Treatment efficacy of febuxostat compared with allopurinol in hyperuricemia patients with hypertensive: A randomized, single-blind controlled trial

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ABSTRACT

Treatment of hyperuricemia with allopurinol and Febuxotate has been shown to be effective in hypertensive patients. Studies comparing the effects of both drugs in hypertensive patients were very limited, especially in the Vietnam population. Evaluating the treatment outcome of febuxostat when compared with allopurinol in hyperuricemia patients with hypertension in Vietnam. We conducted a randomized controlled clinical trial with an allocation ratio of 1:2 on 108 hyperuricemia outpatients with hypertension ≥40 years old. Group A was treated with allopurinol 100 mg, increased to 300 mg if treatment results were not achieved. Group B used febuxostat 40 mg, which increased to 80 mg. The endpoint was to control serum uric acid levels <6.0 mg/dl (<360 μmol/l). Primary outcomes were re-evaluated after 4 and 8 weeks, comparing the reaching endpoint proportion between the two groups. The secondary outcomes were subgroup analysis on characteristic groups of age, gender, and serum lipid indices such as non-HDL-c and triglyceride (TG)/non-HDL-c ratio to evaluate the impact on treatment outcomes within and between two groups. The primary outcomes evaluating the effectiveness between the two regimens showed that the uric acid concentrations after 4 weeks in groups A and B were 343.5 ± 104.0 and 378.0 ± 90.0 μmol/l, respectively ($p = 0.008$), after 8 weeks it was 268.0 ± 97.8 and 310.0 ± 52.8 μmol/l ($p < 0.001$). After 8 weeks of intervention, the reaching endpoint proportion in the A and B groups was 91.7% and 97.1%, respectively [risk ratio (RR) = 1.06, 95% confidence interval (CI) 0.97–1.16, $p = 0.297$]. The secondary outcome was analized subgroup showed that there was a statistically significant difference when comparing group A and group B at age <60 ($p = 0.020$), male gender ($p = 0.021$), non-HDL ≥ 3.37 ($p = 0.042$), TG/HDL-c < 4.5 ($p = 0.006$), in which the allopurinol group showed more optimal serum uric acid lowering results. Both regimens had good outcomes in the ability to reduce serum uric acid and a high proportion of reaching endpoints. Therefore, it could be applied in the clinical of treating hyperuricemia patients with hypertension in Vietnam. When analyzed between the two groups, there was no large difference in treatment outcomes between the two regimens, so preference among the two regimens was not necessary.

INTRODUCTION

There are about 1 billion people with hypertension, and it is estimated to reach 1.5 billion people by 2025

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[1]. Hypertension is a global disease burden, the cause of chronic diseases that require other combined treatments such as hyperhomocysteinemia, ambulatory arterial stiffness index, premature ventricular complexes, left ventricular hypertrophy, and so on [2–4]. Among them, hyperuricemia is still a significant disease burden in hypertensive patients. The prevalence of hyperuricemia in adults ranged from 21.4% to 41.4% and currently had a continuing increasing trend [5,6]. Increased serum uric acid often appears in hypertensive patients. Many studies showed that increased serum uric acid

increases the risk of developing hypertension within 5 years, which was considered a risk factor independent of others [7]. A linear correlation of serum uric acid with hypertension had been demonstrated with each 1 mg/dl increase in serum uric acid leading to a 13% increase in the risk of hypertension [8].

Treatment of hyperuricemia with abstinence and hypouricemic drugs with allopurinol in elderly patients with hypertension helped reduce complications and contributed to good blood pressure control [9]. A recently introduced drug, febuxotate, has been shown to effectively control uric acid in patients with hypertension [10–12]. However, there were lots of studies that only evaluated allopurinol and febuxostat alone, studies comparing the effects of both drugs in patients with hypertension were minimal [8–12]. In addition, very few similar studies have been conducted in the Vietnamese population. Therefore, the Vietnamese population in particular, and the Asian population in general required a study for optimal treatment selection. Our study aimed to evaluate the therapeutic efficacy of febuxostat compared with allopurinol in hypertension patients with hyperuricemia in Vietnam.

