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EVALUATING THE IATROGENIC EFFECTS OF POLYPHARMACY AND DRUG INTERACTIONS IN HIV-POSITIVE PATIENTS ADMITTED TO THE INTENSIVE CARE UNIT: A SINGLE-CENTER RETROSPECTIVE STUDY

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Abstract. *Background.* Polypharmacy and drug interactions are of particular concern in people living with HIV/AIDS, especially those who receive antiretroviral therapy (ARVs). Polypharmacy and drug-drug interactions (DDIs) can impact the efficacy and toxicity of HIV treatment. ARVs used in HIV treatment are often prone to drug interactions if administered with other non-ARV drugs because many of them are metabolized through the cytochrome P450 system. The pharmacological management of HIV patients in the intensive care unit (ICU) is usually complex and typically involves the administration of several classes of drugs. This patient group may be at higher risk for potential DDIs due to polypharmacy in the ICU. The main objective of this study was to assess the iatrogenic effects of polypharmacy in HIV patients treated in the ICU and to describe the DDI profile between ARVs and other non-ARV medications prescribed in the ICU. *Methods and materials.* Between 2018 and 2020, we conducted a single-center, retrospective study evaluating the medical records of 59 HIV patients admitted to the ICU for more than 24 hours at the Infectious Disease Clinical Hospital No. 2, Moscow, Russia. We evaluated the impact of polypharmacy on renal, hepatic and haemopoietic function. The Liverpool HIV Drug Interaction database was used to identify DDIs in ART-treated HIV patients. *Results.* All patients received more than 5 different medications matching the definition of polypharmacy. The average number of concurrent medications prescribed was 15±6.713 (maximum — 40, minimum — 6). All drug interactions recorded were between ARVs and antibiotics: 30 cases of potential interactions in 65.5% patients who received ARV. Of such patients, 94% were exposed to at least two potential interactions. Tenofovir (TDF) and the antibiotic vancomycin underlaid the most common potential interaction (49.2%), followed by lopinavir ritonavir (LPV/RTV) and ciprofloxacin (30.3%). A significant difference in average creatinine levels was found in patients with TDF/vancomycin potential interactions ($p < 0.05$). *Conclusion*. This study demonstrated that potential DDIs frequently occur in ICU patients in line with previous investigations. It is necessary to implement collaborations among clinical pharmacologists and infectious disease/HIV specialists, as well as frequent clinical and laboratory monitoring, aimed at developing effective and actionable strategies that could reduce potential DDIs in HIV patients in the ICU.

Key words: *HIV infection, acquired immunodeficiency syndrome, polypharmacy, medications, drug-drug interactions, intensive care unit.*

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ОЦЕНКА ЯТРОГЕННЫХ ЭФФЕКТОВ ПОЛИПРАГМАЗИИ И ЛЕКАРСТВЕННЫХ ВЗАИМОДЕЙСТВИЙ У БОЛЬНЫХ ВИЧ-ИНФЕКЦИЕЙ В ОТДЕЛЕНИИ ИНТЕНСИВНОЙ ТЕРАПИИ: ОДНОЦЕНТРОВОЕ РЕТРОСПЕКТИВНОЕ ИССЛЕДОВАНИЕ

