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Effect of Flavanoids on Kidney Function in Patients with Chronic Kidney Disease before Dialysis

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Abstract Chronic renal failure is a disease resulting in severe uremic intoxication. In this study, the hypoazotemic efficacy of the domestically produced flavanoid Nephrocizine in patients with chronic kidney disease was studied. The results show, that in the group of patients who took the drug Nephrocizine provided a significant decrease in the levels of urea, creatinine and an increase in the glomerular filtration rate unlike the control group.

Keywords Chronic kidney disease, Glomerular filtration rates, Flavanoids, Nephrocizine

1. Introduction

Improving the quality of life and overall survival of patients with chronic renal failure (CRF), the prevalence of which is steadily increasing in the world, are the urgent problems of modern nephrology [1,2]. According to the results of epidemiological studies, patients with a glomerular filtration rate (GFR) less than 60 ml / min constitute 5% of the total adult population in the world [9,10,11].

The increase in the prevalence of CRF is explained not only by an increase in the number of patients with primary renal pathology, but also by diabetes mellitus, obesity, aging (long life expectancy) and damage to individual renal vessels [4,5,6]. Kidney disease is more severe when multiple risk factors are present. Over the past 15-20 years, the number of patients receiving renal replacement therapy has increased more than 4-5 times [7,8].

In the early stages of the occurring of renal failure, there are no symptoms of renal dysfunction. A further decrease in the loss of functioning nephrons (up to 30% of the norm) leads to a more expressed impairment of renal function - an increase in the concentration of nitrogen metabolites (urea, creatinine), electrolyte imbalance, anemia, and so on. [12,13].

From the literature it can be seen that in cases of hyperazotemia, bioflavonoids made from plant materials are effective drugs, of which flavonoids are the drugs of choice for complex use in the treatment of renal failure (the most widely used) [6,7]. Nephrocizine, a drug belonging to the group of flavonoids, was developed as a substance at the Institute of Plant Chemistry of the Republic of Uzbekistan (reg No. 2 of 12.06.2009). The most valuable property of flavonoids is their excretion of urea and other nitrogenous products from the blood, which is extremely important for chronic kidney diseases of various etiologies. Thus, we considered it necessary to monitor the effect of Nephrocizine on renal function parameters and evaluate its hypoazotemic efficacy for the complex treatment of CKD patients in the pre-dialysis period.

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2. Purpose of the Research

The purpose of the research is to study the effect of Nephrocizine on renal function indicators and evaluate its hypoazotemic efficacy in patients with chronic kidney disease in pre-dialysis stage.

3. Materials and Methods

For the study, 123 patients were selected with CKD with of nephropathy of various origins (GFR 15-59 ml / min / m2), who were treated at the Department of Nephrology of the Tashkent Medical Academy. The age of the patients ranged from 19 to 50 years (averagely 38.63 ± 1.09). The duration of the disease ranged from 5 to 10 years, with an average of 7.8 ± 2.3 years. All patients were randomly divided into 4 groups: 1 A (n-32), 1 B (n-31) (GFR 30 - 59 ml / min) and 2 A (n-30), 2 B (n-30) (GFR 15 - 29 ml / min): group 1 A and 2 A of the patient received traditional treatment in accordance with the recommendations of international standards; group 1 B and 2 B patients, in addition to traditional treatment in accordance with international treatment standards, received Nephrocizine at a dose of 300 mg / day (50 mg in a tablet, 1 tablets 2 times a day, for 3 months). At the time of inclusion in the study, all patients had a documented diagnosis of stage

III or IV CKD based on the eGFR determined from the serum creatinine concentration using the CKD-EPI formulas (2009) modified in 2011 (an on-line calculator was used on the website http://nefrosovet.ru/). At the beginning of treatment, after 10 days, after 1 and 3 months, all patients were determined by the level of urea and creatinine, as well as GFR. The results were statistically analyzed.

