



RESEARCH ARTICLE

Immunosuppressant Therapy Adherence after Kidney Transplantation

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Abstract

Background: Immunosuppressive therapy (IST) is administered to the individual to prolong the graft survival; thus, the survival of the patient after organ transplantation. Adherence of the individual to IST is crucial.

Aim: In this study, it was aimed to find out patients' adherence to immunosuppressant therapy after kidney transplantation.

Material and Methods: The sample of this descriptive study consisted of 50 patients; who underwent kidney transplantation in a university hospital in Istanbul and who applied to the hospital for follow-up in the period between May 2017 and September 2017. Data were collected using the "Descriptive Characteristics Information Form" and the "Immunosuppressant Therapy Adherence Scale".

Results: All of the participants in the study achieved the targeted blood levels of immunosuppressants and 54% had never forgotten/postponed taking the immunosuppressants. The patients; who forgot/postponed taking prescribed medications, reported the associated reasons as follows: Forgetfulness/carelessness (16%), leaving the medications at home forgetfully (14%), unable to take medications because of being away from home (10%), and barriers related to their occupation (6%). The mean score of the Immunosuppressant

Therapy Adherence Scale was 11.40 ± 0.75 and individuals with a post-transplant period of shorter than two years had a higher mean score (11.81 ± 0.40) of the scale in this study ($p < 0.05$).

Conclusions: In the study, immunosuppressant therapy adherence of patients was found high and all patients achieved the targeted blood levels of immunosuppressants after kidney transplantation.

Keywords

Adherence to treatment, Immunosuppressive therapy, Organ transplantation

Introduction

Kidneys are the most commonly transplanted organ in the world and Turkey. Dialysis methods are several but allow for replacing only a minor proportion of the total glomerular filtration function of a healthy kidney. Other renal functions; including the production of erythropoietin, activation of vitamin D, and the maintenance of the acid-base balance cannot be replaced at all. Therefore, kidney transplantation is the most appropriate treatment method for end-stage renal failure as a life-saving and cost-effective treatment modality [1,2].

Immunosuppressive therapy (IST) is administered to the individual to prolong the graft survival; thus, the survival of the patient after organ transplantation. Adherence of the individual to IST is crucial [2]. Medication non-adherence of organ transplant patients is described as medication errors/skipping at least one dose of the medication in a month or taking the drug two-and-a-half hours later than the prescribed time at least once in a month [3].

The rates of immunosuppressant therapy adherence after organ transplantation vary from 15% to 68% [4-6]. Age, gender, the time elapsed after organ transplantation, working status of the individual, cost of immunosuppressants, drug side effects, number of drugs taken in a day, frequent updates to the IST regimen, psychological problems, and disbelief in treatment are reported as factors affecting IST adherence [1,6,7].

In a study conducted by Chisholm, et al. [5] on kidney transplant patients in the United States of America (USA), 65% of the patients were found adherent to IST. The adherent patients were younger; they underwent organ transplantation more recently, and achieved the targeted serum levels of immunosuppressants. Another study by Russel, et al. [2] reported that 86% of the kidney transplant patients included in the study were non-adherent to IST. Gorevski, et al. [8] found out that non-adherence in liver transplant recipients was associated with young age, whereas non-adherence in kidney transplant recipients was associated with depression, decreased physical functioning, and personality traits. In the study conducted by Cheng, et al. [9] on 412 kidney transplant recipients, it was reported that the patients had complaints about the medications used for IST and frequently complained of memory impairment, which acted on IST adherence unfavourably. Madran, et al. [6], reported that IST adherence was higher in women and in individuals with a post-transplant period of shorter than two years.

One of the major factors acting on graft survival, prevention of transplant rejection, and the achievement of low mortality and morbidity rates after organ transplantation is the training of transplant patients about IST adherence in the post-transplantation period. However, most patients fail to achieve full adherence to IST. For this reason; it is critical that organ transplant nurses should determine the level of IST adherence of individuals after transplantation, identify positive and negative factors that act on adherence, and implement the necessary care interventions. Despite the availability of studies in the international scientific literature that investigate adherence to IST after kidney and liver transplantation [7-9], only a few studies have been conducted in Turkey [6,7,10]. In this context, the study was planned and conducted to determine adherence levels of individuals; who underwent kidney transplantation, and to identify factors that act on adherence to IST.

Methods

Study design

This study was carried out descriptively.

