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Original Article

The effect of intradialytic food intake on the urea reduction ratio and single-pool Kt/V values in patients followed-up at a hemodialysis center*

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Aim: This study was conducted to determine the effect of intradialytic food intake on the urea reduction rate (URR) and single-pool Kt/V (spKt/V) values in hemodialysis (HD) patients.

Materials and methods: The study was designed as a quasiexperiment. Twenty-five patients were enrolled in this study. The patients' mean age was 56.5 ± 13.0 years and median time on HD was 63 months. In the first stage of the study, patients were given a standard meal after the first hour of the treatment. The same study group underwent HD without intradialytic food intake 1 week later. Predialysis and postdialysis blood samples for measurement of blood urea nitrogen levels were drawn at the HD sessions with and without food intake. The URR and spKt/V values were calculated. Descriptive statistics, the paired samples t-test, repeated measures analysis of variance, and power analysis were used for the analysis of data.

Results: The mean URR and spKt/V values of the patients were higher in the session without food ingestion compared to the other session. Statistically significant differences were found between the sessions with and without food intake for URR and spKt/V values ($P < 0.001$).

Conclusion: Intradialytic food intake seems to cause a decrease in the URR and spKt/V values.

Key words: Blood urea nitrogen, food intake, hemodialysis, Kt/V, urea reduction rate

Bir hemodiyaliz merkezinde takip edilen hastalarda intradiyalitik gıda alımının üre azalma oranı ve tek havuz Kt/V değerlerine etkisi

Amaç: Bu çalışma, hemodiyaliz (HD) hastalarında intradiyalitik gıda alımının üre azalma oranı (URR) ve tek havuz Kt/V (spKt/V) değerlerine etkisini belirlemek için yapıldı.

Yöntem ve gereç: Çalışmada yarı-deneysel bir tasarım uygulandı. Yirmi beş hasta çalışma kapsamına alındı. Hastaların yaş ortalaması 56.5 ± 13.0 yıl ve ortanca HD süresi 63 ay idi. Çalışmanın ilk aşamasında hastalara tedavinin birinci saatinden sonra standart bir öğün verilirken, bir hafta sonra aynı çalışma grubuna yemek verilmeden HD uygulandı. Kan üre azotu değerinin ölçümü için gıda verilen ve verilmeyen HD seanslarında HD öncesi ve sonrasında kan örnekleri alındı. Üre azalma oranı ve spKt/V değerleri hesaplandı. Verilerin analizi için tanımlayıcı istatistikler, iki eş arasındaki farkın önemlilik testi, tekrarlı ölçümlerde varyans analizi ve güç analizi kullanıldı.

Bulgular: Hastaların gıda alınmayan seansta ortalama URR ve spKt/V değerlerinin diğer seansa göre daha yüksek olduğu belirlendi. Gıda alınan ve alınmayan HD seansları arasında URR ve spKt/V değerleri açısından istatistiksel olarak anlamlı farklılıklar olduğu bulundu ($P < 0.001$).

Sonuç: İntradiyalitik gıda alımı URR ve spKt/V değerlerinde azalmaya neden oluyor gibi görünmektedir.

Anahtar sözcükler: Kan üre azotu, gıda alımı, hemodiyaliz, Kt/V, üre azalma oranı

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Introduction

End-stage renal disease (ESRD) is a chronic illness that is often treated with either dialysis or renal transplantation (1,2). In Turkey, the incidence and prevalence of ESRD has been increasing. The number of patients with ESRD in Turkey is 42,967. Hemodialysis (HD) is the most commonly used renal replacement therapy method in patients with ESRD in Turkey with a rate of 80.5%. While the number of patients keeps increasing, improvements continue to be made in HD conditions with efforts to provide a higher quality dialysis (3).