MATERIALS AND METHODS

Study design and population

We conducted a randomized controlled clinical trial with an allocation ratio of 2:1 on 108 outpatients with primary hypertension ≥40 years old treated at the Can Tho University of Medicine and Pharmacy Hospital from May 2020 to May 2021. The study was approved by the Ethics Committee in Biomedical Research of Can Tho University of Medicine and Pharmacy with Decision with Decision No 27/HDDD. All participating patients filled out an informed consent to participate in the study, and the identities of all research subjects were kept confidential.

Including criteria: (1) Hypertension patients diagnosed based on ESC/ESH 2018, with hypertension when systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg in two measurements of blood pressure or being treated with antihypertensive drugs [1]; (2) patients with hyperuricemia (elevated serum uric acid was confirmed when serum uric acid concentration for men >420 μmol/l and women >360 μmol, initiate treatment in patients received 3 months of lifestyle changes that were ineffective or the patient was unable to adhere to the lifestyle changes [13]); and (3) patients agree to participate in the study.

Excluding criteria: (1) Secondary hyperuricemia such as kidney failure, hemolysis, G6PD deficiency, after chemotherapy, radiotherapy, acute alcoholism [14]; (2) gout patients; (3) patients suffering from acute or malignant diseases: acute heart failure, acute myocardial infarction, acute respiratory failure, cerebrovascular disease, acute gout, liver cancer, acute leukemia, leukemia prayer, polycythemia; (4) patients who are taking drugs that affect the production and excretion of uric acid for 10 days, such as feburic, probenecid, sulfinpyrazole, salicylate, phenylbutazone, ascorbic acid, ethambutol, pyrazinamide, thiazide diuretics, other cytotoxic drugs; (5) patients with severe chronic kidney disease (estimated glomerular filtration rate < 30 ml/minute); (6) patient intolerant with febuxostat or allopurinol; and (7) patients did not agree to participate in the study.

Sample size

The sample size was calculated based on Becker *et al.*'s [14] study, the allopurinol group achieving the uric acid target <6.0 mg/dl (<360 μmol/l) was 21.11% ($p1 = 0.2111$), and the febuxostat group was 53.33% ($p2 = 0.5333$). We calculate $n = 65$ with $\alpha = 0.01$ and $\beta = 0.1$ ($Z_{(\alpha/2)} = 2.57$, $Z_{(\beta/2)} = 1.282$).
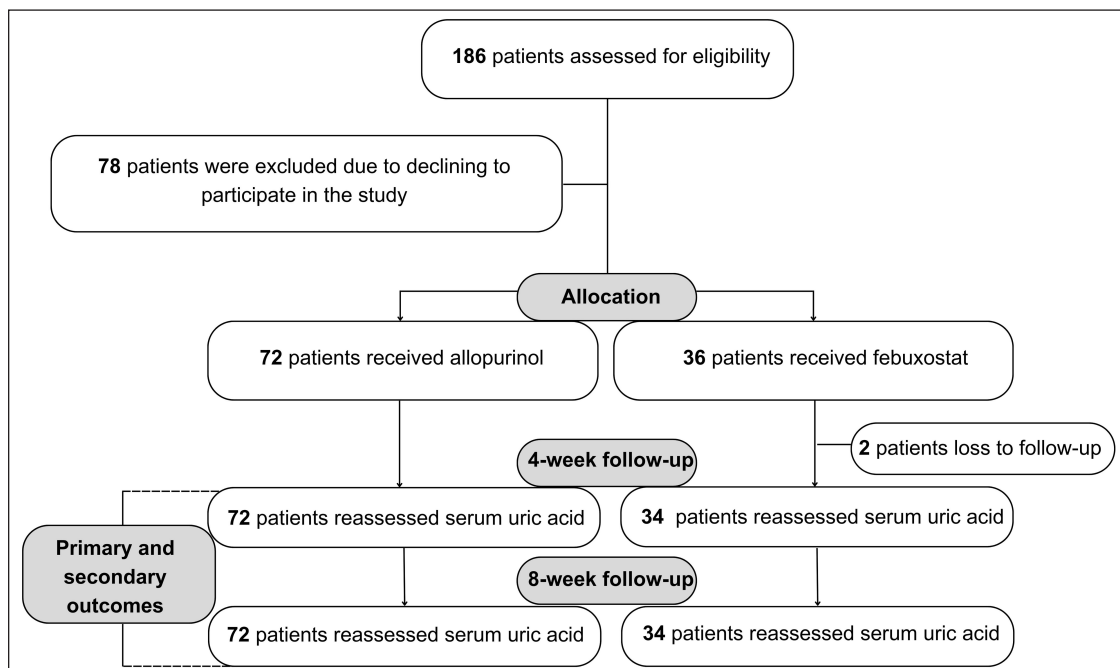
Figure 1. Flowchart of the study population.

