Potential and clinically manifested drug-drug interactions in patients admitted to the hospital: a cross-sectional study

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Introduction

Drug-drug interactions (DDIs) are increasingly common, particularly due to the aging population and the rise in multimorbidity. Some DDIs result in adverse drug events, which may lead to hospitalizations.

Although many studies focus on potential DDIs, only a few examine clinically manifested DDIs.

The aim of this study was to provide information on the prevalence and characteristics of potential and clinically manifested DDIs in patients admitted to the hospital.

Methods

Data source: previous study[1] evaluating the contribution of adverse drug events to unplanned hospitalizations at University Hospital Hradec Králové (Czech Republic).

Population: patients admitted for unplanned hospitalization at University Hospital Hradec Králové with at least two medications in their medication history.

Drug Interaction databases:

- **Uptodate**
- **Micromedex**
- **Stockley**

Definition of Potential DDI:
A combination of two medications for which at least one interaction database indicated moderate or higher severity

Definition of Clinically Manifested DDI: DDI associated with adverse drug events

Limitations

- Cross-sectional design
- Retrospective data collection
  → unknown medication adherence
  → inaccurate medication history (e.g., use of OTC medications)

Results

Potential DDIs

The study included 968 patients with an average age of 73 years and an average of 7 medications in their medical history. Potential DDIs were identified in 90% (95% CI: 88–92) of the patients.

Most of them were classified as pharmacodynamic interactions with moderate severity.

Diuretics (C03), Antithrombotic agents (B01), and Drugs used in diabetes (A10) were the most common medication classes involved in potential DDIs.

Most frequent severe potential DDIs	N	%
ASA + warfarin	34	10.6
amiodarone + warfarin	23	7.2
amiloride + ramipril	18	5.6
ramipril + spironolactone	17	5.3
perindopril + spironolactone	15	4.7
potassium chloride + spironolactone	14	4.4
amiloride + perindopril	12	3.8
bromazepam + tramadol	8	2.5
ASA + dabigatran-etexilate	7	2.2

n=320 (100 %), ASA: acetylsalicyl acid, severity categories according to drug interaction databases: major (Uptodate), major, contraindicated (Micromedex), severe (Stockley)

1252 patients from the previous study[1] → **968** patients with at least 2 medications in their medical history → **867** (90 %) patients with a potential DDI in their medical history → **61** (6 %) patients with a clinically manifested DDI

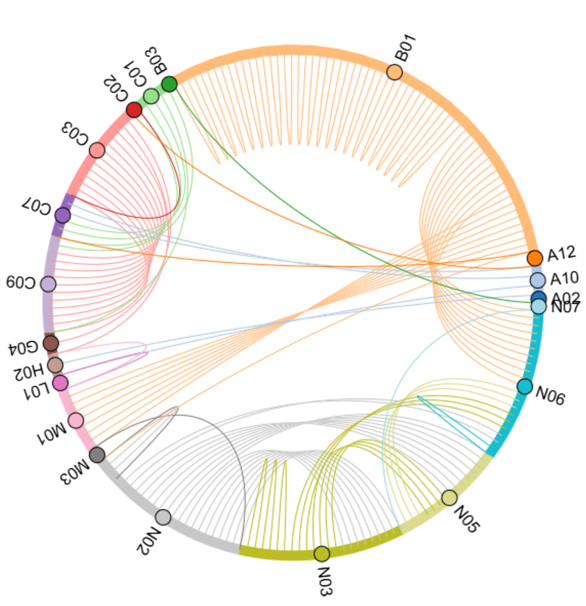
Clinically manifested DDIs

Of the potential DDIs, 1.4% manifested clinically. Clinically manifested DDIs were identified in 6% (95% CI: 5–8) of patients, predominantly presenting as gastrointestinal bleeding. The most common drug class involved in manifested DDIs was Antithrombotic agents (B01). Frequently implicated medications included acetylsalicylic acid, warfarin, tramadol, pregabalin, and clopidogrel.

The most frequent clinically manifested DDIs were combinations of acetylsalicylic acid + warfarin (n=5), acetylsalicylic acid + rivaroxaban (n=4), clopidogrel + warfarin (n=4), and pregabalin + tramadol (n=4).

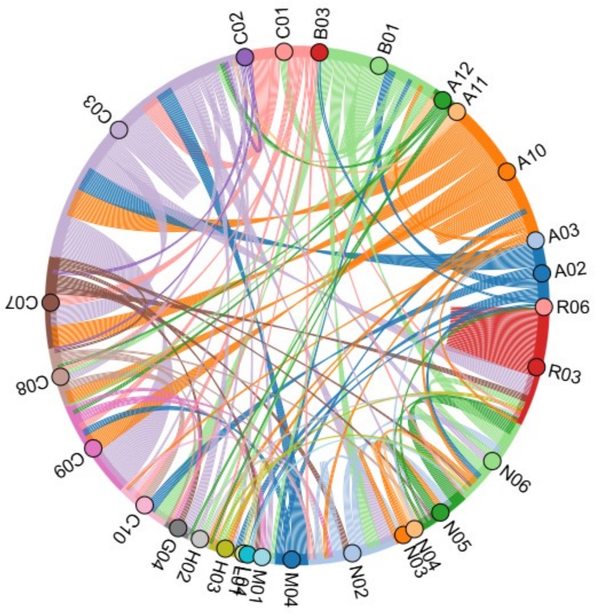
Most common medication classes involved in manifested DDIs	%
Antithrombotic agents (B01)	29.9
Analgetics (N03)	10.7
Antiepileptics (N02)	10.7
Psychoanaleptics (N06)	10.3
Psycholeptics (N05)	7.5
Diuretics (C03)	6.5
Agents acting on the renin-angiotensin system (C09)	6.1
Antiinflammatory and antirheumatic products (M01)	4.2
Beta blocking agents (C07)	2.8
Cardiac therapy (C01)	2.3

n=214 (100 %), number of manifested DDIs: 107



chord diagram of manifested DDIs

Visualization of the relationships between ATC groups of medications involved in clinically manifested DDIs



chord diagram of potential DDIs

Visualization of the relationships between ATC groups of medications involved in potential DDIs

Conclusion

A high prevalence of potential DDIs was found among acutely admitted patients, though clinically manifested DDIs were less common. Compared to previous research,[2] the rate of DDIs was significantly higher, underscoring the issue's growing importance. The discrepancy between potential and clinically manifested DDIs points to the need for targeted alert systems to prevent alert fatigue.

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