Comparison of the Effects of Allopurinol and Febuxostat on the Values of Triglycerides in Hyperuricemic Patients

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ABSTRACT

Introduction: Hyperuricemia is an independent risk factor for the development of many diseases. Aim: The aim of this paper is to compare the effects of allopurinol and febuxostat on the values of triglycerides and uric acid in hyperuricemic patients. Methods: This was a pharmacological-clinical retrospective-prospective study. The research sample comprised 50 examinees of both genders and different ages who were undergoing allopurinol (100 mg/day) or febuxostat (80 mg/day) therapy. Statistical Product and Service Solutions (SPSS) Software and Microsoft Excel were used for statistical analysis. Results: Examinees who were treated with allopurinol had a statistically significant decrease in uric acid concentrations (by 126.28 ± 20.36 µmol/l) at the end of the observation compared to the initial values (p = 0.006). Examinees who were treated with febuxostat had a statistically significant decrease in uric acid concentrations (by 252.80 ± 94.17 µmol/l) at the end of the observation compared to the initial values (p = 0.001). The initial value of triglycerides was 1.58 ± 0.64 mmol/l in allopurinol-treated examinees, and 1.60 ± 0.52 mmol/l in febuxostat-treated examinees. After three and six months of allopurinol use, there was a statistically significant increase in triglyceride values (p = 0.046 and p = 0.042, respectively). A statistically significant decrease in triglyceride values (by 0.16 ± 0.10 mmol/l) was noted after three months of febuxostat use (p = 0.012). Conclusion: The results of this research confirmed the previous findings and pointed out the positive pharmacological effects of allopurinol and febuxostat.

Keywords: hyperuricemia, allopurinol, febuxostat, uric acid, triglycerides.

1. INTRODUCTION

Serum uric acid concentration as a potential marker of cerebrovascular, cardiovascular and diseases such as arthritis and nephrolithiasis, and its association with metabolic syndrome, has been in the focus of medical research for 50 years (1-4). Hyperuricemia occurs when serum uric acid concentration is 416 µmol/l or above (4). Hyperuricemic patients are often diagnosed with hyperlipidemia. Correlation between serum urate and lipid values is interesting, but the results of some studies regarding this are contradictory. Certain studies have shown a significant link between serum lipid values and hyperuricemia in the examinees with metabolic syndrome, with triglycerides, total cholesterol and high-density lipoprotein (HDL) being positively and low-density lipoprotein (LDL) negatively correlated with hyperuricemia (5-9). Some studies on animal models have shown a significant link between serum uric acid and triglyceride values (10, 11). Heimbach and associates showed that drug-altered uric acid values were poorly correlated with triglyceride and LDL values (12). Results of many studies have suggested that allopurinol and febuxostat have undoubted efficacy in the treatment of hyperuricemia and gout (13-16). Target serum uric acid value can be achieved in 22% of the allopurinol-treated examinees (300 mg/day) and 48% of the febuxostat-treated examinees (80 mg/day) (17). Zhang and associates studied the effects of allopurinol and febuxostat on serum lipid values in the examinees with gout. There was no significant difference regarding this before and after the allopurinol treatment, while there was a significant decrease in total cholesterol, triglyceride and LDL values, and a significant increase in HDL values after the febuxostat treatment (18).
2. AIM

The aim of this paper is to compare the effects of the conventional therapy of hyperuricemia (allopurinol) and its novel therapy (febuxostat) on the values of triglycerides and uric acid in hyperuricemic patients.

3. MATERIALS AND METHODS

This was a pharmacological-clinical retrospective-prospective study. Materials were collected at the clinical center, general hospital, family medicine units, and pharmacies. The research sample comprised 50 examinees of both genders and different ages who were undergoing allopurinol or febuxostat therapy. Twenty-five of them (group I) were taking allopurinol (100 mg/day), and the other 25 (group II) were taking febuxostat (80 mg/day).

The inclusion criteria were:

- Verification of hyperuricemia diagnosis by a physician, based on laboratory diagnostics;
- Data availability regarding treatment and its possible complications;
- Availability of indicators by gender and age, and anamnestic data.

Uric acid and triglyceride values were analyzed in serum samples, at the beginning (first measurement), and after three (second measurement) and six (third measurement) months of drug use. Statistical Product and Service Solutions (SPSS) Software for Windows (version 20.0, SPSS Inc., Chicago, Illinois, the United States of America) and Microsoft Excel (version 13, Microsoft Corporation, Redmond, Washington, the United States of America) were used for statistical analysis. Alpha (significance) level was 0.05.

