Effect of Different Antihypertensive Treatment on Serum Uric Acid in Newly Diagnosed Hypertensive Patients

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Abstract:

Background: Hyperuricemia is a risk factor for cardiovascular diseases. Hyperuricemia was found to correlate with hypertension, excluding the influence of other factors such as age and renal function.

Aim: To assess the influence of different antihypertensive drugs on serum uric acid in newly diagnosed hypertension patients.

Patients and Methods: This cohort study that was conducted on 280 patients who are newly diagnosed with hypertension after enrollment of patients classified into three groups (Group A received Beta-blocker, group B received Angiotensin-converting-enzyme inhibitor and group C received calcium channel blocker) followed up in 2 and 6 months for serum uric acid level, the period from July 2022 to January 2023 in El-Fath Health Center- Assiut Government, Egypt.

Results: Group CCBs had highly controlled patients with a normal range of uric acid and normal hypertension measurements, in contrast with the beta blocker group and the ACE group, which had less control than group CCB. There is a significant positive relationship between Hypertension (Baseline) and Uric Acid (Baseline), (r =.033, p <.0001*), Hypertension (After 2 Months) and Uric Acid (After 2 Months), (r =.026, p <.002) and Hypertension (After 6 Months) and Uric Acid (After 6 Months), (r =.011, p <.0001*).

Conclusion: Calcium channel blocker (CCB) was associated with lower serum uric acid level and normal blood pressure measurements than the beta blocker group and the ACE group after 6 months of follow-up.

Keywords: CCB; ACE; beta-blockers; Hypertension; Uric Acid.

Introduction:

The most common condition seen in primary care is hypertension, which can result in myocardial infarction, stroke, renal failure, and death if not treated promptly [1]. According to the guidelines issued by the European Society of Cardiology and the European Society of Hypertension, hypertension is defined as a blood pressure of >140/90 mm Hg. The goal is to keep blood pressure below 130/80 mm Hg only in patients who are at high cardiovascular risk. Still, individual tolerability of the proposed goal is always taken into account [2]. It was found that thiazide-type diuretics, angiotensin-converting enzyme (ACE) inhibitors, and some angiotensin-II receptor blockers (ARBs) increased serum uric acid levels and decreased renal excretion of urate [3]. Serum uric acid levels are also raised by beta-blockers [4].

Hyperuricemia is a cardiovascular disease risk factor. Hyperuricemia was found to be connected with hypertension, barring the impact of different factors, for example, age and renal function [5, 6]. In addition, numerous studies have demonstrated that hyperuricemia was independently associated with cardiovascular events in antihypertensive drug-treated patients [7]. In order to lessen the likelihood of gout and other cardiovascular events in hypertensive patients taking antihypertensive medications, it is essential to monitor serum uric acid levels. Antihypertensive medications' effects on serum uric acid in newly diagnosed hypertensive patients are unknown. Therefore, this study aims to estimate the influence of different antihypertensive treatments on serum uric acid in newly diagnosed hypertension patients.

I.Methods

II.Study Site and Design

El-Fath Health Center, located in El-Fath city in the Assiut governorate of Upper Egypt, was the setting for a cohort study.

III.Study Population

The research was carried out between July 2022 and January 2023. All newly diagnosed hypertensive patients over the age of 30 who met the inclusion criteria for this study were included. Patients under the age of 30 were excluded in order to exclude patients with secondary hypertension, kidney disease, and those taking medications that were known to raise or lower serum uric acid. Patients with kidney disease and those taking renal medications were also excluded.

IV.Sample Size

A study by Ueno et al. found that in hypertensive patients treated with β-blockers in Japan, serum uric acid was elevated in 31.4% of patients, significantly higher than in 16.5% of patients treated with other drugs [8]. The estimated sample size for cohort studies was 256 patients using the open-source calculator OpenEpi Version 3, taking into account a confidence interval of 95 percent and a power of 80 percent. To take into account the dropout cases, we increased the sample size by 10% to 24 patients.

