

NEFROPROTECTIVE PROPERTIES OF FEBUXOSTAT IN CHRONIC RENAL FAILURE

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Abstract

Urgency. Chronic renal failure poses medical, social and organizational problem because of high mortality, disability and complexity of modern treating methods technical support. **The objective:** to evaluate the effectiveness of febuxostat in controlling hyperuricemia in patients with end-stage chronic renal failure. **Material and methods.** 90 patients were divided into three groups in accordance with the use of febuxostat at a dose of 40 mg to reduce uric acid level: group 1 (n=30) - terminal chronic renal failure patients who are not yet receiving renal replacement therapy; Group 2 (n=30) peritoneal dialysis patients; 3 group (n=30)- hemodialysis patients. **Results and discussion.** Febuxostat use led to uric acid level decrease in all groups under study, increase of the functional renal reserve level in the 1st and 2nd groups. In the 3rd group patients (hemodialysis patients), only uric acid level changes were studied in connection with the absence of in this cohort residual functional renal reserve. The use of febuxostat determines, with decrease in uric acid levels, increase in the residual functional renal reserve and improvement the patients' quality of life according to the questionnaire data. These results are best reflected in pre-dialysis patients with terminal chronic renal failure. **Conclusion:** treatment with febuxostat leads to a marked decrease in the level of serum uric acid, increase of residual functional renal reserve and improvement of chronic renal failure patients quality of life, which indicates its good nephroprotective properties.

Key words: terminal renal failure; hyperuricemia; nephroprotective therapy; febuxostat.

Urgency of the problem. Chronic renal failure (CRF) is a symptom complex caused by a sharp decrease in the number and function of nephrons, which leads to impaired kidneys' excretory and incretory function, homeostasis, metabolic disorders on all types, acid-base balance, activity of all organs and systems.

The problem of CRF from medical, social and organizational point of view is associated with high lethality, disability and complexity on this pathology treatment including its technical support.

Currently, there is no doubt that CRF is the inevitable and natural result of virtually all, with rare exceptions, nephropathy, regardless of their nature. At the same time, the spectrum of chronic kidney diseases in the last decades has significantly expanded, which is explained, first of all, by general population aging and increase of hypertension, diabetes and atherosclerosis morbidity rate with simultaneous increase of vascular renal lesions. As a result, in recent years there has been a widespread tendency for a steady increase in the number of CRF patients.

Numerous epidemiological studies suggest the relationship between CRF and asymptomatic hyperuricemia. With that evidences appear that increased uric acid level is a cause of kidney damage. Currently available optimistic data on the effectiveness of medication correction of hyperuricemia at various stages of CRF are based primarily on long-term administration of xanthine oxidase inhibitors (allopurinol, febuxostat) and allow one to consider urate-reducing therapy as potential nephroprotective one. At the same time, further studies are needed to confirm this.

The objective: To evaluate the efficacy of febuxostat in the control of hyperuricemia in CRF patients.

Material and methods. 90 patients were divided into three groups (n=30) according to the use of febuxostat to reduce uric acid:

- I – CRF patients who have not received renal replacement therapy;
- II - patients who were on peritoneal dialysis;
- III – hemodialysis patients.

Clinical and laboratory (blood chemistry, determination of glomerular filtration rate (GFR), residual functional renal reserve - RFRR), instrumental (blood pressure), statistical methods were used as well as quality of life questionnaire.

Results and their discussion. The dependence of uricemia and RFRR under the influence of febuxostat at a dose of 40 mg were analyzed as well as the subjective assessment of CRF patients quality of life.

Febuxostat is a non-purine, selective inhibitor of xanthine oxidoreductase isoforms, it is an alternative to the limited number of drugs used to reduce urate levels in recent decades. The inhibition of xanthine oxidoreductase by febuxostat is more potent and effective than allopurinol, as evidenced by the more frequent achievement of the target urate level in serum, especially in patients with a high concentration of urate. Unlike allopurinol, the pharmacokinetic properties of febuxostat are not significantly dependent on renal clearance, which is important for patients with chronic kidney disease. Also important is that elderly patients do not require a dose adjustment of the drug [1].

The studies done have shown the following.

If before the use of febuxostat in the Ist (pre-dialysis) group the levels of uric acid and functional renal reserve were (291.5 ± 16.07) and (-94.4 ± 0.96) , then after the use of the drug they decreased and amounted to (210.2 ± 4.15) and (-84.8 ± 1.9) , respectively. One-way ANOVA – test revealed an inverse relationship between uric acid level and residual functional renal reserve (Fig. 1, 2).

