Pharmaceutical care and evaluation of adherence to antiretroviral therapy in people living with HIV/AIDS

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Highly Active Antiretroviral therapy (HAART) depends on optimal adherence to be effective. Pharmacotherapeutic follow-up can be used as a strategy for treatment fidelity. To provide pharmaceutical care for HAART patients, to assess adherence, to identify and resolve drug related problems (DRP). This is a prospective, interventional study aimed at people on HAART. Data was collected using the pharmacotherapeutic follow-up form and *CEAT-VIH*. There was a predominance of women (59.1%), older than 33 years (75%), mostly single (43,2%). Regarding adherence, (63.6%) had insufficient adherence at the start of the study, while (36.4%) had strict/adequate adherence. After the pharmacotherapeutic follow-up, (70,4%) presented strict/adequate adherence. Regarding HAART, the relationship between adherence versus time of HAART and adherence versus regimen used was significant, considering that less time of therapy and regimen containing protease inhibitors are predictors for insufficient adherence. Regarding the DRP identified (f=77), missed pills (32.4%), untreated disease, incorrect management frequency, and undue self-medication (11.7%) were the most frequent. Pharmaceutical interventions (f=137) were predominantly advising related to specific pharmacological treatment (32.1%), non-pharmacological measures (19.7%), and medication suspension (8.7%). Pharmaceutical care was shown to be animportant strategy, within the multi professional team, to improve adherence, besides identifying and resolving DRP.

Keywords: HIV infections. Anti-retroviral agents. Medication adherence. Pharmaceutical services.

INTRODUCTION

Human immunodeficiency virus (HIV) infection is a global health problem and a great challenge to be faced. Several studies have been conducted in different regions of the world to study the diagnosis, treatment and prevention of HIV/AIDS (Vieira *et al.*, 2014).

Highly Active Antiretroviral Therapy (HAART) is a great ally in combating morbidity, improving the quality of life and life expectancy of people living with HIV/AIDS.

In 2015, about 455,000 people used these drugs to treat HIV infection (Brasil, 2016).

From 2017 onwards, the first choice of treatment for the HIV infection, the drug Dolutegravir, associated with the combination "2 in 1" Tenofovir + Lamivudine was introduced. This association shows greater effectiveness, greater resistance against mutations and fewer adverse effects, improving adherence to treatment (Brasil, 2017), helping to reduce morbidity and mortality rates (Paraná, 2015). However, it is a challenge to keep adequate adherence indefinitely. The difficulties presented in adherence to treatment are not limited to a characteristic of each person, according to research data, sociodemographic characteristics are poor predictors of adherence (Dunbar-Jacob, Mortimer-Stephens, 2001), but it is related to a complex relationship of factors and determinants, for example, disease, treatment, relationship between health

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professional and patient, characterizing treatment adherence as a complex and multidetermined behavior (Remor, 2018). Its improvement may require modification in lifestyle, and follow-up by health professionals, among them, the pharmacist (Simoni *et al.*, 2003).

Pharmacotherapeutic follow-up has been used to monitor and improve adherence to the use of drugs for people living with HIV/AIDS, revealing a positive effect in relation to the knowledge of the disease and its control. Inserted in the multidisciplinary team, it is the role of the pharmacist to identify and prevent drug related problems (DRP), as well as to guide the patient regarding pharmacotherapy (Molino *et al.*, 2014). Pharmaceutical care comprises actions related to the health care provided by the pharmacist to the person and should be integrated with health services (Correr, Otuki, Soler, 2011).

The presence of the pharmacist, providing pharmaceutical care to patients in antiretroviral therapy, was able to significantly reduce DRP through pharmaceutical-patient interventions (Molino *et al.*, 2017). A study conducted in Peru reported that adherence to antiretroviral treatment improved significantly after pharmaceutical intervention, being able to change patients' attitudes such as not stopping taking medications, not forgetting the correct time or the frequency of their use (Tafur-Valderrama *et al.*, 2012).

In this context, this study intends to provide pharmaceutical care, identify and solve drug related problems (DRP), and compare the degree of adherence to treatment of HIV/AIDS patients in HAART before and after pharmacotherapeutic follow-up.

MATERIAL AND METHODS

Study Design and Data Collection

This is a prospective intervention study conducted with people living with HIV/AIDS in HAART during the period from December 2017 to September 2018, at the Drug Dispensing Unit (DDU) inserted in the Pharmacy of the 4th Regional Health Center of Irati-PR.

The sample for the study was selected from the population of people living with HIV/AIDS in HAART, previously enrolled, and who got the drug from the DDU, through the Logistical Drugs System (Siclom). Siclom is a program developed by the Brazilian Government Ministry of Health for the control and dispensing of antiretroviral drugs. The initial sample consisted of 48 people, who met the inclusion criteria: people living with HIV/AIDS in HAART, aged 18 years or older, who took the antiretroviral drug in the city of Irati, and who accepted to participate in the research signing the written informed consent form (WICF). The exclusion criteria were: to be under 18 years old, pregnant, to take the medication in another city, not accepting to participate in the research. The total sample at the end of the study resulted in 44 people, because 4 people were excluded from the research (one person became pregnant, and three others were transferred to other cities).