V.Study Methods

There were 280 patients in the total sample. After enrollment, 280 newly diagnosed hypertensive patients were divided into three groups according to the type of treatment received as follows: Group (A) included 94 patients who received Beta Blocker (Bisolock 5mg for stage 1 and 10mg for stage 2). Group (B) - included 93 patients who received angiotensin-converting enzyme inhibitors (Capoten 25mg for stage 1 and 50mg for stage 2). Group (C) included 93 patients who received Calcium Channel Blocker (Regecor 5mg for stage 1 and 10mg for stage 2), and their serum uric acid levels were monitored at two and six months.

The following were performed during the initial visit: A history and examination, the completion of the questionnaire, and a treatment decision.

The second visit—the first follow-up—took place two months after the initial visit. Six months after the initial visit, the patient returned for the second follow-up visit.

All patients' phone numbers were taken during follow-up to remind them to come in for follow-up and treatment. A predesigned survey gathered the information. Demographic data such as age, sex, residence, and level of education were included in the first section. Questions about risk factors for hypertension (such as smoking, inactivity, drinking alcohol, and a poor diet) were included in the second section.

The third section consisted of a medical history and a clinical examination. All of the patients who were included will be given a physical examination, which will include taking vital signs and a general examination. Utilizing a mercury sphygmomanometer to measure blood pressure is the method of measurement. A patient's blood pressure was taken while the patient was in a sitting position, from the right arm after the patient rested for no less than 5 minutes before estimation. Three estimations of blood pressure on a solitary visit were required approximately 3 minutes apart, and the average of the three records will be utilized for the calculation of the outcomes.

According to the CDC [9], the patient was considered to have hypertension if the systolic blood pressure was 140 mmHg and the diastolic blood pressure was 90 mmHg. The sphygmomanometer was adjusted before the start of the review.

The body mass index (BMI) can be calculated by dividing the estimated height in meters (m) by the body weight in kilograms (kg). It is also interpreted as either underweight (BMI 18.5), healthy weight (18.5 - 24.9), overweight (BMI 25.0), or obese (BMI 30.0) [10].

Patients' follow-up:

Each patient receiving a different drug treatment was followed up on twice more. The first follow-up was conducted after two months, and the second follow-up was conducted after six months.

Ethical Consideration:

In accordance with the 2013 revision of Helsinki standards, all participants gave written informed consent. The Institutional Review Board of Ethical and Medical Research at the Faculty of Medicine at Assiut University (IRB No 04-10-20-17101205) reviewed and approved the research protocol. All participants were required to provide informed written consent, and the confidentiality of the information was maintained throughout the entire research.

Statistical Analysis

The statistical package for the social sciences, SPSS (SPSS Inc., Chicago, IL, USA), version 22, was used for all statistical calculations. When necessary, the data were statistically described in terms of numbers and percentages. The ANOVA test was used to determine whether the difference between the means of more than two study groups was statistically significant. Pearson's correlation test was utilized to determine the relationship of numeric information. The level of significance was set at P 0.05.

Results

The total percentage of age represented 22.5% ranging between 30 - 39 years old of the total patients; 33% ranged between 40 - 49 years old of the total patients; 27% ranged between 50 - 59 years old of the total patients, and 17.5% ranged between 60 - 70 years old of the total patients (Table 1). Group (A) represented the highest number of hypertensive patients in Stage 1, in contrast with Groups (B) and (C); While Group (B) represented the highest number of hypertensive patients in Stage 2, in contrast with Group (A) and (C) in Baseline (Table 2). After 2 months of follow-up, serum uric acid among Group (A), Group (B), and Group (C) showed non-significant differences, which represent 78.93% for Hyperuricemia and 21.07% for the normal range. However, after 6 months of follow-up, serum uric acid among Groups (A), (B), and (C) showed a significant decrease. The hyperuricemia represented 15.70% of the total patients, and 84.30% were in the normal range (Table 3). Logistic Regression analysis regarding the decrease in uric acid level after treatment. It was found that CCBs were associated with a decrease in uric acid level to normal by three times significantly (Table 4).