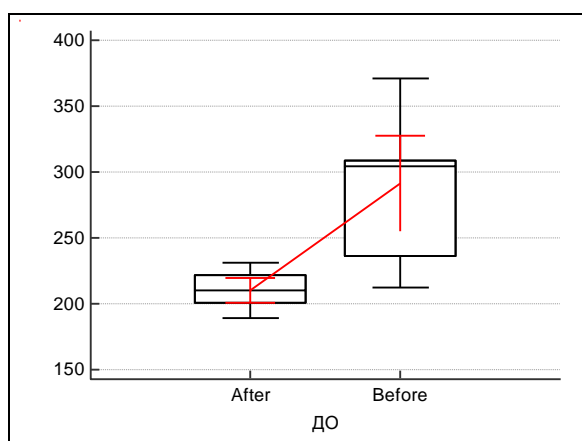


Fig. 1 The result of one-way analysis of variance of uric acid of blood to dialysis in graphical expression

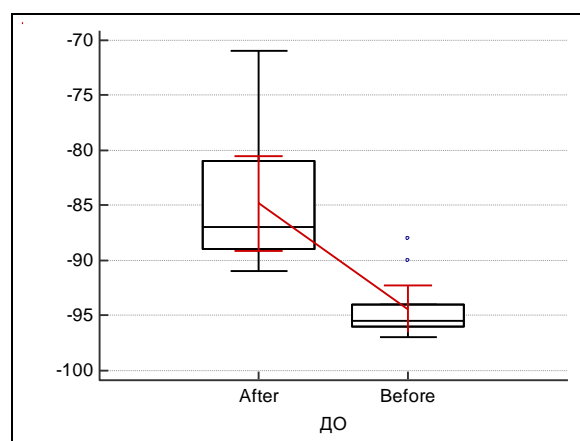


Fig. 2. The result of one-factor analysis of variance of functional renal reserve for dialysis in graphical expression

Improvement of the parameters mentioned above could not but lead to a change in the 1st group of patients' quality of life. The indexes did improve and equaled 123.4 ± 4.99 after the use of febuxostat against 127.05 ± 4.82 , the same was reflected in the questionnaires. The

results of the one-way ANOVA analysis of the 1st group patients quality of life are shown in Fig. 3:

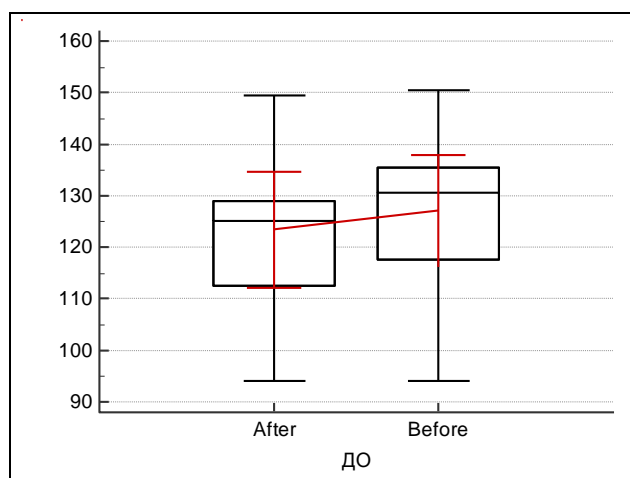


Fig. 3. The result of one-way ANOVA-test analysis of the quality of life assessment in pre-dialysis patients in graphical terms

Thus, the efficacy of febuxostat use in the group of CRF patients who have not yet used renal replacement therapy was proved (Fig. 4).