The information was collected using two instruments. The first was a Pharmacotherapeutic Follow-up Form, adapted from a form prepared by the State Health Department (SESA/PR), which contained questions about the sociodemographic characteristics of the user, diagnosed health problems (with the addition of specific information about HIV, and information on the use of prescribed and non-prescribed medication, including previous treatments) and DRP. The DRP involved the selection and prescription, administration and adherence of the patient to the treatment, dispensing error, discrepancy between levels of health care, problems in drug quality, monitoring, non-effective treatment, adverse reaction and intoxication, and was performed according to the model elaborated by the Ministry of Health (Brasil, 2014). We do not present the detailed classification for the sake of synthesis, only those that were mentioned by at least one patient were included.

Pharmaceutical interventions aimed at optimizing the outcome of treatment by the patient involved, information and counseling, provision of materials and opinion writing, monitoring, direct changes in therapy (medication not prescribed or agreed by the prescriber), and referral to the physician or other health professionals. The pharmaceutical interventions were performed according to the Ministry of Health (Brasil, 2014).

The second instrument used was the Brazilian adaptation for the "Questionnaire for the Evaluation

of Adherence to Antiretroviral Therapy" - CEAT-VIH (Remor, 2002; Remor, Milner-Moskovicsi, Preussler, 2007) authorized by the author in its online version (Remor, 2013a). The CEAT-VIH is a specific questionnaire to evaluate adherence in patients using antiretrovirals. The online version allows self-application, automatic correction, and multidimensional feedback. At the end, a score between 0 and 100 is generated for each dimension of the questionnaire, which uses cut-off points to classify the adherence as insufficient or strict / adequate. The CEAT-VIH is a validated instrument for use in several countries such as Brazil, Chile, Colombia, Mexico, Panama, Peru, Portugal, Puerto Rico, Romania, Spain and Equatorial Guinea (Salmanton-García *et al.*, 2015). According to the meta-analysis by Costa *et al.* (2018), the CEAT-VIH questionnaire is the second most used instrument to measure adherence to treatment throughout Latin American countries. The online CEAT-HIV questionnaire was applied at the beginning of the follow-up (December 2017) and reapplied at the end of the follow-up (between July and September 2018).

Another method used to assess adherence was through the registration dates of dispensed medication in Siclom. "1" was assigned to the patient appearing on the scheduled date or up to six days late, and the value "0" for patients who did not appear on the scheduled date or who delayed seven days or more. At the end of the pharmaceutical follow-up the values were added, considering as adherent (equal to 10), and with insufficient adherence (≤9). Regarding patients inserted during the follow-up who did not complete ten consultations of follow-up until the end, they were considered with insufficient adherence when having one of the values assigned as "0", and adherents, those that had all values equal to "1".

The characterization of the sample was performed by analyzing the sociodemographic (sex, age, education, income, marital status and occupation), clinical (viral load at two moments, CD4 lymphocyte count and comorbidities), and drug related variables (number of HAART pills used per day, total number of pills per day, continued use of other classes of drugs).

Participants in this study attended at least six pharmaceutical consultations. In these consultations, the pharmacist analyzed the pharmacotherapy, identified possible drug-related problems and, when necessary, performed pharmaceutical interventions in an attempt to solve them.

Statistical analysis of data

The statistical analysis was performed in the statistical environment R. The data collected were statistically analyzed, testing the normality for the difference D=(d1-d0), referring to the initial and final results for the dimensions of the CEAT-VIH questionnaire. Lilliefors, Cramer Von Misses and Anderson Darling tests were used in all cases. The Wilcoxon test was performed for cases in which there was no normality (compliance, history of lack of adherence, physician-patient communication, expectations with treatment, and satisfaction with treatment). For the case that presented normality, which was the overall adhesion index, a paired t-test was used.

The variable overall adherence to the questionnaire was categorized as satisfactory (≥86) and inadequate (<86). To evaluate the relevance of some factors in the overall adhesion index to the questionnaire, the methodology of generalized linear models was used, in particular the Binomial model with logistic link function, according to the model below was included:

ceatf ~ income + occupation + age + sex + total number of pills per day + n.comorb + HAART class + time HAART

In order to decide which factors should remain in the model to explain the variable CEAT-Post, the stepwise method was used based on the Akaike criterion and the resulting model was:

ceatf ~ income + HAART class + time HAART.

This project was approved by the Research Ethics Committee of the State University of Maringá - UEM, Process no. 5951/2018, protocol 2,419,649.

RESULTS

Sociodemographic Characteristics

The total sample of this study included 44 patients, who received pharmaceutical follow-up. Their age ranged from 21 to 73 years, with a mean of 43 years, most of them were unmarried, with wage income between 1 and 3 minimum wages, and with some source of income (Table I).

