

A case report of clinical implications of a delayed antiretroviral therapy switch in a patient with multiple treatment interruptions

SAGE Open Medical Case Reports
Volume 10: 1–4
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DOI: 10.1177/2050313X221144209
journals.sagepub.com/home/sco



Mireille A Mpalang Kakubu¹ , Kandali Frans¹, Nelson Gibutai¹
and Patrick DMC Katoto²

Abstract

The Namibia national antiretroviral therapy guidelines recommend that patients living with HIV who interrupt antiretrovirals and in the process disengage from care be restarted on their usual antiretroviral therapy regimen upon return. We introduce a 39-year-old male patient on first-line antiretroviral therapy, namely, tenofovir disoproxil fumarate, lamivudine and efavirenz, from 2015 to 2019 (4 years), who returned to care after the fourth episode of interrupting his treatment, though his adherence to antiretroviral therapy was deemed poor. Thus, he presented with severe immunosuppression and an AIDS-defining condition. Hence, he was switched to second-line antiretroviral therapy, treated with fluconazole for oesophageal candidiasis and reinitiated on cotrimoxazole prophylaxis. The client is currently clinically stable with a suppressed viral load. Medical and drug history taking with an emphasis on the previous history of treatment failure in patients returning to care are paramount in guiding the choice of future prescriptions of antiretrovirals. The multiple antiretroviral therapy interruptions from the patient and the delay in decision-making on the side of the clinician to switch treatments contributed to the emergence of an AIDS-defining condition.

Keywords

ART interruptions, poor adherence, high viral load, treatment failure, treatment switch, case study

Date received: 30 May 2022; accepted: 21 November 2022

Introduction

Adherence to antiretroviral therapy (ART) is the main prerequisite to attain virologic suppression,¹ whereas stigma was found to be among the significant causes of non-adherence to ART.² Suboptimal plasma concentration of antiretrovirals (ARVs) favours HIV mutations and treatment failure.³ The 5th Namibia ART guidelines recommended Tenofovir, Lamivudine and Efavirenz (TDF, 3TC, EFV) as the first-line ART regimen for adults.⁴ EFV is a non-nucleoside reverse transcriptase inhibitor (NNRTI), with a low genetic barrier to viral resistance. Furthermore, in Namibia, the pre-treatment drug resistance to NNRTIs surpasses 10% and can contribute to poorer HIV treatment outcomes in patients on EFV-based ART regimens.⁵ As per the Namibia ART guidelines' recommendation, patients who failed the first-line ART are switched to second-line ART after two consecutive viral loads (VLs) > 1000 copies/mL of plasma with a non-significant drop in the log values, taken 3–6 months apart despite a good adherence to ART.⁴ The Nurse Initiated Management of ART (NIMART),

established in Namibia a decade ago,⁶ is a task-shifting programme whereby nurses while benefitting an ongoing mentorship from medical officers initiate ART with opportunistic infections prophylaxis and review patients for clinic follow-ups.⁶ This approach is efficient, supports the public sector and guarantees that all patients, adults and children, receive standard ART care in a timely manner. Patients with serious conditions are referred from the

¹Ministry of Health & Social Services, Windhoek, Namibia

²Centre for Evidence-based Health Care, Division of Epidemiology and Biostatistics, Department of Global Health, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa

*Patrick DMC Katoto is also affiliated to Cochrane South Africa, South African Medical Research Council, Cape Town, South Africa and Centre for Tropical Diseases and Global Health, Department of Medicine, Catholic University of Bukavu, DR Congo

Corresponding Author:

Mireille A Mpalang Kakubu, Ministry of Health & Social Services, PO Box: 70762, Windhoek, 9000, Namibia.

Email: Mpalangkakubu@gmail.com



NIMART sites to HIV-expert clinicians for specialized care to ensure treatment success.⁷ Here, we describe a patient who presented with multiple episodes of ART interruption, a previous history of poor adherence to the first-line ART and a persistently high VL. This was compounded by a delay to switch the patient to a second-line ART regimen upon his return to the health facility after eventually addressing adherence issues related to ART.

