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Knowledge of oral drug treatment in immunocompromised patients on hospital discharge

Ingrid Chau[a], Virginie Korb-Savoldelli[a,b], Ludovic Trinquart[c], Thibaut Caruba[a,b], Patrice Prognon[a,d], Pierre Durieux[e,f], Christophe Piketty[g], Brigitte Sabatier[a,h]

[a] Pharmacy Department, AP-HP Georges Pompidou European Hospital, Paris, France
[b] Clinical Pharmacy and Pharmacokinetic, Faculty of Pharmacy, Paris Descartes University, Paris, France
[c] Epidemiology Investigation Center 4, INSERM, Paris, France
[d] GCA, EA 40-41, Faculty of Pharmacy, Paris XI, Châtenay-Malabry, France
[e] Department of Hospital Informatics, Evaluation and Public Health, AP-HP, Georges Pompidou European Hospital, Paris, France
[f] Cordeliers Research Centre, University Paris Descartes, INSERM UMRS 872, Paris, France
[g] Immunology Department, AP-HP Georges Pompidou European Hospital, Paris, France
[h] Paris Descartes University, INSERM U765, Paris, France

Summary

PRINCIPLES: Several studies have shown that patients' inappropriate knowledge about their medication is associated with non-adherence. The aim of this study was to assess immunocompromised inpatient knowledge of their oral drug treatment on discharge.

METHODS: We conducted a single-centre, prospective, cross-sectional study from July to November 2008 in the Immunology unit of a university-based hospital. Knowledge of all oral prescribed medication was assessed before discharge of immunocompromised inpatients using a self-administered questionnaire, assessing drug name, dosage, indication and administration guidelines. Prescribed drugs were classified as treatments for chronic disease, or as adjuvant treatments which were differentiated regarding their link with the chronic disease.

RESULTS: Over four months, 17 transplant recipients and 38 HIV-infected patients were included. Overall, 57% of the 497 prescribed drugs were adequately known. The proportions of drugs adequately known were 79%, 91%, 81% and 62% respectively for the drug name, dosage, indication and administration guidelines components. Drugs for the treatment of chronic disease were more adequately known than adjuvant treatments. Older age and a low educational level were significantly associated with poor knowledge of drugs.

CONCLUSIONS: Immunocompromised patients demonstrated moderate to good knowledge of oral drugs on discharge. Adjuvant treatments were less well known than drugs for the treatment of chronic disease. Some recommendations for interventions aimed at utilising the skills of clinical pharmacists are needed. Efforts which encourage patients to be active participants in their own treatment could improve therapeutic adherence and reduce potential complications.

Key words: *immunodeficiency; HIV, transplantation; patient knowledge; drugs*

Introduction

Adherence to the drug regimen is crucial in patients with chronic diseases, especially for immunocompromised patients. In transplant recipients, non-adherence to immunosuppressive drug regimens is known to be associated with the occurrence of late acute rejection episodes, graft loss and death [1]. In HIV-infected patients, non-adherence to combined anti-retroviral therapy has been shown to be associated with increased morbidity and mortality, drug resistance and failure to achieve viral suppression [2–4]. Although adherence to combined anti-retroviral therapy during HIV infection or to immunosuppressive therapy after transplantation is crucial, adherence to the daily adjuvant drugs which aim to treat or prevent side effects or co-morbidities play a key role in immunocompromised patients [5–8].

Furthermore, the patient's knowledge about their medication is a prerequisite for preventing dosage errors, drug interactions and limited adherence [9–11]. Several studies have shown that inappropriate patient knowledge about their medication is associated with a higher likelihood of non-adherence [12, 13]. Other studies have aimed to identify factors associated with poorer knowledge. Expected influencing factors such as sociodemographic characteristics, length of hospital stay or number of drugs were consequently studied [14–16].

Patients' knowledge of their own illness and treatment plan is an important component of patient education [17, 18]. In

the management of chronic diseases, patient education is essential to improve quality of care and to avoid foreseeable iatrogenic events [19, 20]. This approach is integrated into health care and is patient-centred [21].