TABLE I - Sociodemographic characteristics of HAART patients

Characteristics	Category	n	%
Gender	male	18	40.9
	female	26	59.1
Age	<34 years	11	25.0
	≥34 years	33	75.0
Schooling	≤8 years	21	47.7
	>8 years	23	52.3
Income (minimum wage)	1 to 3	38	86.4
	4 to 10	6	13.6
Marital status	married	16	36.4
	single	19	43.2
	widowed/ divorced	9	20.4
Occupation	employed/retired	28	63.6
	unemployed	16	36.4

Clinical features

The results showed that there was a change in the participants' clinical parameters. At baseline, 81.8% (36) of the patients had undetectable viral load (<50 copies / ml), and after the pharmaceutical follow-up, they were 84.1% (37). Patients with viral load between 50 and 1000 copies/ml represented 9.1% at the beginning of follow-up, and at the end they were 13.6%. The proportion of patients with viral load above 1000 copies/ml at the beginning of follow-up, which represented 9.1% of the sample, decreased to 2.3% after follow-up. Considering the CD4 count, approximately 66% of the patients had a CD4 cell count above 500 cells/mm³. Regarding the morbidities, about 65% of the patients had some comorbidity, with dyslipidemia and hypertension being the most frequent (22.4% each).

Characteristics Related to Medications

Regarding the duration of HAART, there was a higher frequency of medication use for a period of less than or equal to 2 years (36.4%) and for a period of 3 to 5 years (27.3%). Regarding the therapeutic regimen used, approximately 45% of the patients used the Nucleoside Reverse Analogue Transcriptase Inhibitor (NRTI) (Lamivudine, Tenofovir, Zidovudine or Abacavir), associated with Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) (Efavirenz or Nevirapine). Another 34.1% used a Protease Inhibitor (PI) (Ritonavir, Atazanavir or Darunavir), associated with NRTI, while 22.7% used an Integrase Inhibitor (INSTI) (Raltegravir or Dolutegravir), associated with NRTI.

Considering the number of pills used per day, 43.2% of patients reported using 3 or more ARV pills, 36.4% used only one pill and 20.4% reported using 2 pills.

In addition to HAART, about 70% of patients reported concurrent use of other drugs to treat comorbidities. The most mentioned therapeutic classes were antihypertensives (21.7%), fibrates (13.3%), and statins (11.7%).

During the pharmacotherapeutic follow-up, 77 drug related problems were identified, including all medications referred by patients, not just ARV drugs. The most frequent DRP identified were omission of doses (32.4%), clinical condition without treatment (11.7%), frequency or schedule of incorrect administration (11.7%) and undue self-medication (11.7%). Considering only the ARV drugs, the main DRP remained the omission of doses, untreated clinical condition and incorrect administration frequency (Table II).

TABLE II - Drug Related Problems identified

DRP	ARV + other drugs*		ARV drugs only**	
	f*	%	f**	%
	77	100	49	100
Omission of doses by the patient	25	32.4	18	36.7
Untreated clinical condition	09	11.7	9	18.5
Incorrect frequency or schedule of administration	09	11.7	7	14.4
Undue self-medication	09	11.7	-	-
Other unspecified administration problems	06	7.8	6	12.2
Undue discontinuation of medication by the patient	05	6.5	-	-
Dose-dependent adverse reaction (Type A)	04	5.2	4	8.2
Unspecified adverse reaction	02	2.6	1	2.0
Incorret patient managment technique	02	2.6	1	2.0
Addition of doses by the patient	01	1.3	1	2.0
Incorrect continuation of medication by the patient	01	1.3	-	-
Abrupt dose reduction by patient	01	1.3	-	-
Wrong storage	01	1.3	1	2.0
Need for self-monitoring	01	1.3	-	-
Chronic exposure to the drug (Type C)	01	1.3	1	2.0

*DRP related to all the drugs mentioned by the patients (ARV + other drugs)
**DRP related only to the use to ARV
f = frequency of DRP found

Considering the use of ARV and other drugs mentioned by the patients, 137 pharmaceutical interventions were performed, 43.2% of the patients received between 3 and 4 interventions, followed by those who received up to 2 interventions (40.9%), and those who received more than 4 interventions (15.9%). The interventions that stood out were related to patient/caregiver counseling on specific treatment (32.1%) and patient/caregiver counseling on non-pharmacological measures (19.7%). It was necessary to suspend the drug in 8.7% of cases, and the pharmacist was responsible for the intervention, because it was self-medication or improper continuation of the drug. Also, 7.3% of the patients were referred to the doctor (Table III).

Among the interventions considering only the use of ARV, the main ones were patient/caregiver counseling on specific treatment (51.2%), and patient/caregiver counseling on non-pharmacological measures (29.1%), change in the frequency or schedule of administration without daily dose change (5.8%), guidance on the use of a tablet organizer or ancillary device (3.5%) (Table III). Overall, patients received guidance about the treatment, its benefits, and risks of non-adherence. The guidelines for non-pharmacological measures included the importance in maintaining healthy eating habits, exercise and leisure practices, as well as regular medical monitoring avoiding extreme emotions and stress.

