

Pharmacokinetic Enhancers (Cobicistat/Ritonavir) And The Potential For Drug-Drug Interactions (An Audit Of Patients Attending A Busy Outpatient HIV Service)

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INTRODUCTION

With the significant advances made in HIV treatment patients are now living longer with a manageable chronic disease. As the HIV positive population age they are succumbing to diseases of old age which often require pharmaceutical intervention. HIV appears to accelerate the aging process, increasing the incidence of frailty and comorbidities.¹ The resultant polypharmacy puts this patient cohort at risk of drug-drug interactions. In addition to prescribed medication patients frequently take natural health remedies and supplements² which can also potentially interact. Clinically significant drug interactions (CSDIs) have been observed in 27% to 40% of patients^{3,4} on antiretrovirals. Independent risk factors for CSDIs have been associated with the use of Protease inhibitors (PIs), number of concomitant medications and recreational drug use.

AIM

An audit was conducted on patients receiving ritonavir and cobicistat, as these are potent CYP 3A4 inhibitors, to ensure this patient cohort was not unnecessarily exposed to potential drug toxicities as a consequence of a CSDI.

METHODS

This study included all patients attending the Infectious Diseases clinic in Beaumont Hospital, Dublin, Ireland who were prescribed the pharmacokinetic enhancer ritonavir or cobicistat. (See Table 1 for patient characteristics.) The clinic primarily treats patients living with HIV with 450 patients currently on antiretroviral therapy (ART). All ART is dispensed by the ID specialist pharmacist from the pharmacy located in the clinic. Each patients demographics, medications prescribed by the ID doctors (ART, anti-infectives for the prophylaxis and treatment of opportunistic infections, lipid lowering medication), medications prescribed by the patients general practitioner, over the counter medications the patients were using, herbal products, supplements, medication ordered on the internet and any recreational medications the patients were taking were collected on a specifically designed data collection sheet. (See Figure 2 for source of comedication.) This record was then compared to the medical notes from their most recent visit to the clinic to determine if these comedications were previously documented.

A colour coded system of red, orange and green were applied to the concomitant medications. (See Figure 3)

- Red indicating medications that should not be coadministered as the combination results in a significant risk to the patient from toxic levels of the co-prescribed medicine or by significantly reducing the antiviral making it subtherapeutic

- Orange indicating a potential interaction that may require close monitoring, alteration of drug dosage or timing of administration
- Green which indicates that no clinically significant interaction is expected.

RESULTS

Table 1 Characteristics of Patients enrolled in audit

Characteristic	N=200	Percentage
Median Age(Range)	41.5(23-76)	
Less Than 50 Years Old	162	81%
Female gender	128	64%
Male gender	72	36%
Irish	77	38.5%
Eastern European	9	4.5%
African	110	55%
Other	4	2%
Recreational Drug Use	14	7%
Antiretrovirals		
Tenofovir in backbone	169	84.5%
Atazanavir	99	49.5%
Darunavir	52	26%
Lopinavir	42	21%
Elvitegravir/cobicistat	7	3.5%
Comedication		
No comedication	27	13.5%
1 comedication	41	20.5%
2 comedications	43	21.5%
3 comedications	36	18%
4 comedications	25	12.5%
5 or more comedications	28	14%
Total	200	100%

