Official journal of the Spanish Society of Chemotherapy

Original

Revista Española de Quimioterapia
doi:10.37201/req/021.2023

Elena Sánchez-Yáñez[1]
María José Huertas-Fernández[2]
María de las Aguas Robustillo-Cortes[3]
Rosa Ramos-Guerrero[2]
Sergio Fernández-Espínola[4]
Rocío Diaz-Acedo[3]
Violeta Montero-Martin[1]
Ramón Morillo-Verdugo[3]

Application of CMO (capacity, motivation, and opportunity) methodology in pharmaceutical care to optimize the pharmacotherapy in older people living with HIV. DISPIMDINAC project

[1]Virgen de la Victoria University Hospital (Pharmacy Department). Málaga, Spain.
[2]Puerta del Mar University Hospital (Pharmacy Department). Cádiz, Spain
[3]Valme University Hospital (Pharmacy Department). Seville, Spain.
[4]Antequera Hospital (Pharmacy Department). Antequera, Málaga

Article history
Received: 20 February 2023; Revision Requested: 21 April 2023; Revision Received: 28 April 2023; Accepted: 14 June 2023; Published: 19 September 2023

ABSTRACT

Objective. To determine the effectiveness of a pharmaceutical intervention, based on the CMO methodology (capacity, motivation and opportunity), to decrease the prevalence of the PIMDINAC concept (potentially inappropriate medication+drug interactions+non-adherence to concomitant medication) in people living with HIV infection.

Material and methods. Longitudinal prospective multicenter study, conducted between October 2021 and October 2022. Patients living with HIV older than 65 years, on antiretroviral treatment and concomitant drug prescription were included. Demographic, clinical, and pharmacotherapeutic variables were collected. Pharmaceutical care was provided for 6 months according to the CMO model in each patient. The main variable was the percentage of patients who simultaneously fulfilled the PIMDINAC concept, comparing the baseline value with the same value at the end of the study. In addition, the percentage of patient's adherent to concomitant and antiretroviral treatment and the percentage of patients meeting the pharmacotherapeutic targets established for the prescribed medication at 24 weeks of follow-up were compared.

Results. Sixty-eight patients were included. Seventy-two percent were men, with a median age of 68 years. The median number of concomitant drugs was 7. A 60.6% of the patients had polypharmacy. The prevalence of the presence of the PIMDINAC concept decreased significantly (10.3 vs. 0%). In isolation, each of the aspects also decreased significantly (p<0.031). The percentage of patients who met the objectives improved significantly from 48,5 at baseline to 88.2 (p<0.001).

Conclusions. The pharmaceutical intervention based on the CMO methodology significantly decreased the prevalence of the PIMDINAC concept and increased the number of patients who achieved the objectives, optimising their pharmacotherapy.

Keywords: Pharmaceutical Care; HIV/AIDS; medication adherence; patient satisfaction; outcome assessment.

Correspondence:
María de las Aguas Robustillo Cortes.
Valme University Hospital (Pharmacy Department).
Av/ Bellavista s/n, Seville, 41014, Spain.
Tel: +34955015467 FAX: 34955015461
E-mail: aguasrobustillo@gmail.com

Intervención farmacéutica basada en la metodología CMO para optimizar la farmacoterapia en pacientes VIH mayores. Proyecto DISPIMDINAC

Objetivo. Determinar la efectividad de una intervención farmacéutica, basada en la metodología CMO (Capacidad, Motivación y oportunidad) para disminuir la prevalencia de criterios PIMDINAC (medicación potencialmente inapropiada-interacciones farmacológica-no adherencia a la medicación concomitante) en pacientes VIH+.

Material y métodos**.** Estudio multicéntrico prospectivo longitudinal, realizado entre octubre-2021 y octubre-2022. Se incluyeron pacientes VIH+ ≥65 años, en tratamiento antirretroviral activo y medicación concomitante prescrita. Se recogieron variables demográficas, clínicas y farmacoterapéuticas. La intervención de atención farmacéutica se realizó durante los 6 meses de seguimiento a través de la metodología CMO. La variable principal fue la diferencia en el porcentaje de pacientes que presentaban los tres criterios PIMDINAC de forma simultánea al inicio-fin del estudio. Se analizó la variación del porcentaje de pacientes adherentes tanto al TAR y a la medicación concomitante, así como el porcentaje de pacientes que alcanzaron sus objetivos farmacoterapéuticos previamente definidos a los 6 meses de seguimiento.

Resultados. Se incluyeron 67 pacientes, 72.0% varones con una mediana de edad de 68 años. El 60.6% de los pacientes tenían polifarmacia de forma basal con una mediana de fármacos de 7.0. La presencia de criterios PIMDINAC disminuyó sig-

nificativamente de un 10.3 a 0%. De forma individual se redujo el porcentaje de cada criterio de forma significativa (p=0.031). Se incrementó el porcentaje de pacientes que alcanzaron sus objetivos farmacoterapéuticos (48,5% vs 88,2%; p<0.001).

