

Use of Complementary and Alternative Medicines in Renal Transplant Patients in Turkey

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Abstract

Introduction: There is limited data concerning the use of Complementary and Alternative Medicine (CAM) among in and worldwide. Our aim in this study to evaluate the use of CAM among patients kidney transplant recipients in.

Patients-methods: This is a cross-sectional study was conducted from May 2019 to May 2020 in the nephrology outpatient clinics of 5 different university hospitals. Demographic, laboratory features were recorded. They answered a self-administered a survey questionnaire, this form is included questions on socio-demographic and clinical features and on the CAM therapies.

Results: A total of 830 patients (496 (59.8%) males, 334 (40.2%) females; mean age 43.9 ± 9.4 years) kidney transplantation recruited for the study. One hundred ninety two (22.89%) of the patients reported the use of one or more forms of CAM. Meanwhile, 78% of CAM users did not report their CAM therapies to their physicians. Herbal therapies used most often parsley+ cinnamon + lemon juice (57.8%), followed by Garlic + lemon juice (51.4%) and *Nigella sativa* and nettle (42.3%). There was a significant correlates for CAM users were older age ($p=0.00$; $OR=0.76$; $95\% CI=0.88-0.93$), occupational status ($p = 0.045$) and monthly income ($p= 0.021$; $OR=2.18$; $95\% CI=1.42-3.3$).

Conclusion: We determined that every five of one kidney transplant patients were using one type of CAM. Some of these CAMs are potentially harmful and may affect patient compliance to immunosuppressive therapies. Doctors and nurses should ask questions about CAM therapies to patients on visit days and healthcare professional should explained their knowledge about CAM therapies.

Keywords: Alternative and complementary medicine • Treatment • Kidney transplant

Introduction

Complementary and alternative medicine (CAM) is popular worldwide and the use of CAM has increased dramatically in recent decades [1,2]. Also, CAM may be dominated especially in developing in countries due to inevitable adverse effects of conventional medicine [3]. The prevalence of CAM usage varies worldwide, accounting for 10-40% in European general population, 40-60% in the USA, 49% in Australia, 75% in Africa, 21.6-90% in Saudi Arabia and up to 21.5-42% in Turkey [4-11].

However, data regarding the use of CAM among patients CKD patients in the world and in the are limited, possibly cause that many patients who used CAM for CKD may withhold this information from their primary healthcare providers.

It is mentioned that used CAM therapy in patients with CKD controlled their symptoms in the pre-dialysis period [12,13]. Several studies showed that prevalence of CAM use in patients with hemodialysis 18-63% [6,7,12,14].

In a study from United States, the prevalence of use CAM therapies in lung transplant patients was found to be 88% (8). This rate was reported as 20% in patients with other organ transplants [9].

Among the CAM therapies there are: acupuncture, body-mind exercises

like yoga, hypnosis or relaxation methods, biological agents like herbal products or dietary supplements and body-based methods like massage or exercise. The healthy population uses CAM to maintain their health status, to feel safe and to protect themselves from chronic diseases [10-12].

The use of CAM in the European general population ranges between 10% and 40% [1,2,4-6]. US national surveys assessing the use of alternative medicine in the general population is 40-60% [7]. In Australia report that 68.9% of the population use CAM. In Asian countries 68.9% of residents used CAM [14].

The prevalence of CAM usage varies worldwide, accounting for 10-40% in different European countries, 40-60% in the USA, 49% in Australia, 75% in Africa and up to 21.6-90% in Saudi Arabia CAM therapies are safe is a widely believed however, it can lead to several adverse effect, such as anaphylaxis, hypertension, dermatitis, liver and nephrotoxicity induction. Also many of herbs therapies can interact with immunosuppressive medicines such as calcineurin inhibitors (cyclosporine and tacrolimus). The interactions may increasing or decreasing the level of the immunosuppressant in kidney transplant patients [15].

We believe that the prevalence of usage CAM therapies in chronic kidney disease patients may be greater in our country like in the worldwide. To our knowledge, there were several studies have evaluated the prevalence of CAM therapies use among patients with CKD and renal transplant recipients [13-15]. Despite the increasing use of CAM therapies among the general population and in CKD patients, there is a very little data about the usage of CAM among patients with kidney transplantation patients in and in the world-wide [14-16].

In this study, we primarily aimed to determine the usage of prevalence and types of CAM therapies among kidney transplant recipients. We second aimed to investigate reasons for using CAM therapies; and the influences, benefits, outcomes, interactions with immunosuppressive medicine and predictors of CAM use.

Materials and Methods

The study was designed in the outpatient nephrology clinics of five

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university hospital in different region of participants were chosen from these transplant clinics randomly. Nine hundred thirty two patients were interviewed and 830 patients were received the complete interview.

