Tripolitana Medical Journal; 2015, Vol. 4, No. 1, pp. 27 - 30

Reseach Article

ISSN 2077-5628

Long Term Medication Adherence in Post-Kidney Transplantation Patients: A Unicenter Controlled Prospective Study.

Nasruddin EL-Reyani@, Noura Elsawsaa and Salma Shebani

Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, University of Tripoli, Libya.

Received 10 May 2015/Accepted 15 June 2015

ABSTRACT

Adherence to drug therapy is a vital behavior to treat chronic illnesses and further to get a better life. Kidney transplanted patients are, therefore, at increasing awareness in terms of adherence and thus satisfaction towards their medication regimen.

Evaluation of factors affecting adherence to the immunosuppressant drugs among a sample of post-renal transplantation Libyan patients in long term follow up.

A questionnaire based study was the sole method used to enroll 52 post kidney transplantation patients at Tripoli Transplant Department, Central Hospital for a period of ten months. A direct patient interview was performed to answer questions by the aid of researchers conducted the study.

Psychological conditions have shown significant impact on adherence to medication regimens among patients, i.e. 63.5% vs. 36.5, $P<0.05$. Interestingly, this was in contradiction with the overall patients estimation who didn't refuse to taking their medication while were in bad mood, i.e. 88.5%, n=46, vs. 11.5%, n=6, $P<0.05$. Young and middle aged patients were more strict to medications as instructed compared to adolescent and elderly, i.e. 39.6% and 22.9%, vs. 16.1% and 14.2%, respectively, $P<0.05$. Moreover, educational level have shown that school level had answered their instruction correctly and showed a significant difference compared with high educational level and non educated patients, i.e. 60%, n=21 vs. 40%, 0% respectively, $P<0.05$.

It is concluded that, the term adherence is a complex issue with cultural, educational and environmental factors are playing a major role.

Keywords- *Post-kidney transplant; Immunosuppressant agents.*

INTRODUCTION

Successful medication-taking behavior is dependent not only on knowledge of medication regimens and the medications' necessity, but also on the ability to successfully and conveniently obtain medications. Participants found it important to have a method for obtaining their medications that they perceived as convenient and effective.[3]

In procedures where medical or surgical intervention will completely change the life style of patients, adherence to drug therapy becomes the principle pillar (but frequently neglected) component of the progress of the patient's condition. Kidney transplantation patients for instance, representing this group and therefore, adherence is a vital behavior to prevent graft rejection after organ transplantation.[4]

There is an emerging evidence to indicate that medication nonadherence in kidney transplant recipients is associated with poor outcomes.[5] Immunosuppressive nonadherence may lead to a number of complications, including acute and chronic rejection, diminished renal function requiring a return to dialysis, or death.[6] Patients returning to dialysis after a failed kidney transplant are at greater mortality risk than are patients receiving dialysis who are waiting for a transplant.[7]

Non-adherence have been categorized into intentional non-adherence; in which the patient refuse to take the medication because of poor education or due to adverse effects caused by the medications.[8] The other type is unintentional non-adherence which is attributed to difficulties in taking the medications (poor memory / physical disability /or life style like working at night or being away from home) or due to the cost of medication or even difficulties with prescription.[8] Studies have shown that in the United States alone, non-adherence to medications causes 125,000 deaths annually and accounts for 10% to 25% of hospital and nursing home admissions.[9] This makes non-adherence to medications one of the largest and most expensive disease categories.

To the best of our knowledge, this is the first domestic study to be conducted on the importance of medication adherence in medical practice. Therefore, factors affecting adherence to the immunosuppressant drugs among a sample of post-renal transplantation Libyan patients in long term follow up was evaluated with special attention on the crucial role of clinical pharmacist in improving the patient adherence.

@To whom correspondence should be addressed: Dr. Nasruddin EL-Reyani; Tel.: +218 91 3721595; E. mail: nelreyani@gmail.com

MATERIALS AND METHODS

Study design

This study is a questionnaire based study where each participant is informed to answer the questions. The questionnaire was designed in a modified form to meet the criterion of the study. After being given a brief explanation concerning the nature of the research, all patients were interviewed in a face to face manner and the questions were confidentially answered.

The questionnaire designed in the study was approved and conformed under the rules and regulation of research of the department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Tripoli-Libya. Accordingly, at commencing the research point, an ethical approval and authorization has been issued while referring to the hospital. At Central Tripoli Hospital, the regulations of research were approved by the ethical committee of the hospital and the department of Nephrology as well.

Data collection

Descriptive study among post-renal transplantation patients was conducted over a period of ten months from April 2014 to December 2014. However, this period was infrequently interrupted owing to domestic violence and catastrophic events paused collecting the data. This has in part limited the patients follow up and on the other part might interfere to the final results of the study.

