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Benefit of a pharmacist-led intervention for medication management of renal transplant patients: a controlled before-and-after study

Jeremy Chambord, Lionel Couzi, Pierre Merville, Karine Moreau, Fabien Xuereb and Sarah Djabarouti

Abstract

Aims: To assess the effect of a pharmacist-led intervention, using Barrows cards method, during the first year after renal transplantation, on patient knowledge about their treatment, medication adherence and exposure to treatment in a French cohort.

Methods: We conducted a before-and-after comparative study between two groups of patients: those who benefited from a complementary pharmacist-led intervention [intervention group (IG), $n = 44$] *versus* those who did not [control group (CG), $n = 48$]. The pharmacist-led intervention consisted of a behavioral and educational interview at the first visit (visit 1). The intervention was assessed 4 months later at the second visit (visit 2), using the following endpoints: treatment knowledge, medication adherence [proportion of days covered (PDC) by immunosuppressive therapy] and tacrolimus exposure.

Results: At visit 2, IG patients achieved a significantly higher knowledge score than CG patients (83.3% *versus* 72.2%, $p = 0.001$). We did not find any differences in treatment exposure or medication adherence; however, the intervention tended to reduce the proportion of non-adherent patients with low knowledge scores. Using the PDC by immunosuppressive therapy, we identified 10 non-adherent patients (10.9%) at visit 1 and six at visit 2.

Conclusions: Our intervention showed a positive effect on patient knowledge about their treatment. However, our results did not show any improvement in overall medication adherence, which was likely to be because of the initially high level of adherence in our study population. Nevertheless, the intervention appears to have improved adherence in non-adherent patients with low knowledge scores.

Keywords: Renal transplantation, pharmacist-led intervention, adherence, Barrows cards, knowledge improvement, adherence

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Introduction

Non-adherence to medications is a patient's deviation from their medical prescription, which leads to adverse consequences. The rate of non-adherence to immunosuppressive medications was found to be 15–30% after renal transplantation, but it was dependent on the measurement method used, non-adherence threshold and population evaluated.[1,2] Non-adherence promotes the rise of *de novo* donor-specific antibodies that are involved in antibody-mediated rejection mechanisms. This results in increased risks of rejection and graft failure, decreased patient survival and an adverse economic impact.[1,3,4]

Several risk factors for non-adherence to medications have been identified, usually grouped into five categories: socioeconomic (age, gender, social support, employment, education); patient-related (knowledge and beliefs, comorbidities and

dependencies); disease-related (time since transplantation, number of transplants, living or deceased donor, complications); treatment-related (intake and dosage, adverse effects, number of medications); and healthcare system-related factors (country-specific).[5,6]

Pharmacist-led interventions can improve patients' knowledge about their therapies and pathologies, especially in those with hypertension, respiratory disease, or chronic kidney disease. However, this has not been demonstrated in patients with renal transplants.[7–10] In the literature, primary interventions used in renal transplant patients have mainly been educational and behavioral. They convey knowledge to patients by promoting active participation in their own care, thus improving adherence.[11–13] However, the main population studies have been conducted in the American population, less adherent than the European population, and many methodological variations exist among studies, such as the time since transplantation and the content and/or duration of these interventions (varying from 8 weeks to 1 year).[11]

Among existing interventions in chronic diseases, self-management education can facilitate the knowledge and skills necessary for self-care. The objectives of this educational approach are to support informed decision-making, self-care behaviors and problem-solving. Barrows cards is a method based on self-management by problem-based learning. Barrows cards have shown self-management improvement with immunosuppressive therapy in oncology, then we hypothetized that this method could be used as a tool to implement knowledge, and adherence in renal transplant patients.[14] To our knowledge, no study to date has assessed the effects of pharmacist-led interventions on renal transplant patients in a French healthcare system as part of routine medical care. Nevertheless, in a multicenter French study, Couzi *et al.*[2] showed that the rate of patient non-adherence to immunosuppressants and co-medications at 3 months post-transplantation was 17% and increased gradually to 31% at 1 year post-transplantation. Therefore, we hypothesized that a pharmacist-led intervention performed during the critical first year post-transplantation will improve patient knowledge about their treatment, medication adherence and exposure to treatment.

