ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Is There Any Contribution of Pancreatic Exocrine Dysfunction to the Malnutrition in Chronic Kidney Disease and End Stage Renal Disease?

Kronik Böbrek Hastalığı ve Son Dönem Böbrek Hastalığı'nda Malnütrisyon Pankreatik Ekzokrin Disfonksiyon ile İlişkili Olabilir mi?

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ABSTRACT

Aim: *Pancreatic exocrine dysfunction has many causes and often results in malnutrition. The relationship between chronic renal disease related malnutrition and pancreatic exocrine function has not been understood clearly yet. There is lack of data in the literature regarding pancreas exocrine dysfunction in kidney diseases. This study aimed to show whether existence of this relationship.*

Material and Method: *40 End stage renal disease (ESRD) patients, 40 chronic renal disease (CKD) patients and 42 healthy volunteers without any diagnosed systemic diseases were included. 'Mini Nutritional Assessment' (MNA) form has been filled up to determine the nutritional status of the participants. Fecal elastase 1 (FE1) levels measured in order to evaluate the exocrine function of pancreas.*

Results: *FE1 values of control group were significantly higher from CKD and ESRD patients both. When considering the sensitivity of FE1 to show pancreas exocrine function, these results worsen pancreas exocrine function in patients with kidney disease.*

Conclusion: *Malnutrition in kidney diseases has various reasons, and pancreatic exocrine dysfunction thought to be one of them. FE1 levels may be used in order to evaluate the exocrine functions of the pancreas.*

Key words: *malnutrition; chronic kidney disease; pancreas exocrine dysfunction; fecal elastase 1*

ÖZET

Amaç: *Kronik böbrek hastalığı (KBH) ilişkili malnutrisyon ile pankreatik ekzokrin disfonksiyon arasındaki ilişki henüz net olarak açıklanamamıştır. Böbrek hastalıklarında pankreatik ekzokrin disfonksiyona ilişkin literatür yeterli değildir. Bu çalışmanın amacı böyle bir ilişkinin olup olmadığının araştırılmasıdır.*

Materyal ve Metot: *40 SDBH, 40 KBH ve 42 sağlıklı gönüllünün dahil edildiği çalışmada katılımcıların beslenme durumlarının belirlenmesi amacıyla "Kısa Nütrisyonel Değerlendirme (KND)" formu doldurulmuş ve pankreasın ekzokrin işlevlerinin belirlenmesi için fekal elastaz 1 (FE1) düzeyleri ölçülmüştür.*

Bulgular: *Kontrol grubunda FE1 düzeyleri KBH ve SDBH ggruplarına göre anlamlı derecede yüksek bulunmuştur. FE1'in pankreas ekzokrin fonksiyonunu göstermedeki duyarlılığı göz önüne alındığında, sonuçlar böbrek hastalarında kötü pankreatik ekzokrin fonksiyonunu işaret etmektedir.*

Sonuç: *Böbrek hastalığında malnutrisyonun çok farklı nedenleri olabilmesinin yanı sıra, pankreatik ekzokrin disfonksiyon bu nedenlerden biri olarak düşünülebilir. FE1 düzeyleri pankreasın ekzokrin fonksiyonunun belirlenmesinde kullanılabilir.*

Anahtar kelimeler: *malnutrisyon; kronik böbrek hastalığı; pankreatik ekzokrin disfonksiyon; fekal elastaz 1*

Introduction

End stage renal disease (ESRD) and chronic renal disease (CRD) are serious health care problems with increasing incidences, and 5 year-mortality rates are about 60% which is due to the disease itself and the complications. Malnutrition is supposed to be one of the leading causes that contributing reasons. Malnutrition prevalence is predicted as 10–70%, and 18–50% receiving hemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD) therapies respectively[1–4].

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There is no gold standard method in order to evaluate the nutritional status. Some tests that combine various parameters may be used; measures of energy and protein intake, visceral protein pools, muscle mass, other dimensions of body composition, serum albumin, prealbumin, cholesterol, urea nitrogen, creatinin and also subjective global assessment (SGA) and mini nutritional assessment (MNA) tests are frequently used[5,6]. The MNA was developed nearly 20 years ago and is one of the most well validated nutrition screening tool. Originally comprised of 18 questions, the current MNA now consists of 6 questions and streamlines the screening process. The current MNA retains the validity and accuracy of the original MNA in identifying older adults who are malnourished or at risk of malnutrition[7]. Malnutrition may be identified with greater sensitivity and specificity using a combination of these factors.

