Comparative Study of Complementary and Alternative Medicine Use in Patients of Chronic Kidney Disease: Predialysis Versus Dialysis

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ABSTRACT

This study was carried out to determine the prevalence and patterns of complementary and alternative medicine (CAM) use in patients of chronic kidney disease (CKD) and to compare CAM use in predialysis patients and patients on dialysis. This was a prospective, cross sectional, questionnaire-based study initiated after approval of institutional ethics committee. Patients suffering from chronic kidney disease for six months or more, of either gender, aged above 18 years were divided into two groups: predialysis and dialysis. Patients were interviewed using a self-designed, semi-structured, open-ended questionnaire to determine the prevalence and patterns of CAM use. CAM use was compared in the two groups. There was no statistically significant difference in the use of CAM between the two groups (19.05% in predialysis and 32.55% in dialysis group, p= 0.1218). Ayurvedic medicines were the most common CAM used in both the groups. Most patients did not disclose CAM use to their doctors. Fifty percent patients of predialysis and 42.8% of dialysis patients considered CAM safer than conventional medicines. Benefits obtained from CAM were: symptomatic improvement, decreased creatinine level, improved sense of wellbeing. Reason for stopping CAM was, no benefit obtained. The matter of concern is that many patients who used CAM along with conventional medicines, didn’t disclose CAM use to their doctors, thereby increasing possibility of potential drug interactions. Hence, it is essential that health care professionals routinely inquire about CAM use as part of their history taking at each follow-up visit.

Keywords: CKD, cross-sectional study, Complementary medicine, Alternative Medicine, Hemodialysis, Treatment adherence.

INTRODUCTION

National Centre for Complementary and alternative medicine (NCCAM), United States has defined Complementary and alternative medicine (CAM) as “a group of diverse medical and health care systems, practices, and products that are not generally considered to be part of conventional medicine.” Various study have reported use of CAM in different chronic disorders including chronic kidney disease (CKD). CKD has been a worldwide health issue affecting millions of people, and has been defined as abnormalities of kidney structure or function, present for more than 3 months, with implications in health. Due to various co-morbidities and the need for multiple medications, most of the CKD patients do not have a satisfactory quality of life (QOL) and turn to CAM to manage several of their issues. Wide variation in the use of CAM in CKD patients has been reported in various studies ranging from 18.8% in Trinidad, 61% in US to 82.3% in Nigeria. In a study conducted in Egypt in patients of CKD, 64% of predialysis patients and 33% of dialysis patients reported using some type of CAM while another study has reported 34% of predialysis patients having used CAM. Extensive search of the published literature revealed only one Indian study evaluating the use of CAM in patients of CKD on hemodialysis in which 26% patients reported of using some type of CAM and Ayurved was the most common CAM used. In another Indian study which basically aimed to evaluate adherence to therapy in patients of CKD, 24.66% patients were reported to use CAM which included Ayurvedic and Homeopathy medicines, nutritional supplements and practicing meditation. This study did not evaluate any other aspects of CAM use. Though CAM may provide new therapeutic options for patients with CKD, not all CAM practices may be safe in these patients because certain herbal constituents and bioactive phytochemical compounds might interact with patients’ medications and there may be accumulation of toxic metabolites of herbal remedies due to the renal dysfunction. Hence, it is important to establish the extent and patterns of CAM use in CKD patients so that health care providers can be better informed and advise their patients accordingly.

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Another concern is, whether use of CAM affects adherence to conventional medication in these patients. Adherence to conventional treatment in CKD patients was affected in 4.2% of CAM users.\(^6\) Poor adherence to conventional medications was also reported in CKD patients using CAM.\(^{11,12}\) Hence, this study was planned with the following objectives: to determine the prevalence and patterns of CAM use in patients of CKD, to compare CAM use in predialysis patients and patients on dialysis and to find association between CAM use and adherence to conventional medications.

