

ORIGINAL ARTICLE

Özgün Araştırma

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Geliş Tarihi : Nisan 02, 2021
Received

Kabul Tarihi : Tem. 01, 2021
Accepted

E Yayın Tarihi : Eylül 01, 2022
Online published

Bu makalede yapılacak atıf
Cite this article as

**Bora F, Asar E, Avşar E,
Sözel H, Yılmaz F.**
Evaluation of Herbal Medicine
Use in Chronic Kidney Disease
Akd Med J 2022; 8(3): 319 - 325

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Evaluation of Herbal Medicine Use in Chronic Kidney Disease

Kronik Böbrek Hastalığında Bitkisel İlaç Kullanımının Değerlendirilmesi

ABSTRACT

Objective:

One of the causes of chronic kidney disease (CKD) may be nephrotoxic herbal products. We wanted to ascertain the rate of herbal product use among CKD patients, the products used, sources of supply, demographic characteristics of the patients, whether acute renal failure develops with these products and the value of predialysis education in this field.

Material and Methods:

The data of 209 patients were collected at the nephrology department and evaluated using a form completed by a CKD education specialist nurse in one-to-one patient interviews.

Results:

The patients' mean age was 57.3 years, and 41% were female. 22% of the patients (n=45) used herbal products. Seven patients followed up with stable GFR had an acute kidney injury episode after using herbal products. The herbal product names used by the patients were as follows: unknown weed mix, black cumin oil, cherry stalk, rosemary, cinnamon, Helichrysum Arenarium, spring water, Galium aparine, reishi mushroom, Ceratonia siliqua, daisy, snail shell, Viburnum opulus, onion juice, Stevia rebaudiana Bertoni, cranberry, malus trilobata leaf, avocado leaf, fig and olive leaf, horse chestnut, ginger, urtica leaf, eating walnut after soaking it in water, pumpkin seed, Vitex agnus-castus, aloe vera, blueberries, juniper molasses, Equisetum arvense L, Lamii albi herbal, yoghurt water. The patients who were followed for more than six months tended to report their herbal product use more than the remaining patients (p = 0.08).

Conclusion:

Due to the widespread use of herbal products, clinicians should be more careful about the use of herbal products by patients.

Key Words:

Chronic Kidney Disease, Herbal Medicine, Education, Communication

Öz

Amaç:

Kronik böbrek hastalığı (KBH) nedenlerinden biri nefrotoksik bitkisel ürünler olabilir. Bu çalışma, KBH hastalarında bitkisel ürün kullanım oranı, kullanılan ürünler, tedarik kaynakları, bu ürünlerle akut böbrek yetmezliği gelişip gelişmediği ve bu alanda prediyaliz eğitiminin yerini tespit etmek amacıyla yapıldı.

DOI: 10.53394 / akd.1059440

Gereç ve Yöntemler:

Nefroloji bölümünde 209 hastanın verileri toplandı ve bir prediyaliz eğitim hemşiresi tarafından birebir hasta görüşmelerıyla doldurulan eğitim formu kullanılarak retrospektif olarak değerlendirildi.

Bulgular:

Hastaların yaş ortalaması 57,3 yıl, % 41'i kadındı. Hastaların % 22'si (n=45) bitkisel ürünler kullanmıştı. Stabil tahmini glomerüler filtrasyon hızı ile takip edilen yedi hastada bitkisel ürünler kullandıktan sonra akut böbrek hasarı atakları yaşandığı tespit edildi. Hastaların kullandıkları bitkisel ürün isimleri şunlardı: Bilinmeyen ot karışımı, siyah kimyon yağı, kiraz sapı, biberiye, tarçın, Helichrysum Arenarium, kaynak suyu, Galyum aparine, reishi mantarı, Ceratonia siliqua, papatya, salyangoz kabuğu, Viburnum opulus, soğan suyu, Stevia rebianadon Bertion, malus trilobata yaprağı, avokado yaprağı, incir ve zeytin yaprağı, at kestanesi, zencefil, cevizi suda bekletip elde edilen su, kabak çekirdeği, Vitex agnus-castus, aloe vera, yaban mersini, ardıç pekmezi, Equisetum arvense L, Lamii albi herbal, yoğurt suyu idi. Altı aydan uzun süre takip edilen hastalar bitkisel ürünleri, diğer hastalardan daha fazla kullanma eğilimindeydiler (p = 0.08).