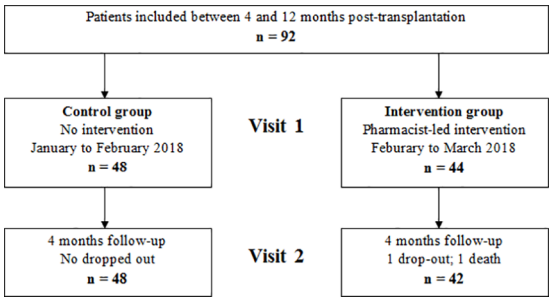

Figure 1. Flowchart of patients through the study.

The objective of our study was to assess the effect of a pharmacist-led intervention, using the Barrows cards method, during the first year after transplantation on patient knowledge about their treatment, medication adherence and exposure to treatment.

Methods

Study design and patients

A controlled before-and-after study was conducted in our department between January and March 2018. The study was conducted in accordance with the Declaration of Helsinki. Patients provided written informed consent and could withdraw from the study at any time. The study was approved by the local Ethics Committee of Bordeaux Hospital University in France (ref. GP-CE2020-35). All patients who underwent renal transplantation at our center received information about their treatment in the first week after transplantation. During the first 3 months post-transplantation, all voluntary patients benefited from an optional post-renal transplant therapeutic workshop delivered by a nurse.

For this study, we enrolled patients who were between 4 months and 1 year post-transplantation at visit 1 (Figure 1). All patients were being treated with tacrolimus, and none had a home-based nurse to prepare their pillbox. In January 2018, 48 patients who attended the outpatient clinic were enrolled at visit 1. During this period, patients' knowledge, adherence and treatment exposure were evaluated by a pharmacist but they did not receive a pharmacist-led intervention (control group; CG). During the next month, 44 patients were attending the outpatient clinic for visit 1. During this period, patients' knowledge, adherence and treatment exposure were

evaluated by a pharmacist and then they received a complementary pharmacist-led intervention (intervention group; IG). At visit 2, 4 months later, patients' knowledge, adherence and treatment exposure were evaluated for the CG and IG by the same pharmacist. During the study, one patient died and another dropped out because of psychiatric complications. Both of them were in the IG.

Process and content of the pharmacist-led intervention

The pharmacist-led intervention, which was performed at visit 1 in the IG patients, consisted of a behavioral and educational interview using kidney transplant-themed Barrows cards.[14] Using the Barrows cards, the patient is presented with a 'situation' that represents a problem they might encounter concerning immunosuppressive treatment or pathology. The patient then chooses one of three 'behavior' cards according to the reaction they would have adopted if placed in this situation. The consequences of the choice were then discussed with the pharmacist leading the interview. For each situation card, the patient had the opportunity to choose a suitable, partially adapted, or inappropriate behavior. The interview was 30 min in duration and involved 11 scenarios. Interventions were only performed by the clinical pharmacist of the nephrology department. The pharmacist who delivered the intervention was a 3-years experienced pharmacist in clinical pharmacy and 6-months experienced in renal transplantation. He was trained in pharmacist-led intervention by a 4-years experienced pharmacist in renal transplantation and therapeutic education nurses. The DEPICT tool was used to describe our pharmacist-led intervention.

Endpoints

Patient knowledge, medication adherence, exposure to tacrolimus, and their evolution between visit 1 and visit 2, 4 months later, were compared between IG and CG (Figure 1). Data were obtained from computerized patient medical records and pharmacy management software.

Data collection. The following patient data were collected, analysed and compared between the IG and CG patients: age, sex, treatments (prescribed immunosuppressants, number of medication a day, pillbox use or not), medical history (number of transplantation, dialysis), lifestyle, employment, level of education, psychiatric pathologies and antidepressant therapy, participation or lack of participation in post-renal transplant therapy workshops, adverse events and related experiences as reported in a patient-completed questionnaire, and rehospitalization rate.