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Резюме. *Введение.* Полипрагмазия и лекарственные взаимодействия вызывают особую озабоченность у людей, живущих с ВИЧ, особенно у тех, кто получает антиретровирусные препараты (АРВП). Полипрагмазия и лекарственные взаимодействия могут влиять на эффективность и безопасность антиретровирусной терапии. АРВП часто вступают во взаимодействие с другими лекарственными средствами, поскольку многие из них метаболизируются через систему цитохрома P450. Фармакотерапия ВИЧ- инфицированных пациентов в отделении интенсивной терапии (ОИТ) обычно включает введение нескольких классов препаратов. Такая группа пациентов может подвергаться более высокому риску потенциального межлекарственного взаимодействия. Целью исследования была оценка ятрогенных эффектов полипрагмазии у ВИЧ-инфицированных пациентов, госпитализированных в ОИТ инфекционного стационара, и описание профиля лекарственных взаимодействий между АРВП и другими классами препаратов, назначаемыми в ОИТ. *Материалы и методы.* Проведено ретроспективное исследование историй болезни 59 ВИЧ-инфицированных пациентов, находившихся в ОИТ более 24 часов в 2018–2020 гг. в ГБУЗ ИКБ № 2 ДЗМ. Оценивалось влияние полипрагмазии на почечную, печеночную и кроветворную функции. Использовался онлайн-сервис «Ливерпульская база данных (Liverpool HIV Drug Interaction database)» для выявления различных межлекарственных взаимодействий возможных при терапии ВИЧ/СПИДа. *Результаты.* Все пациенты получали более 5 различных препаратов, что соответствуют определению полипрагмазии. Среднее количество одновременно назначаемых препаратов составило 15±6,713, максимум 40, минимум 6. Все зарегистрированные лекарственные взаимодействия были между АРВП и антибактериальными препаратами: зафиксировано 30 случаев потенциальных взаимодействий у 65,5% пациентов, получавших АРВП. 94% из этих пациентов подвергались как минимум двум потенциальным взаимодействиям. Сочетание тенофовира (TDF) и ванкомицина было наиболее частым зарегистрированным потенциальным взаимодействием (49,2%), за ним следовали лопинавир/ритонавир (LPV/r) и ципрофлоксацин (30,3%). Средние значение показателя креатинина было выше у пациентов, у которых наблюдалось потенциальное взаимодействие TDF и ванкомицина (345,7±45,2 ммоль/л), чем у тех пациентов, которые не получали TDF и ванкомицин (107,5±33,5 ммоль/л), $p < 0,05$. *Выводы.* Это исследование продемонстрировало, что потенциальные лекарственные взаимодействия часто возникают у ВИЧ-инфицированных пациентов в отделении интенсивной терапии, как сообщалось в других исследованиях. Необходимо осуществлять сотрудничество между клиническим фармакологом и врачом-инфекционистом, а также регулярный клинико-лабораторный мониторинг для разработки эффективных и действенных стратегий с целью снижения рисков межлекарственных взаимодействий у ВИЧ-инфицированных пациентов, получающих лечение в ОИТ.

Ключевые слова: *ВИЧ-инфекция, синдром приобретенного иммунодефицита, полипрагмазия, лекарственные препараты, лекарственные взаимодействия, отделение интенсивной терапии.*

Introduction

Polypharmacy refers to the use of multiple medications in a patient. Numerically or based on the number of medications prescribed, there is no universally agreed definition of polypharmacy, however it can be described in three groups: excessive polypharmacy (use of 10 or more different drugs); polypharmacy (use of 5 to 9 different drugs); and no polypharmacy (use of 0 to 4 different drugs). The use of multiple medications can have a negative effect of treatment and medication adherence. One challenge associated with polypharmacy is drug-drug interaction, which is often a serious complication of taking multiple medications; it accounts for 3% to 5% of all in-hospital medication errors [1]. The consequences of drug interactions vary, ranging from drug toxicities to a reduction in therapeutic effects. These consequences could lead to inadequate treatment of the targeted disease, damage to vital organ systems, or death.

Polypharmacy and drug interactions are of particular concern in people living with HIV/AIDS (PLWHA), especially those who are receiving antiretroviral therapy (ARVs), though ARV naïve patients are also at risk for polypharmacy and drug interactions. PLWHA from regions with low antiretroviral therapy coverage due to limited resources may not achieve sustained viral suppression, putting them at risk for episodic illnesses, hospitalization, or ICU admission with severe forms of disease. Such events would subsequently lead to indiscriminate and uncontrolled use of medication, polypharmacy, and drug-interactions. Polypharmacy and drug-drug in-

teractions (DDIs) can impact the efficacy and toxicity of HIV treatment.

ARVs used in the treatment of HIV are often prone to drug interactions if administered with other non-antiretroviral drugs because many of them are metabolized through enzyme-catalyzed processes. Antiretroviral therapy and other medical therapies for HIV-related infections have been associated with toxicities. Antiretroviral therapy can contribute to renal dysfunction directly by inducing acute tubular necrosis, acute interstitial nephritis, crystal nephropathy, or renal tubular disorders. They can also occur indirectly via drug interactions. The most well-recognized DDI mechanism is that many ARVs, especially pharmacologic boosters (ritonavir) frequently lead to significant drug interactions since they may affect the drug-metabolizing enzyme system or drug transporters as inhibitors. Medications used to treat comorbidities or co-infections, various supplements, and legal or illegal drugs that inhibit or induce the drug-metabolizing enzyme system can lead to organ damage and toxicity to the human body [1].

