiotensin II receptor (type AT1) antagonist

Telmisartan acts by displacing angiotensin II from its binding site at the AT1 receptor subtype, the actions of angiotensin II are mainly mediated by AT1 receptor. Telmisartan binds selectively with AT1 receptor with no affinity for other receptor sub types.

AT1 receptor blockade by telmisartan inhibits the angiotensin II mediated vasoconstriction which causes the reduction in systemic vascular resistance which finally results in the reduction in blood pressure..

PPAR- γ is a nuclear hormone receptor, which acts as a central regulator of insulin and glucose metabolism, improving insulin sensitivity. PPAR- γ receptor agonists (pioglitazone) are approved for the indication of diabetes mellitus. Telmisartan also having a property of PPAR -γ activation.Telmisartan improves both metabolic and hemodynamic abnormalities found in obese hypertensive patients and it also leads improvement in fasting glucose, HbA1c and insulin levels.

Telmisartan have cis-inhibitory effect on URAT1- mediated uric acid transport. The predisposition to hyperkalaemia by Telmisartan is due to decrease in excretion of potassium, which is the cumulative result of aldosterone secretion inhibition and reduction in GFR.

HYDROCHLOROTHIAZIDE[22]

Hydrochlorothiazide is a benzothiadiazine (thiazide) diuretic..It reduces the total plasma volume viaits diuretic effect. In response to reduction in plasma volume there is increase in rennin activity and increase in aldosterone secretion, which subsequently increases the urinary loss of potassium and bicarbonates leading to reduction in serum potassium level. The fluid and electrolyte imbalance caused by Hydrochlorothiazide are as

follows hypokalaemia, hypochloraemic alkalosis and hyponatraemia Hyperuricemia is also a well know thiazide-induced metabolic effects.

With today's scientific advancement and rapid pharmacological research, we have at our disposal a myriad of anti-hypertensive medications which are grouped in various classes like the alpha blockers, beta blockers, ACEi, ARBs and diuretics. They along with their desired pharmacological effect also exert many side effects like electrolyte imbalances and change in various physiological abnormalities. For instance, the alpha blockers can cause nasal stuffiness and impotence; the beta blockers can cause worsening of chronic obstructive lung disease (COPD) and/or derangement in lipid profile; ACEi can cause hyperkalaemia, cough and rashes; ARBs can also cause hyperkalaemia; Diuretics can cause hypokalaemia along with hyperuricemia and deranged lipid profile.

There are myriad beneficial effects of telmisartan and there is ample evidence to support them. They cause reduction in the incidence of myocardial infarction in hypertensive patients as shown by the TRANSCEND trial, similar benefit has been shown in the PRoFESS trial on CV deaths, MI and stroke.[23] Telmisartan significantly reduces the recurrence of AF. Due to its insulin sensitizing properties by being an PPAR-Y agonist telmisartan proves to be very useful in diabetic patients and also patients with metabolic syndrome.[24]

Given the many benefits, Telmisartan has a few notable side effects – they have been shown to cause hyperkalaemia and hyperuricemia, which is a matter of concern because the normal range of serum potassium levels is very narrow (3.5 to 5.5 mEq/L) and any fluctuations might lead to adverse cardiac events.[25]

Hydrochlorthiazide, is a diuretic which along with being an antihypertensive can prove to be beneficial in congestive cardiac failure, Pulmonary oedema or any condition caused or aggravated by fluid retention. But, it being a diuretic and acting on kidneys, it works by altering the Na Cl symport and competes for the same receptor which is involved in the uric acid excretion hence leading to increase in serum uric acid levels.

Hence, Telmisartan, an ARB and Hydrochlorthiazide, a diuretic, is not immune to having side effects, nonetheless, they are a widely used combination therapy for hypertension presently. Thereby, magnifying the occurrence of the side effects associated with them and the need to have a very good understanding of the same.

With this background, our study aims to assess the effects of these drugs on serum uric acid and potassium levels given alone and in combination.

II. Material and Methods

All participants were enrolled after taking written informed consent. BP measurement was done by Mercury Sphygmomanometer in sitting position. During the study days the cases were asked not to change their regular way of life. Care was taken that the person has not smoked or taken tea or done vigorous exercise in previous ½ hour.

For HT patients, anti-hypertensive drugs and dosage were recorded at every visit and compliance of drugs was recorded. Visit of the cases for blood pressure measurement was scheduled in every 15 days from the day of enrolment.