Assessment of treatment knowledge

The knowledge questionnaire was developed from questionnaires previously used by our clinical pharmacy team. It included 18 questions (nine open questions, nine true/false questions) that investigated patients' knowledge of immunosuppressive drugs (name, dosage, benefit, therapeutic follow-up) and health concerns related to kidney transplantation (interactions, infection and carcinogenic risks, self-monitoring). One point was awarded to the patient for each correct answer, and the final score was then expressed as a percentage. Low knowledge score was defined by a score lower than 70%, and high knowledge by a score equal to or higher than 70%. This 70% cut-off was based on the median knowledge score at visit 1.

A topic was considered poorly mastered if less than 30% of patients answered correctly and well mastered if more than 50% of patients answered correctly. A major increase in score was defined as a population score increase of greater than 25% from visit 1 to visit 2.

Knowledge score was evaluated for the CG and the IG at visit 1, and 4 months later at visit 2.

Measurement of medication adherence: proportion of days covered by immunosuppressive therapy

The proportion of days covered (PDC) by immunosuppressive treatment was calculated at the end of the study. Data related to immunosuppressive treatment such as dosage, quantity and date of dispensing, were provided by the patients' pharmacists using community pharmacy management software. The PDC was calculated based on deliveries of the immunosuppressive drug, taking into consideration the hospitalization stay, in which the patients did not use their personal medication supply. The change in dosage over the period was also evaluated, as well as the

remaining medication doses from month to month. We were then able to count the number of days covered by the immunosuppressive drugs between each delivery. The PDC was calculated according to the following formula:

$$\text{PDC} = \left(\begin{array}{l} \text{number of days covered} \\ \text{by immunosuppressive} \\ \text{therapy over the study} \\ \text{period / total study period} \end{array} \right) \times 100$$

PDC by tacrolimus could not be calculated due to its complexity related to dosing variability and the multiplicity of available doses. Thus, we collected mycophenolate quantities and dates of dispensing because the dose of mycophenolate did not change frequently. In cases in which mycophenolate was discontinued, steroids, everolimus, azathioprine and tacrolimus were used.

We defined non-adherent patients as those with a PDC <90%, in accordance with previous studies that used thresholds of 80–95%.[15–17]

Measurement of drug exposure

Drug exposure was monitored by measuring plasma concentrations of immunosuppressants in the pharmacology department of our hospital. Plasma trough concentrations of tacrolimus were used to assess systemic exposure to, and variations in, immunosuppressive treatment by calculating the coefficient of variation. The coefficient of variation of the tacrolimus trough level (CVtac) was calculated using the following formula:

$$\text{CVtac} = \left(\begin{array}{l} \text{standard deviation/mean} \\ \text{trough levels of tacrolimus} \end{array} \right) \times 100$$

Patients with a CVtac >30% were considered to have experienced varying levels of exposure to tacrolimus and were at a higher risk of renal complications.[18] For each patient, the proportion of total tacrolimus trough level values that were <5 ng/mL, a level that is known to be associated with higher *de novo* donor-specific antibodies, was also recorded and expressed as a percentage.[19] CVtac and the proportion of tacrolimus trough levels that were <5 ng/mL were calculated using a minimum of three available plasma concentration values.

Sample size calculation

According to the knowledge score, based on the study of Peipart *et al.*,[20] a standard deviation of 10, a 80% power and a difference of 10% between knowledge score of the two groups led to a sample size of at least 32 patients in each group. The sample size calculation, according to adherence, depends indirectly on the method used to measure adherence, the threshold of non-adherence and the population studied. Based on the study of Chisholm-Burns *et al.*,[21] in which prescription refills were used to measure adherence, a standard deviation of 15, a 80% power and difference of 10% between adherence of the two groups led to a sample size of at least 36 patients in each group.

The sample size needed to be at least 36 patients in each group.

Statistical analyses

The effect of the pharmacist-led intervention was assessed by comparing patient knowledge, medication adherence and treatment exposure in the IG and CG at visit 2. Fisher's exact test and the chi-square test were used for qualitative variables and the Student's *t*-test and the Mann–Whitney test for quantitative variables. Independent samples *t*-tests were used to compare IG and CG at each visit, and the paired samples *t*-test was performed to compare visit 1 and visit 2 in each group. Patient characteristics and pharmacokinetic data were expressed as means (coefficient of variation, %) and medians (interquartile range; IQR). A p value <0.05 was considered to represent statistical significance. GraphPad Prism v8 software was used for the statistical analyses.

