Farm Hosp. 2011;**35(1)**:36–43

Farmacia
HOSPITALARIA

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REVIEW

Drug interactions of new antiretroviral drugs☆

J.I. Serrano López de las Hazas

Servicio de Farmacia, Hospital Son Llátzer, Palma de Mallorca, Spain

Received October 19, 2009; accepted January 20, 2010

KEYWORDS
Systematic review;
Antiretroviral therapy;
Drug interactions;
Darunavir;
Etravirine;
Maraviroc;
Raltegravir

Abstract A systematic review was made of the drug interactions of new antiretroviral drugs. In order to do this a search was made in Pubmed to find articles published from January 2007 to September 2009 and the full-text articles which contained information about new antiretroviral drugs were selected. This search was then complemented with information from the technical specifications of the drugs and consultations made on webpages specialized in antiretroviral interactions: www.interaccioneshiv.com and www.hiv-druginteractions.org. The information about the possible interactions of new antiretroviral drugs with one another and with the therapeutic groups which are most widely used in patients infected with the human immunodeficiency virus was analyzed.

PALABRAS CLAVE
Revisión sistemática;
Terapia antirretroviral;
Interacciones medicamentosas;
Darunavir;
Etravirina;
Maraviroc;
Raltegravir

Interacciones farmacológicas de los nuevos antirretrovirales

Resumen Se realiza una revisión sistemática sobre interacciones medicamentosas de los nuevos fármacos antirretrovirales. Para ello se realiza una búsqueda en Pubmed de artículos publicados entre enero de 2007 y septiembre de 2009 y se consideraron los artículos disponibles a texto completo que aportaban alguna información sobre los nuevos antirretrovirales. Esta búsqueda fue complementada a su vez con la información de las fichas técnicas de los productos y consultas en las páginas web específicas de interacciones de antirretrovirales: www.interaccioneshiv.com y www.hiv-druginteractions.org. Se analiza la información de las posibles interacciones de los nuevos antirretrovirales entre sí, y con los grupos terapéuticos más frecuentemente utilizados en pacientes con el virus de la inmunodeficiencia humana.

Introduction

An increase in life expectancy of HIV-infected patients has made it a chronic disorder. This fact has meant that age-related comorbidities have become apparent (hypertension, diabetes, hyperlipidaemia, psychiatric disorders, erectile dysfunction, etc) HIV-related disorders (neoplasm, transplants) and HIV opportunistic infections. This has meant that HIV patients need to undergo multiple

☆Part of the content of this article was presented to the "Jornadas de Actualización en el tratamiento de la infección por el VIH" (Conference on Updating HIV treatment), organised by the Government of Catalonia Health Department on 10 June in Barcelona.

E-mail address: jserrano@hsll.es

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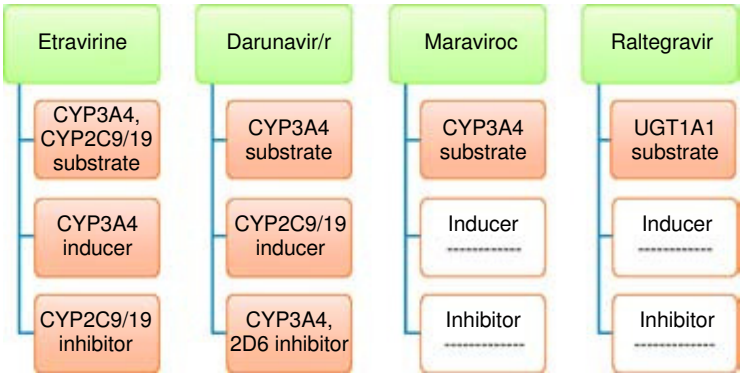

Figure 1 Effect of new antiretroviral drugs on CYP450.

treatments, and as such have become polymedicated patients.[1]

Given the idiosyncratic characteristic of antiretroviral drugs (many of them are enzyme inducers or inhibitors) and other concomitant drugs, drugs interactions are frequent in these patients.