We included patients with kidney transplant who were older than 18 years and following for at least 12 months, currently on immunosuppressive therapy: from 278 deceased and 552 living. We excluded participants if the patients were; unable to manage their therapies independently, who had neurological or psychological disorders, not respond to questions.

Our questionnaire form was containing 28 questions; 12 questions on socio-demographic characteristics (e.g. age, gender, marital status, residency, educational level vs.), 6 questions were about the clinical characteristics of the patients (e.g., urea, creatinine, hemoglobin vs.), 10 questions on CAM therapy. The patients were then asked to fill a form included questions that assessed the prevalence of CAM, CAM types (natural products: herbs, vitamins and minerals, dietary supplements, mind and body practices: Qigong, yoga, acupuncture, massage other complementary health approaches: Ayurvedic medicine, traditional Chinese medicine, homeopathy, naturopathy).

The study was approved by the University Hospital ethics Committee and all patients signed informed consent.

The vitamin supplements that were consumed by the patients were accepted as CAM if not prescribed by a doctor. The demographic data and laboratory results of the patients were recorded from their files.

Statistical analysis

All data were analyzed using the Statistical Package for the Social Sciences version 23 (IBM Corp., Armonk, NY, USA). For descriptive analysis, we computed the means, standard deviations (SD), frequencies and percentages. Pearson's Chi-square test or Fisher's exact test were used to the comparative analysis (stratification of CAM users and non-users). The level of $p < 0.05$ was considered significant for all analyses.

Results

A total of 830 patients were included in the study. Five hundred six (59.8%) of the patients were men with a mean age of 43.9 ± 9.4 years and a mean post-transplant period of 80 ± 22 months. The mean creatinine levels and GFR values were 1.4 ± 0.2 mg/dl and 64.36 ± 24.2 ml/min/1.73m² respectively. The patients' socio-demographic variables and laboratory results are summarized in Table 1.

All the patients were taking immuno-suppressive medications including steroids, calcineurin inhibitors (tacrolimus or cyclosporine-A) and anti-proliferative (mycophenolat mofetil, mycophenolat sodium or azotiyopurin) agents. In addition, some patients had co-morbidities where 38% of the patients had diabetes mellitus and 42% had hypertension.

One hundred ninety two (22.89%) of the patients reported the use of one or more forms of CAM.

Herbal therapies were most frequently used (78.1%) of CAM users. Herbal therapies used most often were Parsley+ cinnamon+ lemon juice (57.8%), followed by Garlic + lemon juice (51.4%) and green tea and nettle (42.3%). Herbal-dietary supplements and their frequency of use are summarized in Table 2.

Thirty-four (17.7%) patients used mind body techniques (relaxation techniques, prayer, bio-feedback, meditation vs.), 8 (4.1%) patients used alternative system such as acupuncture, cuppa (Table 3). None used traditional Chinese medicine (homeopathy, ayurvedic medicine).

The patients were inquired for CAM from their physicians every visit. Only 22% of transplant patients had informed their nephrologist about CAM consumption. The patients who used CAM were not aware of potential interaction risks related with herbal supplements. Percent of 5.7 patients aware about risk of CAM related interactions.

Most of the CAM users were 88% married, 48% unemployed, 68% primary-middle school graduate, 71% living in the city center, 91% living with family,

58% 5000-1000 monthly incoming TL. There was no significant differences socio-demographic features between users and non-users of CAM therapies ($p > 0.05$). Also, no significant difference was observed between CAM users and non-users in terms of serum creatinine, albumin, hemoglobin, leukocyte, thrombocyte count and proteinuria levels. Characteristics of users and non-users of CAM therapies are summarized in Table 4.

Thirty-seven patients (31%) obtained information about CAM therapy from their families, close friends or neighbors, 26 patients (22%) from the internet or media. CAM used was recommended to 22 (18%) patients by health care professionals (such as doctor or nurse) and the remaining obtained them by other different ways (social media, other application). As high as 85% (n=124) of the 146 CAM users did not disclose their use of CAM to their nephrologist.

When we asked to patients why they used CAM, the most frequently responses were to improve physical and emotional well-being (59%), control of diabetes (12%) and treat hypertension (10%). Other commonly responses for indications were prophylaxis of urinary tract infections (8%), treating urinary tract stones (7%), for improving their condition without harm (4%).

Table 1. Demographic features and Laboratory results of all the patients.