Table 1. The state of renal function in patients with stage 3 of CKD

Parameters	Control group (n = 20)	Before treatment	Group 1 A (n-31)			Group 1 B (n-32)		
			After 10 days	After 30 days	After 90 days	After 10 days	After 30 days	Across 90 days
urea mmol / l	6.8 ± 0.13	11.4 ± 0.288 ***	10.6 ± 0.30 ***	10.1 ± 0.24 *** ^^^	13.6 ± 0.411 *** ^^^	10.5 ± 0.25 *** ^	9.8 ± 0.20 *** ^^^	9.4 ± 0.135 *** ^^^
creatinine µmol / l	71.6 ± 1.53	191.1 ± 6.47 ***	180.2 ± 8.73 ***	171.3 ± 7.74 ***	198.9 ± 8.98 *** ^^^	179.6 ± 6.88 ***	167.2 ± 5.83 ***	154.7 ± 4.93 ***
GFR ml / min	104 ± 4.82	39.2 ± 0.92 ***	40.9 ± 1.27 ***	42.1 ± 1.26 ***	37.2 ± 1.30 *** ^^^	41.2 ± 1.14 ***	44.3 ± 1.23 *** ^^	47.3 ± 1.68 *** ^^^

Note: * - significant differences relative to the control group (*** - P <0.001); ^ - differences were significant relative to the parameters of the group before treatment (^ - P <0.05, ^^ - P <0.01, ^^^ - P <0.001).

Table 2. Renal function status in patients with stage 4 of CKD

Parameters	Control group (n = 20)	Before treatment	Group 2 A (n-30)			Group 2 B (n-30)		
			After 10 days	After 30 days	After 90 days	After 10 days	After 30 days	Across 90 days
urea mmol / l	6.8 ± 0.13	16.9 ± 0.52 ***	17.8 ± 0.79 ***	15.8 ± 0.54 ***	19.83 ± 0.56 *** ^^^	17.9 ± 0.42 ***	15.0 ± 0.52 *** ^	13.5 ± 0.29 *** ^^^
creatinine µmol / l	71.6 ± 1.53	347.2 ± 12.37 ***	345.7 ± 18.82 ***	338.9 ± 15.75 ***	379.8 ± 14.24 ***	344.2 ± 10.38 ***	336.7 ± 11.2 ***	326.6 ± 10.67 ***
GFR ml / min	104 ± 4.82	21.8 ± 0.59 ***	22.1 ± 0.80 ***	22.9 ± 0.69 ***	17.5 ± 0.31 *** ^^^	22.6 ± 0.72 ***	23.1 ± 0.56 ***	24.6 ± 0.42 *** ^^^

Note: * - significant differences relative to the control group (*** - P <0.001); ^ - differences were significant relative to the parameters of the group before treatment (^ - P <0.05, ^^ - P <0.01, ^^^ - P <0.001).

4. Results and Its Discussion

The state of renal function: in groups 1A and 1B, the urea level averaged 11.4 ± 0.28 before treatment; the level of creatinine increased by an average of 191.1 ± 6.47, GFR decreased to 39.2 ± 9.2 ml / min.

On the 10th day of treatment in patients of group 1A, the urea level averaged 10.6 ± 0.30; creatinine decreased by an average of 180.2 ± 8.73, GFR increased to 40.9 ± 1.27 ml / min. One month after the start of therapy, the urea level in group 1 A was 10.1 ± 0.24; creatinine decreased to 171.3 ± 7.74, GFR was 42.1 ± 1.26, and after three months, urea parameters increased to 16.6 ± 0.41; creatinine increased to 198.9 ± 8.98, GFR decreased to 37.2 ± 1.30 ml / min. In patients in group 1 B, urea on the 10th day of treatment averaged 10.5 ± 0.25; creatinine decreased to an average of 179.6 ± 6.88, while GFR increased to 41.2 ± 1.14. After a month, the urea values were 9.8 ± 0.20; creatinine decreased to 167.2 ± 5.83, GFR increased to 44.3 ± 1.23, three months after the start of treatment, the urea level was 9.4 ± 0.135;

If we consider each indicator in the assessment of renal function, it can be seen that on the tenth day of treatment there was a slight decrease in the level of urea in both groups (A and B). One month after treatment, despite a positive shift, the levels of urea and creatinine were almost the same in both groups. However, after 3 months there was a significant decrease in the level of urea in group 1B receiving Nephrocizine compared with group 1A, a positive change was evident.