Table (1): Demographic data at the first visit of newly diagnosed hypertensive patients attended at El-Fath Health center (2022-2023)

Demographic Data	Group (A) N = 94	Group (B) N = 93	Group (C) N = 93	Total (N = 280)	P Value
Age					
Mean ± SD	45.40 ± 10.45	50.30 ± 9.50	50.60 ± 9.70		
Median (IQR)	44 (31 - 70)	51 (30 - 68)	51 (30 - 69)		
Age Categories					
30 - 39 Years-old	37 (41.5%)	13 (15%)	13 (15%)	63 (22.5%)	**< 0.03**
40 - 49 Years-old	29 (30.5%)	32 (34%)	31 (33%)	92 (33%)	
50 - 59 Years-old	16 (17%)	30 (32%)	29 (31%)	75 (27%)	

60 - 70 Years-old	12 (11%)	18 (19%)	20 (21%)	50 (17.5%)	
Gender					
Female (N = %)	44 (46.80%)	43 (46.20%)	45 (48.40%)	132 (47%)	**< 0.05**
Male (N = %)	50 (53.20%)	50 (53.80%)	48 (51.60%)	148 (53%)	

Table (1): Demographic data at the first visit of newly diagnosed hypertensive patients attended at El-Fath Health center (2022-2023) ***(Cont.)***

Demographic Data	Group (A) N = 94	Group (B) N = 93	Group (C) N = 93	Total (N = 280)	P Value
BMI					
Mean ± SD	34.13 ± 2.60	35.60 ± 3.10	35.20 ± 2.70		
Median (IQR)	33.5 (30 - 39.5)	36.5 (30 - 39.5)	37.5 (30.5 - 39.5)		
BMI Categories					
Normal	28 (29.7%)	32 (35%)	11 (11.8%)	71 (25.5%)	> 0.080
Over weight	25 (26.3%)	31 (33%)	35 (37.2%)	91 (32.5%)	
Obese	41 (44%)	30 (32%)	47 (51%)	118 (42%)	

Table (2): Diastolic and Systolic Blood Pressure of Stage 1 and Stage 2 of newly diagnosed hypertensive patients attended at El-Fath Health center (2022-2023) in Baseline, After 2 Months, and After 6 Months

	Group (A) (n = 94)	Group (B) (n = 93)	Group (C) (n = 93)	Total patients (N = 280)	P*
(Baseline) Stage 1 (140/90 - 159/99)	44 (46.80%)	38 (40.85%)	40 (43.02%)	122 (12.86%)	**0.241**
(After 2 Months) Stage 1 (140/90 - 159/99)	52 (55.30%)	46 (49.50%)	49(53.20%)	147 (52.5%)	**<0.001**
(After 6 months) Stage 1 (140/90 - 159/99)	77 (82%)	79 (85%)	89 (96%)	245 (87.50%)	**0.002**
Baseline Stage 2 (160/100 - 179/109)	50 (53.20%)	55 (59.15%)	53 (56.98%)	158 (83.93%)	**0.760**
After 2 Months Stage 2 (160/100 - 179/109)	48 (44.70%)	47 (50.50%)	44 (46.80%)	133 (47.5%)	**0.003**
After 6 months Stage 2 (160/100 - 179/109)	17 (18%)	14 (15%)	4 (4%)	35 (12.50%)	**<0.001**