Sonuç:

Bitkisel ürün kullanımının yaygınlaşması nedeniyle, klinisyenler hastaların bitkisel ürünlerin kullanımı konusunda daha dikkatli olmalıdırlar.

Anahtar Kelimeler:

Kronik böbrek hastalığı, Bitkisel ilaç, Eğitim, İletişim

INTRODUCTION

Chronic kidney disease (CKD) is a nephrological syndrome caused by chronic, progressive and irreversible destruction of nephrons due to various causes. Advances in renal replacement therapy offer patients only life-sustaining treatment options; e.g., hemodialysis and peritoneal dialysis. Therefore, some patients pursue solutions beyond traditional nephrological therapies to increase their quality of life. The use of herbal medicine is one of these alternatives and has become increasingly widespread in developed countries (1). However, CKD can also be caused by herbal products that are nephrotoxic substances and/or were previously contaminated with other herbal products (1).

CKD education programs are organized to provide better management of CKD and control of the progression of this disease. An ideal low clearance polyclinic CKD education team should consist of a nephrologist and specialist CKD nurse, a dietician, a psychologist, a social worker, a physical therapist, and the organization representing the patient's interests (2). However, according to a consensus conference and survey conducted in Australia, most educational programs are undertaken especially by a specialist nurse (2,3).

We wanted to ascertain the rate of herbal product use among these CKD patients, the products used, sources of supply,

demographic characteristics of the patients and consequences of usage in low clearance nephrology polyclinic and education in this field.

MATERIAL and METHODS

The ethics committee of our university approved the study protocols. The data of 209 patients were collected at the nephrology out-patient department retrospectively. We included patients with stage 2-5 CKD glomerular filtration rate (eGFR \leq 60 ml/min/1.73m²) that were being followed up in our nephrology out-patient clinic but had not yet started dialysis. Most of the patients lived in the Mediterranean region in Turkey. The patients were evaluated using a form completed by a specialist education CKD nurse during a one-to-one interview with each patient. Demographic information, etiological diagnosis of CKD, dietary habits, hypertension status, regular drug use, renal replacement decision, and any additional treatment were noted.

In our department, standard low clearance polyclinic care consists of informing the patients about CKD and its associated complications, risk of progression, dietary instructions, and different modalities of renal replacement therapy. This process is managed by a CKD education specialist nurse and nephrologists. The number of sessions and duration of CKD educational program vary according to the requirements of each case. For example, the program for adults incorporates different domains of learning and accommodates different visual styles. This education is provided by one nurse and nephrologists.

The approval of the local ethics committee was received (Akdeniz University, Faculty of Medicine, Clinical research ethics committee) (24.02.2021/KAEEK-157). The research complied with the Helsinki Declaration. This study was conducted in accordance with the principles of research and publication ethics. Necessary permissions were obtained from the hospital administration for the study.

Statistical analysis

Data were expressed as mean \pm SD or percentages. Statistical significance was set at the level of p<0.05. The Shapiro-Wilk test was used to assess normality of distribution for continuous variables. Intergroup comparisons were assessed for nominal variables using the Chi-square test. The Mann-Whitney U test was used to determine the differences between nonparametric data. Statistical analyses were performed using statistical software IBM SPSS Statistics v. 23 (SPSS Inc., Chicago, IL, USA).

RESULTS

The sociodemographic characteristics of the patients with CKD are summarized in Table I. The patients' mean age was 57.3 years, and 41% were female. Nearly a quarter of patients (22%) were using herbal products. There was no statistically significant difference between the patients who did and did not use herbal products according to age, gender, education level, and CKD stage (p > 0.05).

