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Adherence to immunosuppressive treatment in post-renal transplant patients: a descriptive-exploratory study

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ABSTRACT
Aim: To check the adherence to the immunosuppressive treatment of post-renal transplant patients.
Method: This is a quantitative, transversal, descriptive-exploratory study performed using 50 patients in the Brazilian state of Santa Catarina. The study involved a semi-structured interview based on the "Measurement Test of Adherence to Treatments".
Results: It was observed that 76% of the patients were considered to be non-adherent to the immunosuppressive treatment; in 62% of the cases it was unintentional behavior; 2% of the cases mentioned lack of motivation to continue treatment; 44% of the cases ingested from 11 to 15 pills/day. The complications reported were hypertension, diabetes and graft rejection.
Discussion: Besides the non-adherence, patients demonstrated understanding and motivation regarding the medication. The excessive umber of drugs ingested on a daily basis influenced the adherence to the treatment. There were two chronic rejections, one of which presented a connection to non-adherence to the immunosuppressive treatment.
Conclusion: The number of medications contributed to non-adherence.
Descriptors: Adherence to Medication; Kidney Transplant; Renal Failure.

INTRODUCTION

Chronic Kidney Diseases (CKD) result from the reduction in the ability of glomerular filtering by the kidneys due to the accumulation of toxins in the blood stream and the loss of electrolytes needed for the functioning of the organic system[1]. The treatment indicated with regard to CKD consists of the prescription of immunosuppressive medication, hemodialysis and renal transplant[2].

Hemodialysis removes toxic substances and filters the blood before returning the cleaned blood to the organism. However, the sessions involved are tiring, and demand an absence from daily activities and work routines; they can be up to five times a week, lasting five hours, making patients dependent on dialysis over periods of weeks, months or even years.

In the case of patients in hemodialysis for a long period, the best option with regard to treating CKD is a kidney transplant. After the proceeding, the patient presents a general health improvement, besides the fact that s/he is no longer dependent on hemodialysis treatment. There are very few counter-indications to kidney transplants. However, it is not performed on all patients due to age, diabetes, seriously debilitated patients, HIV bearers or psychiatric illnesses[3].

After a transplant, it is extremely important to use immunosuppressive therapy with the intention of preventing graft rejection, minimizing the process of graft rejection, and reducing the immune response of the organism against foreign agents[3]. The use of medication starts a short time before the surgical proceeding, and it continues throughout the life of the transplanted patients. However, such medication can also have adverse effects such as pain and discomfort[3].

Besides that, it is necessary to have a high degree of control in terms of adherence to both the immunosuppressive treatment and the treatment of other chronic diseases such as Systemic Arterial Hypertension (SAH) and Diabetes Mellitus (DM), which can lead to CKD. It is important to highlight that such medication is offered free of charge by the

Brazilian Unified Health System (SUS, in Portuguese), guaranteeing access on the part of all renal transplanted patients to immunosuppressive drugs for the rest of their lives.

Despite this fact, (non-)adherence to drug treatment with regard to the many varied chronic diseases is the focus of research[4,5,6], as it is a well-discussed topic among the members of health teams which needs constant reiteration to patients that make use of immunosuppressive drugs after renal transplant.

As the main reasons for adhering to therapy, we stress the following: transportation, the duration of the sessions, pain of fistula puncture, economic factors, dependency of accompanying people and lack of understanding. In addition, we emphasize the new stress factors in the daily lives of patients suffering from renal failure, such as the treatment itself, the changes in lifestyle, the reduction in physical energy, changes in physical appearance and new daily routines[4].

The problems linked to the continuous rise of chronic diseases in Brazil has attracted the attention of health professionals. When promoting the extension of life and the enhancement of the quality of life of bearers – aspects which demands a lot of caring, sensibility and awareness regarding the correct follow-up associated with conservative therapies, it is stressed that besides psychological support, family integration in terms of the treatment and the adherence of the patient to the treatment are essential in order to prevent possible complications and risks that can affect the treatment itself, and the deterioration of the patient's clinical status[7].