Subjects

All patients enrolled in this study were Libyans whom underwent transplantation surgery either in Libya or in other countries. Nevertheless, all patients were performing their regular follow up in Tripoli.

To meet the aims of the study, the study has inclusion and exclusion criteria. The inclusion criterion includes; 1) Patients underwent kidney transplant surgery, and 2) Patients whom on drug therapy achieving the purpose. The exclusion criterion was; 1) Patients in whom organ rejection was an obstacle to continue follow up, 2) Patients whom died for any reason rather than transplant failure, and 3) Patients leaving the country for any reason. Based on these criteria, fifty two questionnaire surveys were conducted to target the aim the of the study. All patients were gently asked to answer the questionnaire in face to face interviews after a brief explanation was given.

Development of post kidney transplantation patient questionnaire

The main focus of the study was to develop a questionnaire that is easy to administer and score due to its simple rating and scoring instructions and clearly specifies areas of evaluation. The content for the Patient's Compliance Questionnaire (PCQ) for use was developed using a questionnaire experts from other sources.[10] The formerly prepared questionnaires from different research areas were used to generate the initial pools of items and helped select the final set of items. The PCQ was formed by established clinical health professionals, with experience in medical practice-related. The PCQ was developed using the consensus of research group of Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, University of Tripoli, Tripoli-Libya.

Data analysis

All data was analyzed using computer-based statistical software package SPSS, version 20.0. The data was not normally distributed and that was confirmed by Kolmogorov-Smirnov (ks) test; therefore, all comparisons were made using non-parametric statistics, and chisquare test was used for comparisons between categorical variables. Wherever significance is found, a *P* value of *<0.05* was considered significantly difference.

RESULTS

Questionnaire and patients descriptions

This study is designed to elucidate the correlation between medication use and possible factors contributing to adherence and compliance. Therefore, thirty questions were contained in the questionnaire applied, in some of them a sub-questions were applied. The levels of questions were categorized into three levels. The first was personal data including sociodemographic ones, the second category was disease course and fate, while the third category was dealing with physician and patients commentaries on the disease management and follow up. As many factors contributing to adherence are patient dependent, the vast majority of questions were targeted the patients.

A total of 100 surveys were distributed and a total of 52 kidney transplant recipients fully completed the surveys, with a non-response rate of 48%. The percentage distribution of these patients was 3.8%, n=2 for the age group 10-20 yrs, 26.9%, n=14 for the age group 21-30 yrs, 36.5%, n=19 for the age group 31-40 yrs, 21.2%, n=11 for the age group 41-50 yrs and 11.5%, n=6 for the age group 51-60 years.

The most common indications for transplant in the kidney transplant recipients were chronic kidney disease (n=26 [50%]), uncontrolled hypertension (n=15 [28.8%]),

diabetes mellitus (n=6 [11.5%]), unknown cause"s" (n=4 [7.7%]), and misuse or overuse of drugs (n=1 [1.9%]).When considering factors affecting adherence to given drugs**,** the psychological condition have shown that patients who had fears about their medications intake along with mistaking their doses was highly significant compared to patients who did not have fears, i.e. 63.5% *vs*. 36.5, *P*<0.05 (Figure 1). Interestingly, this was in contradiction with the overall patients estimation who didn't refuse taking their medication while were in bad mood,

i.e. 88.5%, n=46, *vs*. 11.5%, n=6, *P*<0.05 (Figure 1).

Correlating adherence to medication instruction, only young and middle aged groups have shown to take their medications as instructed with a significant results of 39.6% and 22.9%, vs. 16.1% and 14.2%, adolescent and elderly**,** respectively, *P*<0.05 (Figure 2). Moreover, when measuring educational level and its impact on adherence to following special medical instructions, it has been shown that school level had answered their instruction correctly and showed a significant difference compared with high educational level and non educated patients, i.e. 60%, n=21 *vs*. 40%, 0% respectively, *P*<0.05 (Figure 3).

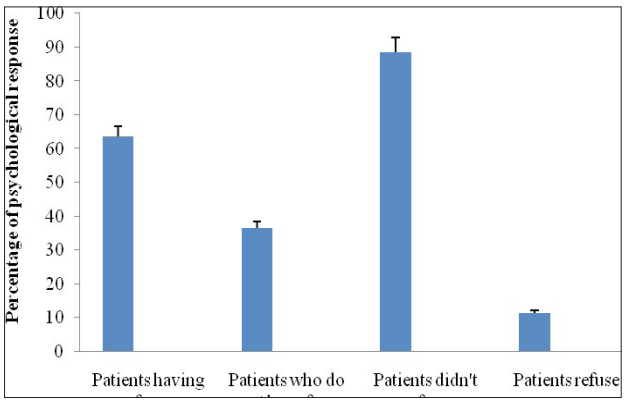

Figure 1: Percentage effects of psychological responses on medication intake.