In clinical practice, the education of immunocompromised patients is focused on oral drugs, because they represent the vast majority of prescribed medications being self-reported after discharge. We hypothesised that the patient's knowledge of his treatment could vary substantially between long-term treatment of the chronic disease, and adjuvant treatment which might be the least known. No data were previously available regarding these adjuvant treatments in immunocompromised patients.

Aim of the study

Hence, the aim of the current study was to evaluate the knowledge of oral drug treatment in immunocompromised patients on discharge, and to examine the relationship between the amount of knowledge and the patient or treatment characteristics.

Methods

Setting

A single-centre cross-sectional survey was conducted in a 720-bed French university hospital from July to November 2008. A patient information system, integrating an electronic patient record and a computerised physician order entry, is used throughout the hospital. Immunocompromised patients were recruited from the 19-bed Immunology unit, which is essentially involved in the care of patients with HIV infection and transplant recipients.

Population

During the study period, all patients hospitalised in the Immunology unit, either HIV-infected patients or transplant recipients, were eligible for the study. Non-French-speaking patients and the mentally impaired (mental retardation and dementia) were excluded. Each patient participated only once in the study. Before inclusion, all patients gave informed consent.

Medication knowledge measurement

Patients' knowledge of drug treatment was assessed using a self-reported questionnaire on discharge. It targeted knowledge according to four items: adequate knowledge of (1) drug name, (2) dosage (number, units and frequency of administration), (3) indication and (4) administration guidelines (specific recommendations about taking the drug in regard to meals, other drugs, or position, for example). The questionnaire was designed by three pharmacists, a statistician and a physician. In a one-week pre-study phase, four patients filled in the self-reported questionnaire and were asked to comment on the questionnaire, which allowed modification of the format and the wording of specific items. These patients were excluded from the present study.

This self-reported questionnaire was given by the pharmacist to inpatients on discharge after they had received all usual pre-discharge information but before the transmission of the written prescription. The doctors, the pharmacists and the nurses never changed their practice during the hospitalisation of the patient and no specific written instructions about medications were given to the patient. The assessed knowledge of the patient was consequently based only on their previous knowledge before hospitalisation, on the information during hospitalisation given by the nurses who brought each drug throughout the day, and on the information orally given by the doctor during his daily visit and the pre-discharge visit to explain the treatment changes regarding the pathology of the patient.

The self-reported questionnaire was introduced by an explanation of the study describing the objective and informing the patient that he could refuse to complete the questionnaire without any justifications. This written notification was also explained by the pharmacist. The signed inform consent forms were systematically collected by the pharmacist.

Patients had to note all long-term oral drugs to be taken after discharge. For each noted drug, the patient then reported the drug name (brand or generic denomination), indication (open-ended questions), the dosage and administration guidelines (multiple-choice questions). The pharmacist reminded the patient about the aim of the study and underlined the importance to only answer the questionnaire only from their memory. For this reason, the subjects were requested not to have access to any written information when they completed the questionnaire (in case of any prescription bottles or any prescription in the patient's room, the pharmacist asked the patient to temporarily keep them out of his room.) If the patient could not answer the self-reported questionnaire alone because it was too difficult or because the patient could not read or to write, the pharmacist could orally interview the patient but must not influence the patient answer. After completion of the study, a pharmacist reviewed all questionnaires and checked the accuracy of the patients' answers by comparing them to the true drug regimens, identified via computer-entered prescriptions and medical summaries. Forgotten drugs, unknown or indeterminate answers were rated as lack of knowledge. To assess whether drug administration guidelines were known, we referred to the French VIDAL Drug compendium [22], the references of the updated Summary Product Characteristics which are authorised and published by the European Medicines Agency or the French Agency for the Safety of Health Products. For example, for the immunosuppressive drug tacrolimus, the referred administration guidelines recommend to be taken in starved conditions, a minimum of 1 hour before or 2–3 hours after a meal. These administration guidelines are very crucial for some drugs because it could have an impact on the efficacy of the drug. For tacrolimus, if these recommendations are not respected the immunosuppressive drug will not be absorbed which represent a risk of graft loss.