Based on that, we decided to research this topic, in terms of investigating the adherence to immunosuppressive treatment, as well as a consideration of the understanding of timetables, prescribed doses, collateral effects and the risks in the case of non-adherence.

The nursing professional has an important role to play in guiding patients regarding the disease timetables and doses, as well as empowering the patient in terms of his self-care and treatment. In this manner, we believe that this study will support the nurse when it comes to verifying the adherence of the patient in immunosuppressive treatment, and in

searching for subsidies that contribute to a rise in adherence. In conjunction with other research it also aims to contribute to this topic and to add consistent data and information that can be used in other fields of study.

Thus, the aim of this study was to verify the adherence to immunosuppressive treatment on the part of post-renal transplant patients.

METHOD

This is a quantitative study, with a transversal approach, with exploratory and descriptive characteristics, performed in a renal clinic in the Brazilian state of Santa Catarina, between the months of March and April 2011. The sample was selected from electronic medical records of patients that were submitted to renal transplant during the period 2007 to 2009. 65 cases were selected. However, from those, a number were excluded: one patient who moved to the capital, four patients who died, and, in one case, besides graft rejection, a patient who was sent back for hemodialysis but in another city, another case involving a patient had a transplant twice during the same year (one of those during this study), one patient who opted out from this study and seven who missed their medical appointments. The instrument used was a semi-structured interview generated from an instrument entitled Measuring Test of Adherence to Treatments, as proposed by Morisky and Green[8].

To collect the data, interviews were scheduled for the day and time of the patients' medical appointment. This research was approved by the Ethics Committee of Santa Catarina Estate University (CEPSH, in Portuguese), under registration number 200\2010, based on the ethics regulations established by Resolution 196/96 of the Brazilian National Health Council.

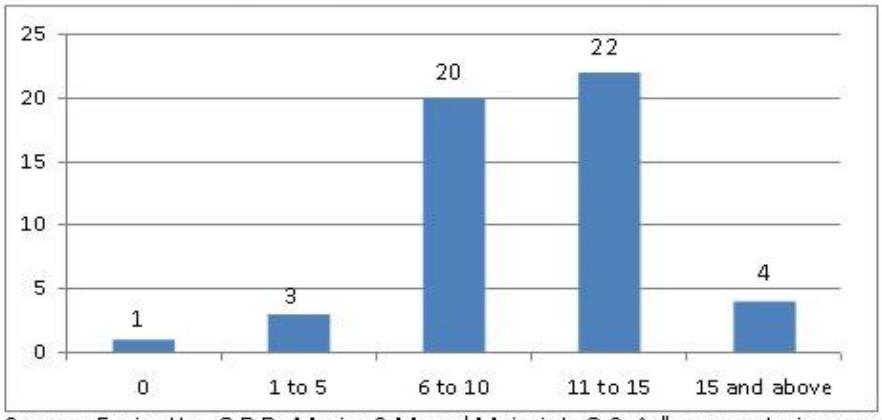
RESULTS

50 patients were studied of which 66% were men, with an average age of 43 years; 76% of them married; 48% were retired; 50% had an average monthly income above the

minimum wage; 46% earned up to the minimum wage; and 25% of the patients did not complete Middle School.

The quantity of daily medication used is presented in Chart 1.