Conclusiones. La estrategia basada en la metodología CMO disminuye significativamente la prevalencia de los criterios PIMDINAC, así como incrementa la consecución de los objetivos farmacoterapéuticos de los pacientes, optimizando su farmacoterapia.

Palabras clave: Atención farmacéutica; VIH/SIDA; adherencia a la medicación; satisfacción del paciente; evaluación de resultados.

INTRODUCTION

HIV infection is now considered a chronic disease due to the extraordinary decrease in mortality after the introduction of antiretroviral treatment (ART) and the subsequent arrival of new, more potent drugs with better dosages and with better dose regimens [1]. Increased survival has been accompanied by parallel ageing of people living with HIV (PLWH). In fact, as of 2030, more than 70% of HIV-infected patient cohorts in both the United States and Europe have a median age of more than 50 years, an aspect that will become more marked in the next decade [2].

At the same time, the older HIV population, considered older than 65 years of age, has also increased in the last decade [3].

The complexity of the approach to the PLWH is increasing. It is well known that aging in this population is more accelerated than in the non-HIV-infected population, which has brought with it the presence of a greater number of associated comorbidities and their necessary management, increasing the prescription of concomitant drugs reaching, according to the latest available data, the presence of polypharmacy is around 30-40% [4,5].

Some authors have highlighted the consequences of this polypharmacy, such as a greater number of interactions, even higher than in the general population, an increased presence of adverse effects and hospitalizations, and a high risk of falls and/or fractures [6,7].

The difficulty in the management of prescription associated with ART in this patient and the possible presence of potentially inappropriate drugs (PIM), is also higher than in the non-HIV population, particularly the prescription of anticholinergic drugs [8,9].

Some authors even mention that there may be an additional decrease in adherence to ART due to the presence of polypharmacy [8,9].

Guaraldi et al. [10] defined the so-called "iatrogenic triad" which includes, in older PLWHIV, the presence of polypharmacy, the prescription of medications that may be PIM for this population, and the possibility of relevant drug interactions (DI) between these drugs.

To carry out this qualitative and multidimensional management of polypharmacy in PLWH, PIMDINAC criteria have been developed. These criteria include interactions, potentially inappropriate drugs, and lack of adherence [11].

On the other hand, the new definition of pharmaceutical care (PC) [12] advocates a change of care orientation based on the direct relationship with the patient and the achievement and achievement of objectives in relation to pharmacotherapy, based on multidisciplinary and multidimensional work. This methodology of PC is called CMO, based on the three pillars that comprise it: capacity (stratification), motivation (objectives in relation to pharmacotherapy) and opportunity (new technologies) has already been developed and used in the PLWH, improving health outcomes, patient activation (knowledge, skills, beliefs, and confidence for managing health and health care), and patient experience [13-15].

The recent study carried out and published by Diaz-Acedo et al. [11] has shown that the prevalence of the PIMDINAC criteria [potentially inappropriate medication (PIM), drug interactions (DI) and non-adherence to concomitant medication (NAC)] is high in elderly PLWH, which requires a multidimensional approach to reduce their presence.

The aim of this study is to determine the usefulness of a pharmaceutical intervention based on the CMO methodology in reducing the prevalence of PIMDINAC criteria in PLWHIV who undergo pharmacotherapeutic follow-up in outpatient pharmacy clinics of participating hospitals.

MATERIAL AND METHODS

Study design and participants. PLWHIV were prospectively recruited between October 2021 and October 2022 in 4 centres across Spain. Patients were 65 years of age or more, clinically diagnosed with HIV infection, receiving ART, with concomitant medication prescribed for at least three months prior to inclusion in the study, attending PC visits in a participating hospital pharmaceutical department for ≥1 year before the beginning of the study, and eligible to sign the informed consent. Patients were excluded if they were unable to complete the study questionnaires or were included in clinical trials during the study period.

Interventions. Patients received routinely applied pharmacotherapeutic interventions in ambulatory care patients according to the CMO PC model [15,16]. It consists of an initial stratification of patients at three levels according to the risk stratified PC model in PLWHIV of the Spanish Society of Hospital Pharmacy [16]. These patients received a structured PC corresponding to the predetermined interventions for each level of care. During the face-to-face visit to the Hospital Pharmacy Service, a motivational interview was conducted for each patient. In each interview, pharmacotherapeutic objectives were established or reevaluated, in consensus with the rest of the medical team taking care of the patient at all times.

Lastly, all patients received permanent contact tools (web: www.farmaciavalmecpv.com, telephone, email, etc.) with study pharmacists to resolve any incident or doubt related to their treatment at any time during the study.