Case description

Using the 2013 care checklist, we report a 39-year-old man who tested HIV positive on 9 January 2015 in a NIMART outpatient clinic of the Ministry of Health of Namibia in the Windhoek district. He complained of tiredness without any other associated symptoms, and the tuberculosis screening was negative with an unremarkable clinical examination. He was assessed as having a World Health Organization (WHO) stage 1 infection. His CD4 count was 96 cells/mm³, weight 76 kg, body mass index (BMI) 21 kg/m², creatinine clearance of 60 mL/min and haemoglobin of 11.3 g/dL. He was counselled on the importance of good adherence, and continuity of care, a treatment supporter was designated and started on TDF, 3TC and EFV on 29 January 2015 with reportedly good tolerance. He is single, self-employed, and does not drink alcohol or smoke. Despite ongoing adherence counselling done at each follow-up, he defaulted to ART on 13 October 2015 and returned to care on 8 September 2016 as he was not well. At this time, his VL and CD4 were, respectively, 52,605 copies/mL and 19 cells/mm³. His adherence was intensified and began personalized enhanced adherence counselling and restarted the same ART regimen. Six months later, on 7 March 2017, he suppressed his VL. However, on 6 April 2017, he stopped his ARVs again due to stigma issues reported by the patient as a mark of disgrace and fear of abandonment. He came back on 7 February 2018, where he was started on an identical regimen on ART and took his ARVs only for 2 months. In July 2018, he continued with enhanced adherence counselling sessions and was reinitiated on the same regimen with a CD4 of 5 (0.9%) cells/mm³, a negative cryptococcal serum antigen and a BMI of 20 kg/m².

He was diagnosed with oesophageal candidiasis, an AIDS-defining illness, and successfully treated with fluconazole. His VL on ART 6 months later, on 31 January 2019, was 11,229 copies/mL. Unfortunately, no consideration for a treatment switch was made at this moment. He was seen again on 29 February 2019 but followed up only on 21 June 2019 with another episode of oesophageal candidiasis and a CD4 of 3 (0.7%) cells/mm³ after he had stopped his treatment. The NIMART nurse who attended to the patient was well trained, NIMART certified, with about a year of experience in ART case management. On 25 June 2019, as the patient returned to the clinic with a complaint of being

unwell, the NIMART nurse referred the man to an HIV expert who oversees complicated cases in the district. The cryptococcal serum antigen remained negative, the minimal state examination was normal, and the VL before restarting ART was 69,706 copies/mL. The man was immediately switched to the second-line ART, comprising TDF, Zidovudine (AZT), 3TC, Atazanavir/ritonavir (ATV/r), and was reinitiated cotrimoxazole and treated with fluconazole. The stigma and the adherence to ART were addressed through enhanced adherence counselling. The client took his ARVs and kept all his clinical appointments. Three months later, his VL (9 September 2019) was suppressed at 30 copies/mL, and his CD4 counts improved to 275/mm³ (Figure 1). With the introduction of dolutegravir (DTG) in Namibia in 2020, the ART regimen was simplified to AZT 3TC DTG in June 2020, and the patient has remained virally suppressed (VL < 40).

Discussion

This case report describes a patient with a history of multiple ART interruptions, poor adherence to ART due to stigma and returning to care in an AIDS-defining condition with a meagre CD4 count.

It is noted that this patient was enrolled and managed at NIMART site. The Namibia national ART guidelines (fifth edition) are used in both the public and private sectors; it is recommended to restart patients if indicated as much as possible on the same ART regimen. The patient discussed in this case benefitted from pre- and post-test adherence counselling and ongoing counselling throughout care. However, he missed his appointments and stopped adhering to his treatment. Hence, the enhanced/personalized adherence counselling revealed that stigma and fear of rejection were the main reasons for non-adherence and were addressed accordingly with the involvement of his treatment supporter.

Multiple ART interruptions and suboptimal adherence to ART contribute to treatment failure, AIDS-defining conditions and death.^{8,9} Our case report described a patient who was 4 years on ART and interrupted treatment more than once with persistent high VLs. He returned to care with a WHO 4 clinical staging of HIV disease and a 97% drop in CD4 counts from baseline. The delay in switching the patient to a second-line ART regimen from NIMART site among others contributed to severe immunosuppression leading to the development of an AIDS-defining illness. However, the referral of this patient from the NIMART to an HIV expert improved this patient's condition. Considering the high mortality and morbidity risk in a patient who was severely immunocompromised, the previous history of high VLs and the fact that the genotyping resistance testing is not routinely indicated in patients failing the first ART line, the client was immediately switched to the second-line ART, including two new drugs: AZT and

