



EFFECT OF ANTIHYPERTENSIVE DRUG THERAPY ON SERUM URIC ACID LEVELS IN HYPERTENSIVE PATIENTS WITH INCIDENT HYPERURICEMIA: A CROSS-SECTIONAL STUDY

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ABSTRACT

Introduction – Serum uric acid (SUA) has been considered as independent factor for cardiovascular disorders through various mechanisms. SUA also showed impact on parameters like body mass index, blood pressure and biochemical parameters like serum lipids.

Material & methods – This was cross sectional observational study carried out on 150 subjects by dividing them in group A, B and C. Group A were normotensives, group B were hypertensives not on antihypertensive (anti HTN) medication and group C were hypertensives on anti HTN medication for more than 6 months. We looked for effect of anti HTN medications on SUA levels and other parameters like blood pressure, body mass index and lipid profile. Statistical tests were applied by using Openepi software.

Result – Age was comparable among all groups. BMI showed significant reduction in group C. Decrease in SUA level in group C was highly significant. Serum triglyceride and HDL didn't show reduction but serum cholesterol declined at significant level.

Conclusion- Anti HTN medication reduces SUA level which is raised in hypertension. Also, reducing blood pressure normalises body mass index and lipid profile.

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INTRODUCTION

High blood pressure represents a major public health problem. Worldwide, approximately one fourth of the adult population has hypertension. Epidemiological and experimental studies suggest a linkage between hyperuricemia and hypertension. Hyperuricemia affects 25-40% of patients with untreated hypertension. A much lower prevalence has been reported in normotensives or in the general population (Gois PHF, 2013). In addition to serving as an independent risk factor for incident hypertension in the general population, hyperuricemia may have important differential effects in age, gender, and racial subgroups (Grayson PC *et al.*, 2011). The prevalence of hyperuricemia has been increasing in recent years, not only in advanced countries but also in developing countries (Chen Li Ying *et al.*, 2007). Present study is therefore designed to understand and confirm positive linkage between hyperuricemia and hypertension and further to explore effect of anti-hypertensive therapy on incident hyperuricemia.

MATERIAL AND METHODS

This was cross-sectional observational study carried out between August-October 2016 at Smt.

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Kashibai Navale Medical College & General Hospital, Pune, Maharashtra (India). In this study, hypertensive patients of either sex between age of 25-60 years attending Medicine outpatient department and inpatient department were included and patients having diabetes with or without complications, heart diseases, psychiatric disease, lipid abnormalities, pregnancy or lactating mothers and not willing to participate or giving consent were excluded. After taking written informed consent depending upon the duration of anti-hypertensive (Anti-HTN) treatment they categorised in to three groups as,

Group A: Normotensive subjects (Blood pressure - Systolic: < 120 mmHg, Diastolic: < 80 mmHg)

Group B: Freshly diagnosed HTN patients with no anti-HTN

Group C: Patients receiving anti-HTN therapy for >6months

BP was measured in the right upper extremity by a mercury sphygmomanometer with the patient in the supine position after at least 10 min of rest. The average of two measurements was used as baseline BP for analysis Person was considered normotensive if SBP (Systolic Blood Pressure) was <120 mmHg and DBP (Diastolic Blood Pressure) was < 80 mmHg and was considered hypertensive if SBP >130 mmHg and DBP > 90 mmHg. These parameters were measured irrespective of any antihypertensive group received by subjects.

Total number of patients studied were 150 [i.e. N=50 in each group]. Apart from the routine tests advised to a patient such as blood sugar and lipid profile, an additional test of uric acid

level in blood performed in all hypertensive patients. Serum uric acid level (Normal - 2.4-6 mg/dl for female and 3.4-7mg/dl for male), serum HDL (Normal - >60 mg/dl), serum cholesterol (Normal - <200 mg/dl), serum triglycerides (Normal - <150 mg/dl) and Body Mass Index (BMI) (Normal – 18.5-24.9) were measured in all subjects of three groups.

Extent of blood pressure control was assessed and effect of anti-HTNs on blood uric acid levels among group was compared. Demography and socio-economic status was also studied. The data collection was started after approval from institutional Ethics Committee (Ref. SKNMC/ Ethics/ APP/2016/181). Data was analysed using one tailed ANOVA test and unpaired t test wherever applicable in OpenEpi statistical software.