Pancreas has exocrine and endocrine functions that regulate glucose homeostasis, digestion of carbohydrates, proteins and lipids. Failure in these processes may occur in course of many diseases and may result with malnutrition. Determination of fecal elastase 1 (FE1) level may be used to evaluate exocrine function of the pancreas[8,9]. FE1 is not affected during the passage through bowels, stays stable for a long time and its level is not influenced by medications, gastric operations, bowel dismotility or intestinal diseases. Also measuring FE1 level is faster and cheaper with adequate sensitivity and specificity when compared to the tests that evaluate direct exocrine dysfunctions[5]. Also FE1 levels are not influenced with age, sex, and underlying renal disease, duration of hemodialysis, creatinin or serum albumin levels[10]. Decreased FE1 levels is rather associated with malnutrition than CRD or hemodialysis.

The relationship between CRD and pancreatic exocrine functions has not been well understood yet, and also any possible association between CRD and pancreas exocrine dysfunction has not been demonstrated.

In this study it was aimed to evaluate the relationship between kidney disease associated malnutrition due to pancreatic exocrine functions in CRD and ESRD patients.

Materials and Method

In this study included 40 ESRD patients who are on hemodialysis therapy at least for 3 years (Group I), 40 CRD consisting stage 3 (estimated glomerular filtration rate between 30–59 ml/min/1.73 m^2) and stage 4 (estimeated glomerular filtration rate between 15–29 ml/min/1.73 m^2) patients (Group II) and 42 healthy volunteers without any established disease (Group III). Exclusion criteria have been set as the presence of chronic pancreatitis, steatorrhea, cystic fibrosis, gluten enteropathy, Zollinger Ellison syndrome, Crohn's disease, diabetes mellitus, short bowel syndrome, prior gastrointestinal surgery, liver parenchymal disease, malignancy, alcohol abuse, proteinuria more than 3 g/day and presence active infection.

CRD patients were under a dietary restriction of 0.8 g/day protein and ESRD patients were under a dietary restriction of 1.2 g/day protein. Adherence to dietary restrictions are examined by using normalisation protein catabolic rate (nPCR) formula; nPCR=0.22 + (. 036 * interdialytic rise in BUN * 24)/(interdialytic interval)

MNA forms have been filled up by participants in order to evaluate their nutritional status after their physical examination and collection of blood and stool samples. MNA scores below 17 has been considered as malnutrition.

One gram of fresh stool samples kept at-20°C for FE1 measurements which are performed using solid-phase enzyme-linked immunoabsorbent assay (ELISA) test (BIOSERV Diagnostics GmbH). FE1 levels below 100 μg/g stool, 100–200 μg/g stool and above 200 μg/g stool considered as severe pancreatic failure, mild pancreatic failure and normal respectively. Amylase and lipase activities have been measured by commercial kits (Roche Diagnostics GmbH, Mainheim-Germany) using enzymatic colorimetric assay. Serum albumin levels are measured by using Abbott Aeroset autoanalyser with photometric method.

The study was confirmed by the ethical committee of Başkent University with number of KA09/330.

Statistics analyses performed using software SPSS for Windows 11.5. The normality of the continuous variables is analyzed by using Shapiro Wilk test. Descriptive data expressed as mean ± standard deviation or median (minimum-maximum). Differences between the groups analyzed using Student's t test, also Kruskal Wallis and Mann Whitney U test when necessary. Categorical variables studied with chi-square test.

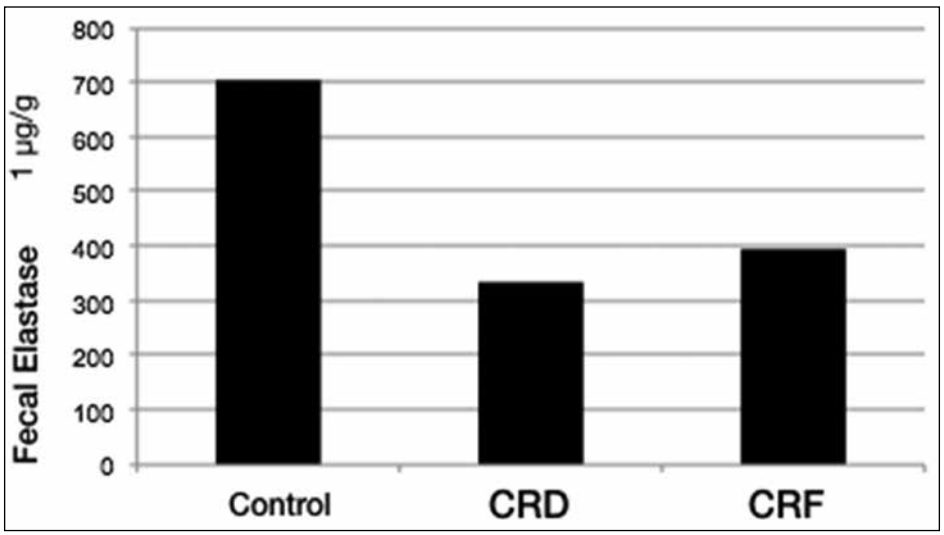

Figure 1. *Fecal elastase level of Control, CRD and CRF groups (CRD: Chronic renal disease, CRF: Chronic renal failure)*

