Renal Transplant Alıcılarında Diyaliz Dönemine Göre Safra Kesesi Taşı Riskinde Artış

Increased Risk of Cholelithiasis in Patients After Renal Transplantation With Respect to Dialysis Period

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ÖZET

Renal transplantasyon sonrası safra kesesi taşı sıklığı ve tedavisinde görüş birliği yoktur. Bu çalışmada, aynı hasta grubunda renal transplantasyon öncesi ve sonrası safra kesesi taşı ve komplikasyonlarını batın ultrasonografisi ile değerlendirdik.

Elli üç renal transplant alıcısında transplantasyon öncesi ve sonrasında vücut kitle indeksi, serum biyokimya değerleri, batın ultrasonografisi ve safra kesesi taşı komplikasyonları değerlendirildi. Aynı zamanda son dönem böbrek yetersizliği ve renal transplantasyon süresi ile birlikte kullanılan immünosüpresif ilaçlar kayıt edildi. Toplam 53 olgu (E/K; 31/22) değerlendirildi ve olguların ortalama yaşları 34.11±9.42 yıl idi. Renal transplantasyon öncesi 47 hasta hemodiyaliz tedavisinde idi. Sırası ile hemodiyaliz, peritoneal diyaliz ve transplantasyon süreleri 2.20±1.97 yıl, 1.32±0.74 yıl ve 44.72±33.68 ay idi. Transplantasyon öncesi 1 (%1.9) ve transplantasyon sonrası 6 olguda (%11.3) safra kesesi taşı saptandı. Olguların hiçbirinde transplantasyon öncesi kolesistektomi öyküsü yok iken transplantasyon sonrası bir olguya pankreatit nedeni ile kolesistektomi uygulandı. Transplantasyon sonrasında safra kesesi taşı olan 6 olgunun beşi siklosporin, biri takrolimus kullanıyordu. Transplantasyon öncesi ve sonrasında, total kolesterol (p=0,043), HDL-kolesterol (p=0,000), kalsiyum (0,045), vücut kitle indeksi (p=0,007) değerleri farklı idi ve safra kesesi taşı için sınırda farklılık vardı.

Özet olarak, safra kesesi taşı sıklığı transplantasyon sonrası %1.9'dan %11.3'e yükseldi ve bir olguda safra kesesi taşı ile ilişkili komplikasyon saptandı. Diğer çalışmalardan farklı olarak çalışmamızda, transplantasyon öncesi ve sonrasında aynı hastalar değerlendirilmiş olup safra kesesi taşı gelişiminde siklosporin kullanımı ve kullanım süresi en önemli faktör olarak bulunmuştur.

Anahtar sözcükler: renal transplantasyon, siklosporin, safra kesesi taşı

ABSTRACT

There is no consensus on the incidence and management of cholelithiasis (Cl) in renal transplant recipients (RTrs). In this study, we assessed Cl and its complications in RTrs before and after transplantation by abdominal ultrasonography in the same patients.

Body mass index, serum biochemistry, abdominal ultrasonography and complications of Cl were evaluated before and after transplantation. Also, duration of end stage renal disease, renal transplantation and immunosupressive drugs were evaluated. A total of 53 patients (M/F; 31/22) were evaluated and the mean age of the patients was 34.11±9.42 years. Before transplantation, 47 of 53 patients were on hemodialysis. The duration of hemodialysis, peritoneal dialysis and transplantation were 2.20±1.97, 1.32±0.74 years and 44.72±33.68 months, respectively. Before transplantation, one patient (1.9%); and after transplantation, 6 patients (11.3%) had Cl. None of the patients had history of cholecystectomy before transplantation and one patient had cholecystectomy due to pancreatitis after transplantation. Five of 6 patients who have Cl were on cyclosporine therapy and one patient was on tacrolimus therapy. Before and after transplantation, total cholesterol (p=0.043), HDL-cholesterol (p=0.000), calcium (0.045), body mass index (p=0.007) were significantly different from each other and borderline differences for Cl before and after transplantation.

In summary, the incidence of Cl increased from 1.9% to 11.3% in RTrs, complication of Cl was detected only in one patient. The incidence of Cl is higher in RTrs than pre-transplant patients. Our study was different from the others because pre- and post-transplant patients were the same patients. The most important factors for development of Cl were the usage of cyclosporine and exposed time of cyclosporine.