Persons with end stage HIV/AIDS are considered critically ill and are frequently admitted (ICU). The pharmacological management of these patients is usually complex and typically involves the administration of multiple drugs of different pharmacological classes due to life threatening illnesses which may be fatal. HIV patients treated at the ICU may also be at higher risk for DDIs due to polypharmacy. In the ICU, most patients with end stage HIV/AIDS present with HIV-related cachexia. Altered body composition and plasma protein concentration may affect drug distribution and induce drug toxicity in these patients [2, 3, 4, 9, 11, 17]. Other factors like prolonged intensive care unit length of stay, age, and death outcome are associated with increased medication administration. Studying the prescription patterns of ICU patients can clarify drug usage patterns in this setting; this is essential for creating favorable conditions for wide scale improvements in therapeutic practices.

To our knowledge, a study that evaluates polypharmacy and drug interactions in people living with HIV/AIDS and the impact on organ functions has never been conducted in Russia. Therefore, the main objectives of this study were: to assess the iatrogenic effects of polypharmacy in HIV patients treated in the ICU; to describe the DDI profile between antiretrovirals (ARVs) and other medications prescribed in the ICU, while evaluating their prevalence; and to classify DDIs as clinically or potentially significant [6, 14, 15, 16].

Materials and methods

A retrospective study was conducted from 2018 to 2020 at the Infectious Disease Clinical Hospital No. 2, Moscow, Russia. We evaluated the medical records of 59 HIV patients who were admitted to the intensive Care Unit (ICU). HIV patients were included in this study: of either sex; older than 18 years; admitted to the ICU for more than 24 hours; and with patients (or their relatives) willing to give informed consent. All patients in the study group received more than 5 medications during ICU stay. Therefore, using the definition of polypharmacy presented in the introduction, patients were divided into two groups according to the number of drugs received. The first group included patients who received five to nine medication (≤ 9 medications), which was considered "polypharmacy". The second group included patients who received ten or more medications (> 9 medications), which was considered "excess polypharmacy".

This design was implemented to assess the impact of the number of drugs prescribed on organ function. We evaluated renal, hepatic, and haemopoietic function taking the mean values of urea, creatinine, liver enzymes, bilirubin, erythrocytes, along with WBC and platelet counts during ICU stay into consideration. Qualitative and quantitative data are expressed with mean±standard deviation (SD). The two-tailed Fisher's exact chi-square test was used to evaluate differences between groups, and results with $p < 0.05$ were considered statistically significant.

Identification of potential and clinically significant drug–drug interactions using the Liverpool HIV drug interaction database. The comprehensive University of Liverpool HIV drug interactions database, which accumulates published findings mainly from various studies, was used to determine drug-drug interaction (DDI) among HIV patients on ART. Two levels of interaction between ARVs and non-ARVs were considered in our study: 1) clinically significant drug-drug interactions revealing contraindicated combinations which could potentially leading to serious adverse events or impaired efficacy; and 2) potential drug-drug interactions wherein patients might require dosage adjustment, close monitoring, or timing-of-administration modification to minimize possible clinical consequences.

Results

We retrospectively reviewed the case records of 59 HIV patients admitted to the ICU. Of them, 74.5% (44) were male, and 25.42% were female (15), with a mean age of 47 (SD±10.7) years. Most patients (81.5%) were diagnosed at HIV stage 4B according to V.I. Pokrovsky's clinical classification of HIV infection (equivalent to CDC category C). The median duration of HIV infection was 8.4 years (IQR 3.5–10.2 years). Their median CD4 count and viral load was 100 cells/mm^3 (IQR: 10–250) and 100 000 copies/ml (IQR: 50 000–500 000), respectively. Thirty patients (51%) were ART treatment naive without valid reasons. Most patients were admitted for *Staphylococcus aureus* bacteremia (44.70%) or infective endocarditis (23.42%). Chronic hepatitis B

Table 1. Comparison between polypharmacy status and demographic and patient clinical data (n = 59)

Variable	≤ 9 medications (n = 38)	> 9 medications (n = 21)	P value
Male	31	13	0.31
Female	7	8	0.7
Age	48±11.7	44±10.2	0.65
Length of ICU stay	8±8.4	6±9.7	0.88
Deaths	33	14	0.70

and C were the prevailing comorbidities, identified in 35% and 32% of patients respectively, but all patients were considered inactive carriers.

