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Allopurinol Effect on Values of Lipid Profile Fractions in Hyperuricemic Patients Diagnosed with Metabolic Syndrome

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ABSTRACT

Subject: The concentration of serum uric acid (SUA) is one of the potential markers of cardiovascular and cerebrovascular diseases, as well as some other severe diseases. In this pharmacological – clinical study we evaluated allopurinol effect on certain values of lipid profile fractions in hyperuricemic patients diagnosed with metabolic syndrome that had pronounced cardiovascular problems, also with diagnosed hypertension. **Methods**: Research sample comprised 40 clinically treated hyperuricemic patients of both sexes, different ages, classified into several subgroups according to the disease diagnoses. The methods used in the study included: assay analysis, statistical and comparative methods. All clinical measurements were performed with standard IFCC methods on suitable biochemical analyzers. **Results**: Study established that after the first three months of allopurinol use, there was statistically significant difference in the average value of uric acid compared to the patients' initial state. During the next three months of therapy no further statistically significant difference in average values of uric acid ($p = 0,936$) was detected, meaning that the desirable effects of drug use were achieved. Simultaneously, the values of triglycerides, cholesterol and LDL fractions in test subjects increased significantly ($p > 0,05$). The values of HDL fractions increased after three month therapy with allopurinol, but later their value remained constant. Atherogenic index increased significantly after three and six months of therapy, therewith retaining at upper limit of reference value. **Conclusion**: The study results confirmed the primary hypothesis, which was that the allopurinol use affects the values of lipid profile fractions in hyperuricemic patients.

Key words: uric acid, hyperuricemia, allopurinol, lipid profile fractions, metabolic syndrome, atherogenic index.

1. INTRODUCTION

The concentration of serum uric acid (SUA) is one of the potential markers of cardiovascular and cerebrovascular diseases, which, arguably, are included in most difficult contemporary diseases. This is reflected not only in increase of number of cases, but also in percentage of lethality of patients with cardiovascular diseases. That is why clinical research is very important, dealing with causes of genesis of cardiovascular disease, as well as evaluation of results of such studies, especially having in mind the fact that there are certain discrepancies among them.

Connection between hyperuricemia and hypertension in humans has been established in series of studies (*1, 2*). The results of recent pilot study entitled "Allopurinol (xanthine oxidase inhibitor lowering concentration of uric acid in serum and urine) leads to the lowering of urates and blood pressure level" (*3*) also speak of link between urates and blood pressure.

It is known also that hyperuricemia occurs as independent risk factor of stroke, and patients with elevated urates have worse outcome of cerebrovascular incident. Elevated urates levels represent a risk factor for peripheral arterial disease (atherosclerosis of carotid artery), in certain heart failures etc.

Even though the results of research up to date pertaining to the effect of serum uric acid concentrations on cardiovascular diseases and lethality (AIM) are partially contrastive, the prevailing opinion is that the connection exists. It is established in the series of known studies amongst which are:

NHANES I – National Health and Nutrition Examination Survey I (5926 subjects) where it was established "that the elevated SUA is the independent cause of occurrence of cardiovascular lethality in general population" (*4*). It was also established that the elevated SUA is the leading risk of cardiovascular diseases in persons between 45 and 55 years of age in both sexes;

In Framingam study (6763 subjects) the "link between SUA and cardiovascular diseases in general population" (*5*) was established, but not as an independent from the other risk markers like hypertension, for example;

Similar results were acquired in some newer studies, such is Rotterdam study which included 4385 subjects, where the "independent connection between SUA and the incidence of coronary heart disease and cerebrovascular insult" (*6*) was

established;

Research of this topic was realized under Chicago Health Association on a sample of 7804 persons of both sexes, where the link between level of SUA and cardiovascular morbidity was established (*7*);

An independent connection between SUA and lethality in population was established as well in MONICA study (sample of 1044 males in age group of 45 – 64 years) (*8*).