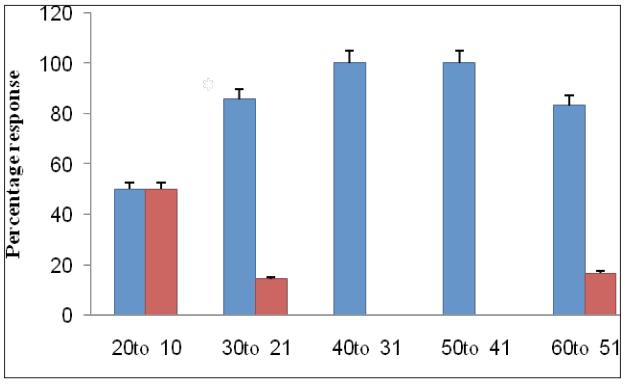

Figure 2: Percentage correlation between medication instructions and patients response.

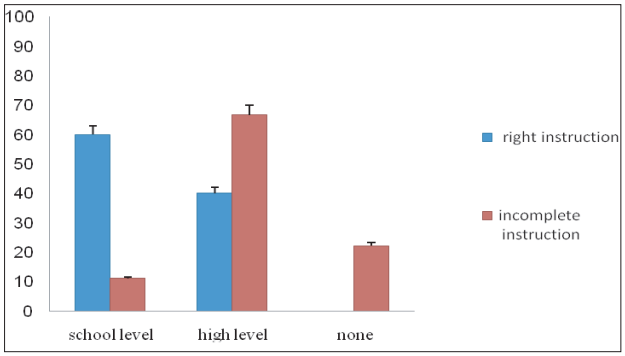

Figure 3: Percentage correlation between patients educational level and adherence to special medication instructions.

DISCUSSION

Medication-taking behavior is extremely complex and individual, requiring numerous multi-factorial strategies to improve adherence. Adherence is a key factor associated with the effectiveness of all pharmacological therapies but is particularly critical for medications prescribed for chronic conditions. In developed countries, 30% of all medication related problems are related to poor medication adherence.[11] At domestic level, a neglected data is available regarding medication adherence in patients with chronic diseases. This can be attributed to the fact that many of the risk factors, adherence can be roughly approximated *via* the measurement of surrogate markers. For instance, adherence to drug therapy of cardiovascular diseases "CVD" can be approximated by CV markers, and adherence to eradication therapy can be approximated by measuring *H. pylori* levels. Because most research is disease-specific and not focused on medication adherence alone, this study was focusing on medication adherence in critically risk patients who had undergone kidney transplantation. Examining adherence in patients with transplanted organ is a useful model for helping physicians and therapists understand medication adherence in other chronic conditions.

It has been shown in many studies that demographic factors like educational status, age, and also psychosocial factors of patients have a major impact on the compliance rate.[12] In our study, it is shown that the psychological status of the patients has a major impact on the adherence process. Patients who have fears or undergo bad mood, missed taking their drugs many times in an increased manner. Nevertheless, this was not associated with refusal of taking their medications. This coincides with others studies which related the depression with compliance when treating renal transplant patients.[13] Depression is a predictive of an increased mortality risk[14], therefore; patients beliefs about the causes and meaning of illness and drugs, which strongly related to their compliance with health care should always be taken into account with factors affecting the adherence.[15]

The different age groups showed in the study indicated that young as well as middle aged people were more adherent than adolescence and elderly. The later might be attributed to the low education level of older patients.

Several studies also attempted to venture plausible reasons for poorer compliance among elderly patients.[16] Elderly patients may have problems in vision, hearing and memory. In addition, they may have more difficulties in following therapy instructions due to cognitive impairment or other physical difficulties such as having problems in swallowing tablets, opening drug containers, handling small tablets, distinguishing colors or identifying markings on drugs. Likewise, low compliance also occurs in adolescents and children with chronic disease.[17] The possible explanation would be that very young children

need more help from their parents or guardians to implement treatment. Therefore, their poorer compliance may be due to a lack of understanding or other factors relating to their parents or guardians.[18] Children usually would prefer to live a normal life like their friends, this priority could therefore influence their compliance.

Regarding the educational status of the patient which is considered the most important factor affecting the adherence, intuitively, it may be expected that patients with higher educational level should be more compliant and adherent to the drug therapy. However, our study showed that patients with lower educational level (school level) have a better knowledge about the disease and about their medication instructions, and therefore, more complied to the drug therapy. This confirms previous studies which found that even highly educated patient may not understand their condition or believe in benefit of being complied to their regimen.[19,20] The possible explanation could be that patients with lower educational levels might have more trust in physician advice and to elucidate that education is not always reflects positive results.