Figure 1 Distribution of CSDIs

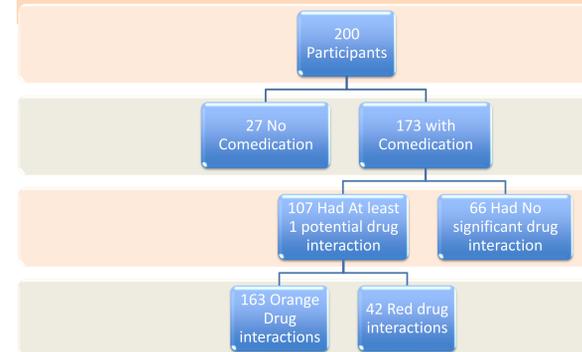


Figure 2 Source of comedication

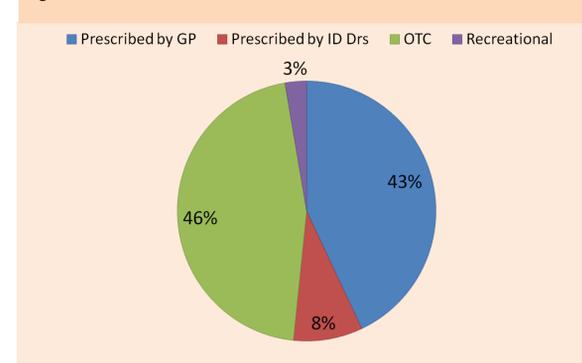
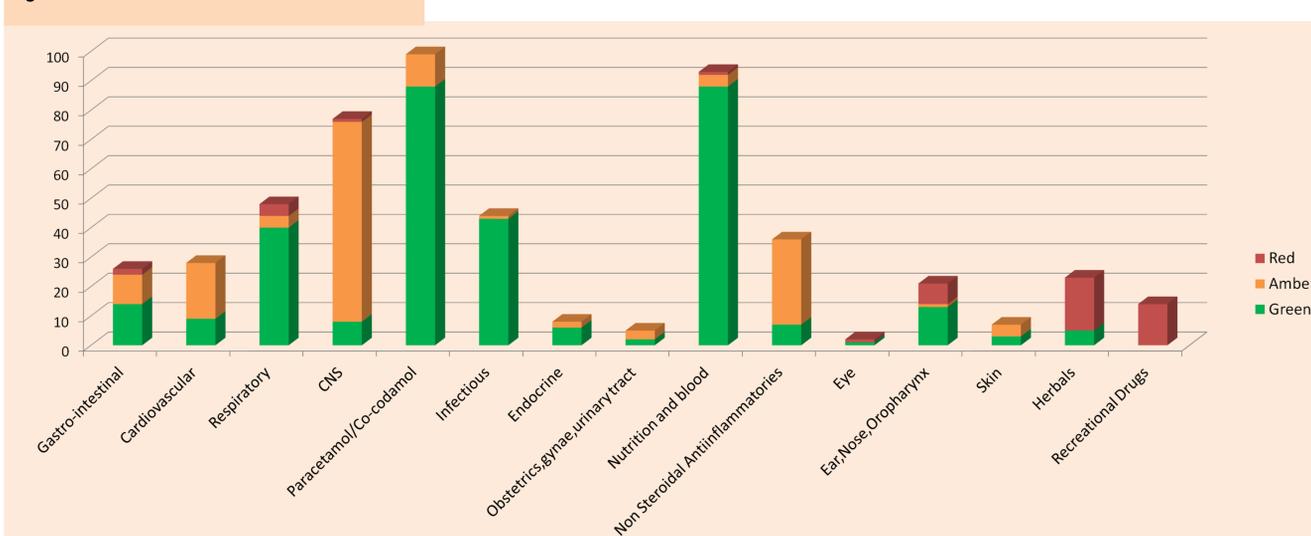


Figure 3 Medicines identified in audit



Of the 173 patients who admitted to taking a comedication, 66 of whom were taking a medication or medications which had no significant drug interaction associated with them. 107 patients had at least one medication which had an interaction which could potentially require a dose adjustment, close monitoring or a recommendation that these agents should not be coadministered. (Figure 1) Only 27 % of these comedications were identified in the normal course of an outpatient visit.

CONCLUSION

Some of the measures we have taken to increase awareness of these interactions and the need for vigilance include regular updates at our team clinical meetings with case presentations and reminders to team Drs to perform a full medication history with each patient. All letters to GPs have a comprehensive footnote highlighting some of the more common and troublesome interactions (steroid inhalers and nasal sprays, statins, PPIs and NSAIDs) and a link to the Liverpools HIV drug interaction website. A list of medications which are regularly prescribed in GP clinics and which are safe to take while on antiretrovirals has been provided to patients GPs or directly to patients in the case of patients who do not wish their GP to know of their HIV status or those who do not have a regular GP.

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