Results

Patient characteristics at visit 1

A total of 92 patients were included in this study between January and March 2018. At visit 1, the median age of the patients was 57 (IQR 47–65) years, and 32.6% of the patients were women (n = 30). The median time since transplantation was 257 (IQR 182.5–332.3) days, and the median number of treatment lines was 10 (IQR 7–13). All patients were treated with tacrolimus, of whom 84 (91.3%) were treated with a sustained-release formulation.

At visit 1, the median knowledge score was 71.7% (IQR 58.3–78.8%). The median PDC by immunosuppressants, obtained from the pharmacy management software, was calculated with mycophenolate, steroids, everolimus, azathioprine and tacrolimus in 72 (78.3%), 17 (18.5%), one (1.1%), one (1.1%) and one patient (1.1%), respectively. The median PDC was 100% (IQR 97.7–100%), and the proportion of non-adherent patients was 10.8% ($n=10$). The median CVtac was 25.6% (IQR 20.3–31.2%), and 29.3% of patients had a CVtac >30%. The median percentage of tacrolimus trough levels <5 ng/mL was 0% (IQR 0–0.05%). Baseline characteristics and treatment were similar between the IG and CG patients (Table 1).

Effect of pharmacist-led intervention on patient knowledge

At visit 1, treatment knowledge was similar between the IG and CG patients [65.8% (IQR 55.0–77.1) *versus* 73.3% (IQR 61.7–80.0), $p=0.21$, Figure 2A]. Topics that were initially poorly mastered included self-monitoring, management of forgotten doses, and management of vomiting. The topic related to the consequences of poor treatment compliance was well mastered in both groups, with more than 90% correct answers.

At visit 2, the IG patients had a significantly higher overall knowledge score than the CG patients [83.3% (IQR 74.8–94.6) *versus* 72.2% (IQR 57.8–85.0), $p=0.001$, Figure 2A]. All topics were well mastered in the IG patients and there were major increases in scores from visit 1 to visit 2 for the following topics: management of forgotten doses, management of vomiting, how to use a pillbox, self-monitoring and drug interactions. There were no significant increases in scores among the CG patients.

Effects of pharmacist-led intervention on patient adherence and treatment exposure

At visit 1, treatment adherence and tacrolimus exposure were comparable between the IG and CG patients (Figure 2B–C). The PDC in the IG was comparable to the PDC in the CG [100% (IQR 97.7–100) *versus* 100% (IQR 97.6–100), $p=0.59$, Figure 2B]. The coefficients of variation of tacrolimus were also comparable between the IG and CG patients [25.1 (IQR 19.8–31.2) *versus* 25.7 (IQR 20.3–31.0), $p=0.86$, Figure 2C]. We were not able to identify the reasons for non-adherence in these patients.

At visit 2, there were no differences between the IG and CG patients when adherence was measured with the PDC [100% (IQR 100–100) *versus* 100% (IQR 100–100), $p=0.89$, Figure 2B]. However, non-adherent patients in the IG (PDC <90%) showed a non-significant decrease from visit 1 to visit 2 (15.9% *versus* 4.8%, $p=0.16$). Non-adherent patients in the CG (PDC <90%) were similar between the visits (6.4% *versus* 8.3%, $p>0.99$). The coefficient of variation of tacrolimus was similar between the two groups (16.6% *versus* 16.9%, $p=0.47$, Figure 2C).

Non-adherent patients and knowledge scores

Based on the PDC by immunosuppressive treatment from renal transplantation to visit 1, 10 patients (10.9%) showed low adherence (PDC <90%) and 82 showed high adherence (PDC >90%). We identified six non-adherent patients (6.7%) based on the PDC from visit 1 to visit 2.

We used patient knowledge scores to identify four subpopulations: low-adherent patients with low knowledge scores (LAd/LK), low-adherent patients with high knowledge scores (LAd/HK), high-adherent patients with low knowledge scores (HAd/LK) and high-adherent patients with high knowledge scores (HAd/HK).