Chart 1: Quantity of daily medication and usage. Santa Catarina, 2011

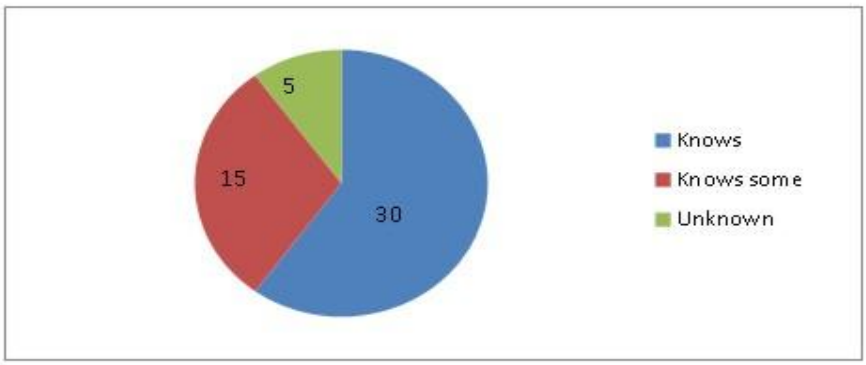


Source: Fuzinatto, C.R.D, Marin, S.M and Maissiat, G.S. Adherence to immunosuppressive treatment in post-renal transplant (2013).

According to Chart 1, 44% of the people used from 11 to 15 different types of drugs on a daily basis and 40% of the subjects ingested from 6 to 10 pills a day.

In Chart 2, we observe that the majority of the patients knew all the drugs prescribed as part of their treatment.

Chart 2: Understanding regarding the medication used. Santa Catarina, 2011



Source: Fuzinatto, C.R.D., Marin, S.M. and Maissiat, G.S. Adherence to immunosuppressive treatment in post-renal transplant (2013).

It was also possible to see that 84% of the patients did not have any support when it came to ingesting the prescribed medication, while 16% were aided by someone from their families: wives, sons or daughters-in-law.

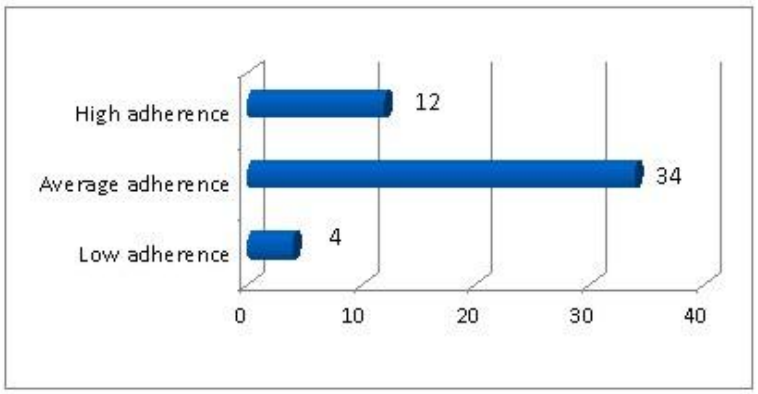
With regard to the use of immunosuppressive medication provided by SUS, it was seen that 72% of the people received all their medication from the public system while 28% of them had part of the medication provided by this same public system.

In terms of post-renal transplant complications, it was seen that 60% of the patients developed SAH, 13% had DM and 10% had both SAH and DM. Other individuals did not report any complications.

It was found that there were four complications associated with the graft. In two cases there was chronic rejection, in one case there was acute rejection, and the final case there was Chronic Renal Failure (CRF) due to an infection in the form of hepatic cryptococcus and septicemia.

With regard to the adherence to drug treatment, including those with low and average adherence, 76% of the patients were classified as non-adherent, as can be observed in Chart 3.

Chart 3: Adherence to immunosuppressive treatment. Santa Catarina, 2011



Source: Fuzinatto, C.R.D., Marin, S.M. and Maissiat, G.S. Adherence to immunosuppressive treatment in post-renal transplant (2013).

Among the patients considered as non-adherents to the immunosuppressive treatment, 62% mentioned that the non-adherence was unintentional, while 2% did not present any motivation regarding the failure to adhere to the treatment prescribed. Other patients demonstrated that they had both understanding and motivation.

DISCUSSION

While characterizing the interviewees, it was seen that the majority of the patients were male, which corroborates with a study performed with 45 patients in hemodialysis, the objective of which was to evaluate the adherence of clients with chronic renal failure to the treatment in hemodialysis[4]. On the other hand, another piece of research performed with 100 patients suffering from Crohn's syndrome, who were clients of a intestinal inflammatory diseases clinic, used the same instrument as this study to evaluate the prevalence and the risk factors associated with low adherence to the drug treatment[9] and showed that the largest number of non-adherents were female.