Table 1. Baseline characteristics of study population.

Characteristics n		Total (n = 108)		Allopurinol (n = 72)		Febuxostat (n = 36)	p^a
		%	n	%	n	%	
General characteristic and risk factors							
Age (year) (X ± SD)		58.80 ± 11.64		59.31 ± 11.69		57.78 ± 11.64	0.523[b]
Male		69	63.9	45	62.5	24	66.7	0.671
BMI (Kg/m^2) (X ± SD)		23.69 ± 2.16		23.11 ± 2.28		24.85 ± 1.26	<0.01[b]
T2DM		22	20.4	16	22.2	6	16.7	0.499
Abuse alcohol		57	52.8	33	45.8	24	66.7	0.041
Smoking		68	63.0	44	61.1	24	66.7	0.573
CAD		56	51.9	34	42.7	22	61.1	0.173
Dislipidemia		14	13.0	12	16.7	2	5.6	0.105
Metabolism syndrome		62	57.4	40	56.6	22	61.1	0.582
Blood pressure (mmHg)	Systolic	158.29 ± 23.88		156.18 ± 28.28		162.50 ± 9.67	0.091
	Diastolic	89.12 ± 10.78		89.93 ± 12.23		87.50 ± 6.92	0.191
Hypertension grade	1	43	39.8	37	51.4	6	16.7	
	2	50	46.3	24	33.3	26	72.2	<0.01
	3	15	13.9	11	15.3	4	11.1	
Serum biochemical variables							
Acid uric (µmol/l) (median ± IQR)		540.5 ± 116.0		540.0 ± 155.0		550.0 ± 81.5	0.665[c]
Ure (µmol/l) (median ± IQR)		6.7 ± 4.5		8.5 ± 5.6		5.8 ± 1.8	<0.001[c]
Creatinin (µmol/l) (median ± IQR)		92.4 ± 60.8		109.0 ± 91.5		85.4 ± 21.2	<0.001[c]
Glucose (mmol/l) (median ± IQR)		5.8 ± 1.5		5.8 ± 1.7		6.0 ± 1.1	0.588[c]
TG (mmol/l) (median ± IQR)		2.15 ± 1.9		1.6 ± 1.15		3.4 ± 2.2	<0.001[c]
Cholesterol (mmol/l) (median ± IQR)		4.9 ± 2.3		4.0 ± 1.8		5.6 ± 1.8	<0.001[c]
LDL-c (mmol/l) (median ± IQR)		2.6 ± 1.6		2.5 ± 1.5		2.9 ± 2.2	0.044[c]
HDL-c (mmol/l)		1.0 ± 0.4		1.0 ± 0.3		1.0 ± 0.2	0.005[c]
Non-HDL-c		3.5 ± 2.1		2.9 ± 1.6		4.6 ± 1.7	<0.001[c]
TG/HDL-c		2.2 ± 2.2		1.8 ± 1.6		3.4 ± 1.9	0.001[c]

BMI = body mass index; CAD = coronary artery disease; HDL-c = high-density lipoprotein cholesterol; IQR = interquartile range; LDL-c = low-density lipoprotein cholesterol; SD = standard devitation; T2MD = type 2 diabetes mellitus; TG = triglyceride.
[a]Chi-squared test.
[b]Independent samples *T*-test.
[c]Mann–Whitney *U* test.