Variables	Results	
Age (year)	<40	413 (49.7%)
	40-60	320 (38.5%)
	>60	97 (11.8%)
Gender	Male	506 (59.3%)
	Female	338 (40.7%)
Education Level	Knows how to read and write	70 (8.4%)
	Primary or Middle school graduate	462 (55.6%)
	High School or University graduate	298 (36%)
Post-transplant period (months)	(<12)	86.3 (10.4%)
	(12-36)	144 (17.3%)
	(>36)	599 (73.3%)
GFR (ml/min)	60.36 \pm 24.44	
Albumin (gr/dl)	4.28 \pm 0.39	
Hb (gr/dl)	13.1 \pm 1.88	

Table 2. Herbal-dietary supplements and their frequency of use.

Supplement	Number of patients (%)
Parsley+cinnamon+lemon juice	111 (57.8)
Garlic + lemon juice	98 (51.4)
Green tea + Nettle	81 (42.3)
chamomile tea	10 (5.2)
Ginger	14 (7.29)
Giloburu plant	8 (4.1)
Black cummin	4 (2)
Green tea	18 (9.3)
Goat horn	10 (5.2)

Table 3. Most frequently reported body-mind practices and alternative therapies used by participants, n (%).

Body-Mind practices	Patient (n:42) (%)
Prayer + meditation	11 (26.1%)
Relaxation techniques	10 (23.8%)
Breathing therapy	9 (21.4%)
Yoga	4 (9.5%)
Acupuncture	3 (7.1%)
Cuppa	5 (11.9%)

Table 4. Demographic features and laboratory results of patients on CAM compared to patients not on CAM.

Variables	CAM+ (n: 192) %	CAM- (n: 638) %	P value
Age (year)			
<40	29 (15%)	291 (45.6%)	0.01
40-60	141 (73.3%)	272 (42.6%)	
>60	22 (11.6%)	75 (11.8%)	
Gender			
Male	68 (35.6%)	424 (66.4%)	0.15
Female	124 (64.4%)	214 (33.6%)	
Married status			
Married	167 (88%)	618 (91%)	0.54
Not-Married	25 (12%)	66 (9%)	
Education Level			
Knows how to read and write	12 (6.3%)	41 (6%)	0.04
Primary or Middle school graduate	89 (46.5%)	404 (59%)	
High School or University graduate	91 (47.2%)	239 (35%)	
Occupation			
Employed	80 (42%)	308 (45%)	0.04
Unemployed	92 (48%)	301 (44%)	
Student	20 (10%)	75 (11%)	
Living Place			
City	136 (71%)	465 (68%)	0.21
Out of City	56 (29%)	399 (32%)	
Monthly Income			
< 5000 TL	42 (22%)	164 (24%)	0.02
5000-10000 TL	112 (58%)	376 (55%)	
>10000 TL	38 (20%)	144 (21%)	
Post transplant period (months)			
<12	19 (10%)	73 (11%)	0.79
12-36	35 (18%)	118 (17%)	
>36	138 (72%)	493 (72%)	
Diabetes Mellitus	72 (32%)	(34%)	0.1
Hypertension	58 (28%)	(31%)	0.13
GFR (ml/min)	56.78 ± 20.523	60.79 ± 25.03	0.22
Albumin	4.24 ± 0.4	4.28 ± 0.38	0.41
Hb (gr/dl)	12.9 ± 1.8	13.1 ± 1.8	0.87
Leukocyte	8.800 ± 2480	7.700 ± 1980	0.62
Thrombocyte	358.000 ± 128.000	374.000 ± 157.000	0.71

Discussion

The present cross-sectional study included 830 kidney transplant participants undergoing treatment in an outpatient nephrology center in 5 different university hospitals in the aim of this study is to evaluate the prevalence, types and adverse effect of CAM use in the renal transplant population.

In a study from our country, the prevalence of CAM use was 28% among hemodialysis (HD) patients [17]. Another study from the Malaysia showed that the frequency of CAM usage was 63% among CKD. The prevalence of CAM use was 14.4% among HD and peritoneal dialysis (PD) patients in US [18]. Nowack, et al. showed that 49% of patients with kidney transplantation use CAM. In our study we reported the prevalence of CAM usage 22.89% [15].

Difference of the frequency of CAM in different region of the world may be related to definition of CAM, cultural and geographic differences. Some of studies CAM definition included nutritional and vitamin supplements as well as, most significantly, prayer [19]. In European countries, prayer is generally not considered a form of CAM. However, National Center for Complementary and Alternative Medicine (NCCAM) [19] and the Institute of Medicine [20] mention prayer as a possible alternative medicine. Liquorice is used as a soft drink in our country and some part of Middle eastern countries, this herb has a diuretic effect and may cause hyperkalemia but patients believe that the diuretic effects and recovery of low urine, which progressively decreases in CKD.