Results

Mean age of the patients was; 45.4±15.3 years consisting 91 males and 31 females (Group I: 45.6±15.3 years, Group II: 45.2±13.6, Group III: 45.4±13.3). There were no statistical differences between the groups in terms of sex and age. Demographical data of the participants are listed in Table 1. nPCR in hemodialysis patients calculated as 1.12±0.21.

Fecal elastase levels measured as 335.3±152.9 µg/g, 395.9±186.6 µg/g, 705.6±225.8 µg/g in Groups I, II, III respectively (Fig. 1). Although there is statistically significant difference between three groups, it faded out when compared between Group I and II ($p > 0.05$).

MNA scores of the CRD, ESRD patients and controls were calculated as 18.7±4.3, 16.8±7.4, 26.9±2.7 respectively. Difference between the groups was statistically significant.

Using MNA scores, we revealed malnutrition rates as 25%, 32.5% and 28.75% in CRD, ESRD and in total respectively.

After evaluating with MNA, 10 CRD and 13 ESRD patients diagnosed with malnutrition. There were not any significant difference in terms of age and sex but serum albumin levels were significantly lower and CRP levels were significantly higher in malnutrition group. FE1 levels in CRD patients were measured as 359.4 µg (299.0–486.5) and 368.5 µg (102.9–494.3) in groups diagnosed with and without malnutrition respectively ($p > 0.05$). Also there was no significant difference between the groups in terms of serum lipase and amylase activities ($p > 0.05$). FE1 levels of the malnutrition group were significantly lower than the patients without malnutrition in ESRD ($p < 0.05$) even amylase and lipase activities were similar. Data is shown in Table 2 and 3.

Table 1. *Demographic features of Chronic renal disease and Chronic renal failure groups*

Variables	CRD (n=40)	CRF (n=40) Control (n=40)	p
Age	45.6±15.3	45.2±13.[6] 45.04±13.3	>0.05
Sex			0.309
Male	27 (% 67.5)	32 (% 80.0) 30 (% 75.0)	>0.05
Female	13 (% 32.5)	8 (% 20.0) 10 (% 25.0)	>0.05

Table 2. *Activities of amylase, lipase and fecal elastase with the relation to malnutrition in CRD group*

Variables	Malnutrition negative (n=30)	Malnutrition positive (n=10)	p
Amylase (IU/l)	92 (23–249)	111 (30–130)	0.612
Amylase activity			0.717
≤110	18 (% 60.0)	5 (% 50.0)	
>110	12 (% 40.0)	5 (% 50.0)	
Lipase (U/l)	58 (14–181)	64 (10–96)	0.701
Lipase Activity			1.000
≤60	16 (% 53.3)	5 (% 50.0)	
>60	14 (% 46.7)	5 (% 50.0)	
Fecal Elastase (µg/g)	368.5 (102.9–494.3)	359.4 (299.0–486.5)	0.988

CRD: Chronic renal disease

Table 3. *Activities of amylase, lipase and fecal elastase with the relation to malnutrition in CRF group*

Variables	Malnutrition negative (n=27)	Malnutrition positive (n=13)	p
Amylase (IU/l)	130 (46–221)	126 (30–293)	0.135
Amylase activity			0.154
≤110	6 (% 22.2)	6 (% 46.2)	
>110	21 (% 77.8)	7 (% 53.8)	
Lipase (U/l)	76 (12–254)	56 (7–150)	0.064
Lipase activity			0.031
≤60	6 (% 22.2)	8 (% 61.5)	
>60	21 (% 77.8)	5 (% 38.5)	
Fecal Elastase (µg/g)	399.0 (299.0–486.5)	368.5 (102.9–494.3)	0.264

CRF: Chronic renal failure

Discussion

This study showed that patients with CRD with malnutrition have lower FE1 levels in comparison to the healthy controls. Even there is no statistically significant difference between CRD and ESRD patients, being significantly lower from the healthy volunteers supports that pancreatic exocrine dysfunction contributes malnutrition in chronic kidney disease.