**MATERIALS AND METHODS**

This was a prospective, cross sectional, questionnaire based study conducted in the Nephrology department (both inpatient and outpatient) (IPD/OPD) of a Superspeciality Hospital. Patients were selected from those admitted in Nephrology wards and those attending the Nephrology OPD. The study was initiated after approval from the Institutional Ethics Committee.

Inclusion criteria were: Patients suffering from chronic kidney disease (all stages) as diagnosed by the treating Nephrologist, since six months or more, either gender and age above 18 years. Following patients were excluded: Patients who received a kidney transplant and seriously ill or mentally incompetent patients who in the opinion of the Nephrologist may not have the ability to communicate verbally, and give informed consent.

Patients meeting the selection criteria were briefed about the study and patient information sheet in vernacular language was provided. Written informed consent was obtained from those willing to participate. Enrolled patients were divided into two groups: Group I-Predialysis patients and Group II- patients on dialysis. All patients were interviewed by a direct face-to-face interview, their prescriptions analyzed and the information was entered in a self-designed, semi-structured, open-ended questionnaire. The questionnaire consisted of three parts.

Part I: Socio-demographic characteristics: age, gender, marital status, educational qualification, occupation, monthly income and residence.

Part II: Clinical characteristics: diagnosis and concurrent illnesses if any, duration of disease and details of medications for chronic use.

Part III: Various aspects of CAM use such as type of CAM product, reasons for use, perceived benefits, influences, effects and consequences, source, and satisfaction with CAM.

The questionnaire was pre-tested in ten patients for its clarity and readability and suitable modifications done. In addition, adherence to conventional treatment was assessed by using the Morisky 4-item medication adherence questionnaire. In this questionnaire, higher score indicates poor adherence.

Outpatients were approached while they were waiting for doctor’s consultation so that they did not need to spent additional time for this purpose. The data obtained was compiled and analyzed.

**Statistical analysis**

Numerical continuous variables, e.g. age, number of drugs prescribed per patient are expressed as mean±standard deviations. Categorical variables (e.g. gender, occupation) are expressed as counts/percentages. Patient demographics and different aspects of CAM use in the two groups are compared by Fisher’s exact test for categorical variables and unpaired-t test for numerical variables, e.g. age. Pearson correlation test was used to find correlation between the level of adherence to conventional medications and CAM use. P value less than 0.05 was considered statistically significant. Graph pad prism version 6.0 was used for statistical analysis.

**RESULTS**

This study was carried out in 127 patients of CKD admitted in Nephrology ward or attending the nephrology OPD of a Superspeciality Hospital. Table 1 shows the demographic characteristics of the study patients. Average age(mean±SD) of the patients in the pre-dialysis group (55.42±16.45 years) was significantly more than in the dialysis group (45.20±16.96 years)(p= 0.0014). Other baseline characteristics were similar in both the groups.

**Table 1:** Baseline socio-demographic characteristics of study patients (n= 127)

| Parameter               | Number of patients | P value |
|-------------------------|--------------------|---------|
|                         | Predialysis | Dialysis |   |
| Total number of patients| 84          | 43       | -  |
| Residence:              |            |         |   |
| Rural                   | 33          | 19       | 0.7033 |
| Urban                   | 51          | 24       |      |
| Gender:                 |            |         |   |
| Men                     | 55          | 28       | 1.0000 |
| Women                   | 29          | 15       |      |
| Age in years (Mean± SD) | 55.42±16.45 | 45.20±16.96 | 0.0014 |
| Education:              |            |         |   |
| Less than SSC           | 40          | 22       | 0.7124 |
| SSC and higher          | 44          | 21       |      |
| Monthly income:         |            |         |   |
| Upto 10,000 INR         | 58          | 32       | 0.6802 |
| More than 10,000 INR    | 26          | 11       |      |