The total number of prescription drugs in the 59 records studied was 723 drugs. Out of 723 prescription drugs, 340 were injectable drugs. The first group had 38 patients with ≤ 9 medications (7.1±1.292). The remaining 21 patients received > 9 medications (17.58±9.343) and were in the second group. The maximum number of prescribed drugs was 40 (minimum 6). There was no statistically significant relationship between the number of drugs prescribed and gender, age, the length of ICU stay, or death outcome (Table 1). Our study also revealed no significant statistical difference between mean values of renal, hepatic or haemopoietic function, and the number of drugs prescribed (Table 2).

The most common non-ARV drugs used in the ICU were antibiotics (100%), antipyretics (99.21%), and antimycotics (88.71%). Among antibiotics, quinolones were most commonly used (79.13%), followed by nitroimidazole (61.25%). The University of Liverpool HIV drug interactions database indicated no cases of clinically significant interaction, but revealed cases of potential interactions among patients who received ARVs (all drug interactions recorded where between ARVs and antibiotics). We recorded 30 cases of potential interactions (Fig.) in 65.5% (19 out of 29) patients who received ARVs. Of these patients, 94% (18) were exposed to at least two potential interactions. The ARV Tenofovir (TDF) most frequently interacted with the antibiotic vancomycin (49.2%), followed by lopinavir/ritonavir (LPV/RTV) and ciprofloxacin (30.3%).

In addition, we investigated the impact of these potential interactions on organ function, revealing a significant difference in average creatinine levels in patients who had TDF/Vancomycin interactions and patients without such interactions during ICU stay (Table 3). After further investigation of the group of patients with TDF/Vancomycin interactions, we found no statistically significant relationship between changes in average creatinine levels and demographic/clinical information including comorbidities.

Discussion

The intensive care unit is considered one of the most neglected departments with respect to drug utilization studies, yet polypharmacy and drug-drug interactions are more common in the ICU [5]. This study was intended to investigate the impact of drug interactions and polypharmacy in HIV patients admitted to the ICU. Previous studies on the subject have demonstrated not only a prevalence of drug-drug interactions with antiretrovirals in HIV outpatients, but also in HIV patients in the intensive care unit [7, 10, 12, 13, 18]. Most studies have revealed that analgesics were the most common ICU medications with ART-related potential DDIs. Our study revealed that antibiotics frequently interacted with antiretrovirals. The basis for a high prevalence of antibiotics in our study was due to a high incidence of bacterial infections in the HIV patients admitted to the ICU. In this study, there was no significant relationship between the number medications prescribed in the ICU and demographic and clinical information. This was probably due to a small sample size which we consider a limitation of the study.

Table 2. Comparison between polypharmacy and indicators of liver, renal, and haemopoietic function

	≤ 9 medications (n = 38)	> 9 medications (n = 21)	P value
ALT	41±2.3 U/L	30±9.1 U/L	0.474
AST	56±7.1 U/L	49.5±8.3 U/L	0.443
Bilirubin	15±2.1 µmol/L	13.25±6.61 µmol/L	0.76
Urea	16.7±7.2 µmol/L	13.45±5.5 µmol/L	0.343
Creatinine	221.5±31 µmol/L	207.5±17.7 µmol/L	0.358
RBC count	3.15±0.76 cells/mcL	3.1±0.75 cells/mcL	0.94
WBC count	13±1.77 cells/mcL	9±2.1 cells/mcL	0.0372
Hemoglobin count	97±13 g/L	88±20.1 g/L	0.61
Platelet count	118±21 µmol/L	105.5±17 µmol/L	0.871

Table 3. Effect of potential TDF/Vancomycin interaction on creatinine levels

	TDF/Vancomycin interaction (n = 14)	Without TDF/Vancomycin interaction (n = 45)	P value
Creatinine	345.7±45.2 µmol/L	107.5±33.5 µmol/L	p = 0.035

Our study also did not reveal any significant relationship between the number medications prescribed and organ function assays (liver, kidney and haemopoietic functions). The Liverpool HIV drug interactions database indicated that more than half of the patients (62%) on ARV were exposed to at least two potential interactions. Data revealed that tenofovir most frequently interacted with the antibiotic vancomycin, followed by lopinavir ritonavir and ciprofloxacin. The following is a summary of the potential tenofovir/vancomycin interaction according to the Liverpool HIV drug interactions database: "Coadministration has not been studied. Vancomycin is eliminated unchanged predominantly via glomerular filtration, and there is little potential for interaction with tenofovir-DF via competition for active renal transport mechanisms. However, both vancomycin and tenofovir-DF are potentially nephrotoxic and tenofovir-DF should be avoided with concurrent or recent use of a nephrotoxic agent. If concomitant use of tenofovir-DF and nephrotoxic agents is unavoidable, renal function should be monitored closely. A case study described renal failure in 2 patients taking tenofovir-DF and a prolonged course of vancomycin".