*Chi-square test was used

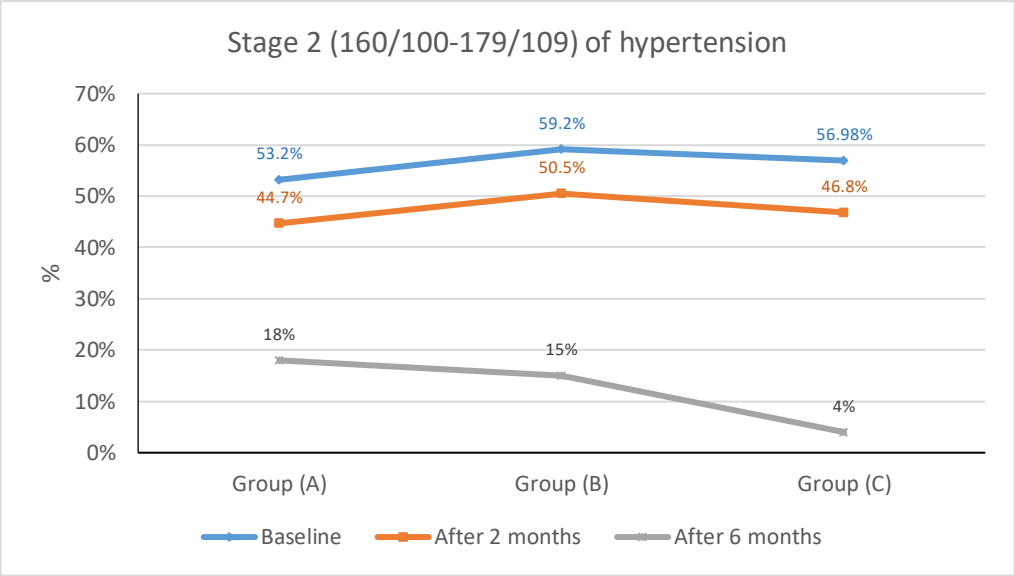

Figure (1): Percentage of Stage 2 (160/100-179/109) of hypertension distribution

Table (3): Serum Uric Acid level in Baseline and follow-up of newly diagnosed hypertensive patients attended at El-Fath Health center (2022-2023)

	Group (A) N = 94	Group (B) N = 93	Group (C) N = 93	Total patients (N = 280)	P Value**
Uric Acid (Baseline)					
Mean ± SD	9.10 ± 0.80	9.12 ± 0.70	9.14 ± 0.72	7.34 ± 3.53	
Median (IQR)	9.5 (7.5 - 10)	9.4 (7.3 - 10)	9.4 (7.5 - 10)		>0.401
Categories					**P1 = 0.008, P2 = 0.061, P3 = 0.395***
Normal	4 (4.5%)	6 (6.5%)	7 (7.5%)	17 (6%)	
Hyperuricemia	90 (95.5%)	87 (93.5%)	86 92.5%)	263 (94%)	
After 2 Months					
Mean ± SD	7.50 ± 1.40	8.01 ± 1.43	7.70 ± 1.30	6.24 ± 2.86	
Median (IQR)	7.9 (5.2 - 9.8)	8 (5.2 - 9.2)	7.3 (5.1 - 8.5)		>0.324
Categories					**P1 = 0.006, P2 = 0.221, P3 = 0.091***
Normal	20 (21.28%)	17 (18.28%)	22 (23.66%)	59 (21.07%)	
Hyperuricemia	74 (78.72%)	76 (81.72%)	71 (76.34%)	221 (78.93%)	
After 6 Months					
Mean ± SD	5.20 ± 1.70	4.30 ± 1.30	6.01 ± 2.43	4.54 ± 1.94	
Median (IQR)	5.9 (3.6 - 7.9)	5.1 (3.5 - 6.1)	4.3 (3.4 - 7.5)		<0.003
Categories					**P1 = 0.508, P2 = 0.123, P3 = 0.057**
Normal	75 (79.80%)	76 (81.70%)	85 (91.40%)	236 (84.30%)	
Hyperuricemia	19 (24.20%)	17 (18.30%)	8 (8.60%)	44 (15.70%)	