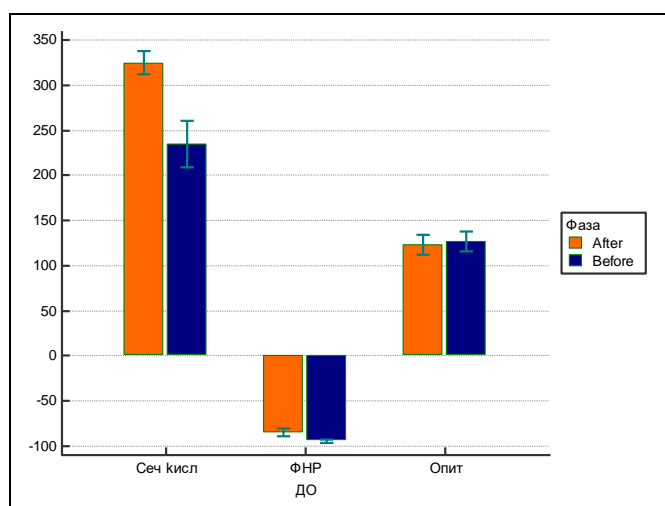


Fig. 4. Evaluation of the effectiveness of febuxostat use before to dialysis in graphical terms

After febuxostat's use in th 2nd group (patients who obtained peritoneal dialysis), level of uric acid and functional renal reserve also decreased and constituted 289.7 ± 15.98 and -92.1 ± 1.5 against 497.0 ± 18.77) and -93.6 ± 1.11 , respectively.

The inverse proportion between the level of uric acid and residual functional renal reserve was established by one-way ANOVA – test (Figs. 5, 6).

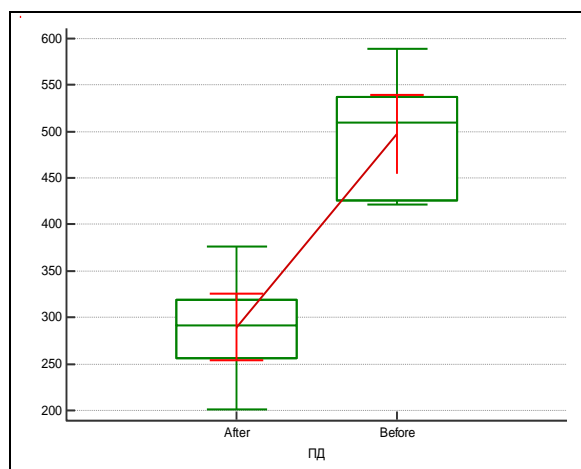


Fig. 5. Result of one-way ANOVA-test of blood uric acid at peritoneal dialysis in graphical expression

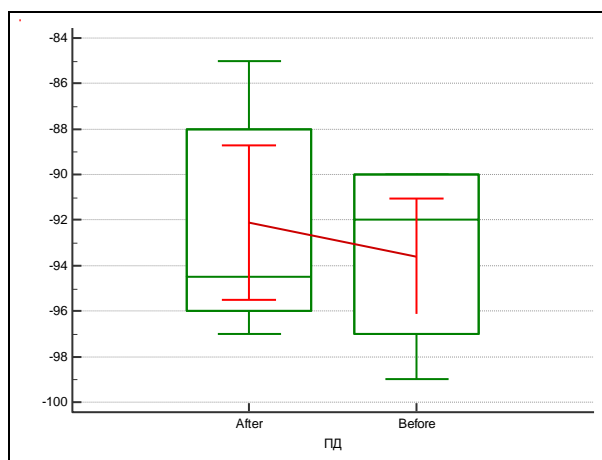


Fig. 6. The result of one-way ANOVA-test of functional renal reserve in peritoneal dialysis in graphical terms

This group patients survey also showed an increase in the quality of life: 99.7 ± 6.92 versus 101.85 ± 7.65 which was proved by one-way ANOVA –test data (Fig. 7).

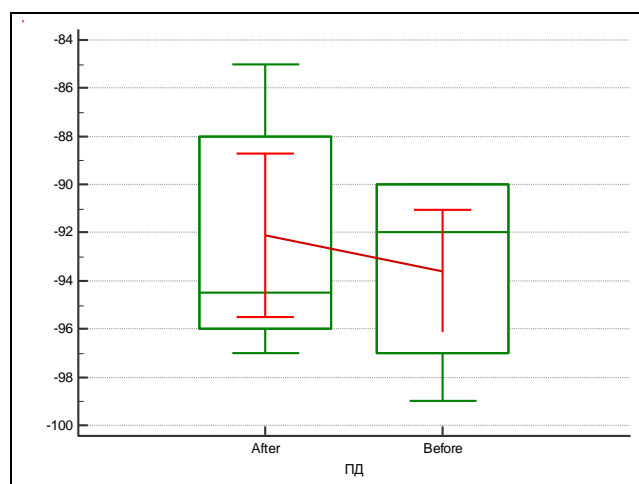


Fig. 7. The result of one-way ANOVA-test of quality of life assessment in peritoneal dialysis patients in graphical terms

Thus, febuxostat use in combination with peritoneal dialysis has led to the patients' improvement quality of life (Fig. 8).