In fact, we conducted the study on 108 patients, more than the sample size to prevent loss of follow-up or nonadherence to treatment.

Table 2. Uric acid concentration before and after treatment.

Uric acid concentration	Total (n = 108)	Allopurinol (n = 72)	Febuxostat (n = 36)	p^a
Baseline (µmol/l)	540.5 ± 116.0	540.0 ± 155.0	550.0 ± 81.5	0.665
4-weeks (µmol/l)	351.5 ± 99.0	343.5 ± 104.0	378.0 ± 90.0	0.008
8-weeks (mmol/l)	289.5 ± 75.3	268.0 ± 97.8	310.0 ± 52.8	<0.001
p^b	<0.001	<0.001	<0.001	
p^c	<0.001	<0.001	<0.001	

CI = confidence interval; HDL-c = high-density lipoprotein cholesterol; p = independent sample T-test.
[a]Analyzed between groups; [b]Analyzed between baseline and 4-week within groups; [c]Analyzed between baseline and 8-week within groups.

Data collection and intervention methods

All outpatients diagnosed with hypertension and hyperuricemia would have their medical history questioned, and examined, general and clinical characteristics recorded by specialist doctors. Some general characteristics include age, gender, overweight, and obesity (classification based on the WHO Asian body mass index (BMI) classification, overweight and obesity when BMI ≥ 23 kg/m^2 medical history of coronary artery disease (CAD) with at least one-time hospitalization, smoking (none if patients have stopped smoking for at least 5 years [15]); type 2 diabetes mellitus (T2DM) (according to American Diabetes Association 2020 guideline [16]), alcohol abuse (drinking ≥2 standard drinks for men (or ≥20 g ethanol/day), and ≥1 standard drink for women (or ≥10 g ethanol/day) [17], metabolic syndrome (according to NCEP-ATP III 2001 [18,19], three out of five criteria of abdominal obesity, high blood triglycerides (TGs), low HDL-c, blood pressure ≥ 130/85 mmHg, blood glucose fasting ≥ 6.1 mmol/l). Quantifies fasting serum uric acid and lipid components in the morning, including baseline, 4 and 8 weeks after intervention. Conduct a blood draw to take 2 ml of venous blood (at least 12 hours before the previous meal) for natural coagulation, serum separation, and quantification of serum lipid components by enzymatic colorimetric method (on the COBAS-C502 machine, HITACHI of Japan). In addition, fasting blood glucose, urea, creatinine were taken.

The intervention was performed in outpatients with high serum uric acid concentration (for men >420 µmol/l and women >360 µmol [13], our research threshold was stricter than previous studies). Group A started treatment with allopurinol 100 mg (once daily), increasing to 300 mg after 4 weeks or 600–900 mg if the treatment goal was not achieved after 8 weeks [1]. Group B used 40 mg febuxostat (once daily), increasing to 80 mg after 4 weeks if the treatment goal was not achieved [1]. All patients participating in the study are numbered from small to large. Equally distributed with a ratio of 1:2, for two groups of patients B and A, respectively. Our study was single-blind, in the study patients were not aware between the two regimens. All participating patients were instructed to use medication, comply with treatment, and make follow-up appointments. Endpoint to control serum uric acid levels <6.0 mg/dl (<360 µmol/l). Record blood uric acid results after 4 and 8 weeks and compare the proportion of controlled serum uric acid concentration between the two groups.

Table 3. Subgroup analysis of uric acid concentration before and after treatment.