Several studies have reported that clinically significant drug interactions are produced in 20%-30% of patients treated for HIV.[2-5]

If we examine the most recently marketed antiretroviral agents in more depth, we are able to observe that etravirine and darunavir/ritonavir act as cytochrome-P450 isoenzyme substrates, inducers and inhibitors. Maraviroc only acts as a substrate, therefore, its metabolism is to be influenced by all potent cytochrome-P450 inhibitors and inducers. On the other hand, raltegravir is mainly metabolised by hepatic glucuronidation, meaning that few drug interactions are expected for this drug (Figure 1).[6]

The relevance of these interactions is justified because they could increase toxicity and reduce other drugs' efficacy, which could cause patients to stop taking antiretroviral treatment (ART). These adverse effects and resistance mutations may develop, causing treatment failure and limiting patients' therapeutic options. As such, antiretroviral combinations should be avoided or used with caution alongside certain therapeutic groups, and alternatives should be prioritised (Table).[7-12]

Each and every day we are having to face several difficulties when assessing antiretroviral drug interactions.

Patient

Most patients need to receive co-medication and some of them are polymedicated patients. Furthermore, this group is interested in using non-prescribed products (20% Canada), herbal medicine and nutritional supplements with significant interactions (60% UK and 20%). Some patients also often use drugs of abuse.[1]

Health care system

Many levels of the health care system intervene within HIV-patient care (primary care staff, emergency doctors, specialists, etc.) and we do not always have access to the patient's complete drug history records.[1]

In Spain, most health care centres are not able to access electronic prescriptions during infectious disorder visits, meaning that the HIV specialist is not able to routinely evaluate possible interactions.

Table Main drugs to avoid with antiretroviral treatment and therapeutic alternatives

Therapeutic group	Prevent	Alternative
Antihistamines	Terfenadine, astemizole	Cetirizine
Opiate analgesics	Fentanyl transdermal	Codeine morphine
Prokinetic agents	Cisapride	Metoclopramide
Benzodiazepine	Midazolam, triazolam	Lorazepam
Anti-migraine drugs	Ergotamine derivatives	Sumatriptan
Antiepileptic drugs	Carbamazepine, phenobarbital, phenytoin	Gabapentin, vigabatrin, levetiracetam
Therapeutic Group	**Caution**	**Alternative**
Antifungal drugs	Ketoconazole>itraconazole>voriconazole	Fluconazol, amphotericin B
Macrolide	Erythromycin>clarithromycin	Azithromycin
H2 Antihistamines	Cimetidine	Ranitidine, famotidine

Furthermore, hospital drug guidelines are limited and not all centres have therapeutic alternatives available for every patient.

Interaction-related studies

Many of the studies that examine drug interactions are performed using single doses, and on other occasions use doses different to those used in clinical practice.

In other cases, studies are conducted on healthy volunteers and not on the patients for whom the treatment is to be indicated. We have also found inconsistencies in study interpretations. For a single adjustable drug, several doses are proposed depending on the regulatory agency.

Lastly, clinical relevance of interactions should not only be based on changes associated with plasma concentrations, but on clinical tests.

Antiretroviral drugs

The likelihood of interactions occurring depends on the very specificity of the antiretroviral families. At present, we know that the antiretroviral families that have the highest interaction potential are protease inhibitors (PI), followed by non-nucleoside reverse transcriptase inhibitors (NNRTI) and lastly the nucleoside analogue reverse transcriptase inhibitors (NRTI), whose interaction potential is really low.

Furthermore, the therapeutic arsenal for treating HIV is quite wide: there are 20 drugs on the market belonging to 6 different families. However, there are many differences in action within the same family and many drug reactions have been found after having been marketed. This means that we should be alert even after the drugs appear on the market.

An added difficulty is the fact that we should combine three active drugs to achieve the best therapeutic response, both for naïve and rescue patients. If patients have resistance mutations to these drugs, then they belong to new therapeutic groups.

The objective of this article is to provide more details about the drug interactions associated with new antiretroviral agents (darunavir/ritonavir, etravirine, maraviroc and raltegravir) in two scenarios: when they are combined with one another or with drugs that are most commonly used for HIV-infected patients.