Table I. Sociodemographic Characteristics of Users and Nonusers of Herbal Product

Patients Characteristics	Herbal nonusers (n=164) (n, %)	Herbal medicine users (n=45) (n, %)	p
Age (Year)	57.52 ± 14.03	56.64 ± 14.34	0.618
Sex			
Female	70 (42.7)	16 (35.6)	0.380
Male	94 (57.3)	29 (64.4)	
Education Level (n, %)			
Illiterate	14 (8.5)	4 (8.9)	0.940
Primary school	85 (51.8)	22 (48.9)	
Secondary school	15 (9.1)	3 (6.7)	
High school	28 (17.1)	8 (17.8)	
University	22 (13.4)	8 (17.8)	

Mann Whitney U test and Chi-square test

Table II presents comparative information on clinical characteristics of the patients. No statistically significant difference was found between the follow-up periods of the patients, but there was a trend showing that the patients who were followed for more than six months were using more herbal products (p = 0.08).

Table II. Some Clinic Qualities of Herbal Product Users and Nonusers of Herbal Product

Patients Characteristics	Herbal nonusers (n=164) (n, %)	Herbal medicine users (n=45) (n, %)	p
Follow – up time (n, %)			
0-6 months	35 (21.5)	4 (8.9)	0.08
More than 6 months	128 (78.5)	41 (91.1)	
Glomerular Filtration Rate (eGFR ml/min)			
Stage 2 (60-89 ml/min)	3 (1.8)	0	0.153
Stage 3 (30-59 ml/min)	51 (31.1)	12 (26.7)	
Stage 4 (15-30 ml/min)	75 (45.7)	16 (35.6)	
Stage 5 (<15 ml/min)	35 (21.3)	17 (37.8)	

Chi-square test

Of the patients that reported to use herbal remedies, 30 (67 %) used only one product and 15 (34 %) more than one product at the same time. It was determined that seven patients (16 %) did not know the content of the herbal product they used. Thirty different types of products were identified.

The product names and the number of patients using each product were as follows: unknown weed mix 7, black cumin oil 7, cherry stalk 3, rosemary 3, cinnamon 3, Helichrysum Arenarium 2, spring water 2, Galium aparine 2, reishi mushroom 2, Ceratonia siliqua 2, daisy 2, snail shell 1, Viburnum opulus 1, onion juice 1, Stevia rebaudiana Bertoni 1, cranberry 1, malus trilobata leaf 1, avocado leaf 1, fig and olive leaf 1, horse chestnut 1, ginger 1, urtica leaf 1, eating walnut after soaking it in water 1, pumpkin seed 1, Vitex agnus-castus 1, aloe vera 1, blueberries 1, juniper molasses 1, Equisetum arvense L 1, Lamii albi herbal, yoghurt water 1 (Table III). Considering the sources from which the plants are provided; 20 patients (44.4 %) from a diary, 10 patients (22 %) by order (internet, phone), 8 (17.8 %) self-collected, 5 (11.1 %) from market, 2 (4.4 %) raised by themselves was determined.

Table III. Name of Herbal Product

Name of Herbal Product	Number
Unknown Weed Mixture	7
Black Cumin Oil	7
Cherry Stalk	3
Rosemary	3
Cinnamon	3
Helichrysum Arenarium	2
Spring Water	2
Galium Aparine	2
Reishi Mushroom	2
Ceratonia Siliqua	2
Chamomile	2
Snail Shell	1
Viburnum Opulus	1
Onion Juice	1
Stevia Rebaudiana Bertoni	1
Plantago lanceolate	1
Cranberry	1
Malus Trilobata Leaf	1
Avocado Leaf	1
Fig And Olive Leaf	1
Horse Chestnut	1
Ginger	1
Urtica Leaf	1
Eating Walnut after soaking it in water	1
Pumpkin Seed	1
Vitex Agnus-Castus	1
Aloe Vera	1
Blueberries	1
Juniper Molasses	1
Thymus vulgaris L	1
Lamii Albi Herba	1
Yoghurt Water	1

