ANALYSIS OF DRUG-DRUG INTERACTIONS IN HOSPITALIZED PATIENTS AT A UNIVERSITY HOSPITAL

Mgr. Olga Svobodová[1,2]
PharmDr. Miroslav Turjap, Ph.D.[1]
[1] Dpt. of Clinical Pharmacy, University Hospital Ostrava, Czech Republic
[2]Dpt. of Pharmacology, Faculty of Medicine, Masaryk University, Brno, Czech Republic
olga.svobodova@fno.cz, miroslav.turjap@fno.cz

66. ČESKO-SLOVENSKÉ FARMAKOLOGICKÉ DNY
13. - 15. 9. 2016, Brno

INTRODUCTION

Adverse events caused by drug-drug interactions (DDIs) can significantly contribute to mortality/morbidity and extend the length of hospital stay. Understanding the mechanisms of DDIs, analyzing own data and adopting and/or optimizing preventive measures may help reduce the risk.

AIMS

Based on experiences from our pilot project [1], the aims of these analyses were to identify drug combinations most frequently involved in serious DDIs in our hospital, assess physicians' responses to DDI risk signals and compare the results in two consecutive time periods.

MATERIALS & METHODS

- **the retrospective analysis was performed at University Hospital Ostrava, Czech Republic (1127 beds)**
- **inpatient electronic medication records with built-in DDI software (Vademecum Infopharm, Prague, Czech Republic) were analyzed from 1-6/2015 and 7-12/2015**
- **DDI data from the records were electronically extracted and the TOP 10 drug pairs/groups most frequently involved in serious DDIs identified (= overall risk ratings 5 and 5! – „very serious“ OR „contraindicated“)**
- **all medical records with occurrence of one of the TOP 10 DDIs were manually reviewed for details**
- **real DDI risk cases and false positive signals were calculated (false positive DDI signal: DDI is dose-dependent and dose limitation was respected OR DDI is diagnosis-dependent and the diagnosis wasn't present OR the drug combination wasn't in fact administered together)**
- **the responses of the physicians to the alerts with ratings 5 and/or 5! were analysed**

RESULTS & DISCUSSION

Tab. 1 THE TOP TEN DDIs AT A UNIVERSITY HOSPITAL FROM JANUARY – JUNE 2015 & JULY – DECEMBER 2015

	JANUARY – JUNE 2015			JULY – DECEMBER 2015		
RANK	DRUG PAIR	RATING Infopharm	RATING LexiComp	DRUG PAIR	RATING Infopharm	RATING LexiComp
1.	RILMENIDINE* - β - BLOCKERS	5	N/A	RILMENIDINE* - β–BLOCKERS	5	N/A
2.	OMEPRAZOLE- CLOPIDOGREL	5	X	OMEPRAZOLE- CLOPIDOGREL	5	X
3.	PROPAFENONE - β -BLOCKERS	5!	C	PROPAFENONE - β –BLOCKERS	5!	C
4.	CLARITHROMYCIN - ATORVA/SIMVASTATIN	5/5!	D/X	AMIODARONE - METRONIDAZOLE	5	D
5.	AMIODARONE - METRONIDAZOLE	5	D	AMIODARONE - CITALOPRAM	5!	X
6.	AMIODARONE - CITALOPRAM	5!	X	AMIODARONE - SIMVASTATIN	5	D
7.	WARFARIN - METRONIDAZOLE	5	D	CLARITHROMYCIN - ATORVA/SIMVASTATIN	5/5!	D/X
8.	AMIODARONE - SIMVA/LOVASTATIN	5/5	D/D	VERAPAMIL - SIMVASTATIN	5	D
9.	CLOPIDOGREL - CLARITHROMYCIN	5	C	VORICONAZOLE - MIDAZOLAM	5	D
10.	VERAPAMIL - SIMVASTATIN	5	D	CYCLOSPORINE - ATORVASTATIN	5	X

5: avoid combination; 5!: contraindicated combination; C: monitor therapy; D: consider therapy modification; X: avoid combination; N/A – not available
*rilmenidine – centrally and peripherally acting antihypertensive, imidazoline receptor agonist

- **in the second time period (JUL-DEC 2015) there were less hospitalizations than in the first time period (JAN-JUN 2015) and therefore less DDIs (a total numbers of grade 5 and/or 5! DDIs were 809 and 627 in first and second time period, respectively)**
- **DDI software is a good tool for warning of possible interaction, but it is important to be able to work with alerts →DDIs usually do not have one universal/unequivocal solution and individual approach to the specific situation is often necessary →consultation with clinical pharmacist/pharmacologist may be a good option**
- **some DDIs which are rated 5 OR 5! are in (reference) DDI software (Lexicomp) rated with lower importance → this may result in interaction signals which physicians have to deal with, but in fact are probably not so clinically relevant**
- **overal ratings of some DDIs were changed during the year 2015:**
  - **metronidazole + warfarin: from 5 to 4**
  - **propafenone + β – blockers: from 5 to 4**
- **the data for this analysis were extracted from electronic medication records, but in some cases physicians used paper form medication records OR the changes in medication were recorded only in paper form and not in electronic form → we found this as one of limits of the analysis**
- **DDI software discusses the present DDIs in detail and usually proposes management of the DDIs, but sometimes physicians didn't read them and misinterpreted the situations**

Tab. 2 STATISTICAL COMPARISON OF TWO TIME PERIODS

PARAMETER	JANUARY - JUNE 2015	JULY - DECEMBER 2015
TOTAL NUMBER OF HOSPITALIZATION EPISODES	25681	23650
TOTAL NUMBER OF AVOID OR CONTRAINDICATED COMBINATIONS	809	627
TOP TEN DDIs	542 (67 %)	386 (62 %)
REAL DDI RISK CASES	249	171
APPROPRIATELY MANAGED REAL DDI RISK CASES	197 (79 %)	118 (69 %)
INCORRECTLY MANAGED REAL DDI RISK CASES	52 (21 %)	53 (31 %)
FALSE POSITIVE DDI SIGNALS	293	212
APPROPRIATELY MANAGED FALSE POSITIVE DDI SIGNALS	234 (80 %)	206 (97 %)
INCORRECTLY MANAGED FALSE POSITIVE DDI SIGNALS	59 (20 %)	6 (3 %)

CONCLUSION

We identified the most frequent drug combinations involved in serious DDIs at our hospital. Periodic analysis of DDIs is currently the routine part of the pharmacotherapy quality assessment at our hospital.

There is still significant number of incorrectly managed interactions between omeprazole & clopidogrel → in these cases, physicians usually don't change the combination in the hospital discharge report → there is no continuity of the medication management and the risk of negative cardiac-related outcomes may be increased.

The software is a valuable tool for preventing serious DDIs. It should be taken as decision support tool for dealing with specific situations rather than rigid set of instructions. DDI alerts should be periodically reviewed to assess the real clinical importance and to avoid "alert fatigue".

Reference: [1] CP-046 Analysis of drug-drug interactions during hospitalisation at a university hospital. *Eur J Hosp Pharm 2016*, 23(Suppl 1):A20.

The work was supported by specific research at the Masaryk University