The course of vancomycin prescription in these patients was not considered prolonged, therefore renal failure as a complication was not observed, although there was a significant difference in average creatinine levels among patients who had tenofovir/vancomycin interactions. Coadministration of lopinavir/ritonavir and ciprofloxacin was the second most common potential DDI recorded. The database (Liverpool HIV drug interaction) indicates that caution should be exercised when prescribing this combination as both drugs have risks of QT prolongation. However, we did not find significant changes from the ECG assessment of patients. We also did not observe any statistically significant relationship between changes in average creatinine levels and demographic/clinical information of patients with tenofovir/vancomycin interactions. These events were probably as a result of a small sample size, which we consider a limitation to the study.

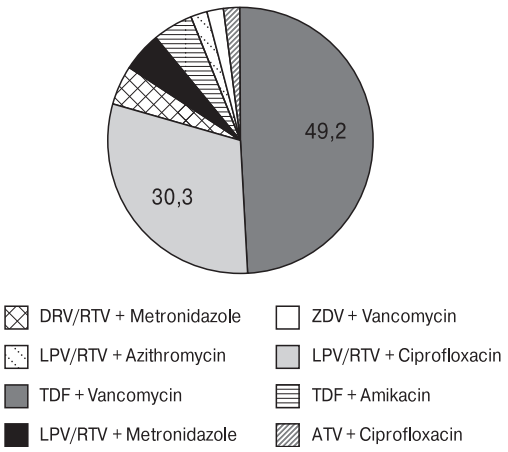

Figure. Potential antiretroviral/antibiotic interactions recorded in HIV-infected patients admitted to the ICU

Note: ATV — Atazanavir; ZDV — Zidovudine; DRV/RTV — Darunavir/Ritonavir; LPV/RTV — Lopinavir/Ritonavir; TDF — Tenofovir.

Conclusion

This study demonstrated that potential DDIs frequently occur in ICU patients, as reported in other investigations. This study also shows the importance of considering the use of an HIV drug interaction database as HIV+ ICU patients are at a high risk for polypharmacy and drug-drug interaction. It is necessary to implement collaborations among clinical pharmacologists and infectious disease/HIV specialists, as well as frequent clinical and laboratory monitoring, with the aim of developing effective and actionable strategies that could reduce potential DDIs in HIV+ ICU patients.

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Conflict of interest

The authors declare no conflict of interest.

References

1. Danielson P.B. The cytochrome P450 superfamily: biochemistry, evolution and drug metabolism in humans. *Curr. Drug. Metab., 2002, vol. 3, no. 6, pp. 561–597. doi: 10.2174/1389200023337054*
2. De Maat M.M., Ekhart G.C., Huitema A.D., Koks C.H., Mulder J.W., Beijnen J.H. Drug interactions between antiretroviral drugs and comedicated agents. *Clin. Pharmacokinet., 2003, vol. 42, no. 3, pp. 223–282. doi: 10.2165/00003088-200342030-00002*
3. Farhoudi M., Khalili H., Karimzadeh I., Abbasian L. Associated factors of drug-drug interactions of highly active antiretroviral therapy: report from a referral center. *Expert Opin. Drug Metab. Toxicol., 2015, vol. 11, no. 4, pp. 471–479. doi: 10.1517/17425255.2014.993606*
4. Hughes C.A., Tseng A., Cooper R. Managing drug interactions in HIV-infected adults with comorbid illness. *CMAJ, 2015, vol. 187, no. 1, pp. 36–43. doi: 10.1503/cmaj.131626*
5. Johnston J.P., Heavner M.S., Liu M., Casal G.L.H., Akgün K.M. The prevalence of drug-drug interactions with antiretroviral therapy in human immunodeficiency virus-infected patients in the intensive care unit. *J. Pharm. Pract., 2021: 8971900211035262. doi: 10.1177/08971900211035262*

