Original Research Article

Effectiveness of allopurinol on triglyceride levels in hyperuricemic patients

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ABSTRACT

Background: In this clinical pharmacological research, we dealt with the action of allopurinol on triglyceride levels in hyperuricemic patients.

Methods: The study included 40 hyperuricemic patients, of both genders and different age groups, that were sorted by comorbid diagnoses in several subgroups. All patients were clinically treated in the period of three years both at UCC Sarajevo, and P.I. General Hospital "Abdulah Nakaš" Sarajevo. All clinical measurements were carried out using standard IFCC methods with the appropriate analysers.

Results: The study was based on mean triglyceride levels before and after three and six months of treatment with allopurinol. It was found out that the mean triglyceride levels were not significantly different from the reference values prior to treatment (p = 0.846) and after three months of therapy (p=0.153). In contrast, after six months of treatment, triglyceride levels significantly increased compared to the reference values. In patients with a diagnosis of gout and metabolic syndrome, triglycerides were statistically significantly increased during the six months of observation. A statin group of patients showed a statistically significant increase in triglyceride levels after three months of therapy (p = 0.032), while, after six months their levels had decreased (p = 0.029). In patients with diabetes mellitus type II, triglycerides rose after three months of treatment (p = 0.039) and retained the same level after six months of observation.

Conclusions: The analysis shows that the use of allopurinol has an effect on triglyceride levels in hyperuricemic patients.

Keywords: Allopurinol, Hyperuricemia, Triglycerides

INTRODUCTION

Hyperuricemia occurs at concentration of uric acid of 416mmol/L, but there are authors that consider the normal values of uric acid to be its values of 392mmol/L for female, and 458mmol/L for male.[1]

It should be noted that men excrete smaller amounts of uric acid than women and therefore more commonly suffer from hyperuricemia.[2] The reason lies in the fact that women in the reproductive age have lower serum uric acid values due to the estrogen effect in the form of enhanced uric acid excretion and inhibition of the renal reabsorption of uric acid.[3]

The concentration of serum uric acid is one of the potential markers of cardiovascular and cerebrovascular diseases and therefore this type of clinical research is very important.[4]

There are some examples of connectivity hyperuricemia and hypertension in humans.

- The prevalence of hyperuricemia is 20-40% in untreated hypertensives, or 50-70% in treated hypertensives or those with impaired renal function,
- Gout prevalence is 2-12% in hypertensives,
- About 20-50% of patients with gout have hypertension,
- The increase in hyperuricemia is directly related to the increase in blood pressure.[5-6]

Within this pharmacological clinical trial, the primary objective was related to the analysis of the values of uric acid and triglyceride levels in patients treated with allopurinol for period of three or six months of treatment. A secondary objective was to monitor values of specified analytes in dependence of comorbidity diagnoses of patients. The starting hypothesis was as follows: initial therapy of hyperuricemic patients with allopurinol for a six-month monitoring period will show additional effects on triglycerides.

METHODS

Our study (retrospective-prospective cohort study) was conducted on 40 clinically treated patients (period from of three years both at the UCC Sarajevo and P.I. General Hospital "Abdulah Nakaš"), of both genders and different age groups, divided into subgroups according to comorbid diagnoses. All patients had already been diagnosed with hyperuricemia. A special group comprised the patients who, in addition to diagnosed hyperuricemia, used statin therapy, prior to treatment with allopurinol, taking in to account that the dose of statins during the six months of our observations was not changed. The first values of uric acid and triglycerides levels (before treatment) were the control values (each patient is his/her own control). The therapeutic effects of allopurinol were monitored (dose of 100mg per day) during the three-month and six-month treatment. Selection of patients in this analysis was carried out according to the following criteria: hyperuricemia verified by doctors, based on laboratory diagnostics; availability of information about the treatment, including possible complications; availability of indicators by gender, age and anamnestic data. While working on this paper the following methods are used: explanatory,

content analysis, statistical and comparative methods. All clinical measurements were carried out using standard IFCC methods with the appropriate biochemical analysers.

