

## THE EFFECTS OF LOW PROTEIN DIET ON NUTRITIONAL AND BONE STATES AND PROGRESSION RATE IN CHRONIC RENAL FAILURE

### KRONİK BÖBREK YETMEZLİĞİNDE DÜŞÜK PROTEİNLİ DİYETİN BESLENME, KEMİK METABOLİZMASI VE PROGRESYON HIZI ÜZERİNE OLAN ETKİLERİ

M. Rıza Altıparmak, D. Deren Oygur, Sinan Trablus, Süheyla Apaydın, Rezzan Ataman  
Kamil Serdengeçti, Ekrem Ereğ

İstanbul Üniversitesi Cerrahpaşa Tıp Fakültesi Nefroloji Bilim Dalı

#### SUMMARY

*In this study we assessed the influence of low protein diet (LPD) and very low protein diet (VLPD) plus ketosteril tablets on the nutritional and the bone status in chronic renal failure and also on its progression. Ten patients (M/F= 5/5, mean age= 45.2±22.3 years) with CRF were enrolled into the study. The nutritional status assessed from anthropometric measurements such as body mass index (BMI) and triceps skin fold thickness (TSF), from biochemical measurements such as serum albumin, transferrin, total cholesterol and triglyceride levels. The serum levels of calcium, phosphorous and intact parathyroid hormone (iPTH) were determined to evaluate the bone status. The progression of renal failure was assessed from creatinine clearance (CCR). All patients were started with LPD containing 0.6 gr/kg/day protein and an energy intake of 35 kcal/kg/day. They were followed for 6 months. At the end of this period the diet was changed to VLPD containing 0.4 gr/kg/day plus ketosteril tablets (1 tablet/5 kgs) and an energy intake of 35 kcal/day. Patients were followed for another 6 months (second period). The initial measurements done were repeated at the end of each period. Paired-sample t-test, two-way Anova test and multiple regression analysis were used as statistical methods. There was no significant difference between the initial, end of first period and end of second period mean values of the parameters studied. The effects of different diets on nutritional parameters, parameters showing bone status and CCR did not differ significantly from each other. CCR was negatively correlated with serum albumin (r=0.12) and transferrin levels (r=0.23) but these correlations were statistically insignificant.*

**Key Words:** chronic renal failure, low protein diet, nutrition, bone metabolism, progression rate

#### ÖZET

*Bu çalışmada düşük proteinli diyet ve çok düşük proteinli diyetin ketosteril ile birlikteliğinin kronik renal yetmezlikli hastaların nutrisyonel ve kemik durumları ve kronik renal yetmezliğin progresyonu üzerine etkileri araştırılmıştır. Çalışmaya kronik renal yetmezlikli 10 hasta alınmıştır (E/K=5/5, ortalama yaş 45.2±22.3). Hastaların nutrisyonel durumları Vücut Kitle İndeksi (VKİ) ve Triseps Deri Kalınlığı (TDK) gibi antropometrik ölçütler ve albumin, transferin, total kolesterol ve trigliserid düzeyleri gibi biyokimyasal ölçütler kullanılarak değerlendirilmiştir. Kemik ölçümü kalsiyum, fosfor, iPTH düzeylerine göre değerlendirilmiştir. Böbrek yetmezliğinin progresyonu kreatinin klirens düzeyindeki değişime göre değerlendirilmiştir.*

*Tüm hastalara 0.6gr/dl/gün protein ve 35 kcal/gün enerji içeren Düşük Proteinli Diyet verilmiştir (DPD). Tüm hastalar 6 ay boyunca izlenmiştir (Unci periyod). Bu periyodun sonunda hastaların diyeti 0.4gr/kg/gün protein ve 35 kcal/gün enerji içeren Çok Düşük Proteinli Diyete (ÇDPD) çevrilmiştir ve bu diyetin yanına ketosteril tablet eklenmiştir.*

*Hastalar 6 ay süreyle tekrar izlenmiştir (2.inci periyod). Çalışmanın başında yapılan ölçümler her periyodun sonunda tekrar edilmiştir.*

*İki örneklem t-testi, Anova testi, çoklu regresyon analizi istatistiksel metodlar olarak kullanılmıştır. Çalışma öncesi, 1. periyod sonu ve 2. periyod sonu ortalama değerler arasında anlamlı fark bulunamamıştır. Farklı diyetlerin nutrisyonel parametreler, kemik statüsünü gösteren parametreler ve kreatinin klirens üzerindeki etkileri arasında anlamlı fark bulunamamıştır. Her iki periyod için hesaplanan kreatinin klirenslerindeki düşüş hızları arasında anlamlı fark bulunamamıştır. Kreatinin klirens, serum albumin ve serum transferin düzeyleri ile negatif korelasyon göstermiştir ancak bu korelasyon istatistiksel olarak anlamsızdır.*

**Anahtar Kelimeler:** kronik böbrek yetmezliği, düşük proteinli diyet, besleme, kemik metabolizması, progresyon hızı

## INTRODUCTION

It has been known that a low protein diet can ameliorate the symptoms in chronic renal failure. This is an expected consequence as many symptoms are caused by accumulation of various end products of protein catabolism like urea and acids. However the possibility of developing malnutrition and especially hypoalbuminemia has cast doubt on the administration of low protein diets as hypoalbuminemia is a well known major risk factor in dialysis patients.