To distinguish patient knowledge of drugs for the treatment of chronic disease from that of adjuvant drug treatments, each prescribed drug was classified into one of the following six categories: 1) treatment of the chronic disease, 2) treatment of ongoing infections, 3) prophylactic treatment of opportunistic infections, 4) treatment of drug side effects (immediate side effects such as gastrointestinal intolerance,

and/or long-term side effects such as osteoporosis with corticoids), 5) treatment of associated pathologies (for example platelet aggregation inhibitors to prevent thrombosis after transplantation or HIV infection), 6) other drugs, which could not be classified in the preceding categories. We considered the categories 2, 3, 4 and 5 as adjuvant treatment.

Two pharmacists and three physicians independently classified all prescribed drugs. Disagreements were resolved by a consensus discussion.

Specific rules of classification were sometimes different when considering HIV-infected patients or transplant recipients. For instance, in transplant recipients, corticosteroids were considered as a treatment of the chronic disease because they are used as a immunosuppressive agent whereas, in HIV-infected patients, they were classified in the category as a treatment of ongoing infection. Another example was treatments for hypertension which were classified as category 4) in transplant recipients, as hypertension is a common side effect of immunosuppressive agents (tacrolimus and ciclosporin), but it was considered as category 5) in HIV patients because hypertension is an associated pathology of HIV infection.

Data collection

This observational study did not require any facility from the Human Subjects Research Committee in accordance with French regulations (article L1121-1 of the Public Health Code), because the opinion of the Ethics Committee which is normally required for biomedical research is not applicable for research where all medical practices and treatments are usually used without any supplementary or unusual procedures of diagnosis or monitoring.

Demographic data (age, sex, marital status, education level) and medication knowledge assessment data were collected through the self-reported questionnaire. Clinical data, including duration of the chronic disease (defined as time since HIV diagnosis or transplantation), hospital length of stay, number of medications on admission and discharge, whether the drug had been introduced during hospitalisation or whether the prescription was modified during the hospital stay, were collected from medical charts. It was hypothesised that these covariates could influence patient knowledge according to our review of the available literature. Drug regimens were collected from computer-entered prescriptions. For each patient, the software displayed all the prescription order lines, one for each drug. This questionnaire remained anonymous and data were consequently treated without name of patients.

Study size and statistical methods

The drug was the principal unit of analysis. A drug was deemed adequately known when the four combined knowledge components were known. We also considered 3-component knowledge adequate (drug name, indication and dosage) because we anticipated that administration guidelines would be less known. We estimated the probability of a drug being adequately known using the ratio of the number of known drugs to the total number of prescribed drugs. Since patients received more than one medication, the calculation of the 95% confidence interval (CI) for this proportion was based on a ratio estimator for the variance of clustered binary data, which includes taking intra-cluster correlations into account [23].

Associations between adequate drug knowledge and patient or drug characteristics were assessed using a General Estimating Equation (GEE) multivariate analysis (a binomial distribution, a logic link and an exchangeable correlation structure were used) [24]. The model also took intra-cluster correlations into account, since patients were prescribed several drugs. The model was estimated for the 4-component and the 3-component definitions of adequate drug knowledge. Results were expressed using odds ratio and associated 95% confidence intervals.

Assuming an *a priori* probability of a drug being adequately known in 60% of cases, that patients are prescribed about 10 drugs and taking intra-patient correlation into account, we estimated that 500 prescribed drugs would ensure a precision inferior to 10% for the 95% confidence interval for the true probability, corresponding to a patient sample size of 50. Moreover, considering that it would provide about 300 adequately known drugs and that we planned to enter 10 covariates in the predictive model, the 10 events per variable rule (to get stable estimates of the regression coefficients) would be met.

Data analysis was performed using SAS software. Two-sided p values inferior to 0.05 were deemed significant.

Results

A total of 66 patients were eligible (hospitalised in the Department during the period of inclusion), and from these 55 patients were included and answered the questionnaire. Exclusion reasons were: (1) two patients not discharged at the end of the study, (2) two patients transferred to another department after one day of stay, (3) seven patients discharged during the weekend or lost. No patient refused to take part in the survey. The characteristics of the excluded patients were disparate regarding chronic disease, age and gender. The characteristics of the 55 patients are presented in table 1.

On discharge for the 55 patients, there were 497 prescribed drugs, with a median of 9 drugs per patient. The median number of prescribed drugs was significantly higher in transplant recipients compared to HIV-infected patients (median number [Q1; Q3]: 12 [11; 15] vs. 7 [5; 10], p <0.0001). In the current study, all transplant recipients always had treatment for drug side effects and associated pathologies.