Besides the majority of transplanted patients being male, the difference between men and women was only 14%, and no meaningful association between gender and adherence was demonstrated in this research.

The 43 year average age of the patients was near to that of a piece of research with 130 patients that had the continuous use of a range of medication of groups C, H02 or L04, from the Anatomical Therapeutic Chemical classification. In this research the level of understanding regarding the pharmacological therapy associated with patients in chronic renal failure (CRF) was observed, together with the factors associated with this understanding, when the average age was found to be 48.8 years[10]. Notwithstanding the possible independence of this age group, it is believed that age does not corroborate with adherence.

The majority of the subjects interviewed were married, a feature also found in a study of 30 patients in hemodialysis in a University hospital in the city of Alfenas, Brazil, that evaluated the quality of life and adherence to immunosuppressive treatment in chronic renal patients[11].

The fact that the patients had studied up to High School level presented higher results than those of a study performed with transplanted patients accompanied by a health team from an ambulatory service of a public hospital in the city of Fortaleza, Brazil. This study described the clinical and socio-demographic profile of renal transplanted patients[12], and it was found that they only had incomplete Middle School education.

Analyzing the occupation of the subjects, retired or unemployed patients were in evident numbers, a data that is compatible with research performed with 30 patients of non-oncologic related pain under treatment at the Pain Ward of the Neurologic Clinic of *Hospital das Clínicas*, part of the Medicine School of São Paulo University[5]. This study aimed to find the prevalence of drug treatment adherence of patients in chronic pain, and showed that retired or unemployed patients were in the majority of patients looking for this service. On the other hand, a study of 45 patients in hemodialysis that evaluated the adherence to hemodialysis treatment of patients with chronic renal failure found that 44% of the patients were involved in paid work of some kind[4].

With regard to adherence of patients to immunosuppressive treatment, the results showed non-adherence in 76% of the cases, similar to a study performed with 100 patients with Crohn's disease, which aimed to observe the prevalence and the risk factors associated with low adherence levels in drug treatment[9], which also revealed a high non-adherence rate of 64%. The voluntary interruption of the treatment was characterized as non-adherence[9].

In the findings of this present study, 31% of the patients showed that non-adherence was non-intentional, which matches the data found in the research with 100 patients with Crohn's disease. This study, which aimed to observe the prevalence and the risk factors associated with low adherence levels in drug treatments, found a low disposition with regard to regular use of prescribed medication and revealed that, in 58% of the cases, the non-adherence behavior, of a non-intentional variety, prevailed[9].

Non-adhesion is an issue faced by health professionals, as it interferes with therapeutic results and in graft support[13]. Based on that, the adherence to treatment and the risks that patients are facing because of non-adherence is being studied in many research projects[4,5,6,9,11]. In this sense, it is extremely important to make the patient feel responsible, as the treatment directly affects the quality of that person's life[14] and requires an adaptation of the lifestyle due to the new situations and personal demands that affect adherence to therapy[2]. These include such aspects as treatment, reduction of

physical strength, alteration of personal appearance, new daily routines[4], diet, hydric ingestion, and the monitoring of arteriovenous fistula.

There is no single method considered as being the gold standard to verify the real adherence to immunosuppressive treatment. However, it is known that the level of non-adherence to the treatment has many associated factors[9], which are in direct correlation with social and cultural environments[6], besides the countless difficulties reported by the clients[4].

The lifestyle of each patient influences how will they face the disease and the adherence to treatment. It is important to identify these factors so prevent them interfering in caring and to help motivate self-care practices[14].

In this sense, there are patients who adhere to the immunosuppressive treatment because they are afraid of dying[4]. In the case of others, it is believed that they stop using the medication due to the fact they do not understand the potential risks of non-adherence.