The aim of the dialysis treatment is to decrease the morbidity and mortality rates, and to increase the quality of life in patients with ESRD (4). Dialysis adequacy is defined by the Renal Association as "a global concept which includes clinical assessment of well-being, the impact on the patient's life and measures of the molecular clearance by the dialysis process" (5). Numerous parameters, such as the sufficient clearance of small, middle, and large molecular weight solutes, sufficient water removal for obtaining dry weight, adequate potassium and phosphorus removal, correction of acidosis and anemia, and sufficient protein/caloric intake to prevent malnutrition and the morbidity score, are used to assess adequacy of dialysis. The urea reduction rate (URR) and single-pool Kt/V (spKt/V), known as urea kinetic parameters, can only determine the clearance of low molecular weight toxins. It is therefore important to evaluate dialysis adequacy using other parameters besides urea kinetic parameters (6-8).

Adequacy of HD has been reported to be associated with cardiovascular disease, the main determinant of mortality in the patients (9). Skipping and shortening HD treatments has been shown to increase the risk of inadequate HD (10). Hemodialysis patients often skip or prematurely end sessions due to the physical discomfort they experience during the treatment (11). Eating during HD session may cause an increase in the number of the skipped or prematurely ended sessions due to reported potential adverse events (12,13).

There are no standards in Turkey as well as in the rest of the world regarding whether patients should eat during HD sessions. Patients are provided food during the session in many HD centers while some ban this for infection control (12). It is important for healthcare staff to be aware of the problems that can be caused by intradialytic food intake and to develop feeding protocols in line with the clinical evidence (13). Several studies have been conducted to assess the hemodynamic effects of intradialytic food ingestion (14-17). However, little is known about the relationship between intradialytic food intake and urea kinetic parameters (18,19). Therefore, the purpose of the present study was to determine the effect of intradialytic food intake on the URR and spKt/V values in HD patients.

Materials and methods

Design and sample

A quasiexperimental design in which participants served as their own control was used in this study. The study was conducted at a HD center that allowed patients to consume food during HD in Ankara, between 7 and 18 May 2007. The Hospital Ethical Committee approved the study protocol, which agreed with the principles in the Declaration of Helsinki. Approval for access to patients was sought from the medical directors of the HD center to collect the data. Participation in the study was voluntary; the study protocol was explained to participants and a written consent form was signed by each participant.

The study sample consisted of clinically stable, volunteer, coherent, and cooperative HD patients aged 18 years or older, undergoing chronic HD thrice weekly for 4 h, and had an arteriovenous fistula. Patients who had a history of diabetes mellitus and autonomic neuropathy were excluded from the study as they are prone to develop intradialytic hypotension (20). Patients undergoing HD with a catheter and arteriovenous graft were also excluded as the blood flow rate is less than for an arteriovenous fistula. The sample included 25 patients. Twenty-seven (51.9%) patients refused to participate or did not meet the inclusion criteria.

Procedure

This study was performed during the midweek HD session (Wednesday and Thursday schedules) because participants had high interdialytic weight gain in the first HD session of the week (Monday and Tuesday schedules). Dry weight was determined by the patient's attending nephrologist. HD was performed with 4008B machines (Fresenius, Bad Homburg, Germany) with a single-use, low-flux Polysulfon dialyzer (1.4 m^2, Gambro, Hechingen, Germany). Bicarbonate dialysate containing 140 mEq/L of sodium was used, and the dialysate temperature was 36 °C. Blood flow rates ranged from 200 to 450 mL/min. The dialysate flow rate was 500 mL/min. Dialysis duration was 4 h. Ultrafiltration rates depended on each patient's requirements but were kept constant during sampling periods. The dialysis prescription (dialysis duration, dialyzer, dialysate, blood flow rate, dialysate flow rate, ultrafiltration rate, etc.) was not changed at the HD sessions with and without food intake. Demographics, cause of ESRD, comorbid conditions, and HD duration were obtained at baseline. In the first stage of the study, patients were given a standard meal consisting of 2 slices of white bread (50 g, 138 kcal, 4.6 g protein), 2 slices of white cheese (100 g, 289 kcal, 22.5 g protein) and 1 glass of tea with no sugar (427 kcal, 27.1 g protein) after the first hour of the HD treatment. The same study group underwent HD without intradialytic food intake 1 week later, in the second stage of the study.