The assessment of medication knowledge is reported in table 2. Overall, 57% of prescribed drugs were adequately known, when considering the four knowledge components combined. The intra-patient correlation coefficient was estimated at 0.41, which means that if one prescribed drug is known by a particular patient, the probability of other prescribed drugs being known by this patient will increase. When considering treatment categories, drugs for the treatment of chronic disease were the most adequately known (71% of 143 prescribed drugs were known). Results were similar when considering adequate 3-component knowledge (drug name, indication and dosage).

When considering the knowledge components separately, knowledge of administration guidelines was the worst item (62% of 228 drugs adequately known). In contrast, drug dosage was almost always adequately known (proportion of known drugs: 97% for treatment of chronic disease and between 83 and 92% for the other categories).

The analysis of the association between medication knowledge on discharge and drug and patient characteristics is reported in table 3. The multivariate analysis demonstrated that adjuvant drug treatments were significantly less known than those for long-term treatment of chronic disease, except for treatment of ongoing infections which was not significant. Concerning patient characteristics, older age, a low educational level and short duration of the chronic disease were significantly associated with lower odds of adequate knowledge of drugs. The knowledge of all treatments was not significantly different between transplant recipients versus HIV infected patients. Conversely, modifications of the treatment during hospitalisation decreased knowledge on discharge (OR = 0.2, p = 0.03). Finally, the length of hospital stay, the number of prescribed drugs, marital status and sex were not significantly associated with medication knowledge on discharge. Results were similar whether we considered the administration guidelines knowledge component or not.

Using the patient as the unit of analysis, 58% of patients adequately knew all their prescribed drugs on discharge when considering the four knowledge components combined. The proportions of transplant recipients and HIV-infected patients who adequately knew all their drugs were similar (59% versus 58%). When the previous analysis of the studied factors was performed on the perfect knowledge of all immunosuppressive or anti-retroviral drugs, no significant difference was found between the two populations and the previous factors were found to be significantly associated. These results confirm the previous results which were obtained with all confounded drugs.

Table 1: Patient characteristics on discharge.

	N = 55	
Variables	**Transplant N = 17* (31%)**	**HIV N = 38 (69%)**
Duration of chronic disease (years)	2 [1; 5]	14 [9; 19]
Associated pathology, n (%)		
Hepatitis B virus	–	4 (11)
Hepatitis C virus	–	12 (32)
Cystic fibrosis	9 (53)	–
Age (years)	31 [23; 57]	51 [43; 56]
Male, n (%)	10 (59)	27 (71)
Higher education level, n (%)	5 (29)	14 (34)
Married or co-habiting, n (%)	7 (41)	11 (29)
Length of hospital stay (days)	7 [3; 16]	7 [3; 13]
Face-to-face interview†, n (%)	4 (24)	12 (32)
Number of patients receiving at least one drug for a chronic disease, n (%)	17 (100)	33 (87)
Number of prescribed drugs per patient, n	12 [11; 15]	7 [5; 10]
Previous AIDS defining event, n (%)		16 (42)

Data were summarised using median [25% percentile; 75% percentile] unless otherwise stated.

*: 6 cardiac transplants, 9 lung transplants, 2 lung and liver transplants

†: some patients were interviewed by the pharmacist because they were not able to read or write, or were too tired to fill in the self-administered questionnaire by themselves.

Table 2: Percentages of known drugs according to treatment category at discharge.

Treatment category	Knowledge of drug name	Knowledge of drug dosage	Knowledge of drug indication	Knowledge of drug administration guidelines	Knowledge of drug name, dosage and indication	Knowledge of drug name, dosage, indication and administration guideline*
Treatment of chronic disease	85 (122/143)	97 (138/143)	96 (137/143)	80 (82/102)	81 (116/143)	71 (102/143)
Treatment of ongoing infections	73 (22/30)	87 (26/30)	77 (23/30)	56 (10/18)	60 (18/30)	50 (15/30)
Prophylactic treatment of infections	79 (33/42)	83 (35/42)	60 (25/42)	34 (11/32)	48 (20/42)	29 (12/42)
Treatment of drug side effects	78 (73/94)	88 (83/94)	67 (63/94)	46 (18/39)	55 (52/94)	49 (46/94)
Treatment of associated pathologies	78 (80/103)	92 (95/103)	81 (83/103)	72 (13/18)	59 (61/103)	56 (58/103)
Other	74 (63/85)	91 (77/85)	87 (74/85)	37 (7/19)	66 (56/85)	56 (48/85)
Total	79 (393/497)	91 (454/497)	81 (405/497)	62 (141/228)	65 (323/497)	57 (281/497)