Uric acid concentration		Total (*n* = 108)	Allopurinol (*n* = 72)	Febuxostat (*n* = 36)	*p*[a]
Baseline (μmol/l)					
Age	<60	556.33 ± 107.39	559.49 ± 125.85	549.85 ± 54.87	0.679
	≥60	569.91 ± 104.48	575.58 ± 120.39	556.81 ± 65.14	0.492
	p[b]	0.532	0.584	0.735	
Gender	Male	567.25 ± 113.65	570.18 ± 132.82	561.75 ± 66.25	0.726
	Female	552.51 ± 91.03	560.15 ± 106.53	535.33 ± 36.61	0.289
	p[b]	0.463	0.726	0.133	
Non-HDL-c	<3.37	576.85 ± 115.40	577.45 ± 118.85	570.25 ± 78.34	0.875
	≥3.37	549.83 ± 97.79	549.07 ± 129.36	550.53 ± 56.68	0.956
	p[b]	0.202	0.353	0.656	
TG/HDL-c	<4.5	557.41 ± 98.60	556.03 ± 111.50	560.63 ± 60.15	0.801
	≥4.5	588.25 ± 144.21	639.11 ± 175.98	522.86 ± 42.75	0.088
	p[b]	0.422	0.202	0.08	
4-weeks (μmol/l)					
Age	<60	349.79 ± 90.13	329.76 ± 99.19	390.85 ± 47.98	0.002*
	≥60	363.20 ± 99.89	354.32 ± 88.48	382.86 ± 122.89	0.444
	p[b]	0.478	0.272	0.820	
Gender	Male	358.59 ± 86.39	336.16 ± 77.69	402.48 ± 87.26	0.004*
	Female	349.92 ± 107.71	347.30 ± 119.52	356.36 ± 75.65	0.782
	p[b]	0.672	0.668	0.128	
Non-HDL-c (mmol/L)	<3.37	349.65 ± 99.69	344.61 ± 101.79	405.00 ± 52.46	0.100
	≥3.37	360.31 ± 89.93	333.61 ± 84.21	385.23 ± 89.24	0.027*
	p[b]	0.568	0.620	0.547	
TG/HDL-c (mmol/L)	<4.5	355.26 ± 94.17	335.87 ± 90.12	400.48 ± 89.19	0.003*
	≥4.5	356.75 ± 97.22	371.56 ± 125.21	337.71 ± 44.46	0.469
	p[b]	0.955	0.430	0.017*	
8-weeks (μmol/l)					
Age	<60	291.34 ± 78.58	278.71 ± 90.56	317.25 ± 34.42	0.020*
	≥60	287.80 ± 80.80	272.84 ± 73.25	320.93 ± 89.45	0.092
	p[b]	0.822	0.762	0.885	
Gender	Male	301.35 ± 84.68	285.73 ± 88.75	331.91 ± 67.90	0.021*
	Female	269.24 ± 64.19	260.26 ± 71.27	291.27 ± 35.93	0.085
	p[b]	0.031*	0.186	0.030*	
Non-HDL-c	<3.37	285.89 ± 83.30	281.89 ± 85.56	330.00 ± 30.82	0.042*
	≥3.37	293.10 ± 76.16	267.21 ± 79.61	317.27 ± 65.18	0.012*
	p[b]	0.646	0.462	0.533	
TG/HDL-c	<4.5	289.62 ± 84.13	275.09 ± 86.77	323.52 ± 67.59	0.006*
	≥4.5	291.06 ± 43.32	283.78 ± 52.67	300.43 ± 28.48	0.434
	p[b]	0.919	0.681	0.184	

*$p < 0.05$. HDL-c = high-density lipoprotein cholesterol; p = independent sample T-test; TG = triglyceride.
[a]Analyzed between intervention and control groups; [b]Analyzed between subgroups within groups.