Predialysis and postdialysis blood samples for measurement of blood urea nitrogen (BUN) levels were drawn at the HD sessions with and without food intake. According to the guidelines of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI), predialysis BUN samples were drawn immediately prior to dialysis, using a technique that avoids dilution of the blood sample with saline or heparin. Postdialysis BUN samples were drawn using the slow flow/stop pump technique that prevents sample dilution with recirculated blood and minimizes the confounding effects of urea rebound. The strategy was to slow the pump to 100 mL per min for 15 s prior to sampling. The pump was then stopped and the blood sample was drawn either from the arterial blood line sampling port or from the tubing attached to the arterial needle (21). All the blood samples were processed in the same laboratory. Concentrations of BUN were determined by routine clinical laboratory methods.

Measurement of variables

Assessment of urea removal. The reduction in urea as a result of HD, or the URR was expressed as percentage. The URR parameter was calculated by the following equation: (predialysis BUN - postdialysis BUN) / predialysis BUN (6). The second measure of urea removal we used was Kt/V (where K is the amount of urea clearance, t represents the duration of treatment, and V is the volume of urea distribution), which is a method of assessing the amount of dialysis that is delivered in terms of urea removal. This parameter was calculated using the Daugirdas formula $Kt/V = -\ln(R - 0.03) + [(4 - 3.5R) \times (UF / W)]$, where UF is the ultrafiltration volume in liters, W is the postdialysis weight in kg, and R is the ratio of the postdialysis-to-predialysis BUN (22).

Assessment of hemodynamics. The hemodynamics of patients were evaluated via blood pressure (BP) parameters and heart rate. BP was measured in all participants in the supine position using aneroid sphygmomanometry. The radial heart rate and BP were measured continuously from the fistula free arm by the same investigator. The measurements were taken 9 times during the treatment consisting of measurements at baseline and at 30-minute intervals. The systolic and diastolic BP levels were used for the mean arterial pressure (MAP) calculation. MAP has clinical and physiologic significance in both the representation of perfusion pressure and its utilization in the calculation of hemodynamic variables (23,24). MAP was calculated using the following equation: Diastolic BP + [(Systolic BP - Diastolic BP) / 3] (25).

Statistical analysis

All statistical analyses were conducted using SPSS, version 11.0. Descriptive statistics included the mean, median, standard deviation (SD), frequency distributions, and percentages. The paired samples t-test was used to compare the means of URR and spKt/V between the sessions with and without food intake. Changes in measured variables (MAP and heart rate) with time were assessed by repeated measures analysis of variance (ANOVA), with the mode of treatment (the HD sessions with or without food intake) as a within-subjects factor. The statistical test of interest was the F-test for the 2-factor interaction between group and time. Post hoc differences were assessed using a Bonferroni correction to the overall alpha level of 0.05.

Post-hoc statistical power and sample size calculations were made with a power and sample size calculation program (PS program version 2.1.31) (26). The necessary sample size was calculated as 10 assuming a difference of 5 units between the 2 sessions for URR values and a general SD of 5 units with 80% power and 95% confidence interval using initial assumptions similar to the results obtained at the end of the study. Similarly, the necessary sample size was calculated as 10 assuming a difference of 0.2 units between the 2 HD sessions and a general SD of 0.2 units for spKt/V values. The level of significance was set at 0.05 for all tests.