Methods

We performed a bibliographical search in PubMed of articles published in English and Spanish between January 2007 and September 2009 on interactions associated with new antiretroviral drugs in human beings. We considered full text articles which provided some information about darunavir, etravirine, maraviroc and raltegravir. We excluded references for new drugs that are yet to be marketed in Spain. This search was then complemented with information from the drugs' summary of product characteristics (SmPC) and we consulted web pages specialising in antiretroviral interactions: www.interaccioneshiv.com and www.hiv-druginteractions.org

New antiretroviral interactions with other drugs used for HIV-infected patients

Darunavir/ritonavir

Protease inhibitors

Lopinavir/ritonavir. Co-administration of this drug with darunavir/ritonavir reduces darunavir's area under the curve (AUC) by 40%. Therefore this co-administration is formally contraindicated.

Saquinavir/ritonavir. Co-administration of this drug with darunavir/ritonavir causes darunavir's AUC to decrease by 26%. This co-administration is therefore not recommended.

Indinavir/ritonavir. Co-administration of this drug with darunavir/ritonavir increases both drugs' AUC by 23% (It should be noted that this drug is currently in disuse due to its secondary effects and high number of tablets.) Therefore, indinavir dosage should be adjusted to 600mg/12hr in intolerant patients.

Atazanavir/ritonavir. Co-administration of this drug with darunavir/ritonavir does not produce any significant changes in both drugs' plasma concentrations. No dosage adjustments are required.

We did not find any studies on the remaining protease inhibitors.

Non-nucleoside reverse transcriptase inhibitors

Efavirenz. We found studies which show that when this drug is co-administered with darunavir/ritonavir efavirenz's AUC increases by 21% and darunavir's AUC reduces by 13%. Dosage adjustment is generally not required, but toxicity in the central nervous system should be monitored due to an increase in efavirenz plasma concentrations.

Nevirapine Co-administration of this drug with darunavir/ritonavir (study performed with a dose not used in clinical practice of 400mg/12hr) causes nevirapine's AUC to increase by 27%. However, it is not considered significant enough for recommending dosage adjustments in either of the two drugs.

Etravirine. Co-administration of darunavir/ritonavir with etravirine (at a dose not used in clinical practice of 100mg/12hr) causes etravirine's AUC to reduce by 37%. This reduction is not considered clinically significant and the efficacy of this combination is supported by DUET studies.

Nucleoside analogue reverse transcriptase inhibitors

Tenofovir. Co-administration of this drug with darunavir/ritonavir (at a darunavir dose not used in clinical practice of 300mg/12hr) causes tenofovir's AUC to increase by 22%. No adjustment dosage are required for either of the drugs, however, toxicity should be monitored in renal failure or if combined with nephrotoxic drugs.

Zidovudine, emtricitabine, stavudine, lamivudine, abacavir, didanosine. This group of drugs is mainly excreted by the kidney, meaning that no significant interactions are expected.

CCR5-receptor antagonists

Maraviroc. Co-administration of this drug with darunavir/ritonavir causes maraviroc's AUC to increase to 305%

meaning that the maraviroc dosage of 300 mg/ 12 hr should be modified to 150 mg/ 12 hr.

Fusion inhibitors
Enfuvirtide. The SmPC does not include any data related to darunavir. According to the University of Liverpool's antiretroviral interaction database, no changes are caused in any of the antiretroviral drugs, meaning that the dosage can be maintained for both antiretroviral drugs.

Integrase inhibitors
Raltegravir. The SmPC does not include any data related to darunavir. We collected data regarding a study on healthy volunteers from the University of Liverpool's antiretroviral interaction database.

Co-administration of this drug with darunavir/ritonavir causes raltegravir's AUC to decrease by 29%, the maximum concentration (Cmax) to decrease by 33%and the minimum concentration (Cmin) to increase by 21%. However, these changes are not considered significant and dose adjustments for either drug are not required.[13-15]