Outcomes. Baseline demographic data (age, gender), HIV infection control variables such as viral load (copies/ml) and CD4 count at the time of inclusion (cells/µL) as well as comorbidities and pharmacological therapy were recorded at the initial clinical evaluation. To describe multimorbidity patterns, we use the categorization proposed by Prados-Torres et al. [17] who classified these patterns according to the comorbidities (Cardiometabolic, geriatric-depressive, chronic obstructive pulmonary disease and thyroid-mechanic pattern).

PIMDINAC evaluation

The prevalence of PIMDINAC criteria was defined as the main variable and classified into 2 categories: total (joint presence of the PIM + DI + NAC criteria) or partial (isolated presence of some criteria).

The STOPP-START (2014) criteria were used to identify PIMs [18].

To identify DI between ART and concomitant medication, the University of Liverpool database was used and only potential contraindications and interactions were considered clinically relevant [19]. For the identification of DI between different non-antiretroviral drugs, the Lexicomp® tool was used, considering DI grade D (potential) or X (contraindications) [20].

Adherence to ART and concomitant medication were measured with the simplified medication adherence questionnaire (SMAQ) and the Morisky-Green questionnaire, respectively. In addition, pharmacy dispensing records were also consulted. In both cases, patients were considered adherent if they obtained a positive score using the appropriate measurement instrument.

The SMAQ is a questionnaire based on the Morisky-Green questionnaire and developed in our setting that consists of six items that assess forgetfulness, routine, adverse events, and missing doses [21]. Meanwhile, the Morisky-Green questionnaire consisted of four items that evaluate forgetfulness, routine, adverse events, and, in contrast to the SMAQ, assesses the impact of feeling better and does not evaluate missing doses; we used the Spanish validated version in Spanish [22].

Adherence rate was quantified as the proportion of days covered (PDC) during the six months prior to the study according to filled e-prescriptions. We estimated the total days of supplies from the first to the last refill during the 6-month observation period divided by the total days of the treatment interval, defined as the time elapsed from the date of the first refilled prescription until the end of the observation period. A PLWH was considered adherent if the PDC was> 95% and was >95% and not positive on SMAQ (where positive means that there was a positive response to any of the qualitative questions), no more than two doses were missed over the past week, or if they had fewer than two days of total non-medication during the last three months.

To evaluate the adherence to concomitant medications, we only considered disease-modifying medications (e.g., treatment for diabetes, cardiovascular disease, etc.) but not symptomatic treatments (e.g., analgesics, medications for gastroesophageal reflux, etc.). Adherence to concomitant medication was defined as a PDC >90% and also the Morisky-Green questionnaire score was four [23].

Polypharmacy

Polypharmacy was defined as the use of six or more different drugs, including ART; major polypharmacy was restricted to the use of 11 or more different drugs [23]. To describe the patterns of polypharmacy, we use the categorization proposed by Calderón-Larrañaga *et al.* [24] who classified those patterns according to the type of disease they were intended to treat (cardiometabolic, depression-anxiety and mechanic-obesity). After categorizing a drug according to the anatomical therapeutic chemical classification system up to the first three levels, a patient was classified into a specific pattern when he received at least three drugs included in the pattern.

Health outcomes

The consequences of the CMO pharmaceutical intervention on health outcomes such as dyslipidemia, hypertension, and diabetes were established by measuring the number of patients who achieved pharmacotherapeutic targets according to their clinical characteristics, including: levels of glycosylated hemoglobin, total cholesterol, triglycerides, low-density lipoproteins, and blood pressure before and after the introduction of the PC model. For the rest of the pathologies without analytical parameters, therapeutic success was confirmed from clinical records of medical histories made by the multidisciplinary team that monitors the patient and the lack of need for new treatments prescribed in the period between two follow-up visits.

Statistical analysis. Quantitative variables were expressed as means ± standard deviations, or medians and interquartile ranges when appropriate. Qualitative variables were presented as counts. Differences in variables collected before and after the intervention were assessed using t-student or Wilcoxon tests for related groups to compare quantitative variables. To analyze the changes in dichotomous variables, McNemar's test was applied.

Data analysis was performed using the R studio program (v 1.1.456). A *p*-value of 0.05 or less was considered statistically significant.