Results

The patients' mean age was 56.5 ± 13.0 years (range 27 - 64) and median time on HD was 63 months (range 10 - 123). Fourteen (56%) patients were female. Fourty-four percent of the patients were elementary school graduates, 92% were married, 56% were housewives, and 40% were retired. The majority (72%) of the patients had a comorbid condition (cardiac disease, hypertension, or other). Hypertension (60%) was the leading underlying etiological factor for ESRD. Three (12%) patients received angiotensin converting enzyme (ACE) inhibitors, 1 (4%) received angiotensin receptor blockers, 1 (4%) received a supplemental vitamin pill, 1 (4%) received statin, 16 (64%) received erythropoietin (EPO), 2 (8%) received IV iron, and 2 (8%) received active D vitamin treatment during the study.

Table 1 presents the differences between the URR and spKt/V values of the HD session with and without food intake. The mean URR and spKt/V values of the patients were higher in the sessions without food ingestion. As shown in Table 1, significant differences were found between the sessions with and without food intake for URR ($t = 5.416$; $P < 0.001$) and spKt/V values ($t = 6.538$; $P < 0.001$).

Figure 1 shows the MAP while Figure 2 shows the heart rate changes during HD sessions with and without food intake. There was a gradual decreasing trend in MAP values and increasing trend in heart rate in both sessions. The session with food intake showed a faster decrease in the MAP value after hour 1 and the value was lower than the other treatment at the end of the session. In contrast, the heart rate increased faster after the first hour in the same session and the value was higher than the session with no food intake at the end of the treatment. There was a statistically significant difference between the HD sessions regarding the MAP ($F = 32.663$; $P < 0.001$) and heart rate values ($F = 18.399$; $P < 0.001$). All dialysis treatments were tolerated without symptomatic hypotension.

Discussion

Adequate clearance of the whole range of molecules by dialysis is important (5,9). The HD Adequacy Work Group reported that URR and Kt/V focus on only one of the different parameters that operationally define the adequacy of dialysis. Urea is only a marker solute and measures of dialysis adequacy, such as the URR and Kt/V, are only surrogates for the clearance of other small molecular weight solutes (27). The KDOQI guidelines

Table 1. Difference in URR and spKt/V values between the hemodialysis sessions with and without food intake (n = 25).

Variables	With food intake Mean ± SD	Without food intake Mean ± SD	t value *	P value
URR [a]	67.8 ± 6.1	72.1 ± 6.0	5.416	<0.001
spKt/V [b]	1.4 ± 0.2	1.6 ± 0.2	6.538	<0.001

* Paired samples t-test.
[a] URR = Urea reduction ratio (%). [b] spKt/V = single-pool Kt/V.

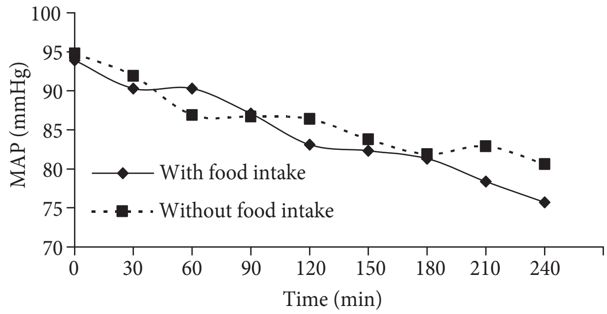

Figure 1. Difference in mean arterial pressures between the hemodialysis sessions with and without food intake

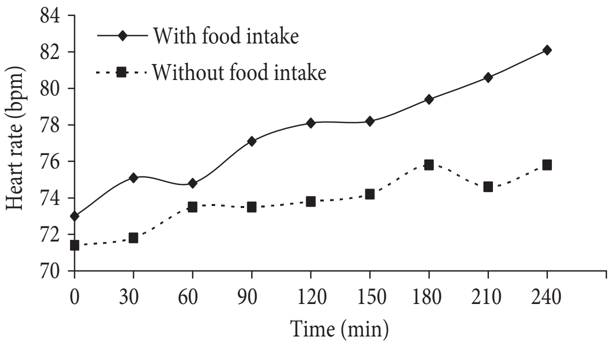

Figure 2. Difference in heart rates between the hemodialysis sessions with and without food intake.

recommend that the minimum delivered dialysis dose per session be a spKt/V of 1.2 or a URR of 65% for HD patients dialyzed three times weekly (7,22,28). In the present study, the URR and spKt/V values obtained from the HD sessions with or without food were in the optimal range as recommended in KDOQI guidelines.