**ANOVA test was used

*P1: Group 1 vs Group 2 p2: Group 2 vs Group 3 P3: Group 1 vs Group 3

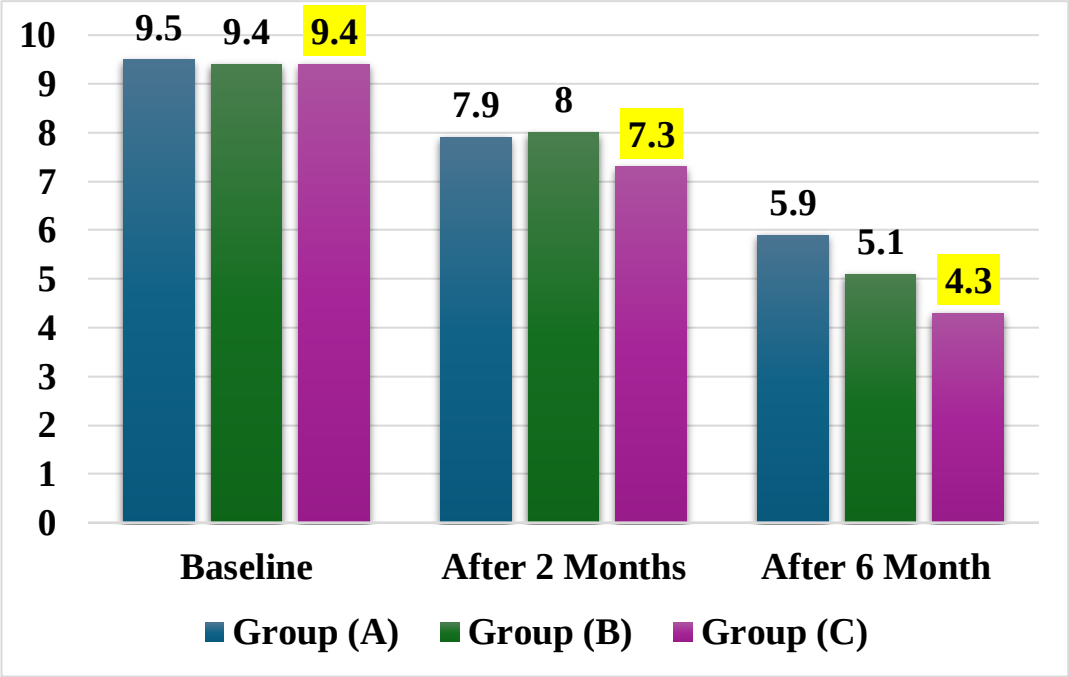

Fig. (2): Median concentration of Uric acid at baseline, after 2 months, and 6 months.

Table (4): Logistic regression analysis for predictors of decreasing serum uric acid among the treatment group.

Variables	P Valu	OR	95% CI
CCBs	<0.001*	3.182	2.203-5.091
Beta-Blockers	0.005	2.531	1.895- 71.104
ACEIs	0.007	3.210	1.39- 18.41
Age	0.321	2.321	0.211, 87.31
BMI	<0.001	1.875	1.023-3.742
Gender Female (reference) Male	0.003	1.543	1.653-3.242

*ANOVA test was used

Discussion

The World Health Organization has set a goal of reducing the prevalence of hypertension by 25% by 2025 (from the 2010 baseline), which affects an estimated 1.13 billion people worldwide. [14].

Therefore, our study assessed the influence of different antihypertensive drugs on serum uric acid in newly diagnosed hypertension patients. In this cohort study was conducted on 280 patients who are newly diagnosed with hypertension, the period from July 2022 to January 2023 in El-Fath Health Center- Assiut Government, with mean Age (30 – 39 represents 22.5%; 40 - 49 represents 33%; 50 - 90 represents 27% and 60 to 70 represents 17.5%) and Gender (total male represents 53% and female represents 47%)

