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CORRECTION OF CALCIUM METABOLISM DISORDERS USING OSTEOBIOS IN PATIENTS WITH CHRONIC RENAL DISEASE

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SUMMARY

Twenty patients with II-III stage chronic renal failure of different origin took part in a study aimed at the demonstration of therapeutic effectiveness of the complex preparation Osteobios.

The patients included in the verum group had to take Osteobios in dosage of 10 drops 30 minutes before meals three times daily. These patients took also the following antihomotoxic preparations: 1 tablet of Reneel N and 10 drops of Lymphomyosot half an hour before meals three times daily to improve the kidney function. The antihomotoxic therapy lasted one month. The first control group (baseline) included 20 patients affected with chronic renal failure as well, and its composition was similar to that of the verum group according to nosological basis of chronic renal failure, age, sex and creatinine level. The patients from this group did not receive any treatment which could influence calcium and phosphorus metabolism. The second control group consisted of 15 healthy people of similar age and sex. The level of general and ionized calcium, inorganic phosphorus, cholecalciferol, parathyroid hormone and serum alkaline phosphatase activity were determined in all patients. After one month of therapy, significant signs of improvement of the mentioned parameters and reduction of lumbar and muscular pain were observed. It was concluded that Osteobios improves phosphorus and calcium metabolism in patients with uraemia, it is safe and can be applied without phosphate binders in these patients.

KEY WORDS **CHRONIC RENAL DISEASE, CALCIUM, CALCIUM METABOLISM, OSTEOBIOS**

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INTRODUCTION

Though the medical approach of chronic renal failure treatment has been constantly improving during the last years, the incidence of this pathology has not decreased.

The conventional factors that enhance chronic glomerulonephritis development are hypertension, immune function disorders, and lipid metabolism disorders, proteinuria and infectious diseases [1, 2].

The influence of mineral metabolism disorders on chronic renal failure is not enough studied. It is known that electrolyte alterations represent the main reason of renal osteodystrophy in chronic renal failure. They also favour the development of cardiovascular failure [1-5]. In general, phosphorus and calcium metabolism disorders during the pre-dialysis period are characterised by secondary hyperthyroidism in 77,8 % of patients. In 13,8 % of the cases a normal or reduced secretion of parathyroid hormone (PTH) was observed, as well as relevant disorders of phosphorus and calcium metabolism, while these disorders were not detected in 10,5 % of patients [3].

There is evidence that tubular and interstitial disorders occur at early stages of chronic renal failure, and sometimes precede glomerular damage; this is one of the major factors leading to the development of the disease [1,2,3].

Just in tubular and interstitial structures cholecalciferol (D3) - the major factor of calcium metabolism - is synthesized.

Cholecalciferol performs different hormonal functions, it takes part in hyperplasia, cell differentiation, cell proliferation, and immune function [4, 5].

In recent studies cholecalciferol and its active hydroxilated form were found out in patients affected from renal failure [3].

It is important to find new solutions aimed at calcium metabolism correction in order to find also effective methods to stabilize and slowdown chronic renal failure development as well as to reduce its incidence and complications.

The aim of this study was to assess the effectiveness of the product **Osteobios** (Guna, Italy) in the treatment of calcium metabolism disorders in *patients with II-III stage chronic renal insufficiency.*

PATIENTS AND METHODS

20 patients with chronic renal failure of different origin (six patients with glomerulonephritis; eight patients with pyelonephritis; six patients with diabetic nephropathy) with an average level of creatinine up to 0,276±0,08 mmol/L took part to the study.

These patients (*verum* group) received **Osteobios**, 10 drops 30 minutes before meal, three times daily for a month. All patients kept to the diet of 700-900 mg/day calcium and reduced protein intake.
In order to improve the renal function the patients of this group received also the homotoxicological preparations **Reneel** N, 1 tablet, and **Lymphomyosot**, 10 drops, three times daily half an hour before meals for a month.

The **first control group** (baseline) consisted of **20** patients affected from chronic renal disease as well, and its composition was similar to that of the *verum* group according to nosologic basis of chronic renal failure, age, sex and creatinine level. The patients of this group did not receive any treatment which could influence calcium and phosphorus metabolism.

The **second control group** consisted of **15** healthy people of similar age and sex.

The content of the general and ionized calcium was determined by calcium selective solid-contact electrode EM-080102 KSRSH.418422.021-01device.
The general calcium and inorganic phosphorus level was determined by means of photocolorimetry; the cholecalciferol level was determined using chromatography, and the level of parathyroid hormone using solid-phase radioimmune analysis (ELISA).
The bone tissue metabolism was measured according to the serum alkaline phosphatase activity that was determined by means of the standard biochemical method.
The results of the study were statistically processed with the methods of variation statistics and using Excel software (Microsoft, USA).

RESULTS AND DISCUSSIONS

All **20 patients** reported chronic back pain, **10** patients (50%) complained about muscle pain, **15** patients (75%) had pain in extremities. Painful symptom intensity in backbone increased in concomitance with the increase of azotemia level.
According to Doppler ultrasound data, nodal secondary hyperthyrodism was not observed in any patient.
In case of diffuse hyperthyrodism a conservative treatment can cause the formation of metastatic calcium deposits [4].

Serum calcium in patients with chronic renal disease at baseline was 1,92±0,11 mmol/L; that was significantly below the same parameter in the control group, 2,29±0,09 mmol/L (p <0,05).
The content of ionised calcium in patients was 0,84±0,03 mmol/L, and was also essentially lower than in the control group, 0,99±0,07 mmol/L (p <0,05).
Renal calcium excretion in the verum group patients was 1,26±0,07 mmol/day and was much slower than the same parameter in the control group, 4,12±0,04 mmol/day (p <0,05).