**Table 1:** Baseline socio-demographic characteristics of study patients (n= 127)
Table 2: Diagnosis of study patients (n=127)

| Diagnosis                  | Predialysis(n=84) | Dialysis(n=43) |
|----------------------------|-------------------|----------------|
| CKD                        | 15(17.85)         | 17(39.53)      |
| CKD + DM                   | 11(13.09)         | 2(4.65)        |
| CKD + HTN                  | 25(29.76)         | 6(13.95)       |
| CKD + DM + HTN             | 16(19.04)         | 4(9.30)        |
| CKD + any other illness    | 5(5.95)           | 6(13.95)       |
| CKD + any other illness    | 12(14.28)         | 8(18.60)       |

Other illnesses include: Benign hypertrophy of prostate, hyperparathyroidism, anaemia, chronic glomerulonephritis, hypothyroidism, liver dysfunction, systemic lupus erythematosus, autosomal dominant polycystic kidney disease, rheumatic heart disease, multiple myeloma, gastritis, pleural effusion. CKD – Chronic kidney disease, DM – Diabetes Mellitus, HTN – Hypertension. Figures in parentheses indicate percentage.

Majority of patients (29.76%) in the predialysis group had CKD with hypertension and in the dialysis group majority of patients (39.53 %) were of CKD alone. (Table 2)

Table 3 shows that ferrous sulphate was the most commonly prescribed drug in both the groups. While vitamin D, calcium carbonate and alpha keto analogue were the other commonly prescribed drugs in pre-dialysis group, erythropoietin and frusemide were commonly prescribed to dialysis patients. Number of patients who were prescribed alpha keto analogue and enalapril/telmisartan were statistically significantly more in the pre-dialysis group (p=0.0059 and 0.0062) while significantly more patients in the dialysis group were prescribed erythropoietin (p=0.0005). Average number of drugs prescribed per patient(mean±SD) was statistically significantly more in the dialysis group (5.51± 1.50) compared to pre-dialysis group(4.12± 1.46) (p<0.0001). (Table 3)

Out of total patients interviewed, 30(23.62%) patients reported using CAM. Patients who used CAM in predialysis group were 19.05% in predialysis and 32.55% in dialysis group. (p= 0.1218)

Table 3: Medicines prescribed to study patients (n =127)

| Name of medicine                  | Predialysis(n=84) | Dialysis(n=43) |
|-----------------------------------|-------------------|----------------|
| Ferrous sulphate                  | 39                | 22             |
| Vitamin D /Calcium carbonate      | 37                | 14             |
| Erythropoietin                    | 8                 | 16*            |
| Alpha keto analogue               | 29*               | 5              |
| Sodium bicarbonate                | 16                | 7              |
| Frusemide                         | 23                | 16             |
| Metoprolol                        | 7                 | 6              |
| Nifedipine/Clindipine             | 26                | 13             |
| Enalapril/ Telmisartan            | 21*               | 2              |
| Antimicrobials (Doxycycline, Amoxclav,Ciprofloxacin, Linezolid, Metronidazole) | 5 | 4 |
| Other drugs                       | 127               | 132            |
| Total drugs prescribed            | 338               | 237            |
| Average drugs prescribed per patient (Mean±SD) | 4.12± 1.46 | 5.5± 1.50 |

*p<0.05 by Fischer’s exact test. Other drugs include: Anti ulcer drugs (ranitidine, pantoprazole), antihistaminics (pheniramine, cetirizine), hypolipidemics (atorvastatin, rosuvastatin), analgesics (aspirin, paracetamol), tamsulosin, levetiracetam, ferrous succrose, prazosin.

