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PEOPLE LIVING WITH HIV IN TREATMENT WITH LONG-ACTING ANTIRETROVIRAL THERAPY: WHICH PSYCHOLOGICAL ASPECTS ARE ASSOCIATED?

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Abstract

Adherence to antiretroviral therapy (ART) is an important health behaviour linked to a reduced chance of drug resistance and lower viraemia in people living with HIV. Several psychosocial factors seem to be implicated both in adherence behaviour and consequently in the management of HIV disease. For example, psychological distress (anxiety and depression), personality traits, dysfunctional coping strategies seem to be related to both poor adherence behaviour and disease severity. Despite advances in the development of ART, several challenges are associated with current treatment involving daily, lifelong oral pills (i.e., stigma concerns, daily reminders of HIV status, medical problems). Long-acting injectable ART allows reduced dosing frequencies, minimising the impact of forgetfulness and high pill burden. Despite this, few studies have yet addressed the psychosocial aspects associated with this new regimen. Therefore, the aim of the present longitudinal study is to investigate the psychological aspects of people living with HIV (PLWH) making the transition from oral antiretroviral therapy to LA injection therapy. Specifically, the objectives are as follows: a) to carry out a baseline assessment of certain personality characteristics; b) to carry out a longitudinal assessment of medical-clinical and psychological variables; c) to investigate which socio-demographic, clinical and psychological factors are associated with a better quality of life (QoL) and lower levels of anxiety and depression. The study project is aimed at PLWH undergoing treatment at the HIV Infection Outpatient Clinic, Amedeo di Savoia Hospital, Turin, in Italy. The study was proposed to PLWH who had been identified by the infectious disease physician as eligible for LA therapy since the time of approval by the Hospital Ethics Committee (reference number 0030555). PLWH were asked to complete questionnaires via an online survey during the first administration of LA therapy (T0), during the fourth administration, 5 months later (T1), and during the seventh administration, 11 months later (T2). The data collected include socio-demographic information (e.g. gender, age, sexual orientation, marital status) and clinical information (e.g. date of diagnosis, course of infection, medical comorbidities). Finally, psychological variables (personality traits, alexithymia, social support, locus of control, stigma, quality of life, anxiety, and depression) will be assessed. Investigating which factors are associated with a better QoL is very important in order to structure tailored psychological interventions. Psychological interventions, if carried out in a timely manner, could reduce the risk of psychological distress in the long term, improving psychological adaptation to the disease and promoting ART adherence.

Keywords: *Long-acting antiretroviral therapy, HIV, quality of life, psychological distress, stigma.*

1. Introduction

At the end of 2023, the World Health Organisation (WHO) estimated that 39.9 million people were living with Human Immunodeficiency Virus (HIV), of which 38.6 were adults. Both studies and clinical practice have shown that, given adequate and consistent antiretroviral therapy (ART), the person with a negative viral load cannot transmit HIV (Menendez-Arias & Delgado, 2022). Considering that therapy usually involves taking oral medication on a daily basis, adherence requires a great deal of commitment on the part of people living with HIV (PLWH) and plays a significant role in the management of the disease.

Adherence management is associated with a number of daily challenges related to medical, social and individual factors (Iacob et al., 2017). The daily assumption of personal responsibility for care, such as swallowing difficulties and drug-food and drug-drug interactions, which make adherence to therapy difficult (Shubber et al., 2016).

The individual factors that may interfere with ART adherence are psychological aspects. For example, psychological distress (anxiety and depression) appears to be involved in increased immune dysfunction and disease severity (Gonzalez et al., 2011). Furthermore, social stigma, perceived social support, more adaptive coping strategies, and an internal locus of control may influence the adherence to ART (Luthuli & John-Langba, 2024; de Oliveira França et al., 2022).

Another psychological factor that seems to be involved both directly and indirectly on the adherence behaviour of PLWH is alexithymia defined as difficulty in identifying, recognising and expressing one's own and others' emotions. PLWH appear to have high levels of alexithymia, with a prevalence ranging from 25% to 40% (Benfante & Romeo, 2022).

Personality traits have also been shown to play a role in the progression of HIV disease and need to be considered in ART adherence (Ironson et al., 2008; John & Gross, 2004).

Given this background and the challenges associated with optimal adherence to daily oral ART, alternative schedules of administration have been developed including less frequent dosing. Long-acting injectable ART (ART-LA) provides administration either monthly or, at higher doses, every two months, minimizing the impact of forgetfulness and high pill burden (Chounta et al., 2021).

Several clinical trials of ART-LA have demonstrated its noninferiority in efficacy to daily oral ART (Landovitz et al., 2023; Wang et al., 2023). To date, patient satisfaction, tolerability, and preference for ART-LA have been high, suggesting that it may help overcome many of the barriers mentioned above (Mills et al., 2022; Slama et al., 2023; Philbin et al., 2022).

Despite this, previous studies that have addressed the individual and social psychological aspects associated with the new treatment have mostly been limited to qualitative assessments (preferences, fears and concerns) and about anxiety-depressive symptoms (Tolley et al., 2020; Fletcher et al., 2023).

1.1. Study aims

The aim of the present longitudinal study is to investigate the psychological aspects of PLWH making the switch from oral ART to LA injectable ART (ART-LA). Specifically, the goals are as follows: to carry out a baseline assessment of some personality characteristics in order to understand whether there are specific clusters; to carry out a survey of medical-clinical and psychological variables during the various administrations in order to understand possible trajectories; to investigate which socio-demographic, clinical and psychological baseline factors are associated with a better quality of life and lower levels of anxiety and depression following the new therapy.