In the IG, we observed a significant increase in the number of HAd/HK patients from visit 1 to visit 2 (36.4% *versus* 80.9%, $p<0.001$), in association with a decrease in the number of HAd/LK patients (47% *versus* 14.%, $p=0.001$), and a trend towards a lower proportion of LAd/LK patients (9.1% *versus* 0%, $p=0.12$, Figure 3). The proportion of LAd/HK patients was similar between visit 1 and visit 2 (6.8% *versus* 4.8%, $p>0.99$).

In contrast, the number of HAd/HK patients in the CG did not increase from visit 1 to visit 2 (57% *versus* 48.9%, $p=0.41$, Figure 3). The other three subgroups also showed similar proportions between the two visits.

Adverse events

According to patient-completed questionnaires, 50 patients (54.9%) experienced expected adverse

Table 1. Baseline patient characteristics.

	Intervention group	Control group	*p*-Value
Sociodemographic factors	*n* = 44	*n* = 48	
Age (years)[a]	59.5 (48–65.7)	55 (43–64.7)	0.16
Women[b]	15 (34.1%)	15 (31.2%)	0.83
Time since transplantation (days)[a]	288 (182.5–363.3)	249 (177.8–326.0)	0.37
	n = 43[†]	*n* = 48	
Living alone[b]	12 (27.9%)	8 (16.7%)	0.22
Unemployed[b]	9 (20.9%)	14 (29.2%)	0.47
	n = 42[‡]	*n* = 48	
Level of education			
Lower than high school degree	4 (9.5%)	10 (20.8%)	
High school degree	16 (38.1%)	14 (29.2%)	0.29
Bachelor to license degree	18 (42.9%)	16 (33.3%)	
Higher than license degree	4 (9.5%)	8 (16.7%)	
Medical history	*n* = 42[‡]	*n* = 48	
Psychiatric disorder	6 (13.6%)	9 (18.8%)	0.58
Anxiolitic/antidepressant therapy[b]	8 (18.2%)	11 (22.9%)	0.62
⩾Two transplantations[b]	6 (13.6%)	8 (16.7%)	0.78
Medical history of hemodialysis[b]	30 (68.2%)	34 (70.8%)	0.82
Medical history of peritoneal dialysis[b]	6 (13.6%)	7 (14.6%)	>0.99
90-Days post-transplantation rehospitalization[b]	21 (47.8%)	20 (41.7%)	0.39
Participation in post-renal transplant therapy workshop[b]	13 (29.5%)	24 (50.0%)	0.06
Treatment	*n* = 42[‡]	*n* = 48	
Number of medications/day[a]	10.0 (7.0–12.75)	10.5 (7.3–13.8)	0.67
Pillbox use[b]	27 (61.4%)	31 (64.6%)	0.83
	n = 44	*n* = 48	
Significant adverse events	10 (22.7%)	10 (20.8%)	1
Tacrolimus ER[b]	40 (90.9%)	44 (91.7%)	0.99
Tacrolimus SR[b]	4 (9.1%)	4 (8.3%)	
Cyclosporin[b]	0	0	NS
Corticosteroids[b]	28 (63.6%)	36 (75.0%)	0.26
Mycophenolate[b]	37 (84.1%)	40 (83.3%)	1
Everolimus[b]	5 (11.4%)	4 (8.3%)	0.73
Azathioprin[b]	1 (22.7%)	1 (20.8%)	1

[a]Quantitative variables are presented as medians (interquartile range).
[b]Categorical variables are presented as numbers (%).
[†]One missing patient.
[‡]Two missing patients.
ER, extended release; SR, standard release.