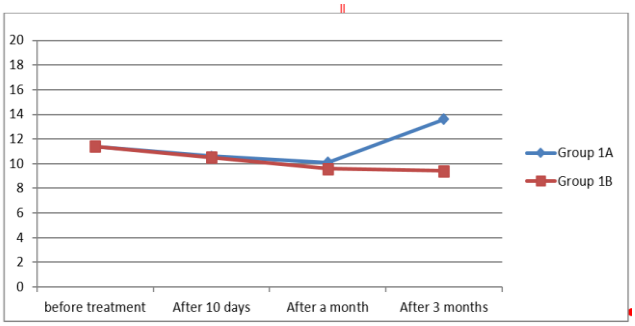

Figure 1. Urea in dynamics

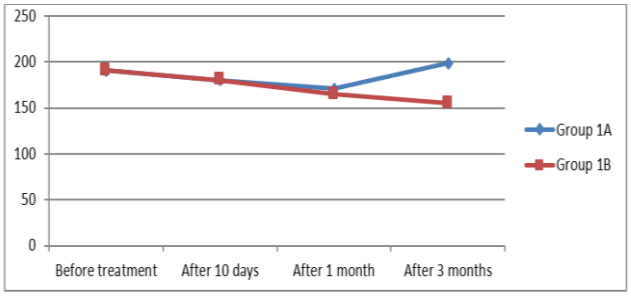

Figure 2. Creatinine in dynamics

On the tenth day of treatment, creatinine levels decreased evenly in both groups (A and B), however, after a month, group 1 B began to lead. After 3 months from the start of therapy, there was a positive shift: the creatinine level in group 1B, who received Nephrocizine, was significantly lower than in group 1A.

If we pay attention to GFR, which is the main indicator in the assessment of renal function, then the positive changes in renal function a month after therapy were at the same level in both groups. However, after 3 months, the positive shift was more pronounced in group 1B, which received Nephrocizine, compared with group 1A. In group 1 A, who did not receive Nephrocizine, GFR was lower than at the beginning of treatment, indicating progression of CKD. Therefore, the effectiveness of treatment in group 1B was significantly higher. This situation can also be seen in the diagram below:

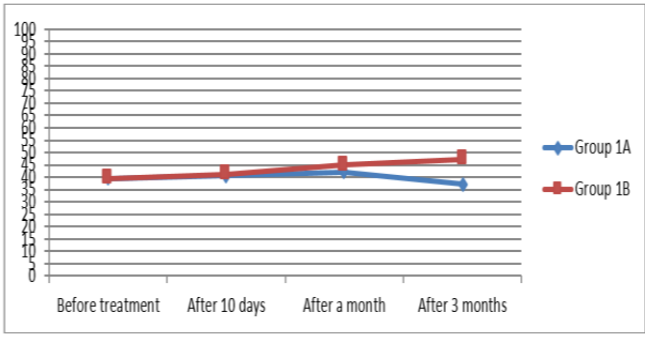

Figure 3. Glomerual filtration rate in dynamics

In the second group, the indicators of renal function before treatment on average were: urea level - 16.9 ± 0.52; creatinine averaged 347.2 ± 12.37, GFR decreased to 21.8 ± 0.59 ml / min.

On the tenth day of treatment in group 2A, urea parameters increased on average to 17.8 ± 0.79; creatinine decreased on average to 345.7 ± 19.31, and GFR slightly increased to 22.1 ± 0.80 ml / min. A month later, in group 2 A, the urea level averaged 15.8 ± 0.54; creatinine decreased on average to 338.9 ± 15.75, and GFR increased to 22.9 ± 0.69 ml / min. Three months later, the urea parameters increased to 19.83 ± 0.561; creatinine increased to 379.8 ± 14.24, and GFR decreased to 17.5 ± 0.31 ml / min. In group 2 B, on the tenth day of treatment, the urea parameters increased to 17.9 ± 0.42; creatinine decreased to 344.2 ± 10.38, GFR was 22.6 ± 0.72 ml / min. After a month from the start of therapy, the urea values were 15.0 ± 0.52; creatinine decreased to 336.7 ± 11.23, GFR increased to 23.1 ± 0.56, and after three months, urea was 13.5 ± 0.293; creatinine decreased to 326.6 ± 10.67, and GFR reached 24.6 ± 0.42 ml / min.

If we look at the indicators that assess renal function, then on the tenth day of treatment in both groups of creatinine and GFR, there was practically no dynamics (A and B). This indicates that as CKD worsens, it becomes more difficult to influence the processes. However, with treatment, there was a significant increase in urea in both groups. This is due to the release of large amounts of urea and other residual nitrogen products into the peripheral blood at the beginning of the treatment process. Although the positive shift in renal function after one month of treatment was almost the same in both groups, the positive shift was more manifested in group 2B, who received Nephrocizine, compared with group 2A after 3 months.