Study outcomes

The primary outcome was the effectiveness of serum uric acid control compared between febuxostat versus allopurinol after 4 and 8 weeks. Treatment was effective when serum uric acid concentration <6.0 mg/dl (<360 μmol/l). Evaluate changes in mean serum uric acid concentration between two groups before and after intervention, after 4 and 8 weeks of treatment. The secondary outcomes were subgroup analysis on characteristic groups of age, gender, and serum lipid indices such as non-HDL-c and TG/non-HDL-c ratio to evaluate the impact on treatment outcomes within and between two groups.

Data analysis and bias control methods

All data collected was ensured: Information bias control (clear and specific definition of research variables, information on diagnosis and classification according to uniform standards, data collection through a unified medical record form); selection bias control (following including and excluding criteria, study protocol, imaging tests interpreted by independent radiologists and cardiologists, entered data and statistical processing by an independent statistician, conducted twice to compare the results); clearly explained to the patient before the procedure.

Data were collected and processed by Statistical Package for the Social Sciences 20.0 software. Quantitative variables with normal distribution were described by mean ± SD, and non-normal distribution variables were characterized by the median, maximum, minimum, and interquartile range (IQR). Qualitative variables are represented by rate and percentage. The difference between two qualitative variables described by the chi-squared test, normal distribution quantitative variables by simple *t*-test (if two groups analyzed) or analysis of variance (if ≥3 groups investigated), quantitative variables with non-normal distribution by Mann–Whitney test (if two groups studied) or Kruskal-Wallis test (if ≥3 groups analyzed), $p < 0.05$ considered to be statistically significant.

Table 4. Proportion of uric acid reaching endpoint compared between groups.

Proportion of reaching endpoint	Total (n = 108)		Allopurinol (n = 72)		Febuxostat (n = 36)		Absolute difference in proprtions, %	RR (95% CI)	p*
	n	%	N	%	n	%			
After 4 weeks	73	67.6	23	67.6	50	69,4	1.8	0.97 (0.73–1.29)	0.852
After 8 weeks	99	91.7	33	97.1	66	91.7	5.4	1.06 (0.97–1.16)	0.297

*Chi-squared test.

CI = confidence interval; RR = risk ratio.

Table 5. Treatment outcomes comparison with other studies.

Study	Duration	Percentage of change		p^a
		Allopurinol	Febuxostat	
Kim *et al.* [20], n = 179	2-week	−51.3*	−39.2*	<0.001
	4-week	−48.5*	−39.5*	<0.001
Gunawardhana [11], n = 121	3-week	NA	−42.3*	NA
	6-week	NA	−42.3*	NA
Kario *et al.* [23], n = 68	12-week	NA	−35.4*	NA
	24-week	NA	−37.2*	NA
Tani *et al.* [12], n = 60	24-week	NA	−28.5*	NA
Soletsky and Feig [25], n = 20	8-week	−41.2*	NA	NA
Kanbay *et al.* [24], n = 59	12-week	−31.2*	NA	NA
Kanbay *et al.* [21], n = 72	16-week	−30.1*	NA	NA
Segal *et al.* [22], n = 115	5-week	−34.8*	NA	NA
Our	4-week	−29.8*	−37.3*	0.029
	8-week	−42.3*	−50.2*	0.001

*$p < 0.05$ analyzed in the percentage of change between follow-up period within group.

NA = not applicable.

^{a}Independent samples *T*-test, analyzed in the percentage of change between groups.

RESULTS

A total of 186 outpatients who met the sampling criteria were included in the study. One hundred eight patients who agreed to participate in the study were randomly put into groups A and B with an allocation ratio of 2:1, of which two patients were excluded from the study due to loss of follow-up. One hundred six patients were included in the analysis, 72 for the allopurinol group and 34 for the febuxostat group (Fig. 1).

Baseline characteristics of the study population

A total of 108 patients participated, mean age was 58.80 ± 11.68 (years old), and 63.9% were male. Among them, smoking was the risk factor with the highest proportion (70.4%). The highest grade of hypertension was grade 2 (46.3%), and BMI had a difference between the two groups ($p < 0.01$) (Table 1).