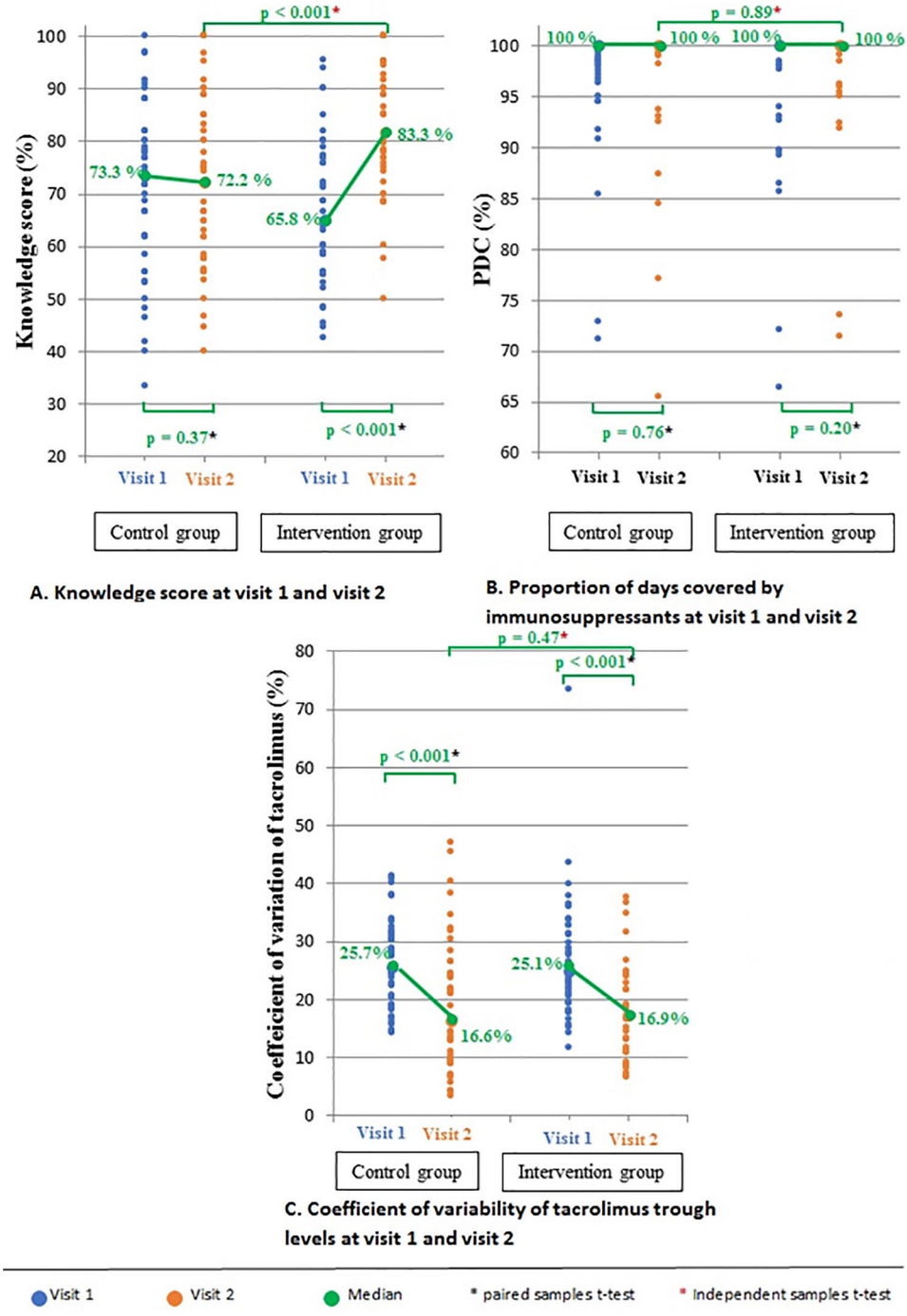

Figure 2. Changes in knowledge scores, adherence and tacrolimus exposure between visit 1 and visit 2.

events at the end of the study. In the CG, 29 patients (60.4%) experienced adverse events: 12 patients (25.0%) suffered from tremor, six (12.5%) from diarrhea, six (12.5%) from abdominal pain, seven (14.5%) from skin problems and 21 patients (43.8%) experienced other adverse events. In the IG, 21 patients (48.8%) experienced adverse events: 10 patients (22.7%) suffered from tremor, five (11.4%) from diarrhea, one (2.1%) from abdominal pain, two (4.5%) from skin problems and 13 patients (29.5%) experienced other adverse events.

