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Short communication

Improving the safety of prescribing and using antibiotics in the treatment of exacerbations of COPD in hospitalized patients in tertiary care

Olivera K. Nakovska[1], Dejan Dokic[1], Dimitar Karkinski[1], Vangel Nechevski[1], Elena Janeva[1], Milena M. Gjorevska[1], Angela Debreslioska[1], Ksenija Bogoeva[2], Zorica Naumovska[3], Aleksandra K. Nestorovska[3], Ljubica Suturkova[3]

[1]*University Clinic of Pulmonology and Allergology, Majka Tereza 17, 1000 Skopje, Republic of North Macedonia*
[2]*PZU Bogoeva, Frederik Chopin 2/1, 1000 Skopje, Republic of North Macedonia*
[3]*Faculty of Pharmacy, University "Ss Cyril and Methodius", Mother Theresa 45, 1000 Skopje, Republic of North Macedonia*

Introduction

Chronic Respiratory Lung Disease (COPD) is a respiratory disease that occurs most often due to prolonged exposure to harmful gases and particles that damage and modify the airways with consequent persistent restricted airflow clinically manifested by dyspnea and frequent prolapse of sputum (GOLD 2022). Hospitalizations of these patients are a consequence of exacerbations that are most commonly caused by respiratory tract infections. 40% –60% of exacerbations are caused by bacteria, especially *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Moraxella catarrhalis.*

An exacerbation of COPD is a sustained worsening of the patient's condition, from the stable state and beyond normal day-to-day variations that is acute in onset and may warrant additional treatment in a patient with underlying COPD (GOLD, 2022). At the PHI UK for Pulmonology - Skopje during the hospital treatment of patients with exacerbations of COPD, the official GOLD 2022 guides are followed, which give directions for the use of antibiotics in this group of patients. Patients with COPD often have a number of comorbidities which inevitably leads to polypharmacy. As a result, there is a predisposition for drug-drug interactions that may contribute to the manifestation of serious side effects and lead to treatment failure or toxicity. The objective of this study was to consolidate the clinical and pharmacologic aspects of drug–drug interactions, develop a compendium of information, provide prescribers with a measure of the risk of interactions, describe the clinical consequences and assess the quality of evidence.

Materials and methods

Observational, longitudinal and prospective study was conducted in The Clinic of Pulmonology and Allergology of Skopje, Republic of North Macedonia. The patients were followed from January to April 2022. Total of 30 patient histories of disease exacerbation with focus on medicament therapy (antibiotics and concominant drugs used to treat comorbidities) have been systematically reviewed by the ward clinical pharmacist. The results of the evaluation were communicated with the pulmology specialists. The average length of hospital stay was 12 days. Additionally, to COPD, 19 out of all patients had a history of heart disease, 6 had diabetes mellitus type II and 5 patients were previously diagnosed with other disorders (gastrointestinal, psychiatric and benign prostatic hyperplasia). The potential drug-drug interactions were identified using Stockley's Drug Interactions manual, subsequently categorized according to the severity of the interaction and sub-classified into: co-administered drugs that alter the pharmacokinetics of antibiotics and *vice versa*, antibiotics that interfere with the pharmacokinetics of co-administered drugs.

Results and discussion

The total number of identified interaction was 52 of which 1 (1.92%) is severe interaction, 22 (42.31%) are moderate and 29 (55.76%) may not be of clinical

*ljsu@ff.ukim.edu.mk

relevance but require counseling about possible adverse effects and additional monitoring.

The identified severe interaction between moxifloxacin-fluconazole is associated with significant risk of QT interval prolongation which might lead to the potentially fatal torsade de pointes arrhythmia and thereby entail avoidance of their concurrent use.

The recognized moderate interactions are mostly associated with concomitant acenocumarol use with antibiotics. The identified side effects and recommendation for their management are as follows: 1) with azitromicin - linked with risk of raised INRs imply it's monitoring over the first 7 days of antibiotic treatment; 2) with ceftriaxone or doxyciclin - occasionally associated with bleeding require monitoring of INR within 3 days of the start of antibiotic; 3) with ciprofloxacin – increases risk of over-anticoagulation and monitor INR within 3-5 days of starting the quinolone is recommended; 4) with clyndamicin no cases of serious increase of INR were identified, however it may be prudent to monitor INR within 3 days of starting the treatment; 5) with moxifloxacin- unpredictably in some patients resulted with bleeding and INR monitoring within 3-5 days of starting the quinolone is recommended.

Moderate interactions leading to increased risk of hipokalemia and torsade de pointes, which requires close monitoring of potassium concentration was identified in case of concominant use of azithromicin or ciprofloxacin or fluconazole with dexamethasone, furosemide, hydrochlorothiazide, salbutamol or methylprednisolone. Case reports describe a large increase in drug concentration of 1) carabamazepine or tamsulosin or verapamil when concomitantly used with fluconazole and 2) digoxin as a result of azithromycin-digoxin interaction. All cases require close therapeutic drug monitoring of carbamazepin or digoxin and subsequent dose adjustment as well as monitoring for signs of digoxin induced bradicardia, tamsulosin or Ca channel blocker adverse effects, respectively. A risk of QT- interval prolongation as a result of ciprofloxacin-olanzapine drug interaction due to the inhibited olanzapine metabolism when used together was also recognized. In general, acenocumarol was the most common drug reported in drug–drug interactions. Nearly all of the observed interactions were pharmacokinetic, with the majority of them affecting the cytochrome P450 mediated metabolism of the concern concomitantly used drug for treatment of the patient comorbidities. Creating a comprehensive and valid list of most common drug interactions of antibiotics in the treatment of COPD exacerbations in hospitalized patients would require a substantial increase in research activities in this area. Improvements in the quality of research methodology are also necessary. Data regarding the most common drug-drug interactions should be estimated with caution due to the small patient number. Further evaluation is needed in order to assess the impact of this intervention on exacerbation and hospital readmission.

Conclusion

This study demonstrates the possibility of treatment failure and life-threatening toxicity associated with complementary use of antibiotics. Additionally, it emphasizes the need of precaution regarding potential and serious drug interactions, particularly where there is no tradition of concomitant drug use (Izzo et al., 2005). Physicians are encouraged to discuss the use of complementary drugs with their clinical pharmacists and patients in order to identify, prevent and manage possible drug- drug interaction.

References

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