Intervention effectiveness after 4 and 8 weeks

Serum uric acid levels decreased significantly after 4 and 8 weeks in both groups and the difference between the two groups was statistically significant ($p \leq 0.01$). The mean uric acid concentration before intervention in both treatment groups with Allopurirol and Febuxobrate was 540.0 ± 155.0 and 550.0 ± 81.5 μmol/l, respectively. After 4 weeks, the mean was 343.5 ± 104.0 and 378.0 ± 90.0 μmol/l, respectively ($p = 0.008$), and was 268.0 ± 97.8 and 310.0 ± 52.8 μmol/l ($p < 0.001$) after 8 weeks (Table 2).

Uric acid concentrations were analyzed according to age groups, gender, non-HDL-c, and TG/HDL-c ratio. After the treatment follow-up period, there was a statistically significant difference when compared between groups aged <60 (p after 4 and 8 weeks were 0.002 and 0.020, respectively), male (p after 4 and 8 weeks were 0.004 and 0.021, respectively), non-HDL ≥ 3.37 (p after 4 and 8 weeks were 0.027 and 0.042, respectively), TG/HDL-c < 4.5 (p after 4 and 8 weeks were 0.003 and 0.006, respectively). When compared within the same group, divided by subgroups, the treatment effect of febuxobrate in women was better than in men ($p = 0.03$) (Table 3).

After 4 weeks of intervention, the proportion of achieving endpoint in the febuxostat and allopurinol groups was 67.6% and 69.4%, respectively (RR = 0.97, 95% CI 0.73–1.29, $p = 0.852$) (Table 2). After 8 weeks of intervention, the proportion was 97.1% and 91.7%, respectively (RR = 1.06, 95% CI 0.97–1.16, $p = 0.297$) (Table 4).

DISCUSSION

Our study evaluated the ability to control serum uric acid levels when comparing the febuxostat regimen in group B and allopurinol in group A. Overall, both regimens clearly showed effectiveness in reducing serum uric acid after 4 and 8 weeks of follow-up ($p < 0.001$) (Table 2). After 8 weeks, the allopurinol regimen showed more effective in the uric acid reduction effect based on mean concentration ($p < 0.001$) (Table 2). However, the febuxostat regimen showed a higher rate of achieving the endpoint (97.1% *vs.* 91.7, RR = 1.06, 95% CI: 0.97–1.16, $p = 0.297$) but was not statistically significant (Table 4). Secondary outcomes were evaluated according to the subgroups analyzed. Allopurinol showed better treatment results in groups with aged <60, male, non-HDL ≥ 3, and TG/HDL-c < 4.5 ($p < 0.05$) (Table 3).

Our study population had a mean age of 58.8 years old, 63.9% male (Table 1), similar to other studies with ages ranging from 50 to 60 years old and men making up the majority

of the population [11,20–22]. The study by Tani *et al.* [12], Kanbay *et al.* [24], and Kario *et al.* [23] recorded a higher age population and the study by Soletsky and Feig [25] was much lower. The mean BMI was 23.69 kg/m^2, significantly lower than other studies due to the smaller physical condition of the Vietnamese population compared to other population groups [11,12,20,22–24].

Subgroup analysis showed that the effectiveness of allopurinol was better in ages <60 years (*p* after 4 and 8 weeks were 0.002 and 0.020, respectively), and male gender (*p* were 0.004 and 0.021, respectively), non-HDL $\geq$ 3.37 (*p* were 0.027 and 0.042, respectively), TG/HDL-c < 4.5 (*p* were 0.003 and 0.006, respectively) (Table 3). When compared within the same group, divided by subgroups, the treatment effect of febuxostat in women was better than in men (*p* = 0.03) (Table 3). Other studies such as Gunawardhana [11] reported that the treatment effect of febuxostat was better in the eGRF group from 60 to 90 ml/phút/1.73 m^2.

