

Gestione delle complicanze in una persona di 66 anni con infezione da HIV e diabete: focus su nuove terapie long-acting.

Managing Complications in a 66-Year-Old person living with HIV and Diabetes: focus on new long-acting therapy.

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Riassunto

Il nostro caso mette in evidenza le probabili interazioni tra i farmaci antidiabetici orali e gli antiretrovirali di cabotegravir e rilpivirina long acting. Con il crescente utilizzo di antiretrovirali long acting, è fondamentale valutare attentamente l'effetto di questi trattamenti combinati sulla sicurezza e sull'efficacia sulle terapie concomitanti, specialmente riguardo le possibili interazioni farmacologiche, che molto spesso non sono segnalate.

Con una popolazione di persone con HIV che invecchia, alcuni di questi possono sviluppare patologie come il diabete mellito, per cui la comprensione dell'interazione tra questi regimi terapeutici è essenziale per ottimizzare la cura dei pazienti. Si vuole cercare quindi di porre l'attenzione sui pazienti trattati con entrambe le categorie di farmaci, valutando la risposta glicemica, la soppressione virale e i potenziali effetti avversi.

Il nostro scopo è di fornire un input ad uno studio più ampio sulle interazioni farmacologiche tra farmaci antidiabetici orali e cabotegravir/rilpivirina long acting, per una gestione ottimale e sicura dei pazienti. L'obiettivo primario è quello di portare alla luce un quadro clinico osservato durante la nostra pratica clinica quotidiana, che possa contribuire all'ottimizzazione del trattamento dei pazienti affetti da queste due complesse condizioni cliniche.

Abstract

This case report aims to highlight the potential interactions between oral antidiabetic drugs and the use of cabotegravir and rilpivirine long acting as therapy in HIV infection.

With the increasing utilization of long-acting antiretrovirals it is crucial to carefully assess the impact of these combined treatments on the safety and efficacy of both therapies, especially concerning drug-drug interactions.

In an aging population of people living with HIV, some of whom are undergoing treatment with long-acting antiretrovirals and are affected by diabetes mellitus, understanding the interaction between these therapeutic regimens is essential to optimize patient care.

Thus, the focus is placed on people treated with both categories of drugs, evaluating glycemic response, viral suppression, and potential adverse effects.

Our aim is to contribute insights to a broader study on pharmacological interactions between oral antidiabetic drugs and cabotegravir/rilpivirine long acting, aiming for the optimal and safe management of patients.

The primary objective is to shed light on a clinical scenario observed during our routine clinical practice that can contribute to the optimization of treatment for patients affected by these two complex clinical conditions.

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Introduction

From a global health perspective, HIV continues to pose significant challenges in both management and therapy, despite the radical shift in its management and the enhanced quality of life for individuals afflicted by this infection over the decades (1).

Currently, the administration of antiretroviral therapy (ART) is a lifelong commitment, with the majority of antiretroviral medications necessitating daily intake to effectively suppress HIV-1 infection. This demands a significant level of adherence from individuals.

The challenge of upholding the potency of ART

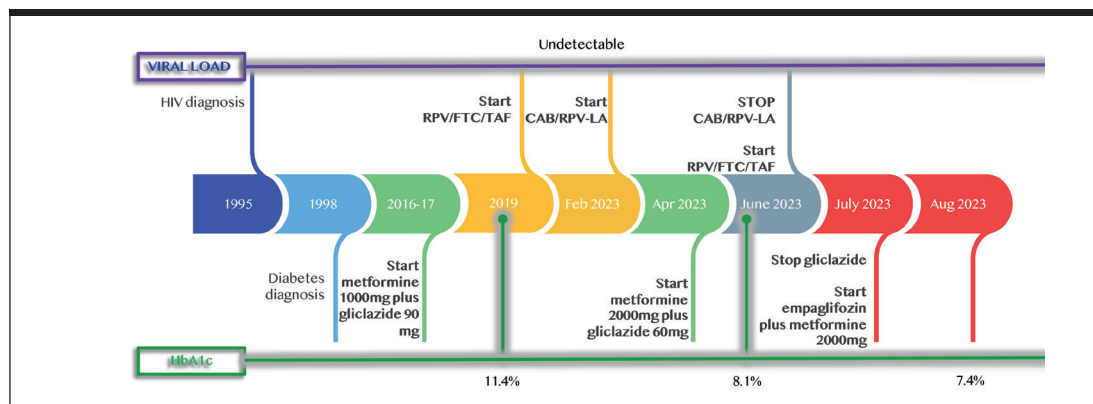


Figure 1. Drug treatments over time.

while contending with the requirement for daily medication is substantial.