4. RESULTS

In both groups, there were 14 (56%) male and 11 (44%) female examinees. Chi-squared test ($\chi^2$-test) did not reveal a statistically significant difference in the gender-structure of the examinees between the experimental groups ($\chi^2 = 0.011; p = 0.609$).

The average age of the examinees was $70.84 \pm 14.51$ years (from 37 to 88) in group I, and $71.84 \pm 11.77$ years (from 38 to 84) in group II. Using Analysis of variance (ANOVA), no statistically significant difference was observed in the average age of the examinees between the experimental groups ($F = 0.072; p = 0.790$).

With the diagnosis of gout, there were 15 (60%) examinees in group I, and 18 (72%) in group II. Gout associated with metabolic syndrome was diagnosed in ten (40%) examinees in group I, and seven (28%) in group II. Using $\chi^2$-test, no statistically significant difference was found regarding the established clinical diagnoses between the experimental groups ($\chi^2 = 0.786; p = 0.276$).

### Analysis of Uric Acid and Triglyceride Values in the Examinees Undergoing Allopurinol Therapy

In Table 1, the initial values of uric acid and triglycerides in the examinees who were taking allopurinol, as well as their values after three and six months of drug use are presented. After the second measurement, a statistically significant decrease in uric acid value was found ($p = 0.015$), as well as a statistically significant increase in triglyceride value ($p = 0.046$). There was no statistically significant difference in uric acid and triglyceride values between the second and the third measurement ($p = 0.344$ and $p = 0.301$, respectively). At the end of the observation, a decrease in uric acid value was statistically significant ($p = 0.006$), as well as an increase in triglyceride value ($p = 0.042$).

### Analysis of Uric Acid and Triglyceride Values in the Examinees Undergoing Febuxostat Therapy

In Table 2, the initial values of uric acid and triglycerides in the examinees who were taking febuxostat, as well as their values after three and six months of drug use are presented. After the second measurement, a statistically significant decrease in uric acid and triglyceride values was found ($p = 0.001$ and $p = 0.012$, respectively). There was no statistically significant difference in uric acid and triglyceride values between the second and the third measurement ($p = 0.089$ and $p = 0.212$, respectively). At the end of the observation, a decrease in uric acid value was statistically significant ($p = 0.001$), but not in triglyceride value ($p = 0.542$).

### Table 1. Average values of uric acid and triglycerides in the examinees treated with allopurinol. $X$ – arithmetic mean; $SD$ – standard deviation

| Observation period | Uric acid | Triglycerides |
|--------------------|-----------|---------------|
|                    | $X^a$ (µmol/l) | SD$^b$ (µmol/l) | $X^a$ (mmol/l) | SD$^b$ (mmol/l) |
| From the beginning to 3rd month | 522.60 | 147.99 | 1.58 | 0.64 |
| From 3rd month to 6th month | 430.48 | 201.25 | 1.77 | 0.70 |
| From the beginning to 6th month | 396.32 | 138.97 | 1.92 | 1.04 |

| Observation period | Uric acid | Triglycerides |
|--------------------|-----------|---------------|
|                    | $X^a$ (µmol/l) | SD$^b$ (µmol/l) | t | p value |
|                    | $X^a$ (mmol/l) | SD$^b$ (mmol/l) | t | p value |
| From the beginning to 3rd month | 92.12 | 17.29 | 2.628 | 0.015 | -0.19 | 0.16 | -2.091 | 0.046 |
| From 3rd month to 6th month | 34.16 | 17.82 | 0.966 | 0.344 | -0.14 | 0.07 | -1.055 | 0.301 |
| From the beginning to 6th month | 126.28 | 20.36 | 3.016 | 0.006 | -0.33 | 0.27 | -2.935 | 0.042 |

Table 1. Average values of uric acid and triglycerides in the examinees treated with allopurinol. $X$ – arithmetic mean; $SD$ – standard deviation
Comparison of the Effects of Allopurinol and Febuxostat on the Values of Triglycerides in Hyperuricemic Patients

At the end of the observation, an increase in triglyceride values was noted, but no statistically significant difference was determined between male and female examinees who were undergoing allopurinol or febuxostat therapy (p = 0.836 and p = 0.840, respectively). At the beginning of the observation, a decrease in uric acid values was noted, but no statistically significant difference was determined (p = 0.065), the mean value of uric acid was 396.32 ± 138.97 µmol/l in group I, and 324.24 ± 45.77 µmol/l in group II (Figure 1).