Study population and sample

The population of the study consisted of all patients, who underwent kidney transplantation in a University Hospital in Istanbul. The study sample consisted of 50 patients; who applied to the same centre for post-transplant follow-up in the period between May 2017 and September 2017 and who met the sample selection criteria of the study. A target sample size was set aiming to include a number of patients 10 times as much as the number of the items in the scale (40 patients). The research was stopped after including 50 patients.

The inclusion criteria of the study were as follows: Undergoing organ transplantation in the centre, where the study was conducted; a period of at least 3 months elapsing after the hospital discharge of the individual after organ transplantation, being 18-years-old or older, using immunosuppressants, being able to take medications on their own, not having medically confirmed cognitive and mental impairments, being able to speak Turkish, and voluntarily agreeing to participate in the research.

Data collection tools and collection of the data

Data were collected using the “**Descriptive Characteristics Information Form**” and the “**Immunosuppressive Therapy Adherence Scale (ITAS)**”.

Descriptive Characteristics Information Form: This form comprised 9 items to collect information about patients participating in the study including age, gender, educational status, working status after organ transplantation, the time elapsed after organ transplantation, donor type, the number of drugs used in a day, the achievement of the targeted immunosuppressant levels in the blood, and the organ rejection history.

Immunosuppressive Therapy Adherence Scale (ITAS): ITAS was developed by Morisky, et al. (1986) to evaluate the adherence of hypertensive patients to antihypertensive drugs. Chisholm, et al. [5] adapted the scale for use in organ transplant patients in order to evaluate adherence to IST. The reliability and validity study of the scale in Turkish was conducted by Madran, et al. [6]. The scale comprises four items that question the adherence of patients to IST in the last three months after organ transplantation. The items are scored on a four-point Likert scale. The answers given to the scale questions are scored to assess adherence to IST as follows: Three points for response values of 0%, two points for 0-20%, one point for 21-50%, and zero points for values of more than > 50%. The lowest and highest scores that can be obtained from the scale are zero and 12, respectively. Increasing scale scores indicate higher ad-

herence to IST. After determining the percentage points correctly conforming to the responses provided by the patients, the suitable options are selected and the total scale score of the patient is calculated. The scale was designed in a way to reflect the degree of patient adherence in percentage points because it was considered that short expressions such as “yes” and “no” answers would limit determining the extent of IST adherence comprehensively. The Cronbach’s alpha reliability coefficient of the scale is 0.65. In this study, the Cronbach alpha coefficient of the scale was found to be 0.80.

After obtaining verbal and written informed consent from the individuals, descriptive characteristics were collected by the face-to-face interview method on the days of outpatient clinic services at the study site. ITAS was filled by patients.

Blood levels of immunosuppressants were not specifically controlled for the study. The patients’ blood levels of immunosuppressants, which were tested once a month, were checked for the previous three months.

Data analysis

The study data were analyzed statistically by the IBM SPSS 22.0 (IBM Statistical Package for Social Sciences Corp.; Armonk NY, USA, 2013) software package. Besides the descriptive statistical methods (mean, standard deviation, and frequencies), non-normally distributed data were analyzed by the Mann-Whitney test between paired groups and the Kruskal Wallis Test across multiple groups. The linear relationship between age and scale scores was evaluated using the Pearson correlation test. The level of significance was assessed at a p-value of < 0.05.

Ethical considerations

Before starting the study, the permission to use the scale was obtained via e-mail correspondence with Madran, et al. [6], who performed the validity and reliability study of the scale in Turkish. The approval of the Clinical Studies Ethics Committee (decision number A-53 dated 06/06/2017); the written permission from the hospital, where the study data were collected, and the written and verbal consent of the individuals included in the study sample were obtained before commencing the study.

Results

The mean age was 43.24 ± 13.92 years in the sample group; which consisted of women at a rate of 50% and primary school graduates at a rate of 44%. Of the participants; 64% did not work actively after the kidney transplant, 78% had a post-transplant period of longer than 2 years, 72% received a kidney transplant from a living donor, 48% took 6-10 pills in a day, 42% took two immunosuppressive medications in a day, all patients achieved the targeted immunosuppressant blood levels, and no patients had a history of transplant rejection (Table 1).

Table 1: Demographic characteristics of transplantation patients (n = 50).