Ethics. The study was carried out according to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use and the Declaration of Helsinki. The study protocol and any other information that required prior approval was reviewed and approved by the ethics committee of the research center *Comité de Ética de Investigación Sevilla Sur (1321-N-21).*

RESULTS

A total of 68 patients were enrolled (Figure 1). Finally, no patients were lost to follow-up. The baseline characteristics of the patients are summarized in Table 1. More than three-quarters of the patients were men (83.3%) with a mean age of

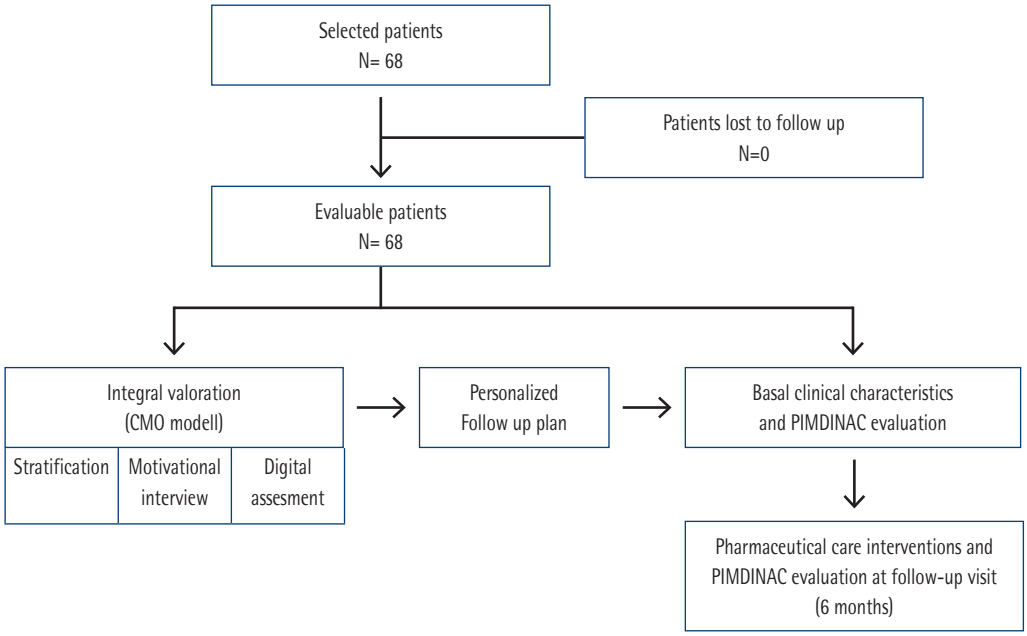

Figure 1 | **Study flow chart**

68±7 years. Most of them (59.0%) had sexually acquired HIV and responded well to the ART, with an undetectable viral load in 92.6% of patients and a CD4 count higher than 200 cells/uL in the 95.6% of them.

The most common ART regimens were those that included a combination of 'other combinations' (58.8), then two nucleoside reverse transcriptase inhibitors (NRTI) plus an integrase inhibitor (23.5%), followed by two NRTI plus a non-nucleoside reverse transcriptase inhibitor (10.4%) and, finally, two NRTI plus a protease inhibitor (2.9%). Among the treatments defined as other combinations, bitherapies such as DTG / 3TC or DRV/c+3TC and monotherapies such as DRV/c stand out.

Following indications from the CMO program, patients were stratified into three groups (Table 1). Six patients (8.8%) were at the high level, 38,2% at the intermediate level, and the remaining 36 patients (52.9%) were at level 3 (basal).

Based on these classifications and the conclusions of the motivational interview, specific pharmacist interventions were then applied to each patient. The interventions performed the most were for each pillar: Concomitant review and validation (91.2%), Review of objectives (82.4), Adherence (73.5%) and Safety (54.4%), and finally Fast Communication (32.4%) and Transversal follow-up (24.9%). Table 2 shows the interventions performed for each of the different patient visits according to the taxonomy of the methodology used.

Regarding the PIMDINAC criteria, a prevalence of 10.3% was found at the beginning of the study. At the end of follow-up, no patient met the concept globally (Table 3).

Regarding isolated criteria, significant differences ($p<0.005$) were found in the decrease in their prevalence at the end of follow-up.

Most of the patients were considered adherent to ART (92.6%). No differences were found at the end of follow-up.

Regarding concomitant medication, adherence was 55.9% at the beginning of the study. A total of 88.2% of patient's adherent to concomitant medication at follow-up at week 24 ($p<0.001$).

At baseline, 39 (57.4%) met the polypharmacy criteria and 10 (14.7%) had major polypharmacy. Among the patients evaluable for this outcome, the most frequent patterns of polypharmacy were cardiovascular and depression-anxiety (Table 1).

The mean number of drugs prescribed at baseline was 7.4 and decreased significantly at 24 weeks: 6.8 ($p<0.05$).

Significant differences were found in the percentage of patients who met the pharmacotherapeutic objectives planned by the health care team for each of the prescribed treatments at the end of follow-up: 48.5 vs 88.2 ($p< 0.001$).