Table 4: Patients’ knowledge and practice about complementary and alternative medicines (n=30)

| Statement                                      | Predialysis (n=16) | Dialysis (n=14) | P value |
|------------------------------------------------|-------------------|-----------------|---------|
| Currently using CAM                           | 05(31.2)          | 02(14.2)        | 0.39    |
| Use CAM with conventional treatment           | 06(37.5)          | 07(50.0)        | 0.71    |
| Disclosed using CAM to your doctor            | 03(18.7)          | 06(42.8)        | 0.23    |
| Benefited from the CAM used                   | 08(50.0)          | 08(57.1)        | 0.73    |
| Stopped conventional treatment after starting CAM | 01(6.2)         | 02(14.2)        | 0.58    |
| CAM is safer than conventional medicines      | 08(50.0)          | 06(42.8)        | 0.73    |
| CAM is more effective than conventional medicines | 06(37.5)        | 05(35.7)        | 1.00    |
| Experienced any adverse effects after using CAM | 06(37.5)        | 05(35.7)        | 1.00    |
| Would recommend CAM to other patients         | 09(56.2)          | 06(42.8)        | 0.71    |

CAM: Complementary and alternative medicine. Figures in parentheses indicate percentage.
Figure 1 shows that Ayurveda was the most commonly used CAM in both the groups.

Figure 2 shows that friends, neighbours and relatives were the most common sources of information about CAM in both the groups.
Table 4 includes only those patients who reported CAM use. Fifty percent patients in the pre-dialysis group and 57.1% in the dialysis group reported to have experienced beneficial effects from CAM use. Very few patients (6.2% of predialysis and 14.2% of dialysis) stopped conventional treatment after starting CAM. Fifty percent patients of predialysis and 42.8% of dialysis patients considered CAM safer than conventional medicines. Majority of the patients (81.2% in predialysis and 71.7% in dialysis group) in both the groups did not disclose use of CAM to their regular doctor. There was no statistically significant difference between the two groups in any of the parameters (Table 4).

Reasons given by patients (13-pre dialysis and 08- dialysis) for not disclosing use of CAM to their doctors were: did not feel it necessary, not asked by doctor and fear about doctor’s reaction.

Average amount spent on CAM per month (in INR) was 1881±2102(mean±SD) for predialysis group and 3050±2717(mean±SD) for dialysis group (p=0.2650). Duration of CAM use (in months) was 5.51±6.98(mean±SD) for predialysis group and 7.96±13.12(mean±SD) for dialysis group (p=0.5213).

Benefits obtained from CAM were reported by six patients in predialysis and eight patients in dialysis group. These were: symptomatic improvement (increased urine output, decreased edema, decreased body ache), decreased creatinine level, improved sense of wellbeing. Adverse events reported by patients using CAM were: body ache, increased edema, acidity, palpitations, joint pains, abdominal swelling, vomiting, weakness, seizures. Reason given by most of the patients who stopped CAM was, no benefit obtained. No association was found between CAM use and adherence to conventional medication.

DISCUSSION

Questionnaire-based studies usually use self-administered questionnaires. These have certain limitations such as: respondents may find it difficult to understand certain terminologies or may interpret some questions incorrectly. This can happen even after translating the questionnaire in vernacular language. These limitations were overcome in this study as respondents were interviewed by the investigators themselves.

This study evaluated the extent of CAM use in CKD patients: predialysis vs dialysis. Out of total patients interviewed, 30(23.62%) patients reported using CAM. CAM use was 19.05% in predialysis group and 32.55% in dialysis group. This is in contrast to another study which has reported higher percentage of patients in the predialysis group using CAM (64% of predialysis patients Vs 33% of dialysis patients). The reason for this wide difference in CAM use between the two groups in different studies is difficult to explain. In another study which is the only other reported Indian study on the extent of CAM use in CKD patients on hemodialysis, the proportion of patients who reported using one or more of the CAM methods was 26%. Wide variation in the use of CAM in CKD patients has been reported in various studies as mentioned earlier. There can be various reasons for this large variation in the extent of CAM use, the major being different definitions of CAM used in different studies. Vitamins, minerals, nutritional supplements, biological products have been the commonly used CAM in other studies while in this study Ayurveda and Homeopathy were the most commonly used CAM. There has been some debate over whether vitamins, minerals and nutritional supplements should be considered as CAM. In this study the respondents were not specifically asked about use of vitamins, minerals and