A promising solution lies in the realm of long-acting antiretrovirals (LA-ARVs).

These hold the potential to enhance adherence to ART, diminish the transmission of HIV-1, and carry the potential for broader public health advantages by decreasing the count of new HIV-1 infections (1-3).

Case report

A 66-year-old Italian male was diagnosed with HIV-1 infection in 1992 in follow up at Infectious Diseases Clinic at Ospedale Policlinico San Martino Genova, on multiple lines of antiretroviral therapy. His past medical history includes HIV since 1995 (CDC C3 classification) diagnosed with CMV retinitis and vision loss in the left eye. Over the years, the patient has undergone multiple antiretroviral therapy regimens. Currently, his last oral the rilpivirine/emtricitabine/tenofovir alafenamide (RPV/FTC/TAF) with excellent compliance, adherence, and suppressed HIV-RNA load. He is affected by type 2 diabetes since 1998, treated with metformin since 2016 and gliclazide since 2017. However, glycemic control has been suboptimal with poor adherence to oral hypoglycemic therapy.

His actual medical history starting in January 2023 when counseling was provided for initiating injectable therapy with cabotegravir-rilpivirine long acting (CABO-RPV-LA), all enrollment criteria were met (virological suppression, stable regimen, without present or past evidence of viral resistance and of previous virological failure to non-nucleoside reverse transcriptase inhibitors (NNRTIs) and/or integrase inhibitors (INSTIs), with BMI 22.5 kg/m²).

The patient received the first injection on January

19, 2023. One month later, during a follow-up visit and second injection, the patient reported peripheral neuropathy and loss of appetite.

Symptoms included diffuse pain, paresthesia, reduced sensitivity in the right upper limb, and occasional balance issues. A third CABO-RPV-LA injection was administered on April 27, 2023, with persistent symptoms and reduced appetite, but no local injection site reactions.

On May the patient underwent a diabetes follow-up visit. His oral antidiabetic regimen consisted of 90 mg gliclazide in the morning and 1000 mg extended-release metformin in the evening (from 2017 and 2016 respectively).

The therapy was modified, reducing gliclazide to 60 mg daily and increasing metformin to 2000 mg daily due to poor glycemic control. A month later, despite an HbA1c of 8.1%, the antidiabetic therapy was maintained.

On June at an infectious diseases follow-up, considering the patient's symptoms and progressive weight loss (from 81 kg in January to 75 kg in June, with loss of 6 kg), the injectable CAB/RPV-LA therapy was discontinued due to suspected interaction with ongoing antidiabetic therapy. The patient was switched back to the previous oral antiretroviral therapy (RPV/FTC/TAF), which he is currently taking (Figure 1).

Furthermore, in June the patient presented an additional health issue.

During the diabetes follow-up, a left plantar lesion was observed.

The patient was referred to an orthopedic specialist on the same day.

The orthopedic examination revealed a planar lesion on the first metatarsal of the left foot with partial detachment of superficial layers and macerated edges, but no serous or purulent discharge. A punch biopsy was performed, and the sample was sent for culture.

An MRI of the left foot was recommended. The culture showed positive results for methicillin-sensitive *S. aureus*, *S. agalactiae*, and *S. mitis/oralis*. The patient started a six-week course of moxifloxacin after the MRI showed partial bone resorption in the left first metatarsal, indicative of osteomyelitis. On July, in terms of diabetes management, the patient's treatment was further adjusted. Gliclazide was discontinued, while he continued with 2000 mg extended-release metformin and started empagliflozin.

At the latest contact with the patient in August, his clinical conditions have shown improvement, with nearly complete healing of the planar lesion. Regarding the initial symptoms, they are still present, with reduced intensity.

Discussion

This case illustrates the challenges of managing a patient with both HIV and type 2 diabetes. The introduction of injectable therapy for HIV posed potential interactions with antidiabetic treatment, leading to symptomatic complications and weight loss.