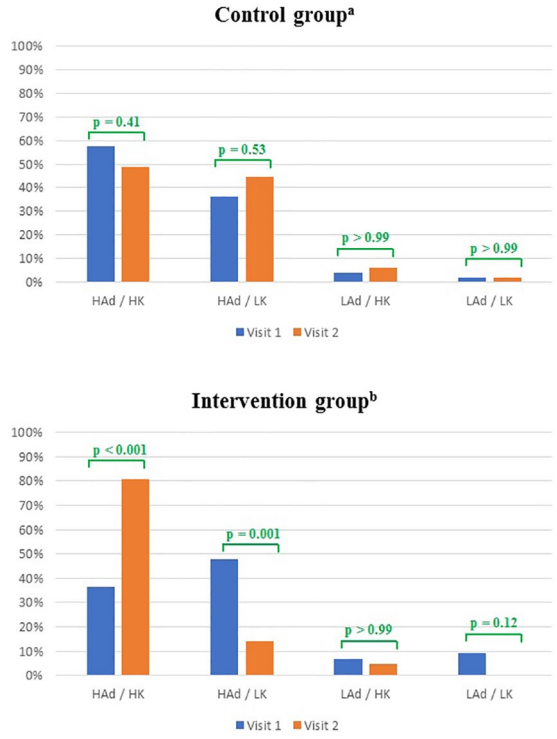

Figure 3. Subpopulations identified according to knowledge score and proportion of days covered by immunosuppressants.
[a]$n = 47$ at visit 1; $n = 48$ at visit 2.
[b]$n = 44$ at visit 1; $n = 42$ at visit 2.
HAd/HK, high-adherent patients with high knowledge scores; HAd/LK, high-adherent patients with low knowledge scores; LAd/HK, low-adherent patients with low knowledge scores; LAd/LK, low-adherent patients with high knowledge scores.

Discussion

Improved patient knowledge versus the pharmacist-led intervention

Our results revealed a higher knowledge score in patients who received a complementary pharmacist-led intervention ($p = 0.001$). These patients improved their knowledge score by approximately 17% (three of 18 questions) at 4 months after the interview . The topics associated with the most significant improvements were those that were less mastered at the beginning of the study, highlighting the need to target interventions that improve patient autonomy in terms of treatment (how to handle missed doses and vomiting, use of pillboxes) and drug interactions. Better patient education leads to a more informed population, and therefore patients are more vigilant about disease pathology and its treatment. Serper *et al.*[22] showed that patients with more knowledge about their treatment reduced the number of post-liver transplant readmissions; thus, we hypothesize that our intervention may improve patient clinical outcomes as well.

No improvement in adherence to treatment versus the pharmacist-led intervention

We failed to show an improvement in treatment adherence in the IG compared with the CG. However, our population had a lower rate of non-adherence compared with previous studies (6–15% *versus* 15–30%).[1] Other studies investigated mainly US patients, who have a higher rate of non-adherence for various reasons (e.g. health-care system-related, socioeconomic factors, ethnicity) compared with other populations.[23] In addition, previous studies were often conducted at later times after transplantation (>1 year post-transplantation) unlike in our study, and some included pediatric patients, who have additional risk factors for treatment non-adherence.[5,6] Our patients had a median post-transplantation time of 8.5 months and were initially considered highly adherent, so demonstrating a difference in adherence between our two groups of patients was more difficult. However, the proportion of non-adherent patients seemed to decrease between visit 1 and visit 2 in the IG, while remaining stable in the CG. Moreover, our intervention increased the proportion of adherent patients with high knowledge scores (HAd/HK patients). We hypothesize that LAd/LK patients responded better to our intervention because of their greater potential for progression, but the initial low proportion of these patients (9.1%) could explain our failure to show an improvement in treatment adherence. For patients with initially high adherence, there is no need for any improvement strategy. For non-adherent patients with initially high knowledge scores (LAd/HK), non-adherence is not related to a lack of knowledge. These cases require other strategies that address the risk factors for the non-adherent behaviors.

Improvements planned for future research

Our study supports the need for pharmacist-led interventions in populations with lower treatment adherence and lower knowledge score. For this purpose, we could assess patients at a later stage post-renal transplantation (>1 year) but also directly target non-adherent patients using different measurement methods. Thus, we propose

that patients with a PDC <90% and poor knowledge may be eligible for a pharmacist-led intervention with Barrows cards.