On the day of enrolment first blood pressure was recorded and as per the routine protocol blood sample for KFT, Serum Electrolyte and Serum Uric acid was taken and again after 2 month the process of data collection was repeated and sent to the central laboratory of the People's Hospital.

Type of study: Prospective Cohort Study

Study area: People's Hospital (Private P.G. Institute)

Study population: Outpatient Department (OPD) and Inpatient Department (IPD) in General Medicine departments of People's Hospital.

The study protocol was presented in front of Institutional Ethical Committee **(IEC- 2016/54)** the study was approved **(**PCMS/OD/2018/1814**)** by the Research Approval Committee of People's College of Medical Sciences & Research Centre. .

A total of 198 subjects in the age group of 20 – 70 years were examined during the study. Among 198 hypertensive patient, 99 Patient were given Telmisartan alone and another 99 hypertensive patients were given telmisartan in combination with hydrochlorothiazide.

Inclusion criteria:

- Patients across both the genders in the Age Group 20-70 years with essential hypertension.

Exclusion criteria:

- Patients under the age of 20 years and above 70 years.
- Patients with secondary hypertension.
- Hypertensive patients on antihypertensive affecting serum uric acid and serum potassium levels.

- Hyperuricemic (male >7mg/dl female >5.7mg/dl) and patients on hyperuricemicdrugs (e.g.Diuretics,beta-blockers,pyrazinamide,ethambutol, cyclosporin, levodopa,ritonavir etc)pregnant and nursing women, patients of CLD,CKD (serum creatinine >1.5 mg/dl. eGFR<60%)
- Hyperkaliaemic patient (k> 5.5mg/dl) and patients on drugs causing hyperkalaemia
- Patients not willing to participate.

Schedule of The Study

The study duration was planned based on the sample size and number of patients visiting Outpatient departments of hospitals. According by the study was scheduled for 18 months from November 2016 to April 2018. A detailed 15 days schedule was prepared well in advance by informing and obtaining consent from authorities of respective study areas. Subjects with written informed consent and following the inclusion and exclusion criteria were recruited in to the study.

Statistical Analysis

The data collected was entered in SPSS (**Statistical Package for the Social Sciences**) version 22.0, for the purpose of data analysis. Chi-square test and t-test was applied to compare qualitative data and determine the statistical significance. p (probability) value ≤ 0.05 was considered to be statistically significant.

III. Result

Intergroup comparison between Group1 (Telmisartan 40 mg), Group 2 - Telmisartan/Hydrochlorthiazide 40/12.5 & Group 3 - Telmisartan/Hydrochlorthiazide - 80/12.5 for different variables

Among 184 patient, 92 were on Group1 (Telmisartan 40 mg), 75 were on Group 2 - T/H 40/12.5 & 17 were on Group 3 - T/H - 80/12.5.

At the base line the total mean SBP was 160.52 ± 11.57mm/Hg, mean DBP was 93.34 ± 9.87mm/Hg, S.Uric acid was 4.07 ± 0.91mg/dl, S. Potassium was 4.31± 0.48 mEq/L

On follow up the total mean SBP falls to 136.53 ± 9.97 mm/Hg, mean DBP falls to 81.30 ± 7.60 mm/Hg, S.Uric acid rose to 4.20 ± 1.02 mg/dl, S. Potassium rose 4.34± 0.54 mEq/L, The mean reduction in SBP and DBP was 23.99± 1.6 and 12.04 ± 2.27.

Intragroup comparison (Group 1- Telmisartan 40mg)

Effect on Systolic Blood Pressure and Diastolic Blood Pressure

In present study, at base line the mean SBP and DBP were 150.72± 4.85 and 86.96± 7.01 respectively. On follow up mean reduction in SBP and DBP was 20.10 mmHg and 10.15 mmHg respectively.

Effect on Serum Uric Acid In the present study, at base line the mean S.Uric acid was 3.94 ± 0.85 mg/dl which on follow up was 3.95 ± 0.88 mg/dl.The mean elevation in S.Uric acid was 0.007 mg/dl which is statistically not significant (p>0.05).

Effect on Serum Potassium In present study, the mean S. potassium at base line was 4.22± 0.43 mEq/L which on follow up increased to 4.25± 0.47 mEq/L. The mean elevation in S. potassium was 0.03 mEq/L, which is statistically not significant (p>0.05).