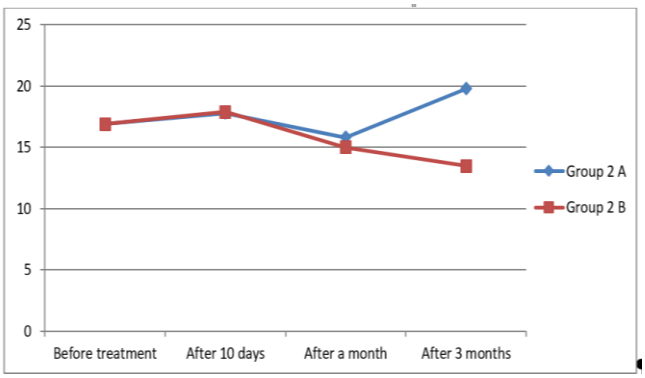

Figure 4. Urea in dynamics

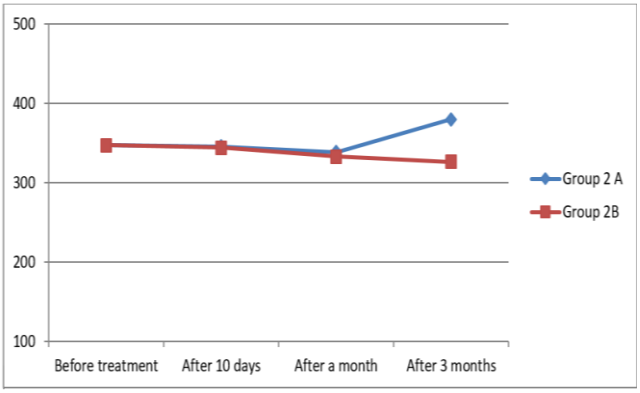

Figure 5. Creatinine in dynamics

GFR, which was the most important criterion or indicator in assessing renal function, also did not change significantly in the first month of treatment. A positive change was observed only in group 2B, which received Nephrocizine, compared with group 2A by the third month. That is, in group 2 B, who received Nephrocizine, the effectiveness of treatment was higher than in group 2 A.

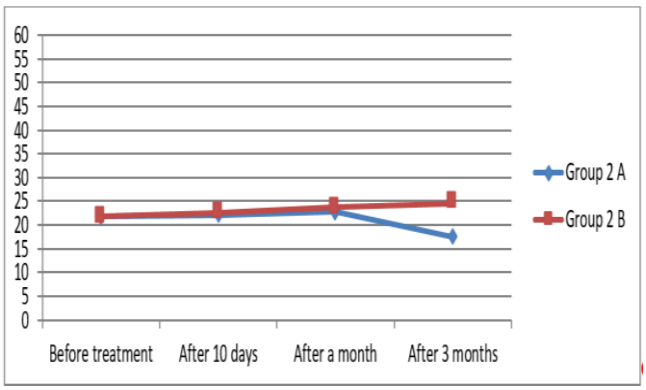

Figure 6. Glomerual filtration rate in dynamics

When comparing CKD stage III and IV groups, the effect of Nephrocizine on the relatively early stages of CKD is observed. In groups "B" with a positive effect, the difference in creatinine and GFR at the beginning and end of treatment was 25.2 μm / l - in group 1 B, 20.6 μm / l - in group 2 B, 8.1 ml / min - in group 1 B, in group 2 B it was equal to 2.8 ml / min.

As this process deepens, the effectiveness of both traditional treatment methods and hypoazotemic drugs decreases. The reason is that as CKD progresses, the number of nephrons, the morphofunctional unit of the kidney, decreases [5]. Like all hypoazotemic drugs, the nephron is a source of Nephrocizine. Thus, in the course of our study, the effectiveness of treatment with hypoazotemic drugs in the relatively early stages of patients with preliminary CKD dialysis is high [3,4]. The main factor that worsens, accelerates and ultimately leads to death is uremic intoxication [3,5,6]. Thus, during the study, we found that the treatment of patients with CKD with Nephrocizine, a hypoazotemic drug that belongs to the bioflavonoid group is the most optimal way to treat the disease, in the pre-dialysis period, as it results of reducing the uremic intoxication.

5. Conclusions

1. In all patients with CKD in the pre-dialysis period, an improvement in renal function and a certain positive shift in treatment are achieved with the use of Nephrocizine.
2. The hypoazotemic effect of Nephrocizine at stage 3 is more effective than at stage 4 CKD.
3. The drug Nephrocizine reduces uremic intoxication and slows down the progression of CKD.

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