TABLE III – Pharmaceutical Interventions performed[1]

Pharmaceutical Interventions	ARV + other drugs*		ARV drugs only**	
	f*	%*	f**	%**
	137	**100**	**86**	**100**
Counseling the patient/caregiver on specific treatment	44	32.1	44	51.2
Counseling the patient/caregiver on non-pharmacological measures	27	19.7	25	29.1
Medication interruption	12	8.7	0	0
Referral to physician	10	7.3	2	2.3
Diary for self-monitoring	09	6.6	0	0
Counseling the patient/caregiver on general treatment	07	5.1	0	0
Change in frequency or schedule of administration without daily dose change	07	5.1	5	5.8
Self-monitoring recommendation	04	2.9	0	0
Pill organizer or device to aid adherence	03	2.2	3	3.5
Counseling the patient/caregiver on self-monitoring	02	1.5	0	0
Counseling the patient/caregiver on drug storage	02	1.5	2	2.3
Other unspecified therapy changes	02	1.5	1	1.2
Laboratory monitoring recommendation	02	1.5	2	2.3
Drug list or schedule	02	1.5	0	0
Counseling the patient/caregiver on access to medications	01	0.7	0	0
Drug replacement	01	0.7	1	1.2
Other counseling (not specified)	01	0.7	1	1.2
Printed education material//pamphlet	01	0.7	0	0

[1]Ministério da Saúde – Cuidado Farmacêutico na Atenção Básica – caderno 2 (2014) (Health Ministry – Basic Care Pharmaceutical Assistance).*Interventions related to all the drugs (ARV + other drugs).**Interventions related only to the use of ARV drugs. f = frequency of interventions

Adherence to Antiretroviral Therapy

The patients'adherence to HAART was classified according to CEAT-VIH. Before the pharmaceutical follow-up, the majority of patients (63.6%) had insufficient adherence, and 36.4% had strict / adequate adherence. After follow-up, an inversion of these values was observed, and the frequency of patients with strict / adequate adherence was 70.4%, while 29.6% presented insufficient adherence (Table IV).

TABLE IV - Adherence to Antiretroviral Therapy according to CEAT-VIH result before and after pharmacotherapeutic follow-up

CEAT-VIH online score	Adherence	Before pharmacotherapeutic follow-up			After pharmacotherapeutic follow-up
		N*	%	N**	%
		44	100	44	100
Less than or equal to 85	inadequatte/insufficient	28	63.6	13	29.6
≥86	strict/adequate	16	36.4	31	70.4

* number of patients before pharmacotherapeutic follow-up. ** number of patients after pharmacotherapeutic follow-up

Regarding the dimensions evaluated in the CEAT-VIH questionnaire, a comparison was made between the means of the patients before and after the follow-up. At a significance level of 5%, the results for the compliance dimensions were statistically significant, antecedents of non-adherence behavior, doctor-patient communication, personal beliefs/expectancies about the treatment, and global adherence index, revealed improvement in adherence after pharmacotherapeutic follow-up (Table V).

TABLE V - Comparison of means of CEAT-VIH parameters according to adherence before and after pharmaceutical monitoring

Dimension	Before	After	*p value*
Compliance	87.9	93.4	**0.000271**
Antecedents of non-adherence behavior	92.7	87.9	**0.01242**
Doctor-patient communication	82.2	87.9	**0.000488**
Personal beliefs/expectancies about the treatment	76.4	80.9	**0.0007685**
Treatment satisfaction	82.0	85.4	0.06701
Global adherence index	83.9	88.2	**7.235 e-0.9 (0.000000007235)**

Regarding adherence based on the dates of dispensation in Siclom and attendance to the pharmaceutical consultations, 61.4% of the patients presented adequate adherence, and 38.6% presented insufficient adherence.

Variables associated with adherence

A possible relationship between adherence to treatment and sociodemographic, clinical and drug use characteristics was evaluated. Among patients with adequate adherence, it was found that more than half (51.6%) used an antiretroviral regimen containing NRTIs associated with NNRTI, and 41.9% used only one HAART pill per day. Another finding was that the majority of patients with adequate adherence (54.8%) had more than 8 years of schooling. Of the patients with insufficient adherence, 46.1% were under treatment for up to 2 years, most of them (53.8%) were using antiretroviral regimen containing IP associated with NRTI, and used 3 or more HAART pills per day (61.5%) (Table VI).