DISCUSSION

Our multicenter study demonstrated that the PC CMO model, based on patient stratification, motivational interview, and the use of new technologies for the follow-up process, has a positive impact on health outcomes in PLWH, specifically with respect to drug optimization by reducing total and partial

Table 1 **Patient baseline characteristics.**

Characteristics	Total cohort (N= 68)
DEMOGRAPHIC	
Mean Age, years (SD)	68 (7)
Male gender, N (%)	57 (83.8)
HIV	
HIV acquisition, N (%)	
Sexual	36 (59.0)
Parenteral	25 (41.0)
Undetectable viral load, N (%)	63 (92.6)
CD4 count> 200 cells / u, N (%)	65 (95.6)
CD4 / CD8 ratio <1, N (%)	14 (20.5)
CLINICAL VARIABLES	
Coinfection HIV-HCV (n, %)	7 (10.3)
Geriatric-depressive comorbidities	17 (25.0)
Cardiometabolic comorbidities	53 (77.9)
Chronic Obstrucive Pulmonary Disease	7 (10.3)
Thyroid-mechanic	8 (11.8)
Charlson Index	5,5 (7)
PHARMACOTHERAPY	
ART (n, %)	
2 NRTI + 1 INI	16 (23.5)
2 NRTI + 1 NNRTI	10 (14.7)
2 NRTI + 1 boosted PI	2 (2.9)
Other combinations	40 (58.8)
STR	18 (26.5)
Polypharmacy	39 (57.4)
Major Polypharmacy	10 (14.7)
Patterns of polypharmacy	
Cardiometabolic	36 (53)
Psychogeriatric-anxiety	12 (17)
Mechanic-obesity	6 (8)
Cholinergic Burden	
High	3 (4.4)
Medium	3 (4.4)
Low	62 (91.6)
Stratification, n (%)	
Level 1 (>32)	6 (8.8)
Level 2 (18-32)	26 (38.2)
Level 3 (<18)	36 (52.9)

Table 2 Interventions carried out according to the CMO taxonomy of pharmaceutical care throughout the study.

	Basal n (%)	12 weeks n (%)	24 weeks n (%)
Capacity Interventions			
1.1 Antiretroviral treatment review and validation	50 (73.5)	45 (66.2)	46 (67.6)
1.2 Concomitant review and validation	68 (100.0)	63 (92.6)	62 (91.2)
1.3 Review of objectives	62 (91.2)	57 (83.8)	56 (82.4)
1.4 Coordination	43 (63.2)	30 (44.1)	19 (27.9)
1.5 Referral	12 (17.6)	3 (4.4)	4 (5.9)
1.6 Planning	59 (86.8)	51 (75.0)	44 (64.7)
1.7 Reconciliation	8 (11.8)	7 (10.3)	7 (10.3)
Motivational Interventions			
2.1 Safety	33 (48.5)	33 (48.5)	37 (54.4)
2.2 Special follow-up	25 (36.8)	19 (27.9)	15 (22.1)
2.3 Adherence	52 (76.5)	52 (76.5)	50 (73.5)
2.4 Motivation	35 (23.5)	35 (23.5)	18 (21.2)
2.5 Co-responsibility	25 (36.8)	23 (33.8)	20 (29.4)
2.6 Commitment	38 (55.9)	23 (33.8)	17 (25.0)
2.7 Information	38 (55.9)	27 (39.7)	29 (42.6)
2.8 Encouragement	24 (35.3)	11 (16.9)	8 (11.8)
Opportunity Interventions			
3.1 Fast Communication	31 (45.6)	20 (29.4)	22 (32.4)
3.2 Transversal follow-up	24 (35.3)	25 (36.8)	19 (27.9)
3.3 Transversal training	4 (5.9)	0 (0)	1 (1.5)
3.4 Social Coordination	1 (1.5)	1 (1.5)	3 (4.4)
3.5 Active Coordination	0 (0)	0 (0)	2 (2.9)

The taxonomy and description of the interventions are detailed in Morillo et al. [15].

Table 3 Prevalence of total and partial PIMDINAC criteria throughout the study.

Variable (n, %)	Pre-Post Analysis		Interaction p-value
	Baseline	Week 24	
PIMDINAC (total)	7 (10.3)	0	P=0.001
PIMDINAC (partial)			P<0.031
PIM	25 (36.8)	10 (14.7)	
DI	6 (8.8)	0	
NAC	27 (39.7)	7 (10.3)	
ART adherence	64 (92.6)	64 (92.6)	0.748
Adherence to concomitant treatment	38 (55.9)	60 (88.2)	0.005

ART: Antiretroviral treatment; DI: drug interactions; NAC: non-adherence to concomitant medication; PIM: potentially inappropriate medication.

prevention of the PIMDINAC criteria. Furthermore, we found that these personalized pharmacist-led interventions improved patient achievement of pharmacotherapeutic goals.