For continuous variables in the research, we first analysed the symmetry of their distribution using the Kolmogorov-Smirnov test. When the distribution was symmetric, we used arithmetic mean and standard deviation to show mean values, and to compare these variables, we used parametric tests (Student's t-test, Paired t-test). When the distribution of continuous variables was not symmetrical, to show the mean values and dispersion measures, we used median and interquartile ranges, and for comparison non-parametric tests. For a statistical analysis of the data SPSS for Windows (version 20.0, SPSS Inc., Chicago, Illinois, USA) and Microsoft Excel (version 13th, Microsoft Corporation, Redmond, WA, USA) were used.

RESULTS

Through the analysis of the mean values of uric acid before treatment and after 3 and 6 months of treatment in patients it was noticed that allopurinol exerted a therapeutic effect. It was determined that the mean value of uric acid before treatment was 523.45µmol/L, after 3 months of treatment with allopurinol 433.25µmol/L, and after 6 months of treatment, 435.77µmol/L. A t-test showed that the mean value of uric acid is significantly different from the reference values prior to treatment (p = 0.04), whereas after 3 and 6 months, the mean values were within the upper (tolerant) reference values. With the analysis of the mean values of triglycerides in the total sample (n = 40) before treatment and after 3 and 6 months of treatment, it was found that the mean value of triglycerides in the study group before treatment was 1.69mmol/L, after 3 months of treatment with allopurinol 1.92mmol/L, and after 6 months of treatment, 2.10mmol/L. A t-test showed that the mean value of triglycerides were not significantly different from the reference values before treatment (p = 0.846), and after 3 months of treatment (p = 0.153), whereas after 6 months of treatment the mean triglyceride levels were significantly higher than reference values (p=0.047), as shown in the following Table 1.

Table 1: Average values of triglycerides during the treatment.

Test period	X	N	SD	SEM	t	df	P
Before treatment	1.69	40	1.21	0.19	-0.195	39	0.846
After 3 months	1.92	40	1.02	0.16	1.460	39	0.153
After 6 months	2.10	40	1.34	0.21	1.759	39	0.047*

Applying a paired t-test showed the difference in triglyceride levels before applying allopurinol and after 3 and 6 months of therapy. There is a statistically

significant difference in mean triglyceride values before applying allopurinol and after 3 months of therapy (p = 0.036). The value of triglyceride has been increased by

0.22mmol/L. and it was within the benchmark of elevated levels. There was no statistically significant difference in mean triglycerides levels after 3 and 6 months of treatment (p = 0.216). as it can be seen from the following Table 2.

Table 2: Differences in average triglyceride levels during test period.

Test period	X	t	df	P
Before treatment- After three months of treatment	-0,22	-2,179	39	0,036*
After three months of treatment- After six months of treatment	-0,15	-1,259	39	0,216

Table 3: Triglyceride levels by defined groups of patients during test period.

	Before treatment			After 3 months			After 6 months		
	X	SD	SEM	X	SD	SEM	X	SD	SEM
Gout	1.69	1.46	0.30	2.00	1.24	0.25	2.19	1.63	0.34
	p<0.05								
Gout+ statins	2.06	0.64	0.28	2.21	0.28	0.12	2.04	0.68	0.30
	p=0.032 p=0.029								
Metabolic syndrome (expressed heart disease-hypertension)	1.35	0.89	0.40	1.42	0.65	0.29	1.73	0.91	0.40
	p<0.05								
Diabetes mellitus type 2	1.48	0.68	0.30	1.97	0.51	0.25	1.88	0.74	0.33
	p=0.039 p=0.721								