TABLE VI - Patient-related characteristics, according to CEAT-HIV adherence

Variable	Insufficient adherence*		Strict adherence*		Total	
	n	%	n	%	n	%
Other classes of drugs used	**13**	**29.6**	**31**	**70.4**	**44**	**100**
Time of HAART in years						
Up to 2	6	46.1	10	32.3	16	36.4
3 - 5	4	30.8	8	25.8	12	27.3
6 - 9	3	23.1	5	16.1	8	18.2
More than 10	0	0	8	25.8	8	18.1
HAART regimen						
NNRTI + NRTI	3	23.1	16	51.6	19	43.2
PI + NRTI	7	53.8	8	25.8	15	34.1
INSTI + NRTI	3	23.1	7	22.6	10	22.7
Schooling						
≤ 8 years	7	53.8	14	45.2	21	47.7
> 8 years	6	46.2	17	54.8	23	52.3
Number of HAART pills per day						
1	3	23.1	13	41.9	16	36.4
2	2	15.4	7	22.6	9	20.4
3 or more	8	61.5	11	35.5	19	43.2
Total number of pills per day (HAART+comorbidities)						
Up to 2	4	30.8	13	41.9	17	38.6
3 - 4	2	15.3	7	22.6	9	20.5
5 - 6	4	30.8	5	16.1	9	20.5
More than 6	3	23.1	6	19.4	9	20.5
Other classes of drugs used						

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TABLE VI - Patient-related characteristics, according to CEAT-HIV adherence

Variable	Insufficient adherence*		Strict adherence*		Total	
	n	**%**	**n**	**%**	**n**	**%**
Other classes of drugs used	**13**	**29.6**	**31**	**70.4**	**44**	**100**
statin	1	5.6	6	14.3	7	11.7
fibrate	2	11.1	6	14.3	8	13.3
antidepressants	1	5.6	4	9.5	5	8.3
Antihypertensive/ beta-blocker/ diuretic	4	22.2	9	21.4	13	21.7
Oral antidiabetic	1	5.6	3	7.1	4	6.7
antimicrobial	1	5.6	1	2.4	2	3.3
anti-inflammatory	2	11.1	2	4.8	4	6.7
Protons bomb inhibitor	3	16.7	3	7.1	6	10.0
Thyroid hormone	0	0	1	2.4	1	1.7
Hormonal contraceptive	0	0	2	4.8	2	3.3
benzodiazepines	0	0	3	7.1	3	5.0
bisphosphonate	0	0	1	2.4	1	1.7
analgesic	3	16.7	1	2.4	4	6.7
Number of DRP (HAART + comorbidities)						
0	0	0	3	9.7	3	6.8
1	4	30.8	12	38.6	16	36.4
2	7	53.8	10	32.3	17	38.6
3	2	15.4	3	9.7	5	11.4
4	0	0	3	9.7	3	6.8
Number of pharmaceutical interventions (HAART +comorbidities)						
Up to 2	5	38.5	13	41.9	18	40.9
3 - 4	6	46.1	13	41.9	19	43.2
More than 4	2	15.4	5	16.2	7	15.9

* Adherence reference at the end of the pharmaceutical follow-up

Statistically analyzing the variables collected and the result of the CEAT-VIH applied at the end of the follow-up, it was observed that, at a significance level of 5%, the variables related to the class of HAART used (PI + NRTI) and the HAART time were statistically significant (p <0.05) (Table VII).

TABLE VII - Relationship between variables and adherence according to final CEAT-VIH

Coefficients	Estimate	Standard error	z	Pr(>|z|)
(Intercept)	-0.34026	0.82682	-0.412	0.6807
Income				
4 to 6	-3.72771	2.71377	-1.374	0.1696
7 to 10	-3.26616	1.95610	-1.670	0.0950
HAART regimen				
PI + NRTI	-6.09097	2.37115	-2.569	**0.0102 ***
NNRTI + NRTI	0.09591	1.33008	0.072	0.9425
HAART time (years)	0.87763	0.36049	2.435	**0.0149 ***

* statistically significant (p<0,05)

DISCUSSION

When discussing the results of the study, it seems important to consider its limitations, for example, the use of questionnaires to assess adherence and drug-related problems, thus depending on the sincerity of the participants at the moment of self-referral and social desirability effects. Therefore, the result of the information collected may not represent the actual situation experienced by the study participant. However, it should be remembered that the literature has systematically shown the usefulness and accuracy of self-report measures in the prediction of biomedical measures (Weldring, Smith, 2013), so they are valid and widely used measures. The second important limitation of the study is the reduced sample size and the selection of the participants for convenience, which may limit the generalization capacity of the data collected by the research. Participants who have not benefited from the pharmaceutical intervention may have been less likely to access the study or have been less willing to accept the invitation to participate.

Although such limitations are considered, the present study also contains a series of strengths, for example, this study complements and expands knowledge about the relationship between pharmaceutical intervention and adherence to pharmacological treatment, showing that the pharmaceutical intervention, including information about the drug, treatment, measures to improve the lifestyle and feeding, correction of schedule of administration, suspension of undue use, among others, brings benefits related to improved adherence. Health education has proven to be effective in increasing the rate of adherence to HAART. Also, the monthly or bi-monthly follow-up strengthens the patients' bond with the service and with the health professionals, generating greater confidence and may also reflect a greater commitment to treatment. Patients who are physically or emotionally debilitated, with little information about medications, feel less able to comply with the treatment (Remor, 2013b).