RESULTS & OBSERVATIONS

There were total 150 subjects in study (50 in each group). Demographic characteristics are mentioned in table 1. There were no statistical difference among three groups with respect to age (p = 0.4882). Sex distribution among groups was comparable. Body mass index showed statistical significant difference among groups (p = 0.002)

Table 1 Demographic characteristics of study groups

Parameter	Group A	Group B	Group C	P value	Turkey Post Hoc Test (P value)		
					Gr A Vs Gr B	Gr B vs Gr C	Gr A vs Gr C
Age (mean±SD)	52.8±3	53.6±4	53.3±3	0.4	0.4	0.8	0.7
Sex (M/F)	27 (23)	24 (26)	25 (25)				
BMI (mean±SD)	23.8±3	26.5±4.8	23.8±5.1	0.002	0.007	0.007	0.9

BMI : Body Mass Index M/F: Male/Female

Table 2 shows comparison among various parameters. When we compared systolic and diastolic blood pressure among groups, the difference was significant (p=0.001 for both parameters in ANOVA as well as post hoc test). Statistical test showed significant difference (p=0.001) for serum HDL values but in post hoc analysis showed no significant difference between group B and group C. There was significance difference was seen between group A and B (p=0.001) with respect to serum triglyceride and like serum HDL, difference was not seen between group B and C (p=0.65). There was statistical difference in Serum cholesterol among all groups (p=0.001). Blood uric acid levels were significantly differed among groups.

Table 2 Effect on various laboratory parameters

Parameter (Mean±SD)	Group A	Group B	Group C	P value	Turkey Post Hoc Test (P value)		
					Gr A Vs Gr B	Gr B vs Gr C	Gr A vs Gr C
SBP	119±0.06	138.4±0.03	126.2±0.04	0.001	0.001	0.001	0.001
DBP	84±0.04	94±0.03	86±0.04	0.001	0.001	0.001	0.001
S. HDL	51.7±20.2	36.7±17.8	42.9±11.3	0.001	0.001	0.16	0.02
S.TG	121.8±6.5	129.3±4.7	128.3±5.7	0.001	0.001	0.6	0.001
Total CH	173.6±2.4	180.6±4.7	178.6±3.7	0.001	0.001	0.02	0.001
SUA	4.49±0.63	7.89±0.54	5.42±0.68	0.001	0.001	0.001	0.001

SBP: Systolic Blood Pressure

DBP: Diastolic Blood Pressure

S.HDL: Serum HDL

S.TG: Serum Triglycerides

CH: Cholesterol

SUA: Serum Uric Acid

When we assessed gender wise relationship between SBP and SUA, we found that females out number males in having raised SUA with respect to SBP range. As shown in table 3, the commonest range of SBP was 161-170 mm of hg.

Table 3 Gender specific prevalence of hypertension and serum uric acid levels

SBP (mm of Hg)	SUA levels (F)	SUA levels (M)	P value
130-140	4.76±0.4	4.29±0.3	0.0001
141-150	6.42±0.5	5.22±0.6	0.0001
151-160	7.26±0.6	5.86±0.2	0.0001
161-170	7.48±0.7	6.08±0.4	0.0001
171-180	8.76±0.8	7.29±0.3	0.0001

SBP: Systolic Blood Pressure

SUA: Serum Uric Acid

F: Females

M: Males

DISCUSSION

Hyperuricemia is an increasingly common medical problem not only in the advanced countries, but also in the developing countries (Chen Li Ying *et al.*, 2007). A large body of evidence has shown that soluble uric acid levels are closely associated with cardiovascular diseases such as hypertension, renal disease, stroke and coronary heart disease. Though it is well known fact, still this fact was ignored due to lack of causal relationship (Zhu P *et al.*, 2012). Approximately 25-40% of untreated hypertensive patients have concomitant hyperuricemia (kuwabara M *et al.*, 2014). There are evidences showing Thiazide diuretics, beta blockers, alpha 1 blocker, CCBs, angiotensin converting enzyme inhibitors and angiotensin II receptor antagonist increase serum uric (SUA) acid level (kuwabara M *et al.*, 2014; Borghi C *et al.*, 2015; Ueno S *et al.*, 2016).