Intragroup comparison Group 2 - Telmisartan/Hydrochlorthiazide - 40/12.5

In the present study group 2 was given Telmisartan 40 mg and in combination with HCTZ 12.5 mg.

The base line mean SBP and DBP was 167.81 ± 5.19 and 97.63± 7.0 respectively. On follow up SBP and DBP was 142.72 ± 8.55 and 85.52 ± 6.55 respectively. The mean reduction in SBP, DBP was 25.09 mmHg, 12.11 mmHgwhich was statistically significant.

Effect on Serum Uric Acid

In this study, at base line the mean S.Uric acid was 4.16 ± 0.97 mg/dl.Which on follow up rose to 4.40 ± 1.09 mg/dl.The mean elevation in S.Uric acid was 0.23 mg/dl, which is statistically significant (p>0.05).

Effect on Serum Potassium

In the present study, at base line the mean S. potassium was 4.4 ± 0.53 mEq/L and on follow up the mean S. potassium was 4.42± 0.61 mEq/L and a mean elevation in S. potassium of 0.01 mEq/L was obtained. Which is statistically not significant (p>0.05).

Intragroup comparison Group 3 - Telmisartan/Hydrochlorthiazide 80/12.5

In the present study group 3 had been given Telmisartan 80 mg and in combination with HCTZ 12.5 mg. In this study group the base line mean SBP and DBP were 181.41 ± 2.8 and 108.94± 5.48 respectively. On follow up SBP and DBP were 141.29 ± 6.4 and 87.06 ± 5.25 respectively. The mean reduction in SBP and DBP were 40.11 mmHg, 21.88 mmHg respectively.

Effect on Serum Uric Acid

In present study, the mean S.Uric acid at base line 4.35 ± 0.94 mg/dl. On follow up it rise to 4.64 ± 1.16 mg/dl. The mean elevation in S.Uric acid was 0.29 mg/dl which is statistically significant ($p<0.05$).

Effect on Serum Potassium

In present study, at base line the mean S. potassium was 4.44 ± 0.48 mEq/L. On follow up the mean S. potassium was 4.42± 0.53 mEq/L and the mean reduction in S. potassium was 0.02 mEq/L obtained which is statistically not significant ($p>0.05$).

Table 1 Intergroup comparison between Group1 (Telmisartan 40 mg), Group 2 - Telmisartan/Hydrochlorthiazide 40/12.5 & Group 3 - Telmisartan/Hydrochlorthiazide - 80/12.5 for different variables

Demographic variables		**Telmisartan 40mg (Group1)**	**T/H - 40/12.5 (Group 2)**	**T/H - 80/12.5 (Group 3)**	**Total**
		Frequency (%)	**Frequency (%)**	**Frequency (%)**	
Age (years)	31-40 yrs	15(16.3)	1(1.3)	0(0)	**16(8.7)**
	41-50 yrs	43(46.7)	14(18.7)	7(41.2)	**64(34.8)**
	51-60 yrs	25(27.2)	32(42.7)	8(47.1)	**65(35.3)**
	61-70 yrs	9(9.8)	28(37.3)	2(11.8)	**39(21.2)**
	Total	**92(100)**	**75(100)**	**17(100)**	**184(100)**
Gender	**Female**	54(79.3)	33(44)	14(97.2)	**101(54.9)**
	Male	38(20.7)	42(56)	3(2.8)	**83(45.1)**
	Total	**92(100)**	**75(100)**	**17(100)**	**184(100)**

Majority of participants in group 1 (46.7%) belonged to 41 to 50 years of age whereas majority of participants in group 2 (42.7%) and group 3 (47.1%) were in age range of 51 to 60 years. Maximum participants in group 1 (79.3%) and group 3 (97.2%) were females.

Table 2 – Comparison of overall mean of all the groups for different variables at baseline & at follow up

Variables	N	Mean ± S.D at base line	Mean ± S.D at follow up	P value
SBP (mm/hg)	184	160.52 ± 11.57	136.53 ± 9.97	0.001*
DBP (mm/hg)	184	93.34 ± 9.87	81.30 ± 7.60	0.001*
S.Uric acid (mg/dl)	184	4.07 ± 0.91	4.20 ± 1.02	0.12
S. Potassium (mEq/L)	184	4.31 ± 0.48	4.34 ± 0.54	0.02*

In present study, test of significance (paired t test) found statistically significant difference between baseline and follow up value for systolic blood pressure ($p=0.001$), diastolic blood pressure ($p=0.001$) and Serum potassium ($p=0.02$).