The initial value of triglycerides was 1.58 ± 0.64 mmol/l in group I, and 1.60 ± 0.52 mmol/l in group II. After conducting ANOVA test, no statistically significant difference was determined (p = 0.903). After the second measurement, a statistically significant difference was determined between male and female examinees who were undergoing allopurinol therapy (p = 0.125).

Comparison of Uric Acid and Triglyceride Values with Regard to the Experimental Groups

The initial value of uric acid was 522.60 ± 147.99 µmol/l in group I, and 577.04 ± 120.25 µmol/l in group II. After conducting ANOVA test, no statistically significant difference was determined (p = 0.160). After the second measurement, a statistically significant difference was determined (p = 0.031), the mean value of uric acid was 340.48 ± 201.25 µmol/l in group I, and 338.12 ± 50.40 µmol/l in group II. At the end of the observation, a statistically significant difference was determined (p = 0.017), the mean value of uric acid was 396.32 ± 138.97 µmol/l in group I, and 324.24 ± 45.77 µmol/l in group II (Figure 1).

The mean value of triglycerides was 1.58 ± 0.64 mmol/l in group I, and 1.60 ± 0.52 mmol/l in group II. After conducting ANOVA test, no statistically significant difference was determined (p = 0.903). After the second measurement, no statistically significant difference was determined (p = 0.065), the mean value of triglycerides was 1.77 ± 0.70 mmol/l in group I, and 1.43 ± 0.56 mmol/l in group II. At the end of the observation, no statistically significant difference was determined (p = 0.123), the mean value of triglycerides was 1.92 ± 1.04 mmol/l in group I, and 1.54 ± 0.59 mmol/l in group II (Figure 2).

Comparison of Uric Acid and Triglyceride Values with Regard to the Gender-Structure of the Examinees

The mean value of uric acid at the beginning of the observation in both groups showed no statistically significant difference with regard to the gender-structure of the examinees (p = 0.090 and p = 0.710, respectively). At the end of the observation, a decrease in uric acid values was noted, but no statistically significant difference was determined between male and female examinees who were undergoing allopurinol or febuxostat therapy (p = 0.836 and p = 0.840, respectively).

The mean value of triglycerides at the beginning of the observation in both groups showed no statistically significant difference with regard to the gender-structure of the examinees (p = 0.692 and p = 0.694, respectively). At the end of the observation, an increase in triglyceride values was noted, but no statistically significant difference was determined between male and female examinees who were undergoing allopurinol or febuxostat therapy (p = 0.017), whereas a decrease in female examinees and an increase in male examinees in triglyceride values were noted, but no statistically significant difference was determined between male and female examinees who were undergoing febuxostat therapy (p = 0.125).

Comparison of Uric Acid and Triglyceride Values with Regard to the Established Clinical Diagnoses

No statistically significant difference was noted in uric acid values in the examinees with the diagnosis of only gout and both gout and metabolic syndrome in both groups at the beginning and at the end of the observation. At the beginning of the observation, the examinees diagnosed with gout and treated with allopurinol...
Comparison of the Effects of Allopurinol and Febuxostat on the Values of Triglycerides in Hyperuricemic Patients

5. DISCUSSION

The examinees diagnosed with gout and metabolic syndrome showed significantly lower triglyceride values compared to the examinees diagnosed with gout and metabolic syndrome and treated with allopurinol (p = 0.042), but at the end of the observation, there was no statistically significant difference in triglyceride values (p = 0.364). The examinees diagnosed with gout and metabolic syndrome and treated with febuxostat showed significantly higher triglyceride values compared to the examinees diagnosed with gout and treated with febuxostat at the beginning and at the end of the observation (p = 0.001 and p = 0.003, respectively) (Table 3).

6. CONCLUSION

Allopurinol and febuxostat both cause a significant decrease in uric acid values in hyperuricemic patients after three and six months of therapy. This decrease is greater with febuxostat, indicating its better efficacy. A significant increase in triglyceride values is noted after three and six months of allopurinol use, whereas allopurinol and benzbromarone modestly decreased triglyceride values, but cholesterol values remained unaffected.

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