Hyperphosphatemia was revealed in all patients with chronic renal disease. Serum inorganic phosphate level in patients with chronic renal disease was 2,18±0,11 mmol/L that was statistically higher than the control parameter (1,59±0,04 mmol/L (p <0,05)). Hypercalcemia is directly caused by increased phosphorus level in chronic renal disease. This can be explained by the fact that increased concentration of phosphorus in blood suppresses the 1α-hydroxylation of 25-hydroxycalciferol in kidneys, and by proximal tubular injury where its synthesis occur in chronic renal disease [1-3].

Serum content of alkaline phosphatase in patients with chronic renal disease before treatment was increased - 1,58±0,19 mmol/L x g (p <0,05 compared to the control group).
This parameter is a biochemical marker of bone remodelling, and the increase of its level proves intensive bone resorption.

PTH blood concentration in patients with chronic renal disease was 60,8±3,2 pg/ml and was twice higher than in the control group, 30,2±3,4 pg/ml (p <0,05). On the contrary, blood cholecalciferol in patients, 1,27±0,07 mmol/L, was much lower than that of the control group 2,42±0,09 mmol/L (p <0,001).
We found a negative correlation between PTH and calcitriol (r = - 0,812, p <0,001).
Many researchers believe that the increase of PTH secretion in chronic renal disease is related to the decrease of cholecalciferol synthesis in proximal tubules and to the increased resistance of different organs and tissues that reduce its action.

Therefore , the parathyroid gland becomes less sensitive to the suppressing action of this hormone. The increase of PTH level is not accompanied by calcemia increase.

The individual analysis revealed that blood calcium level was increased or normal only in 2 patients (10%) with normal blood cholecalciferol level. The latter can be explained by the development of a secondary hyperthyroidism and the increase of PTH level. Thus, increased blood PTH stimulates cholecalciferol synthesis in patients with normal renal function, but this effect is not observed in patients with chronic renal disease.

We studied the possible correlation links between the parameters of calcium metabolism and serum nitric metabolites in patients with chronic renal disease.
Negative correlation between general calcium and blood creatinine (r = - 0,63, p <0,05), ionised calcium and urea (r = - 0,68, p <0,05), PTH and phosphorus (r = - 0,72, p <0,05), PTH and ionised calcium (r = - 0,55 (p <0,05), calcitriol and PTH (r = - 0,73. p <0,05) was found.
Positive correlation was observed between PTH and blood creatinine (r = +0, 67, p <0,05).

- In the treatment of calcium metabolism disorders in patients with chronic renal disease, we used the complex preparation **Osteobios** which contains potentiated mineral, *Suis*-components related to bone

tissue and calcium-metabolism regulating organs (low, middle and high potencies). This formulation allows for a soft, non-invasive therapeutic action, without causing intense systemic reactions, which would lead to undesireable side effects. The composition is addressed to all aspects of calcium metabolism. The potentiated *Suis*-component *Os Suis* (bone tissue extract) acts directly on bone tissue and stimulates the action of other components on the bone tissue. The extract from parathyroid gland *Glandula parathyreoidea Suis* D10/30/200 mediates the parathormone synthesis decrease and regulates the parathyroid function. Calcium is included in **Osteobios** as three salts: carbonate, phosphate and fluoride. The preparation contains two important components: potentiated calcitonin which stimulates the osteoblastic activity and reduces the osteoclastic activity decreasing bone resorption, and the complex of essential amino acids which improves trophism of bone tissue and stimulates tissue synthesis.

- In one month after Osteobios treatment was started, the **concentration of general blood calcium** had increased by **9%** up to **2,16**±0,07 mmol/L in the *verum* group (p <0,05 compared to the baseline; p>0,1 compared to the control group). The ionised calcium level had increased as well (p <0,05 compared to the baseline; p>0,1 compared to the control group). Calcium excretion insignificantly changed compared to baseline. After the treatment with Osteobios blood phosphorus reduced significantly by 21%, up to 1,64±0,09 mmol/L (p <0,05 compared to the baseline; p>0,1 compared to the control group). After one-month of treatment with Osteobios, PTH level decreased by 37% up to 39,6+0,6 pg/ml (p <0,05 compared to the baseline; p> 0,1 compared to the control group). Blood cholecalciferol level in patients with chronic renal disease was twice higher, compared to the control value as a result of Osteobios treatment and this is a significant improvement (p <0,001).
Alkaline phosphatase blood content decreased in the course of therapy up to 1,32±0,26 mmol/L x g (p <0,05 compared to the baseline; p>0,1 compared to the control group), this proves indirectly an activation of the osteogenesis.

After the treatment almost all patients referred that the lumbar or muscular pain had been either reduced or disappeared. Within the same follow-up period (one month) significant changes of phosphorus and calcium metabolism were not observed in lab values. Adverse events of Osteobios were not reported.

It was concluded that **Osteobios** combined with **Reneel N** and **Lymphomyosot** improves calcium metabolism in patients with chronic renal disease. With a creatinine level up to <0,35 mmol/L there is no need for an additional administration of cholecalciferol, minerals and phosphate binders, as well as Klimadinon in women. In these cases the therapy with the complex preparation Osteobios is enough.

CONCLUSIONS

1. The complex preparation Osteobios combined with Reneel N and Lymphomyosot is a reliable, effective and safe method to correct phosphorus and calcium metabolism disorders in patients with chronic renal disease.

2. The treatment of chronic renal disease using the aformentioned preparations for one month help to improve different aspects of calcium metabolism, increasing calcium and cholecalciferol levels, as well as substantially reducing phosphorus and PTH blood levels. The dynamics of alkaline phosphatase blood levels prove the activation of osteogenesis under the influence of Osteobios. ■

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