Seven patients followed up with stable GFR had an acute kidney injury episode after using of herbal products. Two patients with stage 3 CKD who were using a mixture of herbs, whose content was unknown, had a decrease of 6 and 10 ml/min/1.73m² in eGFR. Later, these patients are followed

up with 2 and 3 ml/min/1.73m² eGFR losses. Two patients in stage 5 CKD presented with hypercalcemia and a 4 ml/min/1.73m² decrease in eGFR level. One patient consumed reisha mushroom and the other patient consumed a mixture of yoghurt water, cinnamon and lemon juice. Another patient, who was followed up in stage 4 CKD, had a 5 ml/min/1.73m² decrease in eGFR after the use of Equisetum arvense L and Helichrysum Arenarium. These four patients turned back to basal values when they stopped using the herbs. One patient in stage 4 CKD had a decrease to eGFR 15 ml/min/1.73m² after the use of Viburnum opulus and could not reach the former eGFR level. In another patient who was followed up with the diagnosis of glomerulonephritis, eGFR level decreased from 19.7 ml/min/1.73m² to 6.4 ml/min/1.73m² after the use of avocado leaf.

Table IV presents the herbal products and the purposes of using them. Concerning the patients' using herbal products, 34 (76 %) used them for CKD, two (%4.4) for urinary tract infections, and one each (%2.2) for diabetes mellitus, prostate hyperplasia, gout, losing weight, hyperlipidemia, asthma, osteoarthritis, flu and breast carcinoma.

Table IV. Herbal products used by patients and purpose for using

Purpose- (n=45)(Number,%)	Plants Used for Treatment Purposes, number
CKD 34 (75,6%)	Unknown weed mix 4, black cumin oil 7, cherry stalk 3, rosemary 3, cinnamon 2, Helichrysum Arenarium 2, spring water 2, Galium aparine 2, reishi mushroom 2, Chamomile 2, snail shell 1, Viburnum opulus 1, onion juice 1, Plantago lanceolate 1, cranberry 1, urtica leaf 1, eating walnut after soaking it in water 1, Vitex agnus-castus 1, aloe vera 1, blueberries 1, juniper molasses 1, 1, Lamii albi herba1, yoghurt water 1.
UTI 2 (4,4%)	Reishi Mushrooms, Avocado Leaf, Blueberries
DM 1 (2,2 %)	Stevia Rebaudiana Bertoni
Prostate 1(2,2%)	Pumpkin Seeds
Gout 1(2,2%)	Unknown weed mix
Slimming down 1 (2,2%)	Unknown weed mix
Cholesterol 1 (2,2%)	Malus Trilobata Leaf
Asthma 1 (2,2%)	Fig+Olive Oil
Knee Pain 1 (2,2%)	Horse Chestnut
Flu 1 (2,2%)	Cinnamon, Ginger
Breast cancer 1(2,2%)	Unknown weed mix

CKD: Chronic Kidney Disease, UTI: Urinary tract infection, DM: Diabetes mellitus

DISCUSSION

In this study, there was no statistically significant difference between the follow-up periods of the patients, but it was determined that the patients that were followed for more than six months had a higher tendency to report their use of herbal products. This also corresponded to the patients that visited the education nurse and nephrologist in our hospital more than twice. This might be due to these patients' feeling freer to reveal their herbal product use to their nurse or doctor since they had already established a rapport.

In terms of dietary changes in CKD, there are restrictions on sodium intake, as well as consumption of protein and

phosphorus or potassium containing nutrients for certain patients. Diet change plays an important role in the prevention of the progress of CKD. In KDIGO 2012, it is recommended that adults with CKD should seek medical or pharmaceutical advice before using over-the-counter medicines or nutritional protein supplements (1B) (7). Considering this recommendation of KDIGO, it is important for nephrologists to detect the patient's use of a herbal product that may cause an acute onset on CKD and possibly interfere with the medical treatment for CKD or hypertension.