The introduction of injectable therapy, represented a significant turning point in the patient's care (4). In the case of this patient, we aimed to analyze potential interactions between CABO-RPV-LA, two innovative long-acting therapeutic agents for HIV, and oral antidiabetic drugs, which were being taken prior to the initiation of the new antiviral therapeutic regimen.

The emergence of peripheral neuropathy, loss of appetite, weight loss and other sensory deficits prompted a nuanced examination of potential interactions with the patient's existing diabetes management.

In the literature, no studies highlight the possibility of pharmacological interactions in patients receiving long-acting antiretroviral therapy and oral antidiabetic drugs, with potential implications for gly-

cemic control, as may have occurred in the specific case, or for viral suppression (5) (6).

Careful clinical monitoring of these patients, along with the use of personalized antidiabetic treatment plans, is essential for optimizing both therapeutic regimens.

Currently, there is no available pharmacokinetic profile of antidiabetic agents that could be influenced by the effects of long-acting antiretrovirals on the metabolism of oral antidiabetic drugs. This could have implications for glycemic control and the potential emergence of adverse effects.

The positive results observed in our case emphasize how the potential success of a therapeutic switch, returning to the previous oral antiretroviral therapy, could be linked to a possible interaction between the two therapeutic regimens.

It is noteworthy that our patient maintained an undetectable viral load before and after initiating treatment with long-acting antiretroviral drugs. Therefore, interdisciplinary collaboration between infectious disease specialists and other specialists is necessary for optimizing the ongoing therapies.

At this moment, the major limitation that could certainly help to resolve the probable correlation between these two classes of drugs is the impossibility of performing a pharmacological analysis using the PK/PD model, to assess the drug concentration both at the time of administration and its maintenance over time, hoping that it may be possible in the future, at least for selected individuals as in the case just presented.

Conclusion

In conclusion, with the presentation of this case, the aim is to prompt reflection on the evolving and complex landscape of therapeutic strategies for patients managing both HIV and diabetes.

By shedding light on potential interactions between CABO-RPV-LA and antidiabetic drugs, the intention is to contribute to laying the groundwork for the necessary evidence and exploring broader cohorts to formulate potential evidence-based recommendations, in order to optimize treatment for patients who underwent therapeutic complexities and challenges of managing both HIV and diabetes concurrently. ■



REFERENCES

1. Berruti M, Riccardi N, Canetti D, Lo Caputo S, Taramasso L, Di Biagio A. *Injectable Antiretroviral Drugs: Back to the Future*. *Viruses*. 2021; 13: 228.
2. Ramgopal MN, Castagna A, Cazanave C, Diaz-Brito V, Dretler R, Oka S, et al. *Efficacy, safety, and tolerability of switching to long-acting cabotegravir plus rilpivirine versus continuing fixed-dose bicitegravir, emtricitabine, and tenofovir alafenamide in virologically suppressed adults with HIV, 12-month results (SOLAR): a randomised, open-label, phase 3b, non-inferiority trial*. *Lancet HIV*. 2023; S2352-3018(23)00136-4.
3. Swindells S, Andrade-Villanueva JF, Richmond GJ, Rizzardini G, Baumgarten A, Masiá M, et al. *Long-Acting Cabotegravir and Rilpivirine for Maintenance of HIV-1 Suppression*. *N Engl J Med*. 2020; 382: 1112–23.
4. Wang W, Zhao S, Wu Y, Duan W, Li S, Li Z, et al. *Safety and Efficacy of Long-Acting Injectable Agents for HIV-1: Systematic Review and Meta-Analysis*. *JMIR Public Health Surveill*. 2023; 9: e46767.
5. *EACS Guidelines*. 2022. Version 11.1 October 2022 (last access on August 2023) https://www.eacsociety.org/media/guidelines-11.1_final_09-10.pdf
6. Tarfa A, Sayles H, Bares SH, Havens JP, Fadul N. *Acceptability, Feasibility, and Appropriateness of Implementation of Long-acting Injectable Antiretrovirals: A National Survey of Ryan White Clinics in the United States*. *Open Forum Infectious Diseases*. 2023; 10: ofad341.