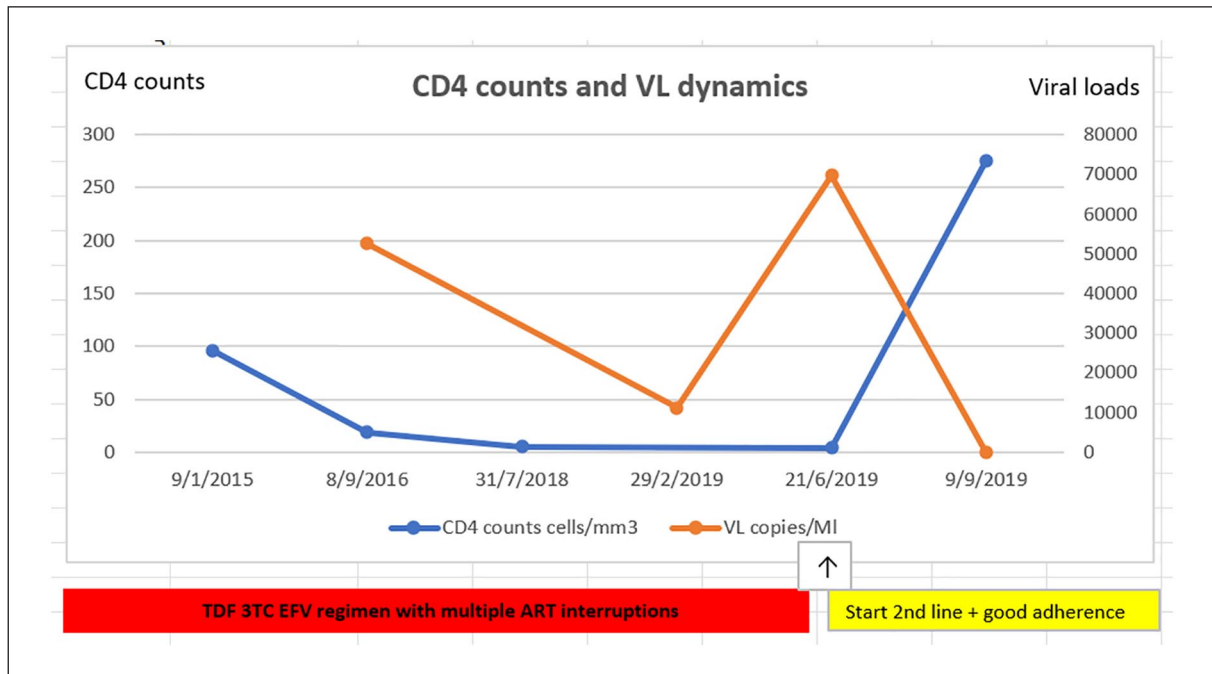


Figure 1. Patient's CD4 (cells/mm³) and VLs (copies/mL) dynamics. This figure explains the CD4 count cells' decline and the VL's rise over a period of 4 years during first-line ART (TDF 3TC EFV) with poor adherence and immunologic recovery + virologic suppression 3 months after starting effective second-line ART (TDF AZT 3TC ATV/r).

a boosted protease inhibitor, Atazanavir/ritonavir (ATV/r). 3TC was kept hypothesizing that the M184V mutation, mainly selected by 3TC and Emtricitabine, has a half-log crippling effect on viral multiplication and can slow down the occurrence of resistance to AZT and TDF. TDF was also maintained with the assumption that the K65R mutation, if present, will re-sensitize AZT.¹⁰

The enhanced adherence counselling addressed the fear of social abandonment by linking the patient to a treatment supporter who was his relative, helped the client to keep up his clinical follow-ups for four consecutive times, improved clinically and managed to suppress his VL 3 months after starting the second-line ART.

Conclusion

The Namibia national ART guidelines are aligned with the WHO recommendations for a standardized treatment. Nevertheless, regarding patients returning to care after ART interruption, previous ARVs exposure and VL results are essential in guiding the management. To avoid treatment switch delays in patients failing ART, we recommend enhancing collaboration between NIMART and HIV-experienced providers, regular and targeted review of patients' records and patients with detectable VL by a multidisciplinary collaborative HIV team. Besides, we suggest linking patients with stigma and fear of rejection to trusted treatment supports and or HIV-differentiated models of care such as community adherence groups for peer support.

Acknowledgements

The authors acknowledge the patient and service providers at Robert Mugabe Clinic.

Author contributions

M.A.M.K. and P.D.M.K. contributed to the study conception and design, prepared, and revised the manuscript before submission. K.F. and N.G. contributed to clinical data collection. All authors proofread the final manuscript and approved the final version of the manuscript.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship and/or publication of this article.

Ethical approval

Patient consent was obtained, and approval was obtained from the Ethical Research Committee of the Ministry of Health of Namibia Review Board on 29 January 2020, approval reference number 17/3/3/MAK.

Informed consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

ORCID iD

Mireille A Mpalang Kakubu  <https://orcid.org/0000-0001-7894-4536>

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