The life expectancy of PLWH has increased substantially. Consequently, older PLWH face many health challenges found in older healthy individuals, although the impact of ageing may be greater among PLWH. Previous studies have shown that personalized interventions led by pharmacists and based on the CMO model are well accepted by both patients and professionals, significantly improving health outcomes and reducing the risk of cardiovascular events [13,14]. In this study, the number of accepted interventions has not been specifically recorded, but given the high number and distribution of interventions carried out, it is reasonable to think that this line has been followed. Furthermore, the fact that the number of patients who reach their pharmacotherapeutic objectives is increasing by almost 40% reinforces this hypothesis and should also be the ultimate goal of this type of health interventions, according to the guidelines established by the different societies and entities around the world.

PIM were found in 36% of our elderly PLWH. This rate is lower than those reported in other studies [25,26]. This difference may be explained by the fact that our study could not include all the criteria that define inappropriate prescribing, for example: drugs prescribed without clinical indication; drugs administered beyond the recommended duration of treatment; drugs not adjusted to the patient's renal function or omission of prescription. Furthermore, the prevalence of drugs with an anticholinergic risk scale 3 was very low compared to the value of 17% reported by other authors [26] in PLWH, but in the line of HIV negative individuals in the same study. This could be explained by the number of drugs prescribed in our study (median 7), similar to the publication by Green et al. (median 6). Furthermore, differences in prescribing patterns between the United States and Europe could also explain this difference. However, it is a priority to develop a guide or tool of our own to establish what the real dimension of this problem is.

Our patients had a low percentage of treatments in the STR format. The use of complex associations of ARVs with comedications is expected to lead to an increased risk of DDI. Our results did not demonstrate a higher frequency of potential DDI in elderly PS compared to other published cohorts. This observation could be explained by the fact that HIV clinicians are aware of the potential for DDI of ART and therefore prescribe drugs without interaction potential, particularly in the elderly, improving the use of integrase inhibitors, with a better profile in this regard. Interestingly, the rate of potential red flag DDI was 8% at baseline and disappeared at the end of follow-up, which is very closely in line with the type of interventions most commonly performed during follow-up.

Another major concern in PLWHIV is the adherence to treatment, a variable negatively impacted by the therapeutic complexity resulting from HIV infection and comorbidities. Establishing PC in PLWH implies an increase in adherence and our results, which showed an increase in primary and secondary adherence, are in line with previous CMO-based PC, supporting the use of this model to improve patient adherence.

The prevalence of polypharmacy identified in our population is in line with studies published in our environment, which reinforces the idea that the characteristics of our population are similar to those of other cohorts from different hospitals [27,28].

Since the exponential growth of this problem is known for the coming years, this type of qualitative approaches should be implemented progressively and as a priority, according to the characteristics and resources of each center [29].

This study presents several strengths, including its prospective and multicenter nature. However, it also has some potential limitations. First, the lack of randomization with a limited sample size could be an important concern. However, we considered that there could exist participant bias when interventions resemble interventions in the putative control group, given the expansion and knowledge of the CMO PC model by many national hospital pharmacists and taking into account the results obtained in previous studies. For this reason, we considered that the best design to consider the influence of our pharmaceutical intervention was to use a pre-post design, so that each patient served as his or her own control. Furthermore, the study follow-up period can be considered relatively short within the life of a PLWH receiving chronic treatment. However, methodologically, it is robust enough to determine the impact of a structured health intervention. In this study, the 2017 stratification tool was used. In this sense, the distribution of patients by typology is within the percentages usually expressed (60-30-10 approximately). Although the tool has repeatedly reported advantages for PLWH, it is an instrument that is considered, at times, too complex. Therefore, a simplified adaptation was recently implemented [30]. This new tool has not yet been tested in the research setting, but given its simplicity, it should be easy to apply and reap greater benefits for practitioners, as it will allow further tailoring of interventions according to the multidimensional characteristics of patients.

Longer study periods will be necessary to determine whether the clinical effects observed after the CMO-based pharmacist intervention are preserved over time. Despite these limitations, this study has significant implications that highlight the importance of specialized PCs in the management of PLWH.

CONCLUSION

In conclusion, the PC CMO model, a pharmacist-led intervention based on stratification of patients according to their specific needs, in agreement with their pharmacotherapeutic objectives, and reinforced by motivational interviews and personalized follow-up using the new technological tools, could induce optimization of the pharmacotherapy of this type of patients and improvement of clinical outcomes frequently associated with HIV disease and improve, this way, their quality of life with the ultimate goal of successful ageing for older PLWH.

FUNDING

This study was founded by Sociedad Andaluza de Farmacia Hospitalaria. Investigator Studies Program-2021.

