

Clinical outcome in patients with chronic kidney disease after use of ketoanalogues

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Abstract

A low-protein diet with increased content of essential amino acids and their ketoanalogues has been applied for patients with chronic kidney disease (CKD). The aim of this study was to assess whether a combination of a low-protein diet with keto-amino acids (KAA) retards progression of chronic renal failure and maintains nutritional status.

One hundred twenty non-diabetic patients in predialytic stages of CKD, randomized as regard the age, sex distribution, blood pressure control, etiology, serum creatinine, glomerular filtration rate (GFR), body mass index (BMI) were included in a randomized, open-label and prospective study. They are divided into two groups: group I, patients receiving low protein diet (0.6g/kg) and group II, receiving low protein diet supplemented with KAA.

After six months, GFR, serum creatinine, BMI did not change significantly between groups, while, serum total proteins, serum albumin were increased significantly in the second group (respectively from 4.8 ± 0.3 g/dl to 6.3 ± 1.1 g/dl, $P < 0.01$ and from 2.2 ± 0.7 g/dl to 3.2 ± 1.3 g/dl, $P < 0.01$), while seric levels of phosphor and blood gas were ameliorated in patients of the second group.

We conclude that the low-protein diet supplemented with KAA is associated with a delay in progression of renal insufficiency, reduction in proteinuria, and maintain BMI.

Introduction

The prevalence of chronic kidney disease (CKD) is rapidly increasing. Studies from the USA, Europe, Australia, and Asia showed that the prevalence of CKD is about 9–13% in the general population [1, 2]. So, every attempts should be done to slow the progression and to avoid the complications of CKD. Dietary protein restriction is an important strategy for delaying the progression of CKD, by reducing the accumulation of nitrogen catabolic substances, and by delaying the progress of CKD [3].

The dietary protein can reduce albuminuria and will prevent uraemic symptoms. Until a means of preventing kidney disease or progression is found, safe methods of management such as dietary manipulation should be available for CKD patients [4].

The purpose of this study is to determine whether low protein diet supplemented with KAA is effective in preventing the progression of CKD.

Patients and Methods

One hundred twenty non-diabetic patients in predialytic stages of CKD, randomized as regard the age, sex distribution, blood pressure control, etiology, serum creatinine, glomerular filtration rate (GFR), body mass index (BMI) were included in a randomized, prospective and parallel group study. The study was performed from June 2013 to September 2014 in patients of CKD attending ambulatory of renal clinic or admitted in Internal Service of the secondary are Center of Durres.

They are divided into two groups:

- group I, patients receive low protein diet (0.6 g/kg/day);
- group II, receive low protein diet (0.6 g/kg/day) supplemented with a KAA named ketosteril for six months (3-9 tablets/day, regarding the stage of CKD).

CKD were classified into 5 stages according to the GFR, estimated by Cockcroft-Gault formula and presence of signs of kidney damage:

- stage 1: GFR > 90 ml/min and signs of kidney damage;
- stage 2: GFR = 60–89 ml/min and signs of kidney damage;
- stage 3: GFR = 30–59 ml/min;
- stage 4: GFR = 15–29 ml/min;
- stage 5: GFR < 15 ml/min [5, 6] (K/DOQI and KDIGO).

Were included in the study patients with CKD in stage 3 and 4 ($15 \text{ ml/min/1.73 m}^2 < \text{GFR} < 45 \text{ ml/min/1.73 m}^2$) receiving conservative treatment for CKD.

Were excluded from the study patients on dialysis, immunosuppressed, pregnant women, those with malignancy.

The changes of GFR, serum total proteins serum albumin, phosphor, HCO_3 blood gas, BMI, were evaluated after six months treatment. The values were expressed as mean \pm SD.

The results were expressed as mean (\pm SD). Statistical significance between pre- and post-treatment values in each group was calculated using Student's paired t-test. Statistical significance between groups was calculated using unpaired t-test. P-values <0.05 were considered statistically significant.

Results

Sixty (31 males and 29 females) patients mean aged 41 years (range 25-68 years) were of group I and sixty (30 males and 30 females) patients mean aged 43 years (range 27-69 years) were of group II (Table 1). None of the patient in either group required dialysis, and till the end of study all patients were alive.

Table 1. Patients' demographics data

| Demographic variable | Total number of patients |
|----------------------|------------------------------|
| N | 120 |
| Sex (M/F) | 61/59 |
| Age (years) | 36.3 \pm 10.7 (27-63) |
| Weight (kg) | 64.2 \pm 6.7 (54-96) |
| Height (cm) | 152.7 \pm 7.4 (150-182) |

After six months, GFR, serum creatinine, BMI, seric level of sodium, potassium did not change significantly in both groups compared with the baseline values, while, serum total proteins, serum albumin were increased significantly after treatment in the group II (respectively from 5.4 \pm 1.3 g/dl to 6.3 \pm 1.1 g/dl, $P<0.01$ and from 2.2 \pm 1.7 g/dl to 3.2 \pm 1.3 g/dl, $P<0.01$).