Demographic Characteristics	Mean \pm SD
Age	43.24 \pm 13.92
	n (%)
Gender	
Male	25 (50.0)
Female	25 (50.0)
Educational status	
Literated	6 (12.0)
Primary school	22 (44.0)
High school	14 (28.0)
Undergraduate and above	8 (16.0)
Working status after organ transplantation	
Yes	18 (36.0)
No	32 (64.0)
The time elapsed after organ transplantation	
Less than 2 years	11 (22.0)
More than 2 years	39 (78.0)
Donor type	
Living donor	36 (72.0)
Cadaveric donor	14 (28.0)
Number of drugs taken in a day	
1-5 pieces	23 (46.0)
6-10 pieces	24 (48.0)
10 pieces and above	3 (6.0)
The achievement of the targeted immunosuppressant levels in the blood	
Yes	50 (100.0)
No	0 (0.00)
Rejection history	
Yes	0 (0.00)
No	50 (100.0)
Total	50 (100.0)
SD: Standard deviation.	

In this study, the mean ITAS score was 11.40 ± 0.75 . The mean ITAS score was higher in patients with a post-transplant period of shorter than two years ($p < 0.05$). There were no differences in the mean ITAS scores by the variables of gender, working status after transplantation, donor types, and the total number of pills taken in a day ($p > 0.05$). It was determined that there was not a relationship between age and the mean ITAS score ($r = 0.229$; $p > 0.05$) (Table 2).

Of the sample group; 54% had never forgotten/postponed taking the prescribed immunosuppressants. The participants; who forgot/postponed taking the prescribed immunosuppressants reported the following reasons as follows: Forgetfulness/carelessness (16%), forgetfully leaving the medications at home (14%), being away from home (10%), and work-related barriers (6%) (Table 3).

Table 2: Comparison of the demographic characteristics and the mean score of the Immunosuppressive Therapy Adherence Scale.

Demographic characteristics	The mean ITAS score	SD	Min.	Max.	p
Age	11.40	0.76	9	12	0.109* r = 0.229
Gender					
Female	11.52	0.65	10	12	0.324**
Male	11.28	0.84	9	12	
The time elapsed after organ transplantation					
Less than 2 years	11.82	0.40	11	12	0.031**
More than 2 years	11.28	0.79	9	12	
Working status after organ transplantation					
Yes	11.22	0.88	9	12	0.269**
No	11.50	0.67	10	12	
Donor type					
Living donor	11.28	0.81	9	12	0.078**
Cadaveric donor	11.71	0.47	11	12	
Number of drugs taken in a day					
1-5 pieces	11.22	0.90	9	12	0.192***
6-10 pieces	11.50	0.59	10	12	
10 pieces and above	12.00	0.0	12	12	
*Pearson's correlation test; **Mann-Whitney U test; ***Kruskal Wallis Test; SD: Standard deviation; Min: Minimum; Max: Maximum.					

Table 3: Reasons of forgotten/postponed taking immunosuppressants (n = 50).

Reasons of forgotten/postponed	n (%)
Forgetfulness/carelessness	8 (16.0)
Forgetfully leaving the medications at home	7 (14.0)
Being away from home	5 (10.0)
Work-related barriers	3 (6.0)
Never forgotten/postponed	27 (54.0)

Discussion

Adherence to IST after kidney transplantation is crucial to preserve graft functions and prevent transplant rejection [11]. Acute rejection has been reported to be related to non-adherence to IST approximately in 50% of acute rejection reactions and approximately in 15% of organ losses in the late post-transplant period in kidney transplant patients [7,11]. Therefore, adherence to IST is expected and aimed after organ transplantation. The rate of non-adherence to IST in kidney transplant patients is reported to vary from 15% to 55% in the literature [1]. Dew, et al. [12] reported the rate of IST non-adherence was as 36% in kidney transplant patients. In the studies conducted by Ichimaru, et al. [13] and Germani, et al. [14] they were reported that the rate of non-adherence to treatment was high in kidney transplant patients. Contrary to the results of that study, Şahin [10], Weng, et al. [15], Promraj, et al. [16], Albekairy, et al. [17], found high adherence to IST in the majority of pa-

tients after organ transplantation. Consistent with the information in the literature [10,15,16], it was found in this study that patients' adherence to IST was high.

Studies in the literature [18,19] report that young individuals have lower IST adherence compared to adults because individuals in younger age groups go to bed late, get out of the bed late, drink alcohol, have an active social life, and disregard treatment assuming that they would never be sick. The high IST adherence found in this study may be explained by the fact that most of the patients included in the study were adults.

In the literature, factors associated with non-adherence to IST after organ transplantation were reported as problems related to young age, the time elapsed after transplantation, black race, daily routines, characteristics and doses of medications, medication costs, and access to medications [11,15,20].

