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Exploring potential interactions between intramuscular cabotegravir/rilpivirine (CAB/RPV) and methadone: a case report

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BACKGROUND

- Antiretroviral drugs may impact the plasmatic levels of **methadone** in people living with HIV (PLWH) who are receiving methadone treatment.
- Methadone is metabolized by enzymes **CYP2B6** and **CYP3A4**.
- Existing literature indicates that concurrent use of oral **rilpivirine** (RPV) and **methadone** does not affect the maximum concentration, area under the curve (AUC), or minimum concentration of RPV, but reduces the AUC of methadone, even though no alterations in dosage are necessary when initiating the concurrent use of methadone and RPV.
- However, **clinical monitoring** may be advisable, as methadone maintenance therapy might require **adjustments** in certain individuals.

CASE PRESENTATION

- This is a case of a 64-yo female living with HIV for 39 years, with history of HCV infection and drug addiction under methadone treatment.
- The history of the patient is characterized by a CD4 cells nadir of 170/mmc and a zenith of HIV-RNA of 680.000 cps/mL, with a CDC classification stage C. She has consistently shown low levels of adherence to ART and follow-up visits, leading us physicians to propose to the patient a switch from non-STR oral therapy (3TC + DRV/c) to long-acting intramuscular antiretroviral therapy with CAB/RPV, which the patient accepted.
- At the latest follow-up visit prior to the switch she had 930 CD4/mmc and non detectable HIV-RNA. No genotypic resistance testing was available at time of switch.
- The **first dose** was injected in November 2023, with **no reported adverse events**. After 28 days a **second dose** was injected.
- Ten days after the second injection, the patient began to exhibit **withdrawal symptoms**, prompting her to seek assistance from **Addiction Services** (AS). She reported absence of such symptoms in recent years, indicating that they had been completely controlled with a daily dosage of **60 mg/die** of methadone. This crisis was managed by temporarily increasing the dosage to **80 mg/day**.
- Suspecting a potential interaction with the new ART, 8 weeks after the second intramuscular administration, a switch to **oral therapy** was performed to TAF/FTC/BIC. Over the following weeks, in accordance with her AS, the patient managed to reduce the daily dosage of methadone, returning it to **60 mg/day**.
- However, after 4 weeks, she again reported adherence issues and severe nausea associated with taking the pill, expressing a desire to return to **intramuscular therapy**. A new administration of CAB/RPV was performed in March 2024, resulting in the recurrence of withdrawal symptoms after a few days, necessitating the patient to seek assistance once again from her AS.
- Currently, the patient is again tapering off the methadone dosage, in anticipation of transitioning back to an oral regimen 8 weeks after the last injection.

CONCLUSIONS

- People who inject drugs (PWID) are generally individuals with **adherence issues** to antiretroviral therapy, where long-acting intramuscular therapeutic strategies can certainly be helpful.
- However, further studies are needed regarding the **potential interaction** between methadone and intramuscular rilpivirine.