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Potential or Contraindicated Drug-Drug Interactions with Antiretroviral Therapy in Taiwanese Patients

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Abstract

The innovative drug development of antiretroviral therapy (ART) has significantly improved the life expectancy of patients with human immunodeficiency virus (HIV) significant increase in the number of elderly individuals with HIV has been observed [1-15]. The complexity of ageing, HIV infection, and ART exposure may alter the risk of comorbid conditions such as cardiovascular disease, metabolic syndromes, or mental disorders in these HIV-infected individuals.As a result, medications were prescribed to address unfavourable comorbidities. Concomitant medications, on the other hand, may contribute to pill burden and drug-drug interactions (DDIs) in the HIV-infected population.

DDIs should be monitored in HIV patients because they can alter the effectiveness and safety of ART or other medications, resulting in negative clinical outcomes. Increased drug exposure of HIV/non-HIV medications may result in unwanted side effects. 5 Subtherapeutic drug concentrations associated with a DDI, on the other hand, may result in the rebound of plasma HIV RNA and ART drug resistance.

Introduction

To our knowledge, the DDI profiles during ART exposure have not been thoroughly addressed in Taiwan. A better understanding of the DDI profiles could aid clinicians in selecting the best ART for patients. Furthermore, patients with DDIs had significantly higher health-care costs than those without DDIs. 11 A thorough examination of DDIs is required to improve medical care for HIV patients while reducing the government's financial burden. As a result, the following are the study's two major objectives to investigate the profiles of comorbidities and comedications among HIV-infected patients stratified by DDI status, and to document the frequency of contraindicated and potential DDIs with recommended 1L-ART and PIs in real-world settings. among The data for this study came from the Health and Welfare Database, which contained all claims data from Taiwan's National Health Insurance (NHI) programme. The NHI programme began in 1995, with a coverage rate of more than 99.9%. 12 In 2019, the programme served approximately 24 million beneficiaries. 12 Data from 2016 was used as the source. Because the patient identification numbers in the database were encrypted and de identified, the Research Ethics Committee of National Taiwan University Hospital waived informed consent and approved the study through expedited review (IRB/REC number: 201802027RIFA). Diagnoses were identified using International Classification of Diseases, Ninth or Tenth Revision, Clinical Modification (ICD-9-CM, ICD-10-CM) codes. The Anatomical Therapeutic Chemical Recognition System was used to identify medications.

Subjective Heading

This study included HIV patients diagnosed between January 1, 2016, and December 31, 2016. HIV patients were those who had at least one inpatient diagnosis or two separate outpatient diagnoses ([ICD-9-CM code]: 042, V08; [ICD-10-CM code]: B20, Z21). Between the two subsequent HIV outpatient diagnoses, at least one examination for CD4 count or viral load ([procedure code]: 12073B, 14074B) was required to confirm the HIV diagnosis further.

In 2016, HIV-infected patients were included in this cross-sectional study. Tenofovir/emtricitabine/efavirenz (TDF/FTC/EFV), TDF/FTC/rilpivirine (TDF/FTC/RPV), and abacavir/lamivudine/dolutegravir (ABC/3TC/DTG) were licenced in Taiwan in June 2010, October 2015, and July 2015, respectively, to ensure a comparable starting point for novel STRs. Because it was not licenced until January 2017, the other STR, elvitegravir/cobicistat/FTC/TDF, was not included in this analysis. Separate studies were conducted on DDIs with the recommended 1L-ART (TDF/FTC/EFV, TDF/FTC/RPV, and ABC/3TC/DTG) and PIs (atazanavir (ATV), ATV + ritonavir (r), darunavir (DRV) + r, and lopinavir (LPV)/r). Atazanavir 200 mg was used as a stand-in for the "ATV alone" group, while atazanavir 150 mg was used in place of the "ATV + r" group. Because ritonavir is frequently used to boost other PIs,

Discussion

First, each HIV-infected patient's antiretroviral therapy exposure period was determined. The index date was the first 1L-ART or PI prescription since January 1, 2016. The ART-exposed period lasted from the index date to the first of the following events, whichever occurred first: discontinuation, death, or the end of the study (December 31, 2016). A 14-day gap between the end of a day's supply and the start of the next prescription was defined as discontinuation. Patients could be included in more than one ART group as long as they were exposed to the specific ART of interest to better outline the real-life circumstances.

