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ANALYSIS OF DRUG-DRUG INTERACTIONS DURING HOSPITALISATION AT A UNIVERSITY HOSPITAL

Background

Adverse events caused by drug-drug interactions (DDIs) can significantly contribute to mortality/morbidity during hospitalisation. Understanding the mechanisms of DDIs, working with own data and adopting preventive measures may help reduce the risk.

Materials & Methods

- **analysis performed at University Hospital Ostrava, Czech Republic (1127 beds)**
- **retrospective analysis of inpatient electronic medication records performed with built-in DDI software (Infopharm, Prague, Czech Republic) from January 2015 to August 2015**
- **DDI data from these records electronically extracted and the top ten drug pairs/groups most frequently involved in serious DDIs identified**
- **only DDIs with highest overall risk ratings (very serious or contraindicated) taken into account. For comparison, risk rating by trusted DDI tool (Lexi-Interact®) added → Tab 1.**
- **subsequently all the medical records with occurrence of one of the top ten DDIs 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)**

Purpose

The aim of the analysis was to asses the utility of the built-in DDI tool and identify drug combinations most frequently involved in serious DDIs in our hospital.

Results

- **a total of 25681 hospitalisation episodes electronically analysed**
- **809 signals of serious DDIs identified in 656 hospitalization episodes**
- **the Top 10 most frequently involved DDIs represented 542 cases (67 % of the DDIs identified) → Tab 2.**
- **after detailed review and exclusion of false positive DDI signals, 249 real risk DDI cases remained → Tab 2.**
- **79 % of the cases were managed appropriately and 21 % incorrectly →Fig 1. ; most frequently clopidogrel – omeprazole combination →Tab 2.**
- **of the 293 false positive DDI signals identified, 80 % of the cases were interpreted correctly and 20 % was misinterpreted →Fig 2; most frequently clarithromycin – atorvastatin combination →Tab 2.**

Tab 1. THE TOP TEN DRUG-DRUG INTERACTIONS – OVERALL RISK RATING & MANAGEMENT

RANK	DRUG PAIR	OVERALL RISK RATING & MANAGEMENT
1	RILMENIDINE* – BETA-BLOCKERS	**Infopharm:** 5 - avoid in heart failure; **LexiComp:** N/A
2	OMEPRAZOLE – CLOPIDOGREL	**Infopharm:** 5 - avoid combination; **LexiComp:** X - avoid combination
3	PROPAFENONE – BETA-BLOCKERS	**Infopharm:** 5! - contraindicated in heart failure; **LexiComp:** C - monitor therapy
4	CLARITHROMYCIN – ATORVA/SIMVASTATIN	atorva (**Infopharm:** 5, **LexiComp**: D - consider therapy modification or limit dose to ≤ 20 mg) simva (**Infopharm**: 5! – contraindicated; **LexiComp**: X - avoid combination)
5	AMIODARONE – METRONIDAZOLE	**Infopharm:** 5! - contraindicated **LexiComp:** D - consider therapy modification
6	AMIODARONE - CITALOPRAM	**Infopharm:** 5! - contraindicated **LexiComp:** X - avoid combination
7	WARFARIN – METRONIDAZOLE	**Infopharm:** 5 - consider therapy modification and closely monitor **LexiComp:** D - consider therapy modification
8	AMIODARONE – SIMVA/LOVASTATIN	simva (**Infopharm:** 5, **LexiComp:** D – consider therapy modification or limit simva dose to ≤ 20 mg) lova (**Infopharm:** 5, **LexiComp:** D - consider therapy modification or limit lova dose to ≤ 40 mg)
9	VERAPAMIL - SIMVASTATIN	**Infopharm:** 5 - limit dose to ≤ 20 mg **LexiComp:** D - consider therapy modification (or limit dose to ≤ 10 mg)
10	CLOPIDOGREL - CLARITHROMYCIN	**Infopharm:** 5 - generally avoid (note: we consider this rating as inappropriate) **LexiComp:** C - monitor therapy

*centrally and peripherally acting antihypertensive; imidazoline receptor agonist

Fig 1. REAL DDI RISK - INTERVENTION

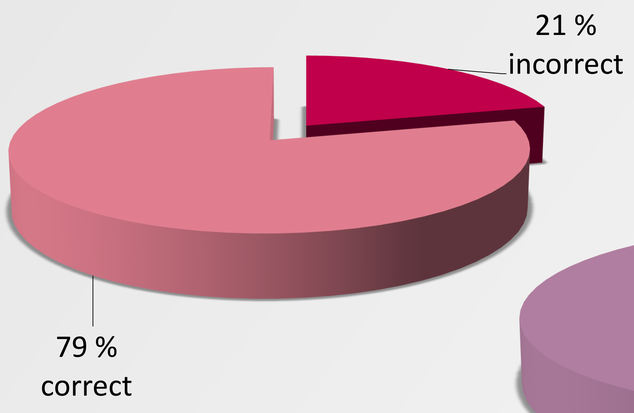
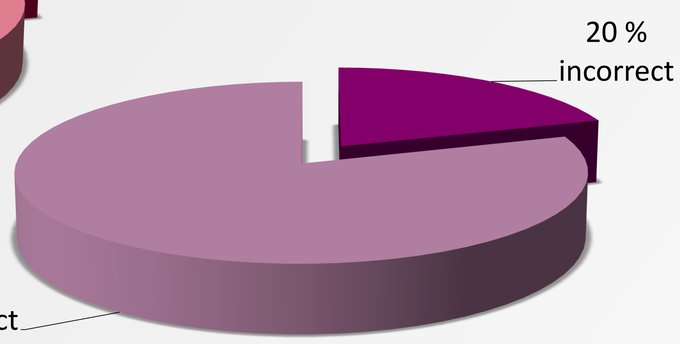


Fig 2. FALSE POSITIVE DDI SIGNALS - INTERPRETATION



Tab 2. THE TOP 10 DRUG-DRUG INTERACTIONS - OCCURRENCE

RANK	DRUG PAIR	TOTAL	REAL DDI RISK*	FALSE POSITIVE DDI SIGNAL*
1	RILMENIDINE – BETA-BLOCKERS	**167**	**15** (10/5)	**152** (148/4)
2	OMEPRAZOLE – CLOPIDOGREL	**108**	**108** (86/22)	0
3	PROPAFENONE – BETA-BLOCKERS	**70**	**5** (3/2)	**65** (52/13)
4	CLARITHROMYCIN – ATORVA/SIMVASTATIN	**59**	**17** (15/2)	**42** (9/33)
5	AMIODARONE – METRONIDAZOLE	**35**	**35** (23/12)	**0**
6	AMIODARONE – CITALOPRAM	**26**	**26** (19/7)	**0**
7	WARFARIN – METRONIDAZOLE	**24**	**24** (24/0)	**0**
8	AMIODARONE – SIMVA/LOVASTATIN	**20**	**1** (0/1)	**19** (16/3)
9	VERAPAMIL – SIMVASTATIN	**17**	**2** (1/1)	**15** (9/6)
10	CLOPIDOGREL – CLARITHROMYCIN	**16**	**16** (16/0)	**0**
		542	**249** (197/52)	**293** (234/59)

*number of cases (solved correctly/solved incorrectly) , for definitions see Materials & Methods

Conclusion

We identified most frequent drug combinations involved in serious DDIs in our hospital and analysed them in detail. Though not flawless, the built–in DDI software proved to be a valuable tool for serious DDIs prevention. It is worth noting, that omeprazole-clopidogrel and clarithromycin – atorvastatin DDIs were relatively often ignored/misinterpreted.

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