The use of alternative treatments in Western societies rapidly increased in the 1990s and the highest consumption was consistently reported among Caucasians, college-educated women, and people with a high socioeconomic status (8-12). In the current study, there was no difference between the demographic characteristics of the patients and the use of herbal products. This indicates that the choice of herbal products for diseases other than CKD was not related to the educational level of our patients.

Most patients do not inform their doctor about their use of herbal products because they believe that these products are not relevant for medical care. In a survey conducted in the United States, it was found that 69 % of the 4.202 patients did not report any supplemental use to their physicians (13). In a survey of hospitalized patients, 3/4 of the physicians were unaware that their patients were using herbal supplements (14,15). The fact that patients hide this information from their doctor may indicate that there is still a barrier against doctor-patient affinity.

Trust is a dynamic and relational process and involves vulnerability and dependency. In chronic illnesses, this process is also referred to as specific reconstructed trust (4). Continuity of services in the low clearance polyclinic unite is also identified as a precondition for the development of trust (5,6). Many publications in different fields suggest that development of mutual trust in a nurse-patient relationship requires time (5,16,18,20-27) although it is not specified how long this process would take. It is easier for an education nurse to build a rapport with patients because as case managers in low clearance polyclinic CKD education, they get to spend more time with patients. This allows patients to get emotional support when they need it. Nurses' professional competencies and personal characteristics are important in the development of trust. Remembering patients' names and knowing about their lives and attitudes prevent depersonalization of patients. Availability and accessibility of nurses, the patients' feeling emotionally and physically safe (16), comfortable and valued as an individual and adequately informed (17), and presence of a respectful communication (5,18,19) constitute an essential part of the relationship between the nurse and patients. Patients tend to have increased trust in staff who know their psychosocial, economic issues, and cultural/religious backgrounds. Nurses can also have a better idea about how informed the patients are and what other requirements they have, which is useful information for the organization of further education programs. Patients tend not to hide their habits and choices regarding their treatment once they get to know the nurse better.

We acknowledge several limitations in this study. First, due to the retrospective nature of the study, it was not possible to determine whether there was a difference between the patients' revealing their herbal product use to their doctor or nurse. At each follow-up visit, the clinician asked the patient whether he or she was using any herbal product, but it was not possible to confirm that the question was fully understood or accurately answered by the patient. Secondly, the results of the study may have been affected by the personal characteristics of the patients. It is easier for some patients to develop trust in the medical team even from the very beginning while for some others, this process might take more than 12 months. Lastly, in our out-patient clinic, the forms were completed for a year, and when some patients were new, others were in the follow-up period. We were not able to determine precisely whether the follow-up patients had used any herbal product in their first presentation to our clinic.

CONCLUSION

The tendency to use and report the use of herbal products was found to be increased in patients who had been followed for more than six months in our low clearance polyclinic out-patient clinic. For the welfare and wellbeing of CKD patients, all health professionals should pay attention to identifying any supplementary drugs, especially herbal products, used by the patients. As the use of alternative medicine becomes more popular and treatments are more available than ever, clinicians should openly talk to the patients about the use of herbal products and help them express themselves clearly. Improved communication, understanding and cooperation between patients and health staff can encourage patients to be more open about their use of herbal remedies.

Ethics Committee Approval:

This research complies with all the relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration, and has been approved by the Medical Faculty Ethical Committee, Akdeniz University (approval number:24.02.2021/KA EK-157).

Author Contributions:

Concept- F.B, E.A, F.Y ; Design-F.B, E.A, F.Y., H.S ; Supervision-F.B, E.A, E.A, H.S.; Resources-F.B, E.A, E.A, H.S, F.Y; Materials-E.A, E.A, F.Y., H.S.; Data Collection and/or Processing-F.B, F.Y., E.A, H.S.; Analysis and/ or Interpretation - F.B.,F.Y, H.S.; Literature Search - E.A, F.Y, H.S.; Writing Manuscript - F.B, E.A, F.Y.; Critical Review - F.B, E.A, F.Y, H.S, E.A.

Conflicts of Interest:

The authors declare that they have no conflicts of interest concerning this article.

Financial Disclosure:

No financial disclosure was declared by the authors.

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