After the follow-up period, the febuxostat group had a lower rate of achieving the endpoint at 4 weeks of evaluation and higher at 8 weeks compared with the allopurinol group (*p* > 0.05) (Table 4). The mean concentrations of uric acid in the allopurinol group were statistically significantly lower compared to the febuxostat group (Table 2) after 4 weeks (*p* = 0.008) and 8 weeks (*p* < 0.001). The uric acid reduction effect when analyzed through the percentage change between periods was lower in the allopurinol group and higher in the febuxostat group when compared with the randomized controlled trials of Kim *et al.* [20]. Our study was different from other studies, which showed that febuxostat provided better treatment results when compared with allopurinol (Table 5) [20]. The difference could be due to differences in populations including ethnicity and BMI. Therefore, in the Vietnamese population, there was no difference in treatment options for both drug groups.

Both regimens showed a high ability to reduce serum uric acid and achieved the endpoint after the follow-up period. Specifically, after 8 weeks of follow-up, >90% of patients achieved the endpoint (Table 4). Similar to other studies, there were good improvement results of either or both regimens over the treatment period [11,12,20–24]. Therefore, the treatment effectiveness of both regimens could be highly recommended for application in the clinical practice of treating hyperuricemia. In addition, our study recorded higher treatment results than other studies. Specifically, after 8 weeks of treatment in the febuxostat group, the percentage change was significantly higher than in previous studies with longer follow-up periods (−50.2% *vs.* 28.5%–42.3%) (Table 5) [11,12,20,23]. However, other populations had much higher BMI than ours, which could lead to bias, but we deliberately selected studies with the most similar populations possible (including hypertension and hyperuricemia). The allopurinol treatment group also showed no different results compared to other studies (42.3% *vs.* 29.8%–51.3%) (Table 5) [20–22,24,25]. Therefore, hyperuricemia in Vietnamese hypertension patients treated with allopurinol and febuxostat was more optimal than compared to other population groups and could be applied in clinical practice.

Strengths and weaknesses of the study

Our study's threshold for intervention in serum uric acid concentration was smaller and stricter than previous studies, so the study brings novelty to the population. The intervention results of the study can contribute to understanding the effectiveness of two types of regimens in controlling serum uric acid. Therefore, our research results could be as medical evidence to choose treatment regimens in the Vietnamese population. In addition, our study has a sample collection process with clearly designed including and excluding criteria. All patients in the study volunteered and had benefited from the study. The intervention research design closely follows the CONSORT 2010 checklist. Research methods and methods were clearly described and reproducible.

However, our study was evaluated in one hospital, which could lead to bias in general and clinical characteristics. Therefore, a study with similar or larger sample sizes in multiple centers in different regions is needed to better represent the characteristics of the population. Our study has the longest treatment period of 8 weeks. In clinical practice, patients use the drug longer than the evaluation period. In addition, our study was conducted with a single-blind design, which was another reason leading to bias. However, our study was designed to minimize this limitation through bias control methods in the method section. Therefore, a double-blind clinical trial with a longer evaluation period is needed to better evaluate the effectiveness and adverse effects of the two regimens in long-term use.

CONCLUSION

In hypertensive patients with hyperuricemia, treatment with febuxostat and allopurinol has been shown to have a high ability to reduce serum uric acid and achieve endpoint. Therefore, both regimens could be applied in clinical practice in the Vietnamese population. There was no difference in treatment outcomes between the two regimens, preference among the two regimens was not necessary.

AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the International Committee of Medical Journal Editors (ICMJEs) requirements/guidelines.

CONFLICTS OF INTEREST

The authors report no financial or any other conflicts of interest in this work.

ETHICAL APPROVALS

The Can Tho University of Medicine and Pharmacy Hospital from May 2020 to May 2021. The study was approved by the Ethics Committee in Biomedical Research of Can Tho University of Medicine and Pharmacy with Decision with Decision No 27/HDDD. All participating patients filled out an informed consent to participate in the study, and the identities of all research subjects were kept confidential.

DATA AVAILABILITY

All data generated and analyzed are included in this research article.

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