When we observed the patients based on their comorbid diagnoses within defined subgroups. we came up with the following results (Table 3).
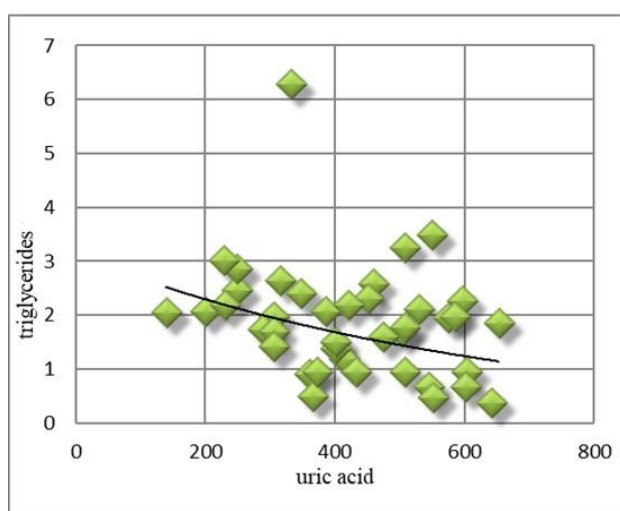

Figure 1: Correlation between the values of uric acid and triglyceride levels.

The analysis of patients with the diagnosis of gout showed that triglyceride levels were significantly increased both. after 3 months. and 6 months after commencing the therapy (p<0.05). In patients diagnosed with gout. and who were treated with statins and allopurinol. it was found that the triglycerides levels were significantly increased after 3 months of therapy with allopurinol (p = 0.032). but later. after 6 months were reduced (p = 0.029). The analysis of patients with metabolic syndrome (expressed heart disease-hypertension) showed that the triglyceride levels were significantly increased during the entire monitoring period (p<0.05). In patients with diabetes mellitus type 2 the triglyceride levels were increased after 3 months of therapy with allopurinol (p = 0.039). and after 6 months they remained the same.

There was a statistically significant negative correlation between the values of uric acid and triglyceride levels after 3 months of therapy r= -0.346; p=0.031. There was no statistically significant correlation between the values of uric acid and triglyceride levels after 6 months of treatment p>0.05.

DISCUSSION

Serum uric acid and lipid levels are analysed in several interesting studies which are. to some extent. contradictory. A certain number of studies have shown a direct link between lipids and hyperuricemia in patients with metabolic syndrome.[7-10] Some studies have shown a positive correlation of uric acid and triglyceride values.[7-9] Also. animal subject studies showed a significant direct relationship between uric acid and triglycerides.[11,12] However. some studies have shown conflicting results. A study by Heimbach EJ and collaborators. which included 66 patients (treatment with allopurinol). diagnosed with metabolic syndrome and gout and observed in the period 2002 to 2012. Showed that the modified values of uric

acid due to medicament therapy are in weak correlation with triglyceride levels.[13]

The mean value of triglyceride before treatment (the total sample) was 1.69mmol/L. and it was increased after 3 months of treatment with allopurinol to 1.92mmol/L. and after 6 months. when it rose further to 2.10mmol/L. A t-test showed that the mean value of triglycerides was not statistically-significantly different from the reference values before treatment (p = 0.846). and after three months of treatment (p = 0.153). whereas. after six months of treatment. mean triglyceride levels were statistically significantly higher than the reference values (p=0.047). The application of comparative t-test revealed a statistically significant difference in mean triglyceride levels before applying allopurinol and after three months of therapy with allopurinol (p = 0.036). There was an increase in triglycerides levels by 0.22 mmol/L and was in an elevated value. After three and six months of treatment with allopurinol. no statistically significant difference in mean triglycerides levels was found (p = 0.216). In an analysis of patients with the diagnosis of gout it was found that triglycerides levels were significantly increased (p <0.05). whereas in patients with a diagnosis of gout. who were treated with statins and allopurinol. triglycerides levels were statistically significantly increased after three months of therapy with allopurinol (p = 0.032). but these decreased after six months of treatment (p = 0.029). Also. with allopurinol therapy of patients with metabolic syndrome with severe heart disease (hypertension present) the mean values of triglycerides were observed. which were in this group. statistically significantly increased (p<0.05) during all six months of follow-up. It was found. in the analysis of triglyceride levels in patients with diabetes mellitus type 2. that the values increased after three months of therapy (p=0.039). and after six months had showed no further increase.

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