Characteristics of clinically relevant potential drug-drug interactions among ambulatory prescriptions in Slovenia

Jazbar Janja 1, Gotar Nina 2, Locatelli Igor 3, Kos Mitja 4.

1University of Ljubljana, Faculty of Pharmacy, A?ker?eva 7, 1000 Ljubljana, Slovenia. 2University of Ljubljana, Faculty of Pharmacy, A?ker?eva 7, 1000 Ljubljana, Slovenia. 3University of Ljubljana, Faculty of Pharmacy, A?ker?eva 7, 1000 Ljubljana, Slovenia. 4University of Ljubljana, Faculty of Pharmacy, A?ker?eva 7, 1000 Ljubljana, Slovenia.

Background A previous study on Slovenian outpatients showed that a total of 9.3% (N = 191,213) of the Slovenian population (N = 2,063,077; 1 July 2015) was exposed to clinically relevant potential drug-drug interactions (DDIs) in 2015. A better understanding of the most frequently occurring potential DDIs may enable safer pharmacotherapy and minimize drug-related problems.

Purpose The aim of the study was to evaluate characteristics of the most frequently prescribed clinically relevant potential DDIs among outpatients in Slovenia.

Method Clinically relevant potential DDIs were selected from the database of all potential DDIs among Slovenian outpatients in 2015, which was constructed based on Health claims data on prescription drugs obtained from the Health insurance institute of Slovenia. A potential DDI was defined as dispensing of two interacting drugs to one patient on the same day. The reference source of interactions was the Lexicomp drug interactions database. Clinically relevant DDIs were defined as drug combinations that should be avoided and drug combinations where therapy modifications should be considered (type X and type D, respectively). Monographs of the 95% of type X DDIs and 75% of type D DDIs were further examined regarding severity, Lexicomp reliability rating (the quality of documentation for an interaction), ATC classification, mechanism of interaction, possible adverse events and patient management.

Findings Drug combinations that should be avoided (type X): The analysis included 58 monographs, which represent 68,280 cases of potential DDIs. The reliability was rated as excellent in 1.3%, good in 34.5%, and fair in 64.2% of cases. The three most frequent possible adverse events were excessive anticholinergic effects (32.9% of cases), QTc-prolongation (24.5% of cases) and prolonged sedative effects (10.9% of cases). Drug combinations where therapy modifications should be considered (type D): The analysis included 62 monographs, which represent 411,646 cases of potential DDI in the population. The reliability was rated as excellent in 7.6%, good in 17.2%, and fair in 75.2% of cases. The three most frequent possible adverse events were increased risk of bleeding (25.0% of cases), enhanced CNS depression (21.6% of cases) and QTc prolongation (15.3% of cases).

Conclusion In the majority of clinically relevant cases of potential DDIs, the quality of documentation for an interaction based on Lexicomp rating is rated as fair. In our study, excessive anticholinergic effects and increased risk of bleeding were the most frequent possible adverse events from type X and type D DDIs, respectively.