In the sample studied, there was a higher frequency of infected women (59.1%) than men. As women historically seek health care more than men, this fact may have been responsible for female prevalence in research. A study conducted in 2015 in West Africa (Salmanton-Garcia et al., 2015) showed that the frequency of infected women (64.5%) was similar to that found in this study. Age, mean age (Silva et al., 2017; Foresto et al., 2017), schooling and income were similarly reported by other authors (Foresto et al., 2017). On the other hand, there are studies that showed a higher frequency of low-education patients (Moraes et al., 2015), and no source of income (Lemos et al., 2016), showing that HIV infection may be present at different social levels.

In this study, most patients maintained a desirable viral suppression level from the beginning to the end of the follow-up (81.8% and 84.1%, respectively). In the treatment of HIV, one of the goals is to maintain the viral suppression. The maintenance of viral load at undetectable levels also acts interrupting the transmission chain, greatly reducing the risk of transmission between people (UNAIDS, 2016; Seidl *et al*., 2007).

In relation to the DRP found, higher frequency was observed to be related to adherence problems (omission of doses), both for the use of any drugs referred by the patient and for the exclusive use of ARV drugs. Similar results were found in a study conducted in Peru (Tafur-Valderrama *et al*., 2012) and another in the State of São Paulo, Brazil (Hernandez *et al*., 2016). The intervention of the pharmacist during the consultation, identifying and correcting DRP, is of great importance to avoid worsening the clinical condition of the patient, reflecting in an improvement in the general condition (Remor, 2013c).

The results of the interventions demonstrated that the patients lack information about the clinical conditions that affect them and the treatments they undergo, and it is important to encourage a change of behavior, besides adopting actions aimed at the rational use of medications. A similar result was presented in a study that reports the relationship between pharmaceutical intervention and improved adherence to treatment (Tafur-Valderrama *et al*., 2012).

A systematic review (Saberi *et al*., 2012) showed that the presence of the pharmacist in the healthcare team who performed the clinical care of the HIV/AIDS patients was related to improvement in adherence and maintenance of the level of viral suppression for longer periods of time.

Relating the variables studied with adherence, higher schooling was seen to favor better adherence, a result that was also observed in other studies (Seidl *et al*., 2007; Resende *et al*., 2012). There was a statistically significant ($p < 0.05$) relationship between adherence and treatment time, and adherence and the antiretroviral regimen used. Shorter HAART time and the use of schedules containing Inhibitors of Protease (PI) predisposes to insufficient adherence. A similar result was observed in another study in Brazil (Foresto *et al*., 2017). This fact can be justified by the fact that PI composed more complex regimens,

using at least three ARV pills per day, making it difficult to insert daily pills into the patients' routine. In a study performed in Portugal (Reis, Guerra, Lencastre, 2013), it was also shown that complex regimens, with higher number of pills per day, constitute a barrier to adherence. This result was also verified in a study performed in Brazil (Cancian *et al*., 2015), reporting that regimens composed of NRTI + NNRTI have a simpler dosage profile, a more favorable toxicity profile, facilitating adherence and viral suppression for longer. Another study performed in Peru (Tello-Velásquez *et al*., 2015) showed that 83% of the patients who used a PI + NRTI regimen had inadequate adherence.

The scores obtained when evaluating adherence using the CEAT-VIH, showed that pharmaceutical care brings considerable improvement in adherence to treatment. A study conducted in Brazil (Foresto *et al*., 2017), which also used CEAT-VIH to evaluate adherence, showed that 75% of the patients had good adherence to antiretroviral treatment. However, there are also studies showing prevalence of non-adherence (Silva *et al*, 2017; Zuge *et al*., 2017).

According to the meta-analysis presented by Costa *et al*. (2018), the CEAT-VIH questionnaire is the second most widely used instrument for measuring adherence to treatment in Latin American countries.

The present study demonstrated statistical significance ($p < 0.05$) in the improvement of adherence evaluated before and after the pharmaceutical follow-up to HIV/AIDS patients, proving the importance of the pharmaceutical professional in the public service as an aid to maintain adherence, providing pharmaceutical care, in the development of health education actions, in the identification and resolution of DRP, and in referral to other health professionals. The simple dispensing of the drug, without effective follow-up by the pharmacist, is not able to identify factors indicative of worsening adherence, resulting in patients with a greater chance of treatment failure, favorable to opportunistic diseases and candidates to use more complex more expensive HAART regimens.

Adherence evaluated based on the dates of attendance at the service for ARV withdrawal showed 62% adequate adherence. We noticed that the value

was not very different from that found in the CEAT-VIH result, which was 70% of adequate adherence. Although the two methods are different, they can be used as complementary.

Many studies have been performed to quantify the adherence of patients in HAART use or the reasons for non-adherence (Salmanton-Garcia *et al.*, 2015; Foresto *et al.*, 2017; Moraes *et al.*, 2015; Padilla, 2016). These are studies of great relevance, which help in the discoveries for the evolution of the treatment. On the other hand, patients who have adequate adherence should also be taken into consideration in order to maintain adherence over the years. This is one of the great challenges of the multiprofessional team seeking reduction of HIV transmission.