The rate of non-adherence to IST is reported to be high in young people because of reasons including the concerns about the body image, the level of cognitive development (the extent of abstract thinking and behaviour control), being in active professional life, and difficulties in adjusting to daily routines due to the lifestyle [18,21,22]. It is reported that the second most non-adherent group are old people after young individuals and it is suggested that forgetfulness plays a major role in the development of non-adherence [18]. Similar to the study conducted by Albekairy, et al. [17],

Muduma, et al. [18] identified old age as a factor acting on IST adherence unfavourably in their study on liver transplant patients. In the studies conducted by Şahin, et al. [10] and Burn, et al. [23], it was found out that adherence to IST increased with progressing age. In the study conducted by Ören and Sucu-Dağ [7], it was found out that individuals under the age of 40 had lower IST adherence. In the study conducted by Özdemir and Talas [20], it was reported that most patients were in the adult age group and that there was not a relationship between age and IST adherence. In this study, it was observed that there was not a relationship between age and the IST adherence rates consistent with the information in the literature [20].

Although it is reported that the socioeconomic factors involved in adherence mainly include education levels, profession, and income levels; the World Health Organization (WHO) consider that gender, age, ethnic origins, and the availability of social support are also included in the group of socioeconomic factors within the context of medication adherence [1,2]. Denhaerynck, et al. [4] and Griva, et al. [21] reported that non-adherence to IST was more common in men in their study. Gheith, et al. [24] showed that the risk of non-adherence to IST was higher in female organ transplant patients. In this study; consistent to the results reported by Butler, et al. [3] and Russell, et al. [25], no differences were found in IST adherence rates by gender.

Another factor associated with non-adherence to IST after organ transplantation is the time elapsed after transplantation. It has been reported that adherence to IST progressively decreased each following year after kidney transplantation [15]. Hamedan, et al. [20] evaluated IST adherence in their study and reported that the highest rate of adherence occurred in the first post-transplant year and the lowest adherence rate occurred beyond the 16-21 years post-transplant. Similarly, Burkhalter, et al. [26] reported that non-adherence to IST increased as the time elapsed got longer after transplantation. Özdemir and Talas [20] reported in their study that adherence to IST increased as the time elapsed after transplantation got longer. Similar to the results reported by the studies conducted by Hamedan, et al. [20] and Burkhalter, et al. [26], it was found in this study that the patients with post-transplant periods of shorter than two years had high IST adherence. The patients' adherence to IST might result from their fear of potential transplant rejection in the early post-transplantation period as they had just been freed of dialysis.

It is reported that the number of medications required to be taken daily by the individual is one of the factors affecting adherence to IST [1,15]. In the study conducted by Weng, et al. [15], it was found out that medication adherence increased as the number of medications to be taken in a day by kidney transplant patients was reduced. Moralesa, et al. [27] found the

medication adherence was very high in kidney transplant patients. In this study, no differences were found in IST adherence by the number of medications to be taken in a day.

In individuals who continue to work actively after organ transplantation, the intensity of working life is considered as one of the factors that act on medication adherence unfavourably [6,7]. In this study, no differences were found in IST adherence between the participants, who were employed, and the ones, who stopped working after organ transplantation. The findings of the study; which showed that neither the employment status nor the number of medications to be taken in a day acted on IST adherence after transplantation, might have resulted from the use of smartphone applications, electronic reminders, and tracking systems commonly utilized today as aids for remembering to take prescribed medications.

Adherence to drug therapy is defined as taking the correct doses of the prescribed medication regularly at proper time intervals [1]. It is important to take immunosuppressants at the right time of the day in order to maintain graft functions and prevent transplant rejection. Forgetfulness is a major factor acting on adherence to IST [15]. It has been shown in the scientific and academic literature that the major cause of non-adherence to IST is forgetting to take medications [1,15]. In this study, it was found that the majority of the patients did not forget/postpone taking the prescribed medications. The participants of this study; who forgot/postponed taking the prescribed medication claimed forgetfulness as the cause consistent with the literature. The results of this research are considered important as it provides grounds for the implementation of interventions that would remind individuals to take the prescribed medication.

Limitations of Study

This study has small sample size and a single-center design which precludes the generalization of the results to the overall organ transplantations patients.

Conclusion and Recommendations

In the study, adherence to IST was found high and all patients achieved the targeted blood levels of immunosuppressants after kidney transplantation. It may be suggested that the causes of forgetfulness specifically at the individual level should be identified and nursing interventions should be applied at the root-cause level when non-adherence is detected. It may also be suggested that further studies on larger sample groups should be conducted.

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