Data are percentages of known drugs (number of known drugs / number of prescribed drugs)

* when there was no specific administration guidelines, we considered the knowledge of name, dosage and indication only.

Discussion

We found that immunocompromised inpatients had moderate to good knowledge of oral prescribed drugs on discharge. Adjuvant treatments were less known than treatment of chronic disease. Moreover, the administration guidelines item was the least known item compared to name, dosage and indication.

Several studies have previously assessed patient knowledge of prescribed drugs in different settings, but to the best of our knowledge, none specifically concerned immunocompromised patients. These studies were interested in inpatients in general [25–27], inpatients hospitalised in internal medicine units [14–16], the elderly population [28, 29], or patients taking specific treatment, such as anti-hypertensive medication [30] or anticoagulants [31].

The only previous study interested in our specific population included HIV outpatients [32]. Whereas we assessed knowledge of all oral drugs, only knowledge of anti-retroviral treatment was assessed in that study. While drugs for the treatment of chronic disease were known by 85% of patients for the name and 97% for the dosage in our study population, these percentages were 69% and 90% respectively for HIV outpatients [32]. This difference was not due to consideration of transplant recipients, because their knowledge was similar to HIV outpatients. As the number of drugs for chronic disease and patient age are similar in this study, the higher education level of our population may be the reason for these better results.

Concerning factors influencing knowledge, we found that recent chronic disease, modifications of the treatment during the hospitalisation stay and demographic characteristics such as older age and lower education level had a negative impact on knowledge. These results regarding age and educational level are in agreement with those found in recent studies [14, 15]. However, the literature shows variable results regarding modifications of treatment [14, 15]. In our study, unlike in previously published studies [14], we found that the number of prescribed drugs had no impact on knowledge of prescribed treatment. Nevertheless, immunocompromised patients have heavy pill burdens compared to the general population of treated patients. Concerning the influence of treatment category on knowledge, adjuvant treatments were always less known than the treatment of chronic diseases. However, it is interesting to note that treatment category had an impact on knowledge. Treatment of infection, particularly prophylactic treatment, treatment of drug side effects and treatment of associated pathologies were less known. One may speculate that patients who have no clinical symptoms feel less concerned about treatment to prevent hypercholesterolemia, osteoporosis or opportunistic infections, for example.

Table 3: Association between patients and drug characteristics and adequate knowledge of 497 drugs taken by 55 patients on discharge.

Variables	Adequate knowledge of drug name, dosage and indication		Adequate knowledge of drug name, dosage, indication and administration guideline*	
	OR [95% CI]	*p* value	OR [95% CI]	*p* value
Treatment of chronic disease	1.0	–	1.0	–
Treatment of ongoing infections	0.3 [0.1; 1.3]	0.10	0.4 [0.1; 1.5]	0.16
Prophylactic treatment of infections	0.3 [0.1; 0.7]	0.01	0.2 [0.1; 0.5]	<0.01
Treatment of drug side effects	0.3 [0.1; 0.7]	<0.01	0.4 [0.2; 0.8]	0.01
Treatment of associated diseases	0.3 [0.1; 0.7]	<0.01	0.5 [0.3; 0.9]	0.03
All other drugs	0.5 [0.2; 1.0]	0.04	0.6 [0.3; 1.0]	0.07
Transplant recipient	1.0	–	1.0	–
HIV patient	0.4 [0.1; 1.4]	0.18	0.5 [0.2; 1.4]	0.18
Duration of chronic disease (↑ 5 years)	1.7 [1.1; 2.6]	0.03	1.5 [1.0; 2.2]	0.06
Length of hospital stay (↑ 5 days)	0.8 [0.7; 1.0]	0.06	0.9 [0.8; 1.0]	0.13
Married or co-habiting	1.0	–	1.0	–
Single or widowed	1.0 [0.4; 2.6]	0.93	0.8 [0.4; 1.8]	0.60
Male	1.0	–	1.0	–
Female	1.1 [0.3; 4.0]	0.88	1.0 [0.4; 2.8]	0.93
Age (↑ 10 years)	0.6 [0.4; 0.8]	<0.001	0.7 [0.5; 0.9]	<0.01
Higher education level	1.0	–	1.0	–
Compulsory or secondary education	0.2 [0.0; 0.8]	0.03	0.4 [0.1; 1.2]	0.10
Newly introduced medication or dosage modification	0.2 [0.1; 0.9]	0.03	0.4 [0.1; 1.0]	0.05
Number of drugs (↑ 5 drugs)	1.1 [0.5; 2.5]	0.86	1.2 [0.6; 2.3]	0.66