Based on several studies, herbal medicines are associated with significant adverse effects, including herb-drug reactions and nephrotoxicity, should be avoided in patients with kidney transplantation. Further, herb-drug interactions can precipitate acute rejection, acute kidney dysfunction or other potential interactions with drugs [21-28].

Patients with kidney transplantation have high risk of herb-drug reactions cause of different mechanisms (such as increasing activity of cytochrome P-450 iso-enzyme metabolism, drug binding or transport proteins e.g., antidiabetics, antihypertensives, anticoagulants). Herbal therapies can cause significant immunosuppressive drug level variability (high or low) and have been related to acute rejection and risk of graft loss (9, cam son). There were no statically significant differences between the use of CAM and mean creatinine levels and mean calcineurin inhibitors levels (Table 2).

Almost 25% of all transplantation patients in this study used CAM and the most frequent CAM therapies was used herbal tea. The most commonly used herbal CAM are parsley+ cinnamon+ lemon juice (57.8%), followed by, Garlic + lemon juice, (51.4%), nettle (42.3%), ginger (38.1%) and turmeric + honey (28.2%).

According to our study approximately 78% of the patients not disclosed the use of CAM their nephrologist, they said that their doctors not asked any questions them about indication or contraindication of CAM. Shelley, et al. showed that most commonly patients expected their doctors to explained

about CAM therapies [25]. If we ask or discussion with patients about CAM therapies, patients may be feeling more comfortable and open to talk about CAM and we can help patients to adverse effects of CAM.

Markell, et al. determinate that the frequency of non-compliances of immunosuppressive treatment was 39% among those using CAM therapies however in our study which is significantly more common in male patients and frequency was 10.2% [26].

In a study in Egypt, they mentioned that five renal transplant patients stopped the immunosuppressive therapy to use CAM [13]. It is also very essential to explain to the patients that some supplements affect the absorption and half-life of many drugs like immunosuppressives and anti-hypertensives [13].

It was observed that the herbal supplements like parsley, nettle juice, garlic, lemon juice, blueberry and black cumin were used as traditional practices by the patients. Most of those products were easily available from local markets or herbalists.

Fortunately the majority of our participants were using CAM in addition to the classic medical therapy prescribed by their doctors.

Studies with different patient groups have reported that a high prevalence (52-72%) of CAM use in patients higher educated [26,27]. We found that the majority of people using CAM are in the highest educational level which might have led to higher occupational and monthly income. On the other hand, Shamsuddin, et al., did not assess the association between CAM usage and patients monthly income [17].

It is also known that the use of CAM therapies also varies by age, gender, occupational, educational, marital status, living region, socioeconomic status, co-morbidities etc. [27,28]. We found no association between the use of CAM and age, comorbidities (such as Diabetes Mellitus, Hypertension), living region, marital status and GFR levels. However, in this study, we found significantly association between the use of CAM gender, educational level and monthly income ($p=0.01$, $p=0.00$, $p=0.01$ respectively).

There are several studies mentioned that the use of CAM is higher among female patients [15,29]. Similarly in our results, the prevalence of usage of CAM therapies was higher among the female patients ($p=0.01$).

We observed that the frequency of body-mind practices 17.7% relaxation techniques, prayer, bio-feedback, meditation, 8 (4.1%) patients used alternative system such as acupuncture, cuppa were the least common CAM type recognised by the participants. Several studies have showed that mind-body practices may be beneficial for patients with CKD and kidney transplant recipients [30,31].

This study provides information about the prevalence of usage of CAM among kidney transplantation recipients in the importance of this study is possibly the first of its kind addressing CAM usage with a reasonable sample size and include five different transplantation centres. We found a relatively low prevalence of CAM usage among kidney transplantation patients. One of the importances of our study is to indicate that CAM usage is not so frequent but closely related to educational, occupational status and monthly income of patients. Another important point of our study the patients who used CAM is generally not disclosed about CAM therapies their physicians or nurses. Healthcare professional who worked transplantation centers must be aware of and discuss patients about their use of CAM.

There are a few limitations to this study. Firstly, it is limited by its cross-sectional designed. Secondly the researchers did not include dose and frequency of herbal products. And finally the benefits of CAM use in kidney transplant patients were not investigated.

Conclusion

Herbal products were the most commonly used CAM therapies with higher prevalence of use in higher socioeconomic status patients. CAM therapies results in a decrease or increase of the immunosuppressive concentration, also it results manifested by electrolyte imbalance or acute rejection. Nephrologist

and other healthcare providers need to be aware about CAM and ask about their use of CAM therapies.

Conflict of Interest

No potential conflict of interest was reported by the authors.

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