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Short communication

Potential drug-drug interactions found in therapeutic treatment during COVID-19

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Introduction

Coronavirus disease 2019 (COVID-19) caused by severe Acute Respiratory Syndrome Coronavirus (SARS-COV 2) was first identified as an outbreak of respiratory illness in Wuhan City, China in 2019. (Wu et al., 2020). Since then, SARS-COV2 has deeply impacted every aspect of health and wellbeing. Patients hospitalized with SARS-COV2 are mostly elders with co-morbidities (*such as hypertension, diabetes mellitus, cardiovascular, lung and kidney diseases*) and getting polypharmacy increases risk factors for developing drug-drug interactions (DDIs). Aging is related with physiological changes that affects the pharmacokinetics and pharmacodynamics of drugs, leading in rise of drug-related toxicity. Patients who already were in polypharmacy treatment, had to deal with the addition of specific treatments for SARS-COV2 infection. Treatment of SARS-COV2 included use of antibiotics, antivirals, corticosteroids, anticoagulants, analgesics, thus when being prescribed to a hospitalized patient with co-morbid disease it may lead to developing DDIs.

Materials and methods

A retrospective, observational study, which includes 20 patients with a proven diagnosis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection who were hospitalized between March and April 2021 in Internal Department in Ferizaj's Regional Hospital. Drugs were analyzed for interactions by utilizing Medscape drug checker, a Computerized Prescription Support System that classifies potential DDIs according to their clinical relevance. When the drugs were entered in the tool, it displayed the potential DDIs and classified them based on severity as contra-indicated, serious (*risk of life threatening drug interaction; use alternative drug*), significant–monitor (*potential for dangerous interaction, use with caution and monitor closely*) and minor (*non-significant interaction*).

Results and discussion

From the total number of hospitalized patients (N=20), female 55% with mean age 66, while 45% were male with mean age 62 years old. Out of 20 patients 5 (25%) of them were prescribed 6 drugs for Covid-19 treatment post-hospitalization, while four patients (20%) were prescribed with 9 drugs also four patients used 5 drugs in treatment. Two patients (10%) were treated with 7 drugs, two other patients were treated with 8 drugs and two patients were prescribed 10 drugs at the same time. Only one patient was prescribed 4 drugs for its treatment. In this study 6 of the 20th patients had zero drug interactions in the therapy, following with 1 DDI was found in 5 patients. Three patients had 2 interactions, 2 patients had 3 interactions also 2 patients had 5 DDI in their discharge therapy. We found only one case with 4 interactions and only one case with 10 interactions.

The most frequently prescribed drugs were oral antibiotics 15.8% (mainly *Cefixime, Levofloxacin, Ciprofloxacin*), followed by proton pump inhibitors-PPIs (*pantoprazole, esomeprazole*), and oral anticoagulants 15% (such as *rivaroxaban* and *aspirin*). Most of the patients were prescribed oral corticosteroids 12.5 % for a short period of time, also Vitamin D was prescribed to 18 patients throughout therapy. All patients have been with chronic therapy and were using antihypertensive agents

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mainly [ACE] inhibitors, β-blockers, diuretics, insulin, hypoglycemic agents, thyroid hormones and statins. Few patients were using bronchodilator, and only two patients were prescribed analgesics to use as needed. Only one patient was using selective estrogen receptor modulator therapy SSRIs at the same time.

We couldn't find any serious interactions, although the highest number of interactions were monitored interactions 13 respectively 54.17% continuing with 11 minor interactions (45.83%).

The monitor drug interactions were:

- Methylprednisolone combined with Atorvastatin has shown that methylprednisolone will decrease the effect of atorvastatin by affecting hepatic/intestinal enzyme CYP3A4 metabolism.
- Tamoxifen increases levels of Rivaroxaban by affecting hepatic/intestinal enzyme CYP3A4 metabolism, we should pay attention in patients with renal impairment receiving Rivaroxaban
- Pantoprazole increases toxicity of Theophylline. Prolonged use of proton pump inhibitors can cause hypochlorhydria, which in turn causes peristalsis in small intestine to increase and peristalsis in the proximal colon to decrease.
- Aspirin combined with Methylprednisolone increases toxicity of the other by pharmacodynamic synergism, also it increased risk of GI ulceration.
- Methylprednisolone and Levofloxacin/ Ciprofloxacin may increase risk of tendon rupture.
- Ciprofloxacin/ Levofloxacin increases the effect Insulin Aspart by pharmacodynamics synergism. Hyper and hypoglycemia have been reported in patients treated concomitantly with quinolones and antidiabetic agents.
- Levofloxacin increases effects of Sitagliptin by pharmacodynamic synergism. Quinolone antibiotic administration may result in hyper- or hypoglycemia.

The minor drug interactions were:

- Methylprednisolone decreases levels of Aspirin by increasing renal clearance.
- Methylprednisolone decreases effects of Insulin Aspart/Detemir and Sitagliptin by pharmacodynamic antagonism, control your blood sugar levels closely.
- Methylprednisolone and Furosemide and Hydrochlorothiazide have a pharmacodynamic synergism in organism. Risk of hypokalemia, especially with strong glucocorticoid activity. Few side effects may be cause muscle pains or cramps, loss of appetite, weakness, dizziness, or confusion.
- Cefixime increases toxicity of Furosemide by pharmacodynamic synergism. Increased risk of nephrotoxicity.
- Hydrochlorothiazide decreases effects of Insulin Detemir/Aspart by pharmacodynamic antagonism. When thiazide dosage >50 mg/day may increase blood glucose.
- Pantoprazole decreases levels of levothyroxine by increasing gastric pH.

The role of anticoagulant-Rivaroxaban in the prevention and treatment of thromboembolic complications of COVID-19 has been widely established. In an observational study involving 320 patients with Covid-19 have received Rivaroxaban 10mg/day resulted in better clinical outcomes, including a reduction in major and fatal thromboembolic events without increasing major bleeding. (Ramacciotti et al., 2022). The fact that 30% of COVID-19 patients had no drug interactions at hospital discharge and zero serious interaction were found comparing with Ali et al. where they have found 41 major interactions (Ali et al., 2020).

On our study 50 % had at least one possible minor DDI, shows that a sufficient assessment of all pharmacologic treatments, including background therapy, was undertaken throughout the hospital stay and all patients were required to come back for a checkup after 7-10 days.

Conclusion

The study shows that drug interactions are frequent but monitored, and among the influencing factors are age, co-morbidities, polytherapy and long hospital stay.

Given the patient's therapeutic priorities and the pharmacological changes that drugs encounter in an organism, the consumption of a single drug may possibly not be more effective but, during co-medication of multiple medications, the risk of drug interaction will be increased.

Adequate knowledge regarding the most common pDDIs is necessary to enable healthcare professionals to ensure patient safety.

References

Ali, I., Bazzar, A., Hussein, N., Sahhar, E., 2020. Potential drug-drug interactions in ICU patients: a retrospective study. Drug Metabolism and Personalized Therapy 35(3), 20200114.

Ramacciotti, E., Barile Agati, L., Calderaro, D., et al., MICHELLE investigators, 2022. Rivaroxaban versus no anticoagulation for post-discharge thromboprophylaxis after hospitalisation for COVID-19.

Wu, C., Chen, X., Cai, Y., Xia, J., Zhou, X, Xu, S., et al., 2020. Risk factors associated with acute respiratory distress syndrome and death in patients with Coronavirus disease 2019 pneumonia in Wuhan. China. JAMA Intern. Med. (108), 934. https://doi.org/10.1001/jamainternmed.2020.0994