We conclude that this study on people living with HIV/AIDS in antiretroviral therapy, presented information that complements previous studies. Pharmaceutical follow-up proved to be effective in improving adherence, showing that the inclusion of the pharmacist in the multiprofessional team, acting in a clinical manner, tended to improve adherence, in addition to acting in the identification and resolution of DRP. The use of a protease inhibitor (PI) class in the HAART, as well as a treatment time of up to two years, proved to be a predictor of insufficient adherence.

Pharmaceutical care proved to be effective in all stages, with emphasis on improved adherence and maintenance of viral suppression by patients on HAART, and was also important to recover of patients with insufficient adherence in the identification and resolution of DRP.

REFERENCES

Brasil. Boletim Epidemiológico – HIV/AIDS. Ministério da Saúde. Brasília; 2016.

Brasil. Capacitação para implantação dos serviços de clínica farmacêutica/Ministério da Saúde, Secretaria de Ciência, Tecnologia e Insumos Estratégicos. Departamento de Assistência Farmacêutica e Insumos Estratégicos. Ministério da Saúde. Brasília; 2014. 308 p.: il.(Cuidado farmacêutico na atenção básica; caderno 2).

Brasil. Nota Informativa 007/2017 – DDAHV/SVS/MS. Ministério da Saúde. Brasília; 2017. Disponível em: http://azt.aids.gov.br/documentos/siclom_operacional/Nota%20Informativa%20007%20-%20protocolo%20de%20uso%20ARV%20-%202017.pdf. Acesso em 09/08/2018.

Cancian NR, Beck ST, Santos GS, Bandeira D. Importância da Atenção Multidisciplinar para resgatar o paciente com HIV/AIDS apresentando baixa adesão ao tratamento Antirretroviral. Rev Atenção Saúde. 2015;13(45):55-60.

Correr CJ, Otuki MF, Soler O. Assistência farmacêutica integrada ao processo de cuidado em saúde: gestão clínica do medicamento. Rev Pan-Amaz Saude. 2011;2(3):41-49.

Costa J D M, Torres T S, Coelho L E, Luz P M. Adherence to antiretroviral therapy for HIV/AIDS in Latin America and the Caribbean: Systematic review and meta-analysis. J Int AIDS Soc. 2018;21(1):01-20.

Dunbar-Jacob J, Mortimer-Stephens MK. Treatment adherence in chronic disease. J Clin Epidemiol. 2001;54(Suppl. 1):57-60.

Foresto JS, Melo ES, Costa CRB, Antonini M, Gir E, Reis RK. Adesão à terapêutica antirretroviral de pessoas vivendo com HIV/Aids em um município do interior paulista. Rev Gaúcha Enferm Porto Alegre. 2017;38(1):e63158.

Hernandez CD, Lucchwetta RC, Nadai TR, Galduróz JCF, Mastroianni PC. Self-perception of knowledge and adherence reflecting the effectiveness of antiretroviral therapy. Patient Prefer Adher. 2016;10:1787–1793.

Lemos LA, Fiuza MLT, Reis RK, Ferrer AC, Gir E, Galvão MTG. Adherence to antiretrovirals in people coinfected with the human immunodeficiency virus and tuberculosis. Rev Latino-Am Enfermagem. 2016;24:e2691.

Molino CGRC, Carnevale RC, Rodrigues AT, Visacri MB, Moriel P, Mazzola PG. Impact of pharmacist interventions on drug related problems and laboratory markers in outpacients whit human imunodeficiency virus infection. Ther Clin Risk Manage. 2014;10:631-639.

Molino CGRC, Carnevale RC, Rodrigues AT, Moriel P, Mazzola PG. HIV pharmaceutical care in primary healthcare: Improvement in CD4 count and reduction in drug-related problems. Saudi Pharm J. 2017;25(5):724-733.

Moraes DCA, Oliveira RC, Motta MCS, Ferreira OLC, Andrade MS. Terapia antirretroviral: a associação entre o conhecimento e a adesão. Rev Fund Care Online. 2015;7(4):3563-3573. DOI: 10.9789/2175-5361.2015.v7i4.3563-3573.

Padilla HLE. Adherencia al tratamiento antirretrovial en los pacientes de la consulta de VIH del Iahula y su posible relación sobre el comportamiento de la epidemia del VIH/SIDA em el Edo. Mérida durante el quinquenio 2011-2015. 76f [Tese]. Curso de Postgrado de Medicina Interna, Universidad de Los Andes, Faculdad de Medicina. Mérida, Venezuela. p.54-59; 2016.

Paraná. Boletim Epidemiológico – HIV/AIDS. Secretaria de Estado da Saúde. Paraná; 2015. Disponível em <http://www.saude.pr.gov.br/arquivos/File/boletimhivaids2015__1.pdf>. Acesso em: 06 nov 2018.