The prevalence of malnutrition in dialysis patients is reported as 10–54% in literature[11,12]. Biochemical parameters in order to establish the diagnosis of malnutrition in dialysis patients has been described before and which may be evaluated by assessing serum albumin, prealbumin, transferrin, insulin like growth factor-1, creatinine, potassium, phosphorus and amino acid levels[13,14]. Serum albumin levels were not significantly different between the groups I, II and III. But when grouping the participitans according to status of malnutrition, albumin levels were significantly lower and CRP levels were significantly higher, this finding may support the relationship between malnutrition and inflammation.

Establishing the diagnosis of malnutrition in course of chronic renal disease has great value. Even when using MNA in patients included in our study, we revealed malnutrition rates as 25%, 32.5% and 28.75% in CRD, ESRD and in total respectively, which are comply with the data reported in the literature[11]. MNA scores were lowest in ESRD patients when compared to CRD patients and controls, also CRD patients had lower MNA scores than healthy volunteers with statistical significance. This finding supports that nutrition status is deteriorated in CRD and ESRD.

It has been demonstrated that mild to moderate exocrine pancreatic insufficiency is not infrequent in patients on ESRD[10,15]. Mild to moderate pancreatic

exocrine insufficiency in not uncommon in end-stage renal disease patients. Hypermetabolism is thought to be a major reason for malnutrition in CRD patients, our results point that pancreatic exocrine dysfunction may be considered as a contributing factor[10]. Even it has been reported that vitamin D levels are associated in individuals with high BMI (35–40 kg/m^2) none of our patients had BMI higher than 25 kg/m^2 [9].

Even there are some choices in order to evaluate exocrine functions of the pancreas; most of them are invasive and difficult to perform. It has been reported that measurement of FE1 levels may have a valuable role in evaluating the exocrine functions of pancreas[16]. There are some studies aimed to set the cut-off value of FE1 in chronic pancreatitis and to show the association with serum lipase level which is used to diagnose and monitor chronic pancreatitis[17–19].

Insufficiency in exocrine functions of pancreas is often associated with maldigestion and malabsorbtion causing excessive excretion of fat and nitrogenous organics with feces, so may result with malnutrition[19,20]. Pancreatic exocrine dysfunction may be a contributing factor to the malnutrition in course of CRD and ESRD, which results in higher mortality and morbidity rates.

FE-1 not affected by intestinal motility, medications, gastric operations and stays stable for a long time and also faster and cheaper choice with reasonably high sensitivity and specifity when compared to conventional direct tests[16,22,23].

Loser et al.[24] reported that when comparing secretine-cerulein test results in FE1 measurements; FE1 evaluation has 93% sensitivity and specitivity in case that the margin value was set as <200 μg/g. In another study by Soldan et al.[25], 16 cystic fibrosis patient with established pancreatic failure using secretine-pancreozymine test, compared with healthy volunteers in same range of FE1 sensitivity and specificity were measured as 100% and 96% respectively with the threshold of <200 μg/g. Another study by Walkowiak et al.[26] aimed to compare FE1 and secretine-cholecystokinin test revealed that measuring FE1 levels has 100% sensitivity in cases of moderate and severe pancreas failure, in mild cases the sensitivity decreases to 25% with a specificity of 96.4%.

Even there was statistically significant difference between CRD and ESRD patients in terms of amylase levels, it faded out when compared according to the status of nutrition. It is well known that serum levels of amylase rises in cases of CRD, because of this reason serum amylase levels are insignificant in establishing the diagnosis of pancreatic exocrine dysfunction in CRD[27].

Our data shows that in patients with CRD and ESRD have significantly lower levels of FE-1 levels in comparison with healthy volunteers. It may be stated that altered pancreatic functions may accompany with kidney diseases. Due to its high sensitivity and specificity of FE-1 is a useful marker in evaluation of pancreatic exocrine dysfunction. FE-1 levels were not statistically significant different between the groups diagnosed with malnutrition by using MNA test. There are many factors that may contribute the malnutrition in kidney diseases, it should be noted that pancreatic functions are affected in course of kidney diseases which may worsen malnutrition.

FE1 levels were not significantly different between groups in case of malnutrition using MNA. This result may rise because of being fewer patients in malnutrition group. Studies with more patients may light up the significance.

In case of kidney diseases, alterations in nutrition and complications due to these alterations are thought to be some the leading causes of mortality and morbidity. Malnutrition in these patients has various reasons, and pancreatic exocrine dysfunction may be one of these. FE-1 levels may be used in order to evaluate the exocrine functions of the pancreas, Even FE-1 levels are associated with pancreatic exocrine functions; it does not seem to be a suitable marker in order to establish the diagnosis of malnutrition, the value of this marker in diagnosing malnutrition needs further research.

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