The pharmacist-led intervention performed was similar for all patients and presented the same scenarios to each patient. An individualized intervention adapted to the needs of each patient would allow a more relevant approach. In other chronic conditions, motivational interviews are conducted to explore factors related to non-adherence, assess ambivalence and/or patient resistance and encourage patient adherence.[24] First, it is necessary to determine whether non-adherence is intentional or not. If not intentional, it may be worth discussing integration of the treatment into the patient's daily life and methods to help remember taking the prescribed dose (e.g. alarms, intake during meals, use of a pillbox). In the case of intentional non-adherence, which is more complex, discussions with the patient regarding their beliefs, knowledge about the treatment and its complications, associated pathologies, and follow-up may be beneficial.[7] Given that significant side effects tended to be more prevalent in our non-adherent population, counselling patients to avoid or minimize medication non-adherence seemed necessary.

A pharmacist-led intervention, condensed into one interview, was conducted in our study. Although organization of several interviews is more complex, repeated interventions over longer periods have shown better results in improving adherence.[11,12] In a systematic review from 2017, Nevins *et al.*[13] suggested that interventions should be maintained throughout the treatment course and integrated into standard care practice. These repeated interventions would allow clinicians to follow and guide the patient throughout the process to improve treatment adherence.

Although the clinical pharmacist plays an important role in identifying non-adherent patients, non-adherence remains a complex phenomenon that requires collaboration with other health professionals (e.g. dieticians, psychologists, nurses, and doctors) to ensure an appropriately multidimensional approach.

Limitations of the study

The before-and-after study design is recognized to overestimate the effect of the intervention. The values measured before intervention may change after intervention because of temporal change or because of statistical phenomenon called 'regression to the mean' (especially for extreme values) not due to the intervention. However, we used a control group to decrease these limitations. There was no randomization in our study because the pharmacist-led intervention was implemented from February 2018 for all patients as part of the evolution of routine care. No method of measuring adherence is 100% reliable. The PDC by immunosuppressants, calculated using the pharmacy management software, may be subject to bias if the patient retrieves the medication from a pharmacy that we are unaware of. This is a rare event because of the difficulties in ordering immunosuppressive treatments. To reduce this bias, patients were asked to report any potential pharmacy changes. Moreover, this method cannot establish whether the patient actually ingested the correct drug or dose.

Another limitation was that the plasma concentration of tacrolimus may vary depending on drug interactions or therapeutic thresholds defined by the clinician. The questionnaire on treatment knowledge was created for this study and inspired by the questionnaires used by the clinical pharmacy team at our hospital, and was not previously validated in the literature. The results of this questionnaire should be used with caution because they are difficult to compare with those from other studies.

Finally, our patient population was small (<50 patients per group) for the purpose of evaluating the effects of pharmacist maintenance. Further investigations in larger cohorts are necessary to confirm our results.

Conclusion

To our knowledge, this is the first study to evaluate the effect of pharmacist-led intervention on adherence and knowledge score on kidney transplant patients in the French population. Our intervention showed a positive effect of the intervention on the patients' knowledge about their treatment. However, we did not find any improvement in adherence to immunosuppressive therapy, probably because of the initially high adherence in our population. Nevertheless, our intervention decreased the proportion of non-adherent patients with low knowledge scores (LAd/LK patients). Thus, we encourage

further interventions for these patients. We could proactively identify these patients during the 6–8-month period after renal transplantation. A pharmacist individualized intervention based on Barrows cards could be performed and followed up by a third interview a few months later to help patients improve their adherence and knowledge. The benefit of our intervention on adherence should be assessed in randomized and large cohort studies, especially in patients who underwent renal transplantation more than 1 year before and who are at high risk of non-adherence associated with low knowledge of their treatment.

The English in this document has been checked by at least two professional editors, both native speakers of English. For a certificate, please see: http://www.textcheck.com/certificate/mk0n6g.

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Conflict of interest statement

The authors declare that there is no conflict of interest.

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Supplemental material

Supplemental material for this article is available online.

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