Reis A, Guerra MP, Lencastre L. Treatment Adherence, Quality of Life and Clinical Variables in HIV/AIDS Infection. World J AIDS. 2013; 3(3):239-250.

Remor E, Milner-Moskovicsi J, Preussler G. Adaptação Brasileira do "Cuestionario para la Evaluación de la Adhesión al Tratamiento Antirretroviral". Rev Saúde Pública. São Paulo. 2007;41(5):685-694.

Remor E. Self-reported adherence to antiretroviral therapy in HIV+ Colombian population. Sage open [Internet]. 2013b;3(3):1-7. Available from: < https://doi.org/10.1177/2158244013497727>. Access on 25 jul 2018.

Remor E. Systematic Review of the Psychometric Properties of the Questionnaire to Evaluate the Adherence to HIV Therapy (*CEAT-VIH*). Patient. 2013a;6(2):61–73.

Remor E. Valoración de la adhesión al tratamiento antirretroviral en pacientes VIH+. Psicothema. 2002;14(3):262-267.

Remor, E. Release of an Online Self-Reporting Tool for Assessing Adherence to Antiretroviral Therapy (CEAT-VIH). J Antivirals Antiretrovirals. 2013c;5:178-179.

Remor, E. Adesão ao Tratamento Médico. In: Elisa Kern de Castro; Eduardo Remor. (Org.). Bases Teóricas da Psicologia da Saúde. 1ed.Curitiba: Editora Appris; 2018, p. 199-214.

Resende RC, Podesta MHMC, Souza WA, Barroso TO, Vilas Boas OMGC, Ferreira EB. Adesão ao tratamento antirretroviral de pacientes vivendo com HIV/AIDS atendidos pelo Sistema Único de Saúde. Rev Univ Vale do Rio Verde. 2012;10(2):186-201.

Saberi P, Dong BJ, Johnson MO, Greenblatt RM, Cocohoba JM. The impact of HIV clinical pharmacists on HIV treatment outcomes: a systematic review. Patient Prefer Adherence. 2012;6:297-322.

Salmanton-Garcia J, Herrador Z, Ruiz-Seco P, Nzang-Esono J, Bendomo V, Bashmakovic E, et al. Self-reported adherence to antiretroviral therapy in HIV+ population from Bata, Equatorial Guinea. AIDS Care. 2015;28(5):543-553.

Seidl EMF, Melchíades A, Farias V, Brito A. Pessoas vivendo com HIV/AIDS: variáveis associadas à adesão ao tratamento antirretroviral. Cad Saúde Pública Rio de Janeiro. 2007;23(10):2305-2316.

Silva RAR, Nelson ARC, Duarte FHS, Prado NCC, Rodrigo JRR. Avaliação da adesão à terapia antirretroviral em pacientes com Aids. Rev Fund Care Online. 2017;9(1):15-20. DOI: http://dx.doi.org/10.9789/2175-5361.2017.v9i1.15-20.

Simoni JM, Frick PA, Pantalone DW, Turner BJ. Antiretroviral adherence interventions: a review of current literature and ongoing studies. International Aids Society-USA, Topics in HIV Medicine. 2003;11(6):185-198. Available from:https://www.iasusa.org/wp-content/uploads/2003/11/11-6-185.pdf>. Access on 17 nov 2018.

Tafur Valderrama EJ, Ortiz Alfaro C, García-Giménez E, Faus Dader MJ, Martínez Martínez F. Impacto de la intervención farmacéutica en la adherencia al tratamiento antirretroviral en pacientes de un hospital de Lima (Perú). Pharm Care España. 2012;14(4): 146.

Tello-Velásquez JR, Díaz-Lianes BE, Mezones-Holguín E, Rodrígues-Morales AJ, Huamaní C, Hernández AV, et al. La mala calidad de sueño se asocia a una menor adherencia al tratamiento antirretroviral de gran actividad en pacientes peruanos con infección por VIH/SIDA. Cad Saúde Pública Rio de Janeiro. 2015;31(5):989-1002.

UNAIDS. Report on Viral suppression is an important tool in HIV. Switzerland: Unaids; 2016. Available from: https://unaids.org.br/2016/12/testando-supressao-viral/. Access on 15 nov 2018.

Vieira ACS, Rocha MSG, Head JF, Casimiro IMAPC. A epidemia de HIV/Aids e a ação do Estado. Diferenças entre Brasil, África do Sul e Moçambique. Rev Katál. 2014;17(2):196-206.

Weldring T, Smith SM. Patient-reported outcomes (PROs) and patient-reported outcome measures (PROMs). Health Serv Insights. 2013;6:61-68.

Zuge SS, Primeira MR, Remor E, Magnago TSBS, Paula CC, Padoin SMM. Fatores associados a adesão ao tratamento antirretroviral em adultos infectados pelo HIV: estudo transversal. Rev Enferm UFSM. 2017;7(4):577-589.