CONCLUSION

Given its potentially devastating consequences, adherence deserves attention. It is irrelevant which immunosuppressive medications are prescribed if the patient simply does not, or cannot, adhere to them. The reasons for non adherence are complex and related to many factors that control success and patient survival.

If the patients do not follow or adhere to the treatment plan faithfully, the intended beneficial effects of even the most carefully and scientifically-based treatment plan will not be accomplished.

REFERENCES

1. Sabaté E, ed. (2003) Adherence to Long-Term Therapies: Evidence for Action. Geneva, Switzerland: World Health Organization.

2. Van Boekel GA, Kerkhofs CH and Hilbrands LB (2013) Treatment satisfaction in renal transplant patients taking tacrolimus once daily, *Clinical Therapeutics*. **35**(11), 18211829.

3. Takemoto S, Pinsky B, Schnitzler M, Lentine K, Willoughby L, Burroughs T and Bunnapradist S (2007) A Retrospective analysis of Immunosuppression compliance, dose reduction and discontinuation in kidney transplant recipients, Am J Transplant. 7(12), 2704-2711.

4. Todd M. Ruppar, and Cynthia L (2009) Medication adherence in successful kidney transplant recipients, *Prog Transplant*. **19**(2), 167-172.

5. De Geest S, Abraham I, Dunbar-Jacob J and Vanhaecke J (1999) Behavioral strategies for long-term survival of transplant recipients. In: Metry J, Meyer U, editors. Drug regimen compliance: Issues in clinical trials and patient management. chichester, NY: John Wiley & Sons, pp. 163180.

6. Takemoto S, Pinsky B, Schnitzler M, Lentine K, Willoughby L, Burroughs T and Bunnapradist S (2007) A Retrospective analysis of Immunosuppression compliance, dose reduction and discontinuation in kidney transplant recipients, *Am J Transplant*. **7**(12), 2704-2711.

7. De Geest S, Borgermans L, Gemoets H, Abraham I, Vlaminck H, Evers G and Vanrenterghem Y (1995) Incidence, determinants, and consequences of subclinical noncompliance with immunosuppressive therapy in renal transplant recipients, *Transplantation* **59**(3), 340-347.

8. Rao PS, Schaubel DE, Jia X, Li S, Port FK and Saran R (2007) Survival on dialysis post- kidney transplant failure: Results from the scientific registry of transplant recipients, *Am J Kidney Dis.* **49**(2), 294-300.

9. Nicholas T, Nadeem E, Evelyn W and David T (2010) Renal transplantation. Medical management of transplant recipients, *Oxford specific book*, pp. 308-310.

10. Smith DL (1989) Compliance packaging: a patient education tool, *Am Pharm*. **29**(2), 42-45, 49-53.

11. www. kidney.uk, www.nice.org.uk

12. Osterberg L and Blaschke T (2005) Adherence to medication, *N Engl J Med*. **353**(5), 487-497.

13. Jin J, and Li SC (2006) PMC9 A review of factors affecting therapeutic compliance, *Value in Health* **9**(6), A272-A273.

14. Cynthia L. Russell and *et al*. (2013) Time-in-a-Bottle (TIAB): A Longitudinal, correlational study of patterns, potential predictors, and outcomes of immunosuppressive medication adherence in adult kidney transplant recipients, *Clin Transplant*. **27**(5), 10.1111/ctr.12203.

15. Quinn DK, Alan JC, Austin SB and William JL (2010) Association between depressive symptoms and mortality risk in chronic kidney disease, *Health Psychol.* **29**(6), 594600.

16. Kyngas H and Rissanen M (2001) Support as a crucial predicator of good compliance of adolescents with a chronic disease, *J Clin. Nurs*. **10**, 767-774.

17. Salzman C (1995) Medication compliance in the elderly, *J Clin Psychiatry* **56**(1),18-22.

18. Buck D, Jacoby A, Baker GA and Chadwick DW (1997) Factors influencing compliance with antiepileptic drug regimes, *Seizure* **6**(2), 87-93.

19. Tebbi CK (1993) Treatment compliance in childhood and adolescence, *Cancer* **71**, 3441-3449.

20. Hahn SR (2009) Patient-centered communication to assess and enhance patient adherence to glaucoma medication, *Ophthalmology* **116**(11), S37-42.

21. Senior V, Marteau TM and Weinman J (2004) Genetic Risk Assessment for FH Trial (GRAFT) Study Group. Selfreported adherence to cholesterol-lowering medication in patients with familial hypercholestremia: the role of illness perceptions, *Cardiovasc Drugs Ther.* **18**(6),475-481.