Hyperuricemia occurs at concentration of uric acid of 416 mmol/L. At concentration below the said value, uric acid is released from monosodium urate, and above this concentration the formation of precipitate crystals was observed. There are authors that consider the normal values of uric acid to be its values of 458 mmol/L for male and 392 mmol/L for female. (*9*)

It is also known that the increase of uric acid production can be the effect of increased nucleoprotein degradation, excessive intake of purines with food or excessive synthesis of uric acid as a consequence of rare enzyme mutation defect (*10*).

Since the concentration of serum uric acid is a risk factor of genesis of certain diseases, including those most difficult, with which we deal here, it is of utmost medical importance to putt it under effective control.

In this pharmacological-clinical study the primary objective pertained to the analysis of uric acid values and lipid status in patients on therapy with allopurinol, starting from its primary values, i.e. before the start of therapy, as control values (each patient is his/her own control). The therapeutic effects of allopurinol (daily dose of 100 mg) on values of triglycerides, cholesterol and LDL and HDL fractions were monitored during three months and six months of treatment of hyperuricemic patients with the additional diagnosis of metabolic syndrome and pronounced cardiovascular diseases and diagnosed hypertension.

The eventual change of atherogenic index was also monitored.

2. STUDY SAMPLE AND METHODS

Our research encompassed 40 clinically treated patients of both sexes and belonging to different age groups, divided according to the diagnose of disease in several subgroups. All patients were diagnosed with hyperuricemia, hospitalized in MKC Sarajevo and JU Opšta bolnica (General Hospital) "Abdulah Nakaš" in Sarajevo (2010 – 2013.). Inclusion criteria for patient acceptance in this analysis were as follows: hyperuricemia verified by medical doctor based on laboratory diagnostics; availability of treatment data including eventual complications; availability of indicators of sex and age determination and anamnestic data.

During the study the following methods were used: explicative, assay analysis, statistical and comparative methods.

All clinical measurements were carried out by using standard IFCC methods on suitable biochemical analyzers.

	Before treatment			After 3 months			After 3 months		
	X	SD	SEM	X	SD	SEM	X	SD	SEM
Uric acid	499.40	54.87	24.54	447.60	123.51	55.23	396.00	66.07	29.54
	P<0.05								
Triglycerides	1.35	0.89	0.40	1.42	0.65	0.29	1.73	0.91	0.40
	P<0.05								
Cholesterol	3.42	1.57	0.78	4.04	1.59	0.71	4.87	1.51	0.67
	P<0.05								
HDL	0.60	0.07	0.01	2.16	1.86	1.07	2.07	1.83	0.91
	P<0.05								
LDL	1.38	0.19	0.13	2.16	1.15	0.66	3.39	0.68	0.34
	P<0.05								

Table 1. Average values of uric acid and lipid fractions during the treatment of subjects with metabolic syndrome (pronounced heart problems)

Subjects with metabolic syndrome (heart patients)	Before treatment	3.06	1.35	0.60	p=0.031
	After three months of treatment	5.00	1.97	0.88	
	After six months of treatment	4.95	0.88	0.39	

Table 2. Analysis of average values of atherogenic index with regard to the established diagnosis of subjects on allopurinol therapy during test period

3. RESULTS

Out of total of 40 subjects on allopurinol therapy, 60% were males, and 40% were females. Four patients were below 40 years of age, one 41-50, four 51-60, eight 61-70 and 23 patients were above 70 years of age. Chi-squared test showed no statistically significant difference in sex structure of the subjects included in this study, χ^2=1.6; DF=1; p=0.205.