Etravirine

Protease inhibitors
Darunavir/ritonavir. Co-administration of this drug with etravirine causes darunavir's AUC to increase by 15%and etravirine's AUC to decrease by 37%. These plasma concentration changes are not considered clinically significant, meaning that dosage adjustments are not required.
Tipranavir/ritonavir. Co-administration of this drug with etravirine causes etravirine's AUC to decrease by 76% and tipranavir's AUC to increase by 18%, meaning that this combination is not recommended.
Fosamprenavir/ritonavir. Co-administration of this drug with etravirine causes fosamprevanir's AUC to increase by 69%. This combination should be administered with caution. We have found different data depending on the evaluation agency: the FDA considers it as a contraindicated combination; however the EMEA states they can be used together only when the fosamprenavir dose is reduced, however it does specify a recommended dosage in this case.
Atazanavir/ritonavir. Co-administration of this drug with etravirine causes etravirine's AUC to increase by 30%and atazanavir's AUC to decrease by 14%, and Cmin to decrease by 38%. Recommendations differ depending on the regulatory agency, as the FDA considers that this combination should be contraindicated, while the EMEA recommends that it is used without dosage adjustments.
Lopinavir/ritonavir. Combination of this drug with etravirine causes etravirine's AUC to increase by 17% and lopinavir's AUC to decrease by 20%. Recommendations differ depending on the regulatory agency, as the FDA considers that this combination should be indicated with caution, while the EMEA recommends that it is used without dosage adjustments.
Saquinavir/ritonavir. Co-administration of this drug with etravirine causes etravirine's AUC to decrease by 33%and saquinavir's AUC to decrease by 5%. Dosage adjustments are not considered necessary.

Non-nucleoside reverse transcriptase inhibitors
Co-administration of two non-nucleoside reverse transcriptase inhibitors is not currently justified in usual clinical practice.
Efavirenz. Co-administration of this drug with etravirine causes etravirine's AUC to decrease by 41%. This combination is not recommended.
Nevirapine. Co-administration of this drug with etravirine causes etravirine's AUC to increase by 55%. This combination is not recommended.

Nucleoside analogue reverse transcriptase inhibitors
Tenofovir. Co-administration of this drug with etravirine causes tenofovir's AUC to increase by 15%and etravirine's AUC to decrease by 19%. Dosage reduction is not recommended.
Didanosine. The co-administration of this drug with etravirine causes etravirine's AUC to increase by 15%. Dosage adjustment is not recommended.
Abacavir, emtricitabine, lamivudine, **stavudine, zidovudine.** No interactions are expected with etravirine. Dosage adjustments are not required.

CCR5-receptor antagonists
Maraviroc. Co-administration of this drug with etravirine causes maraviroc's AUC to decrease by 53%, meaning that the maraviroc dose should be adjusted to 600mg/ 12hr, except for patients treated with protease inhibitors or potent cytochrome-P450 inhibitors (consult maraviroc SmPC).

Fusion inhibitors
Enfuvirtide. No interactions are expected.

Integrase inhibitors
Raltegravir. Co-administration of this drug with etravirine reduces raltegravir's AUC by 10%and increases etravirine's AUC by 10%. Dose adjustments are not considered necessary for this combination.[16-20]

Maraviroc

Maraviroc dosage guidelines, in accordance with the accompanying drugs, are summarised in Figure 2.

Protease inhibitors
Darunavir, lopinavir, saquinavir, indinavir, atazanavir (ritonavir-boosted). Combination with any of these PI increases maraviroc's AUC by between 3.5 to 9 times, and its Cmax by between 2 to 4.7 times. Maraviroc dosage should be decreased to 150 mg/ 12 hr for all of these PI.
Fosamprenavir. We have only found population pharmacokinetics data (healthy volunteers). We have found different data depending on the regulatory agency. The FDA suggests maintaining the same dose as any other PI, i.e. 150 mg/ 12 hr. However, the EMEA considers maintaining dosage at 300 mg/ 12 hr.
Tipranavir. Co-administration of this drug with maraviroc caused maraviroc's AUC to increase by 2%and its Cmax to decrease by 14%. Recommendation in this case is to maintain dosage at 300 mg/ 12 hr.