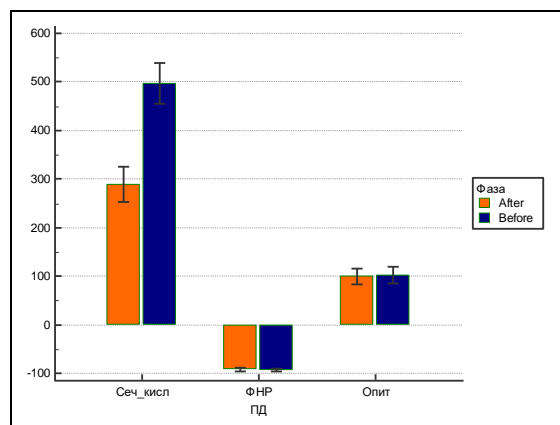


Fig. 8. Evaluation of the efficacy of febuxostat use in PD in graphical terms

In the 3rd group patients who were on hemodialysis, only changes of uric acid changes have been analyzed. Residual functional renal reserve was not investigated in this cohort. The researches made have shown its significant decrease after febuxostat use from 324.5 ± 5.78 to 234.9 ± 11.4 .

The inverse proportionality between the levels of uric acid was also established by one-way ANOVA - test (Fig. 9).

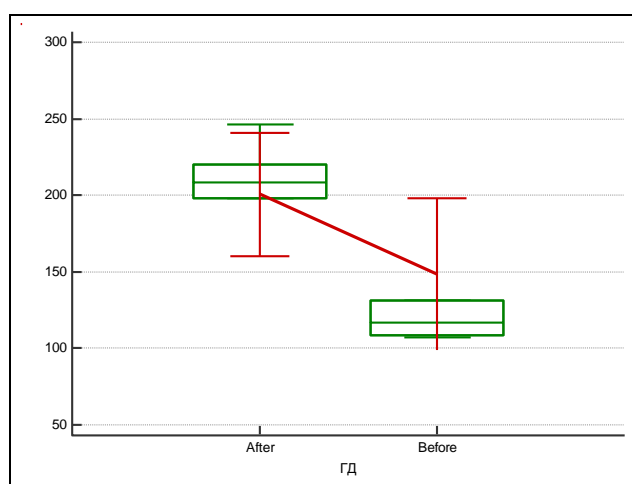


Fig. 9. The result of one-way ANOVA-test of blood uric acid levels at hemodialysis in graphical terms

According to the data of questionnaire's analysis reduction of uric acid levels contributed to the improvement of quality of life in hemodialysis patients from $111,1 \pm 3,81$

to $114,5 \pm 3,16$ and that was reflected in the graphical expression of the results of the one-way ANOVA-test (Fig. 10).

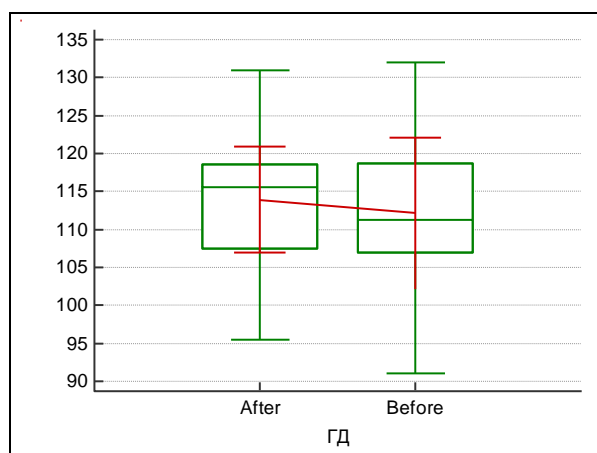


Fig. 10. The result of one-way ANOVA-test of variance in quality of life in hemodialysis patients in graphical terms

Thus, with uric acid levels decrease, residual functional renal reserve increases, the patients' quality of life improves according to the questionnaire's data, and this is best reflected in pre-dialysis patients with CRF.

The studies made allowed us to conclude that the treatment with febuxostat leads to a marked decrease in serum uric acid level, increase of residual functional renal reserve level and improvement of the quality of life in patients with chronic renal failure, which indicates febuxostat's good nephroprotective properties.

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