CONFLICT OF INTEREST

Authors declare no conflict of interest

REFERENCES

1. Antiretroviral Therapy Cohort C. Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies. Lancet HIV 2017;4:e349-e56. doi 10.1016/S2352-3018(17)30066-8
2. Smit M, Brinkman K, Geerlings S, Smit C, Thyagarajan K, Sighem Av, et al. ATHENA observational cohort. Future challenges for clinical care of an ageing population infected with HIV: a modelling study. Lancet Infect Dis. 2015;15(7):810-8. doi: 10.1016/S1473-3099(15)00056-0. Erratum in: Lancet Infect Dis. 2015;15(9):998.
3. Milic J, Russwurm M, Cerezales Calvino A, Brañas F, Sánchez-Conde M, Guaraldi G. European cohorts of older HIV adults: POPPY, AGEhIV, GEPPO, COBRA and FUNCFRAIL. Eur Geriatr Med. 2019;10(2):247-257. doi: 10.1007/s41999-019-00170-8.
4. Schouten J, Wit FW, Stolte IG, Kootstra NA, van der Valk M, Geerlings SE, et al; AGEhIV Cohort Study Group. Cross-sectional comparison of the prevalence of age-associated comorbidities and their risk factors between HIV-infected and uninfected individuals: the AGEhIV cohort study. Clin Infect Dis. 2014;59(12):1787-97. doi: 10.1093/cid/ciu701.
5. Guaraldi G, Menozzi M, Zona S, Calcagno A, Silva AR, Santoro A, et al. Impact of polypharmacy on antiretroviral prescription in people living with HIV. J Antimicrob Chemother. 2017;72(2):511-514. doi: 10.1093/jac/dkw437.
6. Justice AC, Gordon KS, Skanderson M, Edelman EJ, Akgün KM, Gibert CL, et al; VACS Project Team. Nonantiretroviral polypharmacy and adverse health outcomes among HIV-infected and uninfected individuals. AIDS. 2018;32(6):739-749. doi:10.1097/qad.0000000000001756.
7. Allavena C, Marzolini C. Polypharmacy and risk of admission to hospital in people ageing with HIV: what is the contribution of drug-drug interactions? Lancet Healthy Longev. 2021;2(10):e606-e607. doi: 10.1016/S2666-7568(21)00227-0.
8. Vinuesa-Hernando JM, Gimeno-Gracia M, Malo S, Sanjoaquin-Conde I, Crusells-Canales MJ, Letona-Carbajo S, et al. Potentially inappropriate prescriptions and therapeutic com-

plexity in older HIV patients with comorbidities. Int J Clin Pharm. 2021;43(5):1245-1250. doi: 10.1007/s11096-021-01242-1.