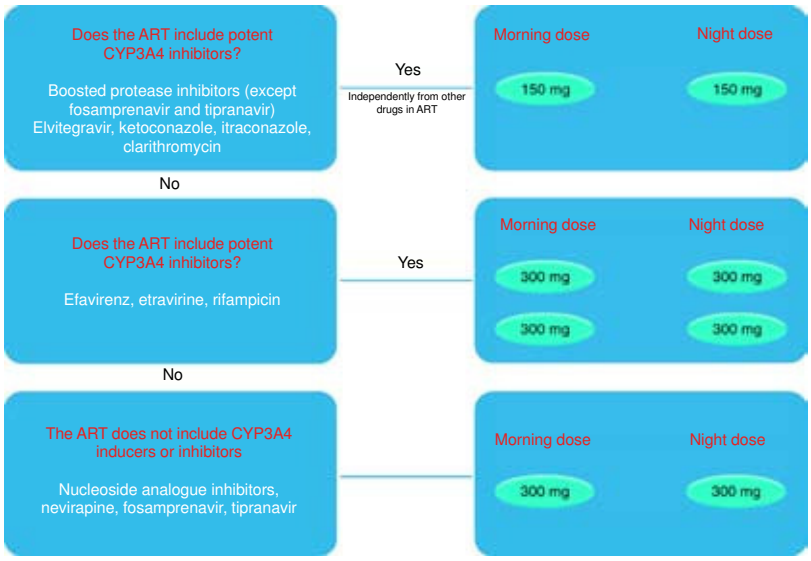

Figure 2 Summary for MARAVIROC dosage according to concomitant drugs.

Nucleoside analogue reverse transcriptase inhibitors
Lamivudine, tenofovir, zidovudine. The dosage of both these drugs is practically not modified, meaning that the recommendation is to maintain the usual dosage of 300 mg/ 12 hr (the accompanying drugs should be also taken into consideration).

Non-nucleoside reverse transcriptase inhibitors
Efavirenz. The co-administration of this drug with maraviroc causes maraviroc's AUC to decrease by 45%and its Cmax to decrease by 51% Therefore, when there are no potent cytochrome P450 inhibitors present, dosage should be increased to 600 mg/ 12 hr.
Etravirine Co-administration of this drug with maraviroc causes maraviroc's AUC to decrease by 53%and its Cmax to decrease by 60% Therefore, when there are no potent cytochrome P450 inhibitors present, dosage should be increased to 600 mg/ 12 hr.
Nevirapine No interactions between nevirapine and maraviroc are expected, therefore, maraviroc should be used at its usual dosage of 300 mg/ 12 hr, provided that it is not co-administered with potent cytochrome-P450 inhibitors.

Fusion inhibitors
Enfuvirtide. No interactions are expected. Dosage of 300 mg/ 12 hr should not be modified when potent cytochrome-P450 inhibitors are not present.

Integrase inhibitors
Raltegravir. No information is provided on the SmPC. Data have been extracted from a study on healthy volunteers cited in the University of Liverpool's antiretroviral interaction database. Co-administration of this drug with maraviroc reduced maraviroc's AUC to by 14%and its Cmax by 21%. It caused raltegravir's AUC to reduce by 37% and its Cmax to decrease by 33% Despite these data no dosage adjustments are required (300mg/ 12hr). When dosing maraviroc, not only raltegravir should be taken into consideration, but other antiretroviral drugs which are included in the ART.[16,17,21-23]

Raltegravir

Protease inhibitors
Darunavir. No information is provided on the SmPC. Data have been taken from the University of Liverpool's antiretroviral interaction database. Co-administration of this drug with raltegravir causes raltegravir's AUC to decrease by 29%and its Cmin increase by 38% However, dosage adjustments are not required.
Lopinavir. No information is provided on the SmPC. Data have been taken from the University of Liverpool's antiretroviral interaction database. Co-administration of this drug with raltegravir does not modify raltegravir's AUC or Cmax, but it does cause its Cmin to reduce by 30% However, dosage adjustments are not required.
Fosamprenavir, indinavir, saquinavir. No information is provided on the SmPC. Data have been taken from the University of Liverpool's antiretroviral interaction database. No interactions are expected. Dosage adjustments are not required.
Atazanavir. Co-administration of this drug with raltegravir increases raltegravir's AUC by 41% SmPC states that dosage adjustments are not required, but the main web pages recommend precaution with this co-administration.
Tipranavir. Combining this drug with raltegravir causes raltegravir's AUC to decrease by 24% The SmPC states that dosage adjustments are not required, but the main web pages recommend precaution with this co-administration.

Nucleoside analogue reverse transcriptase inhibitors

Tenofovir. Combining this drug with raltegravir causes an AUC increase of 49%. However, dosage adjustments are not required.

Abacavir, emtricitabine, lamivudine, stavudine, zidovudine, didanosine. No information is provided on the SmPC. Data have been taken from the University of Liverpool's antiretroviral interaction database. No interactions are expected, therefore, dosage adjustments are not required.