Keywords: renal transplantation, cyclosporine, cholelithiasis

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Introduction

The real incidence of cholelithiasis (Cl) in renal transplant recipients (RTrs) is not known. Some reports about Cl in RTrs offered the same inciden-

Table I. Biochemical parameters, BMI and abdominal ultrasonography of the patients

Parameters	Before transplantation	After transplantation	p value
Glucose (mg/dL)	92.48±12.49	86.53±17.37	0.006
BUN (mg/dL)	73.02±27.22	21.10±9.67	-
Creatinine (mg/dL)	9.05±2.65	1.46±0.67	-
Total cholesterol (mg/dL)	165.23±33.62	183.12±41.17	0.043
HDL-cholesterol (mg/dL)	39.94±8.65	55.16±15.74	0.000
LDL-cholesterol (mg/dL)	95.11±27.09	98.16±32.16	0.86
Triglyceride (mg/dL)	144.23±49.22	159.76±83.74	0.40
AST (U/L)	17.69±8.92	18.51±9.87	0.46
ALT (U/L)	19.75±13.55	18.53±16.34	0.054
Total bilirubin (mg/dL)	0.57±0.18	0.62±0.25	0.17
Ca (mg/dL)	9.75±0.91	9.95±0.46	0.045
P (mg/dL)	4.72±1.47	3.49±0.61	0.000
BMI	22.35±3.04	23.45±3.38	0.007
Cholelithiasis	1 (1.9%)*	6 (11.3%)	0.063
Complications of cholelithiasis	0	1 (pancreatitis)	-

* tacrolimus based

ce in general population (1). Also, appropriate management in these patients is controversial (1,2). But, these studies were based on patients on the waiting list or after transplantation cross-sectionally.

In this study, we assessed Cl and its complications in RTrs before and after transplantation by abdominal ultrasonography. According to our knowledge, this is the first report of evaluation of Cl in RTrs before and after transplantation in long-term period.

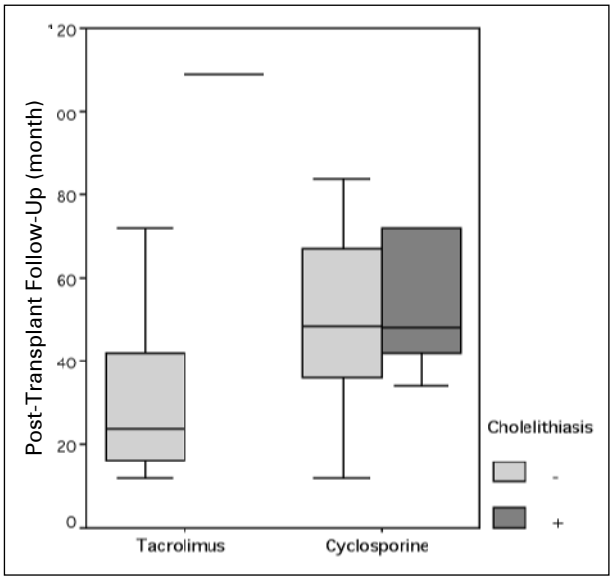

Figure 1. Cholelithiasis in renal transplant recipients.

Patients and Method

Candidates for renal transplantation on the waiting list were evaluated retrospectively for age, Cl, history of cholecystectomy, serum biochemistry, duration of dialysis, number of maternity, diabetes mellitus, body mass index (BMI) and abdominal ultrasonography. After renal transplantation, duration of transplantation, serum biochemistry, immunosuppressive drugs, abdominal ultrasonography, cholecystectomy, biliary colic, pancreatitis due to Cl, and antihypertensive medication were noted in post-transplant follow-up (PTFU) in the same patients. Abdominal ultrasonography was performed by General Electric (GE) Lopic 500 series and 3.5 mHz convex transducer. Statistical analysis was performed by Wilcoxson Signed Ranks Test and data were expressed as mean±SD.

Results

A total of 53 patients were evaluated and 31 of 53 patiens (58.5%) were male. The mean age of the patients was 34.11±9.42 years. Before renal transplantation, 47 patients were on hemodialysis and 6 patients were on CAPD. The duration of hemodialysis and periton di-

alysis were 2.20±1.97 and 1.32±0.74 years, respectively. None of the patients had diabetes mellitus, and 7 female patients had a total of 11 children (1 patient had 3, 2 patients had 2 and 4 patients had 1 children). Also, none of the patients had history of cholecystectomy before transplantation. The post-transplant duration was 44.72±33.68 months. Twenty-three patients were on cyclosporine based, 27 patients were on tacrolimus based and 3 patients were on sirolimus based immunosuppressive treatment. In all patients, target levels of these drugs were achieved. The biochemical parameters and findings of abdominal ultrasonography are shown in Table I. The post-transplant follow-up and cholelithiasis of the patients are shown in Figure 1.