Figure 3 shows that seven patients in each group used CAM because they had heard about its benefits.
nutritional supplements but none of them mentioned about use of these products on their own. Hence, it is likely that patients may have been using other forms of CAM not specifically addressed by the study questionnaire. This might have resulted in underreporting of CAM use. The probable reason for Ayurveda and Homeopathy being the common CAM used may be the belief prevalent in the Indian population that these medicines are safe and are effective in various chronic disorders for which modern medicine offers no satisfactory cure.\textsuperscript{17} This is a matter of concern since there is no definitive evidence to prove the safety and efficacy of Ayurvedic or Homeopathic medicines administered concurrently with conventional medicines.

The reason for using CAM given by majority of the patients in both the groups was that they had heard about beneficial effects of CAM. Benefits of CAM use as reported by respondents in both the groups were similar to those reported in other studies.\textsuperscript{11} It is difficult to comment on the efficacy of these treatments in CKD due to non-availability of adequate evidence. It is known that some unproven and alternative therapies may at times prove effective and some alternative therapies may have placebo effects, which impart more therapeutic benefit and improved quality of life.\textsuperscript{18}

Among patients who stopped using CAM the major reason was no benefit obtained with CAM in both the groups. Most of the adverse events reported by patients in both the groups were mild to moderate in severity. All the adverse events reported are non-specific and it is difficult to attribute these either to conventional medicines or CAM.

In this study, relatives, friends, neighbors and paramedical staff were the main sources of information about CAM in both the groups. Similar factors influencing CAM use have been reported in earlier studies.\textsuperscript{3} Media like television, radio and internet have also been reported as sources of CAM information in other studies but very few patients reported the same in this study.\textsuperscript{11}

In this study, 37.5% predialysis and 50% dialysis patients reported CAM use along with prescription medicines. Other studies have reported approximately 46% of patients using CAM with prescription medicines.\textsuperscript{7} Using CAM with prescription medicines needs to be considered seriously since patients who are totally unaware of the potential for drug interactions are exposed to risk. Though data on drug interactions between conventional medicines and CAM is sparse, some combinations of conventional medicines and CAM likely to be involved in serious interaction are reported.\textsuperscript{19}

Number of patients not disclosing CAM use to their regular physician was 81.2% and 57.1% in predialysis and dialysis group respectively. Earlier studies have also reported that a high proportion of patients, ranging from 70 to 79% do not disclose CAM use to their physicians.\textsuperscript{6,11} Major reason for not disclosing CAM use in this study as well as in earlier studies was that doctor did not ask.\textsuperscript{12} A less common reason reported in this study was fear about doctor’s reaction which is also reported in another study.\textsuperscript{20} Considering widespread use of CAM along with conventional medicines and not disclosing this to the treating physician creates an additional potential hazard for patients which they may be totally unaware of. Hence, it can be suggested that health professionals routinely inquire about CAM use as part of their history taking at each follow-up visit. But even this may not be of much benefit most of the times since conventional health care providers may not always be able to advice the patient about CAM use due to lack of knowledge or education about CAM during their training.

The average monthly expenditure on CAM was more than 1500 INR in both the groups. Though the expenditure on CAM cannot be compared between different studies, in this study since most of the patients were from low socio-economic background, the amount spent on CAM is significant and may be economically exhausting for the family. This appears to be pitiable as a major portion of the already meager income is spent on therapy of which the safety and efficacy in these disorders is not established.

CONCLUSION

Use of CAM was similar in predialysis and dialysis groups with Ayurvedic medicines being the most commonly used CAM. The matter of concern is that many patients who used CAM along with conventional medicines, didn’t disclose CAM use to their doctors, thereby increasing possibility of potential drug interactions. Hence, it is essential that health care professionals routinely inquire about CAM use as part of their history taking at each follow-up visit. It is also necessary that concurrent use of CAM and conventional medicines should be monitored for safety and efficacy.

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