9. Zheng C, Meng J, Xiao X, Xie Y, Zhao D, Wang H. Polypharmacy, Medication-Related Burden and Antiretroviral Therapy Adherence in People Living with HIV Aged 50 and Above: A Cross-Sectional Study in Hunan, China. Patient Prefer Adherence. 2022;16:41-49. doi: 10.2147/PPA.S340621.
10. Guaraldi G, Pintassilgo I, Milic J, Mussini C. Managing antiretroviral therapy in the elderly HIV patient. Expert Rev Clin Pharmacol. 2018;11(12):1171-1181. doi: 10.1080/17512433.2018.1549484.
11. Díaz-Acedo R, Soriano-Martinez M, Gutiérrez-Pizarraya A, Fernandez-Gonzalez-Caballos JA, Raya-Siles M, Morillo-Verdugo R. Prevalence of PIMDINAC criteria and associated factors in elderly HIV patients. Enferm Infecc Microbiol Clin (Engl Ed). 2021:S0213-005X(20)30417-1. English, Spanish. doi: 10.1016/j.eimc.2020.11.014.
12. Morillo-Verdugo R, Calleja-Hernández MÁ, Robustillo-Cortés MLA, Poveda-Andrés JL. A new definition and refocus of pharmaceutical care: the Barbate Document. Farm Hosp. 2020;44(4):158-162. English. doi: 10.7399/fh.11389.
13. Morillo-Verdugo R, Robustillo-Cortes MLA, Navarro-Ruiz A, Sánchez-Rubio Ferrandez J, Fernández Espínola S, Fernández-Pacheco García-Valdecasas M, et al. Clinical Impact of the Capacity-Motivation-Opportunity Pharmacist-Led Intervention in People Living with HIV in Spain, 2019-2020. J Multidiscip Healthc. 2022;15:1203-1211. doi: 10.2147/JMDH.S361305.
14. Cantillana-Suárez MG, Robustillo-Cortés MLA, Gutiérrez-Pizarraya A, Morillo-Verdugo R. Impact and acceptance of pharmacist-led interventions during HIV care in a third-level hospital in Spain using the Capacity-Motivation-Opportunity pharmaceutical care model: the IRAFE study. Eur J Hosp Pharm. 2021;28(Suppl 2):e157-e163. doi: 10.1136/ejhpharm-2020-002330.
15. Morillo Verdugo R, Villarreal Arevalo AL, Alvarez De Sotomayor M, Robustillo Cortes ML. Development of a taxonomy for pharmaceutical interventions in HIV+ patients based on the CMO model. Farm Hosp. 2016;40(n06):544-568. English. doi: 10.7399/fh.2016.40.6.10567.
16. Morillo-Verdugo R, Martínez-Sesmero JM, Lázaro-López A, Sánchez-Rubio J, Navarro-Aznárez H, DeMiguel-Cascón M. Development of a risk stratification model for pharmaceutical care in HIV patients. Farm Hosp. 2017;41(3):346-356. English. doi: 10.7399/fh.2017.41.3.10655.
17. Prados-Torres A, Poblador-Plou B, Calderón-Larrañaga A, Gimeno-Feliu LA, González-Rubio F, Poncel-Falcó A, et al. Multimorbidity patterns in primary care: interactions among chronic diseases using factor analysis. PLoS One. 2012;7(2):e32190. doi: 10.1371/journal.pone.0032190.
18. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. Age Ageing. 2015 ;44(2):213-8. doi: 10.1093/ageing/afu145. Erratum in: Age Ageing. 2018;47(3):489.
19. HIV Drugs Interactions. University of Liverpool. Interaction Checker [accesed 3 Ago 2022]. Available at: https://www.hiv-druginteractions.org/.
20. UpToDate®. Drugs & drug interaction [accesed 3 Ago 2022]. Available at: https://www.uptodate.com/home/drugs-drug-interaction.
21. Knobel H, Alonso J, Casado JL, Collazos J, González J, Ruiz I, et al; GEEMA Study Group. Validation of a simplified medication adherence questionnaire in a large cohort of HIV-infected patients: the GEEMA Study. AIDS. 2002;16(4):605-13. doi: 10.1097/00002030-200203080-00012.
22. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care. 1986;24(1):67-74. doi: 10.1097/00005650-198601000-00007.
23. Documento de consenso sobre edad avanzada e infección por el VIH (2015). Available at: https://www.segg.es/media/descargas/Documento-de-edad-avanzada-y-VIH.pdf
24. Calderón-Larrañaga A, Gimeno-Feliu LA, González-Rubio F, Poblador-Plou B, Lairla-San José M, Abad-Díez JM, et al. Polypharmacy patterns: unravelling systematic associations between prescribed medications. PLoS One. 2013;8(12):e84967. doi: 10.1371/journal.pone.0084967.
25. Courlet P, Livio F, Guidi M, Cavassini M, Battegay M, Stoeckle M, et al; Swiss HIV Cohort Study. Polypharmacy, Drug-Drug Interactions, and Inappropriate Drugs: New Challenges in the Aging Population With HIV. Open Forum Infect Dis. 2019;6(12):ofz531. doi: 10.1093/ofid/ofz531.
26. Greene M, Justice AC, Lampiris HW, Valcour V. Management of human immunodeficiency virus infection in advanced age. JAMA. 2013;309(13):1397-405. doi: 10.1001/jama.2013.2963.
27. López-Centeno B, Badenes-Olmedo C, Mataix-Sanjuan Á, McAllister K, Bellón JM, Gibbons S, et al. Polypharmacy and Drug-Drug Interactions in People Living With Human Immunodeficiency Virus in the Region of Madrid, Spain: A Population-Based Study. Clin Infect Dis. 2020;71(2):353-362. doi: 10.1093/cid/ciz811.
28. Halloran MO, Boyle C, Kehoe B, Bagkeris E, Mallon P, Post FA, et al. Polypharmacy and drug-drug interactions in older and younger people living with HIV: the POPPY study. Antivir Ther. 2019;24(3):193-201. doi: 10.3851/IMP3293.
29. Yu X, Lobo JD, Sundermann E, Baker DJ, Tracy RP, Kuchel GA, et al. Current Challenges and Solutions for Clinical Management and Care of People with HIV: Findings from the 12th Annual International HIV and Aging Workshop. AIDS Res Hum Retroviruses. 2023;39(1):1-12. doi: 10.1089/AID.2022.0079..
30. Morillo-Verdugo R, Aguilar Pérez T, Gimeno-Gracia M, Rodríguez-González C, Robustillo-Cortes MLA; representing the project research team belonging to the HIV Pharmaceutical Care group of the (SEFH). Simplification and Multidimensional Adaptation of the Stratification Tool for Pharmaceutical Care in People Living With HIV. Ann Pharmacother. 2023;57(2):163-174. doi: 10.1177/10600280221096759