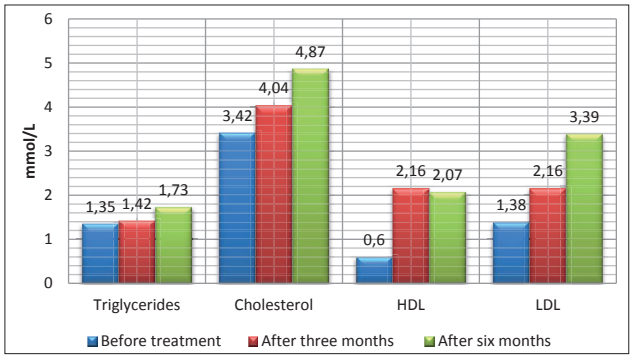

Figure 1. Average values of uric acid and lipid fractions during the treatment of subjects with heart diseases

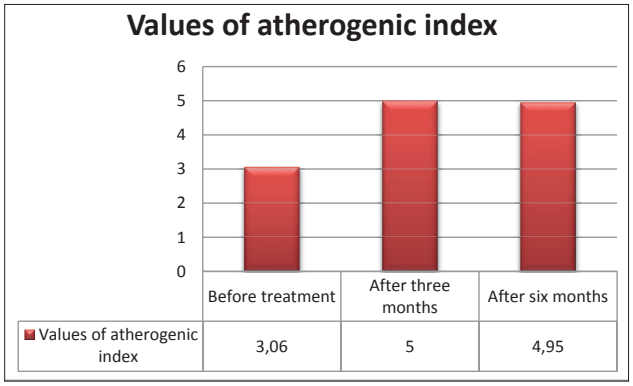

Figure 2. Analysis of average values of atherogenic index with regards to the established diagnosis of subjects on allopurinol therapy during the test period

By analysis of average values of uric acid before and after three months and six months of treatment, it was established that the average value of uric acid in subjects before the treatment was 523.45 mmol/L, after three months of allopurinol use 433.25 mmol/L, and after six months of treatment it was 435.77 mmol/L. This indicates that the uric acid value decreased for 90.2 mmol/L and was within the reference values. There was no statistically significant difference in average values of uric acid after three and six months of treatment ($p = 0.936$), implying that the desired effects of therapy were achieved.

As can be seen from *Table 1* and *Figure 1*, the average values of uric acid in tested patients decreased significantly after three and six months of allopurinol therapy, while the values of triglycerides, cholesterol and LDL fractions statistically significantly increased ($p > 0.05$). The values of HDL fractions increased after three months of therapy, while later their value stayed constant.

Graphical depiction of the afore-mentioned indicators:

In subjects with metabolic syndrome (pronounced heart diseases) the atherogenic index increased statistically significantly after three and six months of therapy and was at lower limit of reference values, which can be seen in *Table 2,* as well as Figure *2*:

4. DISCUSSION

It is evident from the presented indicators that during the allopurinol therapy of the subjects with metabolic syndrome (pronounced heart problems) there was statistically significant decrease of average values of uric acid, but the values of triglycerides, cholesterol and LDL-fractions increased statistically significantly ($p > 0.05$), while the value of HDL fraction increased after three months of treatment, but afterwards, during the next three months, remained constant.

Atherogenic index in subjects with metabolic syndrome (pronounced heart diseases) statistically significantly increased after three and six months of therapy, even though it remained at the upper limit of reference values. Due to these findings, it is advisable, along the control of uric acid values, to monitor the values of the available fractions of lipid profile, as well as the value of atherogenic index, due to the fact that these are patients with pronounced risk factors for development of KV incidents, thus keeping them inside tolerable limits.

5. CONCLUSION

By evaluation of efficacy of allopurinol on the values of lipid profile fractions in hyperuricemic patients treated on three and six months regime, it was established that the average value of uric acid statistically significantly differed from the reference values before the start of the allopurinol treatment of patients ($p = 0{,}04$). After three months and six months of therapy the value of uric acid decreased and was at the upper tolerable limit of reference values. Since no statistically significant differences in average values of uric acid were established after the third to sixth months of treatment, it could be concluded that the desirable effects regarding the decrease in SUA were achieved.

With allopurinol therapy of the subjects with metabolic syndrome and pronounced heart diseases, the average value of uric acid statistically significantly decreased, but the values of triglycerides, cholesterol and LDL fraction statistically significantly increased ($p > 0.05$). The value of HDL fraction increased after three months of therapy, and afterwards during the next three months of therapy remained constant.

Atherogenic index statistically significantly increased after three and six months of therapy, even though it remained at the upper limit of reference values.

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