One of the causes of non-adherence to the treatment is ignorance on the part of the patient and accompanying relatives with regard to the importance of the treatment[6]: "The adequate understanding of the patients regarding the drugs they use is considered a fundamental factor to adhere to treatment"[10].

Besides, all the interviewees reported that they have information regarding the importance and the benefits of consuming medication at an appropriate time and manner. However, it is seen that 2% of the patients reported as non-adherents showed that they do not have enough motivation to continue treatment. Other patients described as non-adherents showed understanding and motivation. This is interesting information as it demonstrates a tendency to neglect treatment due to forgetfulness or carelessness[9].

On the other hand, it was observed that even with a low educational level, patients are interested in knowing about the medication they are using, as, among the non-adherent patients, 40% recognize the drugs prescribed. This result is compatible with research

performed with patients under hemodialysis treatment in a University hospital in the city of Alfenas, Brazil. This study evaluated the adherence to immunosuppressive treatment on the part of chronic renal patients[11] and also found that 40% of the patients knew all the drugs used. The high level of understanding by the patients regarding the medication they use is a supreme factor when it comes to generating adherence to the treatment[10]. From another point-of-view, a study of patients in constant use of specific medication types, which aimed to check the level of understanding about pharmacologic treatment of patients with CRF and the factors associated with this understanding, revealed that the majority of the patients did not have sufficient understanding to safely and effectively manage the use of medication[10]. Another study of patients with Crohn's disease, that aimed to evaluate the prevalence and the risk factors associated with low adherence to medicament treatment[9] found a reduced use of the prescribed drugs. Furthermore, it also demonstrated that in 58% of the cases the non-adherent behavior of a non-intentional nature prevailed, and it was seen that it was a lack of understanding or motivation in 42.2% of the patients, which directly affected adherence.

At the same time, the excess of medication ingested every day influences adherence of treatment, as the majority of the patients observed used between 11 and 15 different drugs a day, which can be seen as up to 18 immunosuppressive pills taken on a daily basis. Besides that, other medications are used to fight collateral effects and to treat comorbidities such as SAH, DM and cardiac illnesses. In research into patients diagnosed with CRF that have a continuous usage, it was seen that they used from 1 to 9 pills a day in the form of immunosuppressive medication[10]. Yet it is important to highlight that only one single case of renal rejection, loss of graft and a return to hemodialysis was noted, and in which the continuous use of drug therapy was interrupted.

The higher the number of different ingested medications, the higher are the chances of non-adherence[6]. Therefore, the quantity of drugs taken in the post-transplant period can interfere with adherence, not only because of the quantity, but also because of the elevated doses and the presence of collateral effects from them. On the other hand, in

the literature, we find conclusions that do not indicate a correlation between the number of pills a day and adherence[5].

Immunosuppressive medication is expensive, and that is why SUS demands a new drug prescription for the patients. Besides that, there was one single case in which the patient did not renew his prescription and stopped receiving the medication because of the general procedure adopted by the government. Later, the patient used this situation as an "excuse" to interrupt the treatment. Yet, patients receive their medication through the clinic and must come to it every two months to be examined, meet medical appointments and also renew their prescription, as demanded by SUS.

In this case, 72% reported they had their medication provided free for them, while 28% mentioned a partial expense because of some missing medication, which are not immunosuppressive drugs made available free at the public clinics, and therefore, had to be bought. In other studies, there was also seen to be a predominance of free medication provided by SUS[5,9]. The major part of the investment in public health in Brazil involves the purchase of medication, which is distributed freely, albeit not in enough quantities to meet the national demand[6]. It is believed that the large number of drugs per day is also associated with non-adherence, even when this medication is provided at no cost[6].