2. Material and methods

The present project is a longitudinal and prospective study. The Department of Psychology of the University of Turin together with the Infectious Diseases Unit have originally conceived the study idea and design. The study has already been approved by the Hospital Ethics Committee (n. protocol 0030555) and will be conducted in accordance with the Declaration of Helsinki.

2.1. Recruitment procedure

The final sample will be made up of 120 PLWH, consecutively recruited from the HIV Infection Outpatient Clinic, Amedeo di Savoia Hospital, in Turin, Italy.

The participation in the project is on a voluntary basis and with prior signing of informed consent. It entails no additional burden or change to the patient's treatment plan, which will be continued as current clinical practice even if they do not join the study.

Study participants will be required to complete a battery of self-report psychological questionnaires in combination with 3 administrations of ART-LA. The questionnaires are expected to be completed through an online survey that allows for pseudonymized data to be managed by creating a personal code. Inclusion criteria will be as follows: >18 years old, having a diagnosis of HIV infection; be eligible for ART- LA; cognitive ability and language skills to participate in the study.

These assessments will be distributed over the course of the study as follows:

T0: baseline assessment, during the first administration of the new injectable therapy;

T1: evaluation carried out at five months after T0 (during the fourth administration);

T2: evaluation at eleven months after T0 (during the seventh administration).

2.2. Assessment instruments

The data collected include socio-demographic information (ethnicity, gender, age, sexual orientation, marital status, children, education, occupation, income) and clinical information (date of diagnosis, course of infection, duration and type of previous therapy, medical comorbidities). Finally, psychological variables will be assessed (personality, alexithymia, perceived social support, locus of

control, stigma, quality of life, anxious and depressive symptoms) in accordance with the scheme presented in **Table 1** and with the help of the following instruments:

- PID-5 BF5 - The Personality Inventory for DSM-5 - Brief Form (PID-5 BF) is a 25 item self-related personality trait assessment scale for adults age 18 and older (Anderson et al., 2018).
- TAS-20 - The Toronto Alexithymia Scale (TAS-20) is a self-report instrument designed to assess alexithymia (Taylor et al., 1985).
- MHLC-C - The Multidimensional Health Locus of Control Form-C (Ubbiali et al., 2008) is an 18-item self-administered questionnaire, useful for assessing Locus of Control beliefs with any medical or health-related condition.
- HIV Stigma Scale - brief version has been implemented from the 40-item HIV Stigma Scale to create a short version with 12 items (three from each of the four stigma subscales: personalized stigma, disclosure concerns, concerns with public attitudes and negative self-image) (Berger et al., 2001).
- HIVDQOL - (HIV Dependent Quality of Life) (Romaine et al. 2018) is a self-report questionnaire, assessed to measure QoL and the impact on QoL in PLWH. The HIVDQoL includes two overview items which measure present 'generic QoL' and 'HIV-specific QoL' and 26 domain-specific items.
- HADS - The Hospital Anxiety and Depression Scale (HADS) will be employed to assess symptoms of anxiety and depression (Zigmond and Snaith, 1983).

Table 1. PID-5 BF5 - The Personality Inventory for DSM-5 - Brief Form (PID-5 BF); TAS-20 - The Toronto Alexithymia Scale (TAS-20); The Multidimensional Health Locus of Control Form-C (MHLC-C); HIV Stigma Scale- brief version; HIV Dependent Quality of Life (HIVDQOL); The Hospital Anxiety and Depression Scale (HADS).

	T0 (1° Injection)	**T1** (5 months later)	**T2** (11 months later)
1. Socio-demographic information	X		
2. Clinical information	X	X	X
3. PID-5 BF	X		
4. TAS-20	X		
5. MHLC-C	X	X	X
6. HIV Stigma Scale	X	X	X
7. HADS	X	X	X
8. HIVDQOL	X	X	X

2.3. Statistical analysis

The sample size has been determined based on an a priori power analysis, using the software G*Power 3.1 (Faul et al., 2009), with a medium effect size F2: 0.15 (Cohen, 1988; Greene, 2000), and an alpha level of .05, as being sufficient for repeated measures Analysis of Variance (ANOVA) and t-test. To answer the first question, i.e., to monitor the trend of the variables under consideration over time, repeated measures ANOVA will be used. This will allow us to compare the results obtained from the questionnaires during the assessment, in order to highlight the presence of statistically significant differences in the scores at the different times.

To investigate, however, which factors can have the greatest impact on the outcome measures (quality of life, anxiety and depressive symptoms), bivariate Pearson or Spearman correlations will first be conducted in order to investigate the relationships with the demographic, clinical and psychological variables. The variables, which are found to be statistically significant correlated with the criterion variables, will then be inserted as independent variables in multiple hierarchical regression models.

All analyzes will be performed using the "Statistical Package for Social Sciences – SPSS" software, version 28 or later.

3. Discussion

Through the present study we expect to know which factors may significantly contribute to a better mental and physical health in PLWH. Furthermore, our aim is to show the trajectory of psychological well-being and QoL in the PLWH during LA therapy. These future data could have an important clinical implication. Timely psychological interventions could reduce the risk of long-term psychological distress, improve psychological adjustment to the disease and promote adherence to pharmacological treatment.

Finally, integrating psychological intervention into the complex treatment of PLWH means considering a biopsychosocial model of care that overcomes reductionist and ineffective models of care.

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