Five patients who have cholelithiasis were on cyclosporine based immunosuppressive treatment and 1 patient was on tacrolimus based immunosuppressive treatment. The median time of Cl detection was 60 months (min 34-max 136). After adjustment for duration of the transplantation, the usage of cyclosporine increased the risk of Cl 9 times. When the patients who have Cl after transplantation were evaluated for serum lipid levels, AST, ALT, BMI, and CaxP before and after transplantation, there was no significant difference for each other, except HDL-cholesterol (p=0.046).

Discussion

Epidemiological studies have reported an incidence of Cl of >10% in general population (3,4). Studies showed that the incidence of Cl in dialysis patients was higher than that of in general population. Vecchi et al have reported that incidence of Cl in pre-dialysis patients was higher (22%) than in general population and lower than patients in dialysis. In this study, it was claimed that the higher incidence of cholelithiasis was not associated with age, BMI, diabetes mellitus, usage of oral contraceptives and dyslipaemic alterations (5). But, Paydas et al found an incidence of cholelithiasis of 8% in 100 patients with end stage renal disease in our local area (6). Interestingly, we found an incidence of cholelithiasis of 1.9% in pre-transplant patients. These differences can be related with the higher age and incidence of diabetes mellitus. In a study, Graham et al screened 423 transplant patients when they were placed on the waiting list or following transplantation and the incidence of Cl was found as 10%. Also, 29 patients had history of cholecystectomy. They reported that combined incidence was 17% (7). In our study, the incidence of Cl increased from 1.9% to 11.3% after transplantation. We found that the incidence of Cl in transplantation was similar with general population. It is known that the incidence of Cl shows an increase with age. The highest Cl incidence was in 50-60 years of age (5.3% for males, 13.5% for females) (8). The mean age of our patients was 34.11±9.42 years and when this value is taken into consideration, we can say that the incidence of Cl in our patients is higher than in general population of similar age. This increase can be related to weight gain after transplantation, the usage of cyclosporine, dyslipidemia and increase in Ca levels. It is well known that Cl is related to obesity (3). In our study group, BMI increased after transplantation. If we consider water retention in pre-transplant patient, the increase in BMI may be more important after transplantation. But our patients on PTFU were not over-weighted or obese. It has been claimed that the usage of cyclosporine for more than 2 years shows increased risk for Cl (9). Our results are similar to these reports and 5 of 6 patients who have Cl were on cyclosporine therapy and the median time of Cl detection was 60 months. The usage of cyclosporine increased the risk of Cl for 9 times when we adjusted the duration of the transplantation. Also, it has been reported that the incidence of Cl increased in patients with dyslipidemia (10). Our study group showed a significant difference for total cholesterol before and after transplantation. This difference is probably due to immunosuppressive treatment.

Calcium and phosphorus may play a partial role for formation of gallbladder stone because these minerals have been found in the core and outer layers of both cholesterol and pigmented gallbladder stones (11). Our patients have significant increase in Ca while phosphate levels decrease.

As long as gallbladder stones remain asymptomatic, treatment is not warranted. It has been reported that only 7.85% of 662 RTrs devoleped symptoms from Cl requiring cholecystectomy (1). In RTrs, prophylactic cholecystectomy is not recommended because of low incidence and morbidity of Cl (1). But, some authors recommended that prophylactic (especially laparoscopic) cholecystectomy is appropriate management for patients on the waiting list who have Cl to prevent its complications such as biliary colic, acute cholecystitis and

gallbladder stones, pancreatitis after transplantation (2). Melvin et al notified that 52 (7.85%) of 662 RTrs had required cholecystectomy for Cl disease and its complications (1). Only one of our patients has cholesystectomy due to pancreatitis.

In literature, it has been claimed that azathioprine and angiotensin converting enzyme inhibitors (ACEI) also caused Cl via cholestatic hepatitis (12,13). Three of 6 patients who have Cl were taking ACEI and one of 6 patients was taking angiotensin receptor blocker.

In summary, we detected the incidence of Cl as 11.3%. Cyclosporine usage was an important factor for Cl. The median time of Cl detection was 60 months. Although the incidence of Cl increased from 1.9% to 11.3% in RTrs, complication of Cl was detected only in one patient. We can say that the incidence of Cl is higher in RTrs than pre-transplant patients. Our study was different from the others because pre- and post-transplant patients were the same and only one patient had Cl before transplantation. The most important factors for development of Cl were the usage of calcineurin inhibitors, especially cyclosporine, and exposed time of cyclosporine.

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