The unit of analysis is the drug.
OR [95% CI]: odds ratios and 95% confidence interval. Intra-patient correlation was taken into account.
*: when there was no specific administration guidelines, we considered the knowledge of drug name, dosage and indication only.

This study has several limitations. It is a single-centre study targeted to a specific sample of immunocompromised patients. This may limit the generalisation of our results. Moreover, the comparison between HIV infected patients and transplant recipients would be interesting, but the primary objective was to assess the knowledge of immunocompromised patients in general because this specific population has heavy pill burdens for a long time. If a comparison between the two populations was analysed, the found results could be criticised because of the population sizes (38 HIV patients versus 17 transplant recipients). Our study showed that, when regarding all confounded drugs and specifically regarding treatment of chronic disease, the knowledge of the HIV infected patients did not significantly differ from the knowledge of transplant recipients. Concerning drug administration guidelines, we made reference to the Vidal compendium. Consequently, our interpretation criteria could be too restrictive compared to clinical practice. The strict administration guidelines, which are described in the Summary Product Characteristic of products, are difficult to respect for the patient considering daily life. In clinical practice, doctors prefer to favour adherence rather than administration guidelines. Another limitation should be the fact that in practice even if the patient does not know the exact name of the drug, he is able to describe it. In this study, we considered that to know the exact name of the drug was relevant to assess the patient knowledge because it is part of an active participation of the patient regarding his disease. Although the number of taken drugs is high in immunocompromised patients, the study showed that it was not an influencing factor. We considered in this study that even if the patient forgot the exact name but was able to describe the drug, this could not impact the other items. The results proved this because the most known item was the dosage of the drug.

Despite the limits of our methodology, our proposed self-reported questionnaire could be useful to assess the effectiveness of interventions aimed at increasing patient knowledge via education programs, for instance. The actual involvement of all medical and paramedical staff, during patients' stays and on discharge, can be improved. Numerous studies have demonstrated that written and oral information improves patient knowledge [33]. A number of tools could be introduced such as a treatment card given by the medical team on discharge [15], verbal counselling or a list of instructions given on discharge by a pharmacist [34], repeated oral information during drug administration by nurses, and participation in a self-medication program [19, 21]. All activities encouraging the patient to be an active participant in their own treatment could improve therapeutic adherence and reduce potential complications. The skills of clinical pharmacists could be an additional way to strengthen the doctors' information and the nurses' counselling.

Conclusion

This study demonstrated that immunocompromised patients' drugs were very well known but that adjuvant treatments were less well known than the treatment of chronic disease. The least known component was the administration guidelines, compared to name, dosage and indication. Age, low educational level, duration of the chronic disease and modifications of the treatment during the hospitalisation stay influenced knowledge, whereas length of stay and the number of drugs had no impact. Even if immunocompromised patients know their treatment of chronic disease regimen better than their adjuvant treatment, the goal of the medical team is to improve patients' knowledge in order to ensure their understanding. In future, some interventions delivered by clinical pharmacists could encourage patients to be active participants in their own treatment and could improve therapeutic adherence.

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Correspondence: *Virginie Korb-Savoldelli, Pharmacy Department, AP-HP Georges Pompidou European Hospital, 20, rue Leblanc, F-75908 Paris cedex 15, France, virginie.savoldelli@egp.aphp.fr*

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