On the other hand as they can ameliorate the uremic symptoms low protein diets prevent anorexia and therefore malnutrition. The effects of these diets on slowing the progression of renal failure is another rationale for their use. This slowing of progression has been showing in some studies. This consequently causes a delay in the initiation of dialysis. This delay in part may also be attributed to decreased symptoms of uremia due to protein restriction. In most of the studies however ketosteril tablets solely had not been shown to have any beneficial effects on delaying the progression of chronic renal failure. Osteodystrophy is a well known complication of chronic renal failure which at least can be ameliorated by using some measures. Administration of low protein diets for amelioration of uremic osteodystrophy has been studied in some of these studies a positive effect has been shown. The aim of this study is to find out the effects of diets with low protein content on the nutritional status, the bone status and the progression of chronic renal failure and to compare the effects of these diets with different protein contents on each of these parameters.

## PATIENTS AND METHODS

The study group consisted of 10 patients with chronic renal failure. There were 5 males and 5 females with mean age of  $45.2 \pm 22.3$ . The etiology of CRF was unknown in 2, chronic glomerulonephritis in 3, chronic pyelonephritis in 3, nephrolithiasis in 1, amyloidosis in 1 of these patients. Their mean CCr was  $25.7 \pm 5.7$  ml/min (R-8-38 ml/min), 6 patients had CCr below 20 ml/min (advanced CCr).

The nutritional status was assessed from anthropometric measurements such as body mass index (BMI) and triceps skin fold thickness (TSF), from biochemical measurements such as serum albumin, transferrin, total cholesterol and triglyceride levels. The serum levels of calcium, phosphorous and intact parathyroid hormone (iPTH) were determined to evaluate the bone status. The progression of renal failure was assessed from creatinine clearance (CCr) changes with time.

All patients were started with LPD containing 0.6 gr/kg/day and an energy intake of 35 kcal/kg/day (55% carbohydrate, 30% fat, 15% protein). They were followed for 6 months. Then they were switched to

VLPD containing 0.4 gr/kg/day protein and ketosteril tablets \* (1 tablet/ 5kg) and an energy intake of 35 kcal/day and were followed for another 6 months which constituted the second study period. The initial measurements done were repeated at the end of each period. Paired sample t-test was used to evaluate the difference in mean values of the parameters initially, at the end of first and second periods of the study. Two way Anova test was used to assess the effects of two different diets on parameters studied. Multiple regression analysis was used to determine the relation of nutritional parameters on CCr.

Ketosteril film tablet= Calcium-3-methyl-2-oxo-valerate 67mg, calcium-4-methyl-oxo-valerate 101mg, calcium-2-oxo-3-phenylpropionate 68mg, calcium-3-methyl-2-oxo-butyrate 86mg, calcium-DL-hydroxy-4-(methyl-thio)-butyrate 59mg, L-lysine-acetate 105mg, L-threonine 53mg, L-tryptophane 23mg, L-histidine 38mg, L-thyrosine 30mg, total nitrogen content 36mg, calcium/tablet 0.05gr

## RESULTS

The mean values of the measurements taken initially, at the end of 6<sup>th</sup> month and at the end of 12<sup>th</sup> month are shown in table 1. No significant difference was found between the initial, end of first period and end of second period mean values of the parameters studied. The effects of two diets on nutritional parameters, parameters showing bone status like  $\dot{\text{I}}\text{p}^{\text{th}}$ , serum calcium and serum phosphorous levels and CCR did not differ significantly from each other. The decline of CCR in different periods was not found to be significantly different. CCR was negatively correlated serum albumin ( $r=-0.12$ ) and serum transferrin levels ( $r=-0.23$ ) but these correlations were statistically insignificant.

## DISCUSSION

Malnutrition is a well known important risk factor for morbidity and mortality in maintenance dialysis patients [2]. It is also well known that this malnutrition starts in predialysis patients especially due to anorexia. Therefore it is important to demonstrate the safety of LPD and VLPD plus ketosteril tablet usage as a conservative therapy in predialysis patients. Many studies were done in order to evaluate the safety of these diets [3,4]. MDRD (Modification of Diet on Renal Disease) Study has confirmed the adequacy of protein restricted diets [4]. In this study no significant decline was detected in nutritional parameters. In fact albumin and transferrin levels increased at the end of study but increases were insignificant. Weight, BMI, TSF also did not change significantly with both diets.

With protein restriction intakes of phosphorous and hydrogen also decreases hence osteodystrophy and acidosis. Amelioration of renal osteodystrophy is

Table 1: Results

	INITIAL	3 MONTH Period 1	9 MONTH Period 2	P
<b>NUTRITIONAL STATUS</b>				
TSF (cm)	6.5	6.4	6.4	NS
BMI (kg/m <sup>2</sup> )	21.5	21.4	21.9	NS
ALBUMIN	3.6	3.7	3.9	NS
TRANSFERRIN	225.1	226.3	237.5	NS
T. CHOLESTEROL	197.2	199.5	211.7	NS
TRIGLYCERIDE	148.3	149.4	148.4	NS
<b>BONE STATUS</b>				
CALCIUM	9.1	9.1	9.3	NS
PHOSPHOROUS	5.0	4.7	4.5	NS
INTACT PTH	152.3	148.8	139.6	NS
<b>RENAL STATUS</b>				
CCR	25.7	23.6	21.7	NS
CCR DECLINE		3.45	2.66	NS

shown in some studies [5,6]. In our study no significant differences were noted in the levels of calcium, phosphorous and iPTH therefore neither deterioration nor regression was noticed with respect to hyperparathyroidism; it stayed stable.

The usage of diets with low protein content in order to slow the progression of renal failure is still debatable however some studies proved that these diets can slow this progression [7]. In fact apart from this slowing the referral to dialysis is delayed due to decrease in uremic symptoms when on low protein containing diets. In some studies it was shown that a low protein diet prevents the adaptive increase in glomerular capillary pressure occurring in RF and it was proposed that this is the mechanism leading to progressive glomerular sclerosis [8] however in some studies protein restriction had shown to have no effect in slowing the progression of renal failure [9]. In **our** study we did not show any significant difference in the decline of creatinine clearance during each period.

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