In our study, there were 3 groups and 50 participants in each group. There was no statistical difference between number of males and females in each group. Females showed to have raised SUA level than males for all blood pressure ranges with significance, particularly from 161 -170 mm of hg of SBP category. Ueno S *et al* found that beta blocker use raised SUA level in women. The mechanism may be decreased eGFR, also, beta blockers may produce alpha receptor mediated renal vasoconstriction thereby affecting filtration rate (Ueno S *et al.*, 2016). Age factor didn't show any difference among groups. Age may be the influencing factor on SUA, as Peter C *et al* concluded that relation between SUA and blood pressure is stronger in younger individuals but diminishes over time (Grayson PC *et al.*, 2011).

Body mass index (BMI) was increased in group B. And there is significant difference between group A and B and B and C. Group A and C shows no difference which means BMI was normalised after taking anti HTN drugs. We have excluded diabetes from our inclusions so we are not hoping metabolic syndrome here. There is strong relation between weight and SUA. In a study by Yue JR, they found that weight loss of 8 kg was associated with 11% decrease in SUA level and Ishizaka *et al* concluded that weight reduction is thought to be effective non-medical strategy to reduce SUA (Yeu Ji Rong *et al.*, 2012; Ishizaka *et al.*, 2010). Leptin is one of the factors considered as culprit for this association (Bedir A *et al.*, 2003) Chen Li found that SUA is markedly associated with waist circumference (Chen Li Ying *et al.*, 2007).

Though SBP and DBP didn't reach to level of normotensive subjects, still their reduction in group C was highly significant as compared to group B. SUA is considered as independent factor for the development of hypertension also, patients with hyperuricaemia needed to take higher doses of anti HTN drugs compared to patients with normal SUA (Zhu P *et al.*, 2012; kuwabara M *et al.*, 2014; Ueno S *et al.*, 2016). Inability of

group C patients not attaining normal blood pressure as group A may be because of requirement of higher doses anti HTN drugs. Uric acid may contribute to hypertension through oxidative stress. It also stimulate expression of endothelin 1 associated with nicotinamide adenine dinucleotide phosphate oxidase to block release of nitric oxide and to promote oxidation of LDL (Zhu P *et al.*, 2012). Uric acid can directly stimulate Renin Angiotensin System (Grayson PC *et al.*, 2011; Chen Li Ying *et al.*, 2007). These findings are matching with our findings as SUA in our study was significantly higher in group B and was significantly reduced in group C after anti HTN drugs. So, SUA and hypertension are deeply related with each other and anti HTN therapy showed impact on SUA level which got reduced after treatment which we can indirectly correlate with reduction in BMI. Choi *et al* reported that risk of development of gout was modified by antihypertensive drugs (Choi HK *et al*, 2012)

SUA has effect on blood lipids levels. In our study, serum HDL levels were increased in group C patients as compared to group B but this difference was not significant. Studies have shown inverse relationship of SUA and HDL (Grayson PC *et al.*, 2011; Peng TC *et al*, 2015; Sarmah D & Sharma B, 2013). SUA has major impact on serum triglyceride and total cholesterol but our study showed not significant and significant result respectively when compared between group B and C. Increase in TG level might be related to accumulation of glycerol-3-phosphate (Chen Li Ying *et al.*, 2007). Overall reducing blood pressure had beneficial impact on lipid profile.

CONCLUSION

Anti HTN drugs have notable impact on various parameters like SUA, BMI and lipid profile. SUA level reduced significantly to normal level. Surprisingly we couldn't see remarkable effect on serum lipid levels. BMI reduced to near normal value. So we are at conclusion that Anti HTN drugs modify SUA level and this indirectly modifies other parameters in positive way.

Limitations

First, this study didn't consider exact anti HTN given to patients, because various anti HTN drugs have effect on SUA level. Diuretics, beta blocker, alpha blockers and ACE inhibitors increase SUA level. Second, sample size could have been increased to come at definite conclusion.

Conflict of Interest: No

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