Non-nucleoside reverse transcriptase inhibitors

Efavirenz. Co-administration of this drug with raltegravir reduces raltegravir's AUC by 36%. Dosage adjustments are not required.

Nevirapine No information is provided on the SmPC and no interactions are expected, therefore dosage adjustments are not required.

Etravirine No information is provided on the SmPC. Data have been taken from the University of Liverpool's antiretroviral interaction database. Co-administration of this drug with raltegravir reduces raltegravir's AUC by 10% and increases etravirine's AUC by 10%. However, dosage adjustments are not required.

CCR5-receptor antagonists

Maraviroc. No information is provided on the SmPC. Data have been taken from the University of Liverpool's antiretroviral interaction database. Co-administration of this drug with raltegravir causes raltegravir's AUC to decrease by 37% and its Cmax to decrease by 33%. Furthermore, it causes maraviroc's AUC to decrease by 14% and its Cmax to decrease by 21%. However, dosage adjustments are not required for either drug.

Fusion inhibitors

Enfuvirtide. No interactions are expected. Dosage adjustments are not required.[16,17,24]

New antiretroviral interactions with therapeutic groups most frequently used for HIV-infected patients

Proton pump inhibitors and H2 antihistamines

Darunavir and lopinavir are the only PI that are completely exempt from interactions with proton pump inhibitors and H2 antihistamines. We should take precaution with the remaining PI (fosamprenavir, tipranavir, saquinavir, indinavir), as their plasma concentrations decrease. Proton pump inhibitors are totally contraindicated with atazanavir and nelfinavir, given that their plasma concentrations decrease dramatically.

There are no interactions with NNRTI (efavirenz, nevirapine, etravirine).

Maraviroc does not interact with CCR5-receptor antagonists.

There is a certain interaction with stomach protectors and raltegravir. In a study on healthy volunteers, with a single dosage of both drugs, raltegravir's AUC increased by 212% and its Cmax increased by 315%. Raltegravir can be used with medicinal products that increase gastric pH only if unavoidable, according to the EMEA SmPC recommendations. FDA does not make any recommendation.[16,17,25,26]

Antituberculosis drugs

Combination of any boosted PI with rifampicin is contraindicated, given that this drug could induce infra-therapeutic levels of the antiretroviral drug, with serious consequences for the patient.

Rifabutin is generally recommended to be used with a dosage of 150mg/48hr or 3 times a week. PI Dosage adjustments are not required in any case for the protease inhibitor.

With regard to NNRTI, co-administration of efavirenz with rifampicin produces a decrease of efavirenz's plasma concentrations: AUC by 26%, Cmax by 32% and Cmin by 32%. Rifampicin should be administered 600 mg/day or three times a week and efavirenz at the standard dosage or 800 mg/day in patients weighing more than 50 kg. Rifabutin combined with efavirenz reduces rifabutin's AUC by 35% and there is very little clinical experience with this combination, meaning that it is not recommended.

On the other hand, co-administration of nevirapine and etravirine with rifampicin is not recommended as plasma concentrations decrease, and in some cases mortality is increased. Rifabutin is therefore the recommended antituberculosis drug, and dosage adjustments are not required in any case.

Co-administration of CCR5-receptor antagonists (maraviroc) with antituberculosis drugs (rifampicin or rifabutin) causes maraviroc's plasma concentrations to decrease significantly. Therefore, when there are no potent cytochrome-P3A4 inhibitors present, maraviroc dosage should be increased to 600 mg/12 hr.

Lastly, the co-administration of integrase inhibitors with rifampicin causes raltegravir's Cmax, AUC and Cmin to significantly decrease by 38%, 40% and 61%, respectively. An increase in raltegravir dosage to 800mg/12hr should be assessed. One of the review articles considers that this co-administration should be contraindicated. Dosage adjustment would not be necessary with rifabutin.[15-17,19,23,24,27]

Statins

Co-administration of PI with simvastatin and lovastatin is contraindicated due to severe toxicity.

General recommendation is to use fluvastatin or pravastatin (taking precaution with darunavir/ritonavir, given that pravastatin's AUC increases. Treatment should be initiated at low doses, gradually increasing it.)

Pravastatin is recommended for NNRTI, including etravirine.