In the location of this study, nurses and nephrologists guide patients, clear doubts and provide general information regarding the medication prescribed: doses, schedules, counter-indications, collateral effects, specific caring, the importance of adherence, correct use of medication and the damage that may occur as a result of inadequate usage. The need to assuage the doubts of the patients, as well as to calm them, demands some guidelines for the whole team and some nursing care. In this sense, the nurse must act as a base, giving psychological and educational support to the patients and relatives[2,4], as data show that many patients who are non-adherents to drug treatment have little information regarding the effects of renal substitution therapy[10].

The education of patients with regard to self-care is a decisive factor in terms of adherence to treatment, as the knowledge generated by proper guidance and the continuous use of medication produce benefits such as SAH control, prevention of SAH complications (strokes, heart attacks), a new routine of healthy habits and special caring.

These benefits can reduce the negative consequences of the disease, and moreover, the delay in terms of renal transplants and the promotion of the quality of life[2].

Besides that, based on the current number of chronic diseases, in the present context of public health in Brazil, the presence of relatives is relevant in the caring, treatment and adherence of the patient, in order to diminish possible secondary illnesses, complications and risks[7].

The complications can appear on the first days or even months after the transplant. Some of the most worrying complications that follow renal transplant are those linked to the graft. In this study, 8% of the patients, all of whom were categorized as non-adherents to the treatment, reported some complication with the graft.

In one of the cases of chronic rejection to the graft, there was a loss of the grafted material and the patient had to return to hemodialysis. The main reason for losing the graft, due to chronic rejection, was the lack of adherence to the immunosuppressive treatment, as it was seen that this was a patient with low adherence and the treatment was interrupted for 20 consecutive days.

Regarding the other case of chronic rejection, the patient was treated with plasmapheresis and was able to recover the functioning of the graft, continuing the immunosuppressive treatment with Tacrolimus and Sodium Mycophenolate. However, this patient presented, following examination, a low serum level for the drugs, which represents a lack of adherence to immunosuppressive treatment.

All transplant cases that presented chronic and acute rejection were SAH holders, and patients that did not present rejection did not have DM. However, we cannot affirm that these two comorbidities are connected to rejection, as there has been no study to prove the relationship between SAH and/or DM to the rejection of a renal graft. The treatment to control DM includes education, change in lifestyle that includes a non-smoking, abstinence from alcoholic beverages, practicing of physical activities, reorganization of diet habits and the use of medication prescribed by a doctor[2].

To guarantee a higher survival of the graft, it is necessary to observe the signs and symptoms of post-transplant rejection. Despite the fact there are immunosuppressive

drugs that are indicated to prevent organ rejection, one should pay attention to the occurrence of infections[12].

The transplant team must have adequate protocols with regard to patient care, according to the ideal level of immunosuppression for each individual, in order to prevent acute and chronic rejection, and to guarantee a lower risk to infection[3].

Data showed that the majority of the graft donors are deceased, as indicated in the statistics observed from another study that aimed to identify the profile of renal transplanted patients[12].

In a study performed with 288 adult patients that underwent renal transplant, the objective was to evaluate the prevalence of non-adherence to immunosuppressive treatment, and the risk factors associated with this attitude. It revealed that the recipients of deceased donors are more adherent to the treatment than those whose donor was still alive[13].

In this research, no association was seen between adherence and the origin of the graft. But non-adherence can be related to a higher level of possible rejection of the graft.

CONCLUSION

This study enables the understanding of the variables of education and the number of ingested medication daily, as factors that influence the adherence to immunosuppressive treatment. Besides patients understanding the drugs that are being used in the treatment, it is necessary to pay higher attention to those with few school years, to those who are demotivated to continue treatment, and to those who are prescribed a large number of pills/day.

We conclude that the lack of adherence to immunosuppressive treatment can lead to many risks to the health of the patient. It interferes in the evolutional process in the post-renal transplant period, and also it is a factor that causes complications and can lead to the rejection of the graft.

We hope that the data found here can guide health professionals so they can work on the factors associated with non-adherence in order to minimize them. In this way they can

achieve better results regarding the benefits to the patient when continuing with immunosuppressive treatment.

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