Table 3 - Intragroup comparison (Group 1- Telmisartan 40)

Group 1		Mean	N	Std. Deviation	Mean differences	T value	P value
SBP (mmHg)	Baseline	150.7	92	4.85	20.10	28.4	0.001*
	Follow up	130.6	92	7.87			
DBP (mmHg)	Baseline	86.9	92	7.01	10.15	25.24	0.001*
	Follow up	76.8	92	5.93			
S.Uric acid (mg/dl)	Baseline	3.94	92	0.85	-0.007	-0.18	0.85
	Follow up	3.95	92	0.88			
S. Potassium (mEq/L)	Baseline	4.22	92	0.43	-0.03	-1.05	0.29
	Follow up	4.25	92	0.47			

Table 3 reveals a statistically significant reduction in both systolic and diastolic blood pressure. ($p<0.05$). Though Serum uric acid and Serum potassium also rose from the baseline but the increase was not statistically significant.

Table 4 – Intragroup comparison Group 2 - Telmisartan/Hydrochlorthiazide - 40/12.5

Mean age of the patients was 57.57 ± 7.66 years.

Group 2		Mean	N	Std. Deviation	Mean difference	T value	P value
SBP (mmHg)	Baseline	167.81	75	5.19	25.09	26.95	0.001*
	Follow up	142.72	75	8.55			
DBP (mmHg)	Baseline	97.63	75	7.00	12.1	17.14	0.001*
	Follow up	85.52	75	6.55			
S.Uric acid (mg/dl)	Baseline	4.16	75	0.97	-0.23	-3.57	0.001*
	Follow up	4.40	75	1.09			
S. Potassium (mEq/L)	Baseline	4.40	75	0.53	-0.01	-0.28	0.77
	Follow up	4.42	75	0.61			

Table 4 revealed a statistically significant reduction in both systolic and diastolic blood pressure ($p<0.05$). There was statistically significant increment in Serum uric acid also. Though on follow up Serum potassium rise.

Table 5 – Intragroup comparison Group 3 - Telmisartan/Hydrochlorthiazide 80/12.5

Group 3		Mean	N	Std. Deviation	Mean differences	T value	P value
SBP (mmHg)	Baseline	181.41	17	2.80	40.11	24.59	0.001*
	Follow up	141.29	17	6.40			
DBP (mmHg)	Baseline	108.94	17	5.48	21.88	14.49	0.001*
	Follow up	87.06	17	5.25			
S.Uric acid (mg/dl)	Baseline	4.35	17	0.94	-0.29	-2.06	0.05*
	Follow up	4.64	17	1.16			
S. Potassium (mEq/L)	Baseline	4.44	17	0.48	0.02	0.17	0.86
	Follow up	4.42	17	0.53			

Above table reveal a statistically significant reduction in blood pressure both systolic and diastolic ($p<0.05$). There was increase in Serum uric acid from base line though not statistically significant. Also statistically insignificant decline in Serum potassium was found.

IV. Discussion

Present study was conducted in People's College of Medical Sciences and Research Centre in the Department of General medicine among 198 Essential Hypertensive patients. In the study the patients were divided into three groups, Patients in group 1 were given Telmisartan Monotherapy (Telmisartan 40mg) once daily, Patients in group 2 were given Telmisartan 40 mg in combination with Hydrochlorothiazide 12.5mg once daily and that in group 3 were given Telmisartan 80 mg in combination with Hydrochlorothiazide 12.5mg once daily.

During the study, 7 patients were lost to follow up in group 1, 5 patients were lost to follow up in group 2 and 2 patients were lost to follow up in group 3.

There was no adverse drug reaction reported during the study. 184 patients completed the study protocol.

Intergroup comparison between Group1 (Telmisartan 40 mg), Group 2 - Telmisartan/Hydrochlorthiazide 40/12.5 & Group 3 - Telmisartan/Hydrochlorthiazide - 80/12.5 for different variables

On follow up the mean reduction in SBP and DBP was 23.99± 1.6 and 12.04 ± 2.27, S.Uric acid rise to 4.20 ± 1.02 mg/dl, S. Potassium rise 4.34± 0.54 mEq/L,

Intragroup comparison (Group 1- Telmisartan 40mg)

Effect on Systolic Blood Pressure and Diastolic Blood Pressure

The mean reduction on follow up in SBP and DBP was 20.10 mmHg and 10.15 mmHg. Similar reductions in blood pressure were also found in studies done by Michel MC et al[26], Yvueslacourciere et al[27], Pavel Prikryl et al[28].