Our findings revealed that there were significant differences in group A, B, and C regarding Age (30 - 39 represents 22.5%, 40 - 49 represents 33%, 50 - 90 represents 27% and 60-70 represents 17.5%) and Gender (total male represents 53% and females represent 47%). Our findings revealed that: Stages of hypertension among the treatment

group of hypertensive patients in El-Fath Health center, 2022. Regarding Stages of Hypertension, there was no statistically significant difference between the three studied groups (p= 0.241). Group (A) represented the highest number of hypertensive patients in Stage 1, in contrast with Groups (B) and (C); While Group (B) represented the highest number of hypertensive patients in Stage 2, in contrast with Group (A) and (C) at baseline. Our findings revealed that there **were n**o differences between Groups A, B, and C of hypertension in baseline, as regards systolic and diastolic. Significant decreases were observed between Groups A, B, and C of systolic and diastolic after 2 months, since Group C had the largest decrease in systolic and diastolic, followed by Group (B) and Group (A). There was a significant decrease in hypertension after 6 months in all groups, but Group C had the largest decrease, followed by Group A and Group B. All the included patients were under controlled hypertension after using different drugs.

***White*[15]** found that patients with stage 2 hypertension respond better to ACE inhibitors and CCB therapy for blood pressure control.

In agreement with our findings, ***Abdul-Razak et al.*** **[16]** demonstrated that the effect of calcium channel blocker therapy would be five times greater than that of doubling the dose of a beta-blocker antihypertensive drug, which is consistent with our findings.

In contrast with our study findings, ***Marshall et al.*** **[17]** observed that the inverse association between use of beta-blockers and risk of incident hyperuricemia may be due to their effect on renal function, in contrast to our study's findings. An expansion in uric corrosive discharge has been seen with Beta-blockers.

Yang et al. **[18]** discovered that patients with heart failure and chronic kidney disease prefer to take ACE inhibitors and CCBs as their antihypertensives. They should be used as the first line of treatment for people who have chronic kidney disease and show signs of hyperuricemia. Except for patients with chronic kidney disease, for whom ACE inhibitors or ARBs are the first-line treatment, the JNC8 guidelines recommend calcium channel blockers as a first-line treatment alone or in combination with other antihypertensives in all patients with HTN, regardless of age or race.

In agreement with our findings, ***Stewart et al.*** **[19]** found that people with hypertension who had CCBs had a lower risk of developing hyperuricemia, which was in line with our findings.

Other studies were not in agreement with our study findings. ***Krajčoviechová et al.*** **[20]** found that many antihypertensive medications, including diuretics, RAAS antagonists, and beta blockers, can raise the level of uric acid (UA), which was inconsistent with our findings. Contrary to our findings, it has been demonstrated that ACE inhibitors and CCB significantly lower UA concentrations.

Contrary to what we found in our study **[21],** UA can have multiple effects on BP, and ACE can help lower UA levels. This positive association may be explained by another mechanism related to hemodynamics.

Other studies were not in agreement with our study findings. ***Stewart et al.*** **[19]** found that current hypertensive patients' use of diuretics, blockers, angiotensin converting enzyme inhibitors, and non-losartan angiotensin II receptor blockers was linked to an increased risk of developing hyperuricemia. These findings were inconsistent with those of our study. The current use of diuretics was associated with the greatest multivariate relative risk, compared to not using them at all. Except for beta-blockers and non-losartan angiotensin II receptor blockers, these multivariate relative risks tended to increase with increasing duration of use among people with hypertension (P 0.05 for trend). Except for angiotensin converting enzyme inhibitors, these associations tended to be stronger with higher doses than with medium or low doses. Except for the relationship between duration of use and non-losartan angiotensin II receptor blockers, these relative risks tended to be

comparable among people without hypertension. The low rate of such use in this group was especially noteworthy.

Conclusion:

There was a positive correlation between hypertension and serum uric acid level through the decrease caused by antihypertensive drugs. Since all the included antihypertensive drugs decreased serum uric acid levels, ACE inhibitors and beta-blockers had the lowest records, in contrast to calcium channel blockers (CCB). Group C (CCBs) was highly controlled patients with a normal range of uric acid and normal blood pressure measurements, in contrast with the beta blocker group and the ACE group, which were less controlled than group CCB.

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