Second, using the University of Liverpool drug interaction database, the comedications that could cause contraindicated or potential DDIs with the ART of interest were identified. 13 The Liverpool drug interaction database made interactive charts available for assessing the

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risk of DDIs between HIV/HIV and HIV/non-HIV medications. Icons were used to categorise the severity of the interactions. Only red and amber icons, representing contraindicated and potential DDIs, were estimated in this study. The DDIs were defined as having used systemic medications at least once during the ART-exposed period. Even if a person had multiple prescriptions for the same DDI pair, each person would only be calculated once. For each drug pair and ART of interest, the frequency was estimated.

Finally, we classified patients based on their DDI status and examined their baseline characteristics. Patients with potential or contraindicated DDIs were assigned to the "with DDI" group, while everyone else was assigned to the "without DDI" group. Age, gender, comorbid conditions, and concomitant medications were the variables of interest. The total number of comorbidities and medications was also added together as two independent variables. Among the comorbidities were cerebro cardiovascular diseases, metabolic syndromes, respiratory disease, liver disease, renal failure, psychiatric disease, and cancer. In 2016, comorbidities were defined by at least one inpatient record or two separate outpatient records. The co medications were made up of various medication classes, such as glucose-lowering agents, cardiovascular agents, central nervous system agents, gastrointestinal agents, and anti-infectives. Concurrent medications were identified in at least one prescription.

To see if the categorical variables were significant, the chi-square test was used. Instead, if more than 20% of the cells in the table had an expected value of less than five, Fisher's exact test was used. A 2-sided p-value of 0.05 was used to determine whether there were significant differences between patients with and without DDIs. According to the Health Data Research Center, Department of Statistics, Ministry of Health and Welfare of Taiwan, a cell size less than five is represented as "5". SAS version 9.4 was used for all statistical procedures (SAS Institute Inc., Cary, NC, USA). A total of 25,863 HIV-infected people were identified; 92 percent of them were men, with a mean age of 39. There were 5877 TDF/FTC/EFV users, 3519 TDF/FTC/RPV users, and 2517 ABC/3TC/DTG users among 1L-ART patients. We identified 2314 ATV users, 656 ATV + r users, 1291 DRV + r users, and 3440 LPV/r users among PI users.

Table 1 shows the number of patients divided by the number of contraindicated or potential DDIs. Patients with contraindicated DDIs were most frequently observed among 1L-ART users with TDF/FTC/RPV (4%) followed by TDF/FTC/EFV (2%) and ABC/3TC/DTG (1%). (1 percent). Patients with potential DDIs were more prevalent in those who received TDF/FTC/EFV (50%) than in those who received TDF/FTC/RPV (32%). (15 percent). Patients who were prescribed various types of PIs, on the other hand, were processed. A similar trend was discovered among those with potential DDIs: ATV alone (50 percent), ATV + r (48 percent), DRV + r (48 percent), and LPV/r (48 percent) (44 percent). Patients with more than three potential DDIs had the highest frequency among ATV + r users (19%), followed by ATV users (17%), DRV + r users (13%), and LPV/r users (7%). (12 percent). Supplemental Tables 1-4 show the detailed frequencies of contraindicated or potential DDI pairs. Because a single patient may contribute more than one DDI pair, the total number of DDI pairs may exceed the number of 1L-ART or PI users.

presents the top three most commonly observed comedications that lead to contraindications and potential DDIs. Midazolam (2 percent of TDF/FTC/EFV users) and dexamethasone (1 percent of TDF/FTC/RPV users) were the most commonly coadministered medications for contraindicated DDIs among 1L-ART users. Diclofenac (13 percent of TDF/FTC/EFV users and 11 percent of TDF/FTC/RPV users) and polyvalent cation-containing antacids (12 percent of ABC/3TC/DTG users) were the most frequently coprescribed medications related to potential DDIs. Domperidone (3-4%) was the most commonly coadministered contraindicated medication for all of the protease inhibitors of interest, followed by quetiapine (2%) and midazolam (1%). (1–2 percent). The medications that were most frequently associated with potential DDIs with PIs were zolpidem, betamethasone, polyvalent cation-containing antacids, and loperamide..

Conclusion

The baseline characteristics of patients receiving 1L-ART are shown, stratified by DDI status. Patients with DDIs were more likely to be female and to have more comorbidities and polypharmacy than patients without DDIs, regardless of which 1L-ART groups were included. Similarly, Table 4 shows the baseline characteristics of patients prescribed PIs based on their DDI status. Patients with DDIs were also more likely to be elderly, to have multiple comorbidities, and to be on multiple medications. Supplemental Tables 5 and 6 provide detailed comorbidities and medications stratified by DDI status. Psychiatric disease and liver disease were the most common conditions across all groups among the selected comorbidities. The most commonly prescribed medications for all patients were anxiolytics, hypnotic agents, and gastrointestinal agents.

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Conflict of Interest

The authors declare that they are no conflict of interest.

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