6. Kacha H.V., Mundhava S.G., Kubavat A.R. Assessment of drug use pattern, their cost and safety in emergency department at a tertiary care teaching hospital, Rajkot. *Int. J. Pharm. Sci.Res., 2018, vol. 9, no. 4, pp. 1638–1643. doi: 10.13040/IJPSR.0975-8232.9(4).1638-1643*
7. López-Centeno B., Badenes-Olmedo C., Mataix-Sanjuan Á., McAllister K., Bellón J.M., Gibbons S., Balsalobre P., Pérez-Latorre L., Benedí J., Marzolini C., Aranguren-Oyarzábal A., Khoo S., Calvo-Alcántara M.J., Berenguer J. Polypharmacy and drug-drug interactions in people living with human immunodeficiency virus in the region of Madrid, Spain: a population-based study. *Clin. Infect. Dis., 2020, vol. 71, no. 2, pp. 353–362. doi: 10.1093/cid/ciz811*
8. Masnoon N., Shakib S., Kalisch-Ellett L., Caughey G.E. What is polypharmacy? A systematic review of definitions. *BMC Geriatr., 2017, vol. 17, no. 1: 230. doi: 10.1186/s12877-017-0621-2*
9. Miller C.D., El-Kholi R., Faragon J.J., Lodise T.P. Prevalence and risk factors for clinically significant drug interactions with antiretroviral therapy. *Pharmacotherapy., 2007, vol. 27, no. 10, pp. 1379–1386. doi: 10.1592/phco.27.10.1379*
10. O'Dwyer M., Peklar J., McCallion P., McCarron M., Henman M.C. Factors associated with polypharmacy and excessive polypharmacy in older people with intellectual disability differ from the general population: a cross-sectional observational nationwide study. *BMJ Open, 2016, vol. 6, no. 4: e010505. doi: 10.1136/bmjopen-2015-010505*
11. Pal D., Kwatra D., Minocha M., Paturi D.K., Budda B., Mitra A.K. Efflux transporters- and cytochrome P-450-mediated interactions between drugs of abuse and antiretrovirals. *Life Sci., 2011, vol. 88, no. 21–22, pp. 959–971. doi: 10.1016/j.lfs.2010.09.012*
12. Ray S., Bhattacharyya M., Pramanik J., Todi S. Drug-drug interactions in the ICU. *Crit Care., 2009, vol. 13 (suppl. 1): P495. doi: 10.1186/cc7659*
13. Schlaeppi C., Vanobberghen F., Sikalengo G., Glass T.R., Ndege R.C., Foe G., Kuemmerle A., Paris D.H., Battegay M., Marzolini C., Weisser M.; Kilombero and Ulanga Antiretroviral Cohort (KIULARCO) study group. Prevalence and management of drug-drug interactions with antiretroviral treatment in 2069 people living with HIV in rural Tanzania: a prospective cohort study. *HIV Med., 2020, vol. 21, no. 1, pp. 53–63. doi: 10.1111/hiv.12801*
14. Sharma N., Parakh R., Sharma D., Sharma P., Sharma P., Sharma N. A drug utilization study in critically ill patients in a tertiary care teaching hospital in North India. *Am. J. Pharmtech. Res., 2014, vol. 4, no. 1, pp. 780–789. doi: 10.18203/2319-2003.ijbcp20195778*
15. Shinde R.M., Kale A., Chube S., Sawant M. Drug utilization study in medical intensive care unit in a rural tertiary care teaching hospital in Maharashtra. *Int. J. Med. Sci. Public Health., 2017, vol. 6, no. 4, pp. 733–737. doi: 10.5455/ijmsph.2017.1165030112016*
16. Smythe M.A., Melendy S., Jahns B., Dmuchowski C. An exploratory analysis of medication utilization in a medical intensive care unit. *Crit. Care Med., 1993, vol. 21, no. 9, pp. 1319–1323. doi: 10.1097/00003246-199309000-00014*
17. Stolbach A., Paziana K., Heverling H., Pham P. A Review of the toxicity of HIV medications II: interactions with drugs and complementary and alternative medicine products. *J. Med. Toxicol., 2015, vol. 11, no. 3, pp. 326–341. doi: 10.1007/s13181-015-0465-0*
18. Xia H., Gao L., Gong X., Zaongo S.D., Zhang T., Wu H., Ma P., Huang X. The challenge of potential drug-drug interactions among people living with HIV on antiretroviral therapy: a cross-sectional study in selected provinces in China. *Front. Pharmacol., 2020, vol. 11: 800. doi: 10.3389/fphar.2020.00800*

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