Multiple variables influence the delivery of an adequate dialysis dose. Hemodialysis adequacy is associated with dialysis-related factors, such as the duration of a dialysis treatment, the type and size of the dialyzer membrane used during the treatment, the blood flow rate during the treatment, recirculation, the adequacy of vascular access, and the BUN sampling procedure and personal characteristics (18,19,29). Teixeira Nunes et al. found better HD adequacy findings in female and younger patients (29).

Nutrition is an important part of the treatment because of its influence on morbidity, mortality, and quality of life (25,30,31). The protein-energy intake in HD patients is generally inadequate (25) and the prevalence of malnutrition varies between 10% and 70% (29). In addition, it has been reported a significant reduction in nutrient intake on the day of the HD session (12,13,25). Kalender et al. found that the protein catabolic rate, a marker of nutritional status, is associated with URR and Kt/V values (4). Furthermore, Teixeira Nunes et al. reported an association between Kt/V and anthropometric or biochemical parameters (29). These results indicate that adequate HD treatment has an improving effects on patients' appetite and nutritional status (4,12).

In the literature, there is limited information regarding to relationship between intradialytic food consumption and URR and spKt/V values in HD patients. San Juan Miguelsanz et al. found that intradialytic food consumption led to a significant change in the Kt/V value in 14 HD patients (18). Singri et al. reported that food consumed before treatment did not influence the URR and spKt/V values in 42 patients (19). We did not find any other study investigated the relationship between food consumption during treatment and urea kinetic parameters. In the present study, we found that food intake during HD session decreased the mean URR and spKt/V values. However, we analyzed the effects of food ingestion 1 h after treatment was started in HD patients. Eating at different periods of treatment may have different effects on HD adequacy. In this study, the study power was 98% for URR and 88% for spKt/V. The study power was found to be acceptable (>80%) for both values (26).

Both sessions showed a trend for a gradual decrease in the MAP value and an increase in the heart rate. The MAP value for the participants was lower in the session with food intake than the other session. The heart rate was also higher in the session with food intake than the other session. A healthy individual is predicted to have a 20% decrease in systemic vascular resistance, 35% increase in the splanchnic blood flow and 69% increase in the hepatic blood flow following a meal (16). A large amount of blood flow is diverted from large vessels to the splanchnic organs and the venous return and systemic vascular resistance decrease considerably during intradialytic food ingestion. Intradialytic food ingestion therefore causes hypotensive attacks by decreasing the cardiac output (12,13,32). A recent study involving 20 stable nondiabetic patients found that food intake during HD caused significant reductions in relative blood volume (17). Intradialytic food consumption and intradialytic hypotension also influence the adequacy of the treatment (18,33). Digestion of food decreases the amount of blood filtered during a certain period, which could influence the urea removal (12). Decreasing blood flow and ultrafiltration rate in hypotensive patients further decrease HD adequacy. The patient receives less than the prescribed HD dose and cannot reach the ultrafiltration target. Prolonged hypotension during the HD session also increases urea rebound (10). The relationship between intradialytic food intake and urea kinetic parameters needs to be assessed with further studies.

In conclusion, in the present study, although URR and spKt/V values obtained from the HD sessions with or without food were in optimal range according to recommendations of the KDOQI, food consumption during HD seems to cause a decrease in the URR and spKt/V values. It is not possible to generalize the results of the present study due to potential confounding factors, such as the use of antihypertensive drugs, supplemental vitamin pill, statin, EPO, IV iron, or active D vitamin during the study. However, we feel that our study will guide the way for future studies as the current amount of clinical evidence on the subject is limited.

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