Effect on Serum Uric Acid

The mean elevation on follow up in S.Uric acid was 0.007 mg/dl which is statistically not significant ($p>0.05$). This was similar to study done by Yayoi Nishida et al[29] where mean elevation in S.Uric acid was 0.13mg/dl. In study done Masanobu Sato et al[25], Yan LI et al[30], BurcuBarutcuoglu et al[31] no significant elevation of S. Uric acid was found. However, in study done by MinakshiSumbria et al[32] state that there was reduction of S.Uric acid by 0.7 mg/dl.

In our study, we found that monotherapy with telmisartan increased SUA level though it was not statistically significant.

Effect on Serum Potassium

The mean elevation in S. potassium on follow up was 0.03 mEq/L, which is statistically not significant ($p>0.05$). This was similar to study done by Salim Yusuf et al[33] in which hyperkalaemia was found in 3.8% patients. In study done by R.Anantharaman et al[34]Hyperkalamia was observed in 2 out of the 30 patients. However, in studies done by Schierok H et al[35], Michel MC et al[26], Aranda P et al[36] no change in S. potassium level was found.

Intragroup comparison Group 2 - Telmisartan/Hydrochlorthiazide - 40/12.5

The mean reduction in SBP, DBP on follow up was 25.09 mmHg, 12.11 mmHg which was statistically significant. Similar results were found in studies done by Y Lacourciere[27], Schmieder Re[37], Narsimha Reddy RA et al[38],Helmut Schumacher et al[39], Kondo K et al[40] they all found significant reduction in SBP and DBP.

Effect on Serum Uric Acid

The mean elevation in S.Uric acid on follow up was 0.23 mg/dl, which is statistically significant ($p>0.05$) similar results were found in studies done by Minami J et al[41], Ando K et al[42], Toshihiro Hamada et al[43], Kondo K et al[40]. However, in contrast to this study by Hamada T et al[44] no change in S.Uric acid level could be found.

Effect on Serum Potassium

The mean elevation in S. potassium on follow up was 0.01 mEq/L was obtained. Which is statistically not significant ($p>0.05$). This was contrasting to results of study done by Y Lacourciere[27] who found reduction of just 0.064 mEq/l.

Intragroup comparison Group 3 - Telmisartan/Hydrochlorthiazide 80/12.5

The mean reduction in SBP and DBP on follow up was 40.11 mmHg, 21.88 mmHg respectively. Similar results were found in studies done by Schmieder RE[37], Joel M. Neutel et al[45], Helmut Schumacher et al[39].

Effect on Serum Uric Acid

The mean elevation in S. Uric acid on follow up was 0.29 mg/dl which is statistically significant ($p<0.05$). Similar results were also obtained in studies done by William B. White et al[46], Ando K et al[42] and Hirose Hiroshi et al[47].

Effect on Serum Potassium

The mean reduction in S. potassium on follow up was 0.02 mEq/L obtained which is statistically not significant ($p>0.05$). This result is similar to results obtained in study done by William B. White et al[46]. In a study by Y Lacourciere[27] also in study by Arya M Sharma et al[48], Rubanova A et al[49] no significant change in S. potassium was found.

V. Conclusion

1. In telmisartan monotherapy (group 1) though there was no significant change in S.Uric acid and s. potassium.
2. Telmisartan 40 mg in combination with hydrochlorothiazide12.5mg (group 2) did not show a significant change in s. potassium but there was significant increase in S.Uric acid.
3. Telmisartan 80 mg in combination with hydrochlorothiazide12.5mg (group 3) showed a significant increase in S.Uric acid but there was no significant change in s. potassium.
4. The present study shows that telmisartan Monotherapy and Telmisartan in combination with hydrochlorothiazide are well tolerated in patients with no adverse drug reactions.

VI. Recommendation

Telmisartan alone and in combination with hydrochlorothiazide are effective in controlling blood pressure. There is significant increase in S. Uric acid when telmisartan is used in combination with hydrochlorothiazide. Regular monitoring of S. Uric acid is recommended in patients who are prone to hyperuricemia

VII. LIMITATIONS

1. Sample size
2. Duration of study

By increasing the sample size and the duration of study we can generalized the outcome of the study and the power of the study can be improve.

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