Also, seric levels of phosphor were decreased significantly in the group II after six months of treatment with KAA. Bicarbonates in blood were

ameliorated in patients of the group II, compared with the baseline values (Table 2).

Table 2. Comparison of biochemical parameters before and after treatment

| | Baseline values | After 6 months of treatment | | |
|-----------------------------------|-----------------|-----------------------------|-----------------|----------|
| | | Group I | Group II | P |
| GFR (ml/min/1.73 m ²) | 26.1 \pm 7.9 | 25.9 \pm 9.3 | 25.9 \pm 9.3 | NS |
| Serum creatinine (mg/dl) | 2.66 \pm 1.83 | 2.47 \pm 1.6 | 2.2 \pm 1.1 | NS |
| BMI (kg/m ²) | 24.8 \pm 5.3 | 24.2 \pm 3.8 | 23.9 \pm 3.6 | NS |
| Phosphor (mg/dl) | 5.1 \pm 1.3 | 4.8 \pm 1.2 | 4.2 \pm 0.6 | $P<0.05$ |
| Total protein (g/dl) | 5.4 \pm 1.3 | 5.7 \pm 0.5 | 6.3 \pm 1.1 | $P<0.01$ |
| Albuminemia (g/dl) | 2.2 \pm 1.7 | 2.8 \pm 0.7 | 3.2 \pm 1.3 | $P<0.01$ |
| HCO_3 | 18 | 19.2 | 20 | NS |
| Proteinuria (24 hour g/dl) | 3.1 \pm 1.5 | 2.8 \pm 0.7 | 2.7 \pm 0.6 | NS |
| Seric level of sodium (mmol/l) | 140 \pm 3.5 | 141 \pm 2.6 | 142.6 \pm 2.3 | NS |
| Seric level of potassium (mmol/l) | 4.2 \pm 0.5 | 4.3 \pm 0.2 | 4.2 \pm 0.9 | NS |

Discussion

The chronic dialysis programme in Albania began there in 1985 using three dialysis machines. At present a total of 12 patients (4 per million populations) receive hemodialysis [7]. Since that period the number of patients requiring dialysis is increased tremendously, arriving in these days at about 1000 patients in all Albania, receiving from the Albanian budget an important part. This high number is because of higher incidence of CKD in nowadays, better diagnostic for CKD, increased number of hemodialysis machines in all country. In these conditions, conservative management is very important to prevent CKD and to prevent progression of CKD to end-stage renal disease (ESRD). Consequently, CKD patients accumulate salt, phosphates, uric acid and many nitrogen-containing metabolic products, and secondary problems of metabolic acidosis, bone disease and insulin resistance become prominent [8]. These problems can be avoided with dietary planning. Protein-restricted diets do not produce malnutrition and with these diets even patients with advanced CKD maintain body weight, serum albumin and normal electrolyte values [8].

Hence, newer treatment modalities are being searched, which can halt nephron damage, delay the development of ESRD, and cost-effective. KAA might be useful in the treatment of uremia [8]. Ketoacids reduce protein degradation and urinary protein excretion, producing a reduction of plasma urea, urea synthesis and urea excretion and an improvement in nitrogen balance in CKD patients [9]. These might be

the probable mechanisms for beneficial effects of KAA in our study.

In concordance with study of Di Iorio [10], also in our study results a reduce of phosphate burden from KAA may decrease proteinuria and slow the progression of renal disease in CKD patients. In our study KAA are showed to be beneficial in stages 3 and 4 of CKD, with an improvement in clinical features as well as biochemical parameters. So, the KAA therapy in predialysis CKD patients can be consider an essential part of therapy [11]. A limitation of our study is the small number of patients. These results need to be followed by more studies.

Conclusion

We conclude that the low-protein diet supplemented with ketoanalogs is associated with a delay in progression of renal insufficiency, reduction in proteinuria, and maintain BMI. Ketoanalogues are safe, well tolerated, and efficacious in retarding the progression of renal failure and preserving the nutritional status of CKD patients, but cost may still be a limiting factor.

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Biography

Anita Krrashi is graduated in Medicine Faculty in University of Tirana. She graduated in Nephrology Dialysis Transplantation, in University Hospital Center "Mother Teresa" in Tirana, Albania in 2006.

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