No significant interactions are expected for the remaining new antiretroviral drugs (maraviroc and raltegravir).[28]

Methadone

Most protease inhibitors slightly reduce methadone concentrations, by around 20%. Precaution should be taken

with lopinavir/ritonavir and with tipranavir/ritonavir in case methadone dosage needs to be increased. Reductions in methadone AUC to 50% have been reported.

First-generation non-nucleoside inhibitors cause methadone's AUC to significantly decrease by approximately 50%, and abstinence syndrome can appear during the first 4-10 days. However, etravirine does not interact with methadone.[16,17]

No interactions are expected with maraviroc and raltegravir.

Antifungal drugs

Darunavir's interactions with antifungal drugs are the same as its therapeutic group representatives. Co-administration of PI with amphotericin B seems to be safe, given that there are no significant interactions. However, there are no specific studies on darunavir and atazanavir. There are no interactions between PI and fluconazole, except with tipranavir/r. When co-administered with fluconazole, tipranavir's Cmin can double. Therefore, dosage should not exceed 200 mg/day. Co-administration of PI with itraconazole and ketoconazole increases the antifungal drug's plasma concentrations. Dosage should therefore not exceed 200 mg/day.

Any voriconazole-boosted PI is considered contraindicated because the antifungal drug's concentrations are reduced significantly (approximately 40%).

Etravirine has the same antifungal interactions as the other non-nucleoside inhibitors (NNRTI). Amphotericin B with NNRTI is a safe combination: there are no clinically significant interactions.

NNRTI with ketoconazole or itraconazole is contraindicated because the antifungal drug's plasma concentrations are significantly reduced, approximately by 50%.

The maintenance dose of caspofungin should be increased to 70 mg/day for co-administration of NNRTI and caspofungin, given that caspofungin's plasma concentrations are decreased by being associated with non-analogue inhibitors.

There are no studies on the effect of voriconazole with nevirapine, therefore it is contraindicated.

Efavirenz used with voriconazole: the voriconazole maintenance dose should be adjusted to 400 mg/12 hr and efavirenz's dose reduced to 300 mg/day.

Co-administration of etravirine and voriconazole is not recommended as no clinical tests have been performed with this combination.

Maraviroc has potential interactions with itraconazole, voriconazole and ketoconazole, which could increase maraviroc's plasma concentrations (dosage adjustment to 150 mg/12 hr). Antifungal dosage adjustments are not required.

There are no data provided for other antifungal drugs.

Raltegravir does not have any clinically significant interactions with fluconazole, ketoconazole, itraconazole and voriconazole, however, there are no data provided for caspofungin and amphotericin B.[16,17,29]

Hormonal contraceptives

Barrier contraceptives are the general recommendation.

Ethinylestradiol is contraindicated with PI given that the contraceptive's plasma concentrations are significantly reduced.

First-generation non-nucleoside inhibitors also have a significant interaction with ethinylestradiol. Only etravirine can be administered with reasonable safety, given that no clinically significant interactions exist.

No significant interactions are produced when maraviroc and raltegravir are co-administered with ethinylestradiol.

Medroxyprogesterone is the only contraceptive that does not produce interactions when co-administered with antiretroviral agents.[16,17]

H1N1 antiviral drugs

The safest antiviral drug to co-administer with antiretroviral drugs is intranasal zanamivir. However, caution should be taken when administering oseltamivir with PI given the increased risk of neurotoxicity; and with lamivudine, emtricitabine and tenofovir given their competition in renal excretion.[17]

Discussion

Antiretroviral drug interactions are common and can be clinically significant. Interactions can potentially occur between antiretroviral drugs and with other drugs used to treat other disorders, to prevent or treat opportunist diseases and other problems related with antiretroviral drugs' adverse effects. The development of new drugs such as darunavir, etravirine, maraviroc and raltegravir means that we have to continuously be alert when searching for information, given that new mechanisms of action may result in unpredictable results. The hospital pharmacist should know the pharmacological profile of new antiretroviral drugs so as to provide quality pharmaceutical care. Antiretroviral interactions databases (www.interaccioneshiv.com, www.hiv-druginteractions.org) and the summary of product characteristics should be used in day-to-day practice when searching for these drugs. The hospital pharmacist needs to be actively involved in this subject.

Conflict of interest

The author affirms having no conflict of interest.

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