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# Drug-Drug Interactions Control of Cardiac Patients in Nation Heart Institute-Bach Mai Hospital

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**ABSTRACT**

**Background**: The incidence of cardiovascular diseases has increased in recent decades. Our main goal is to study the incident ratio of drug interaction and analyze the relationship between the number of used drugs and incident occurrence.
**Subject:** 100 in-patients clinical record in the Institute of cardio-vascular diseases, Bach Mai hospital from January 2007 to June 2007.
**Methods:** Retrospective analysis.
**Results and Conclusions:** Both the software Drug Interaction Facts 1998 and Mims Interactive 2001 revealed the incident ratio of drug interaction in the records in the Institute of Cardio-vascular diseases were rather high (80-91%).
**Conclusions**: The incident ratio was higher when the number of used drugs increased. ACE inhibitors with a potassium-sparing diuretic or loop diuretics, furosemide with digoxin, cephalosporin with an N-metylthiotetrazole ring.

**Keywords**
cardiac diseases, drug-drug interactions, polypharmacy, complications.

## Introduction

Drug–drug interactions (DDI) are defined as two or more drugs interacting in such a manner that the effectiveness or toxicity of one or more drugs is altered. DDI in patients receiving multidrug therapy is a major concern [1-3]. Drug therapy is growing more complex, thus making appropriate decision on drug therapy increasingly challenging [4]. Such interactions may lead to an increased risk of hospitalization and higher health care costs. Patients with cardiovascular diseases are particularly vulnerable to DDI due to their advanced age, polypharmacy and the influence of heart disease on drug metabolism [5, 6]. These interactions can be either pharmacokinetic or pharmacodynamic. Pharmacokinetic interaction is said to occur when one drug affects the effect of other drug by change in absorption, distribution, metabolism or excretion of another drug. On the other hand, pharmacodynamic interaction is seen when the two drugs either exhibit synergism or antagonism in their mechanism of action [7, 8]. Computational techniques can be used to predict potential drug-drug interactions [9-11]. Thirty-six percent of older adults in the U.S. regularly use five or more medications or supplements, and 15% are potentially at risk for a major drug-drug interaction (DDI) [12]. 75.9% patients taking 7 or more drugs were having at least one DDI [13-15].

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Researchers have found that the drugs commonly involved in DDI include cardiac glycosides, NSAIDs, diuretics and calcium channel block [16]. A study conducted in South India demonstrated that hospitalized cardiac patients are at an increased risk of potential drug interactions (30.67%) [17]. As these kind of events cannot be prevented without recognizing the need to adjust medications according to DDI risks, there is a need for carefully planned preclinical and clinical DDI studies during drug development, and typically also after marketing approval, as well as for modeling studies, databases, and clinical decision support systems that can be easily implemented and used to improve clinical decision making [18].

In order to initially assess the drug interactions met in clinical practice at the Heart Institute - Bach Mai Hospital, we conducted this study with the goal:

1) Survey the proportion of medical records experiencing drug interactions.
2) Analyze the relationship between the amount of medicine used in the medical record and the drug interaction.
3) Survey the prevalence of drug interactions in clinical practice according to severity.

## Materials and Methods

Subjects of the study included 100 cases of inpatient patients at Heart Hospital - BVBM from 1/2007 to the end of June 2007.

Retrospective research was provided. Random stratification and inclusion criteria: the number of drugs used in the medical record does not change with the whole course of treatment, it is the number of drugs studied. If the number of drugs used in the medical record changes during the course of treatment, that medical record may choose a prescription with the longest number of treatment days. 100 medical records were selected with 6 patient groups, each group consisting of 15-20 medical records, including the disease codes: I.10 - Idiopathic hypertension, I.20 – Angina pectoris, I.21 – Acute MI, I .49 – Arrhythmia, I.50 – Heart failure, I.80 – Phlebitis and thrombophlebitis. Detection of drug interactions was provided by software: MIMs Interactive 2001 and Drug Interaction Facts 1998.

**Categorize the level of interaction according to Mims interactive**

- Grade 0: No interactive classification.
- Grade 1: Monitor treatment.
- Grade 2: Be cautious, monitor patients.
- Grade 3: Consider the benefits and risks.
- Grade 4: Dangerous coordination.

**Classification of interaction levels by Drug Interaction Facts:**

- Dangerous interactions, life-threatening patients, there are evidence-controlled studies. Contraindications to coordination.
- Interactions may be the cause of affecting the clinical condition of the patient, there are evidence-controlled studies.
- The interaction caused a small number of effects, there were evidence-controlled studies.
- Interaction causes some effects from moderate to severe, the data proves to be limited.

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- Interaction causes some effects from mild to severe, there is no conclusive evidence to prove that it has clinical effects.

Evaluation of drug interactions was providing by using monographs: Stockley's Drug Interaction (e-version 2006), Ministry of Health (2006), Drug interaction and attention when indicated, Medical Publishing House [19]. Data processing: Using SPSS 13.0 software.

## Results and Discussion

The number of medical records using 10 drugs accounted for the highest proportion (22%). The number of medical records using 13 drugs accounts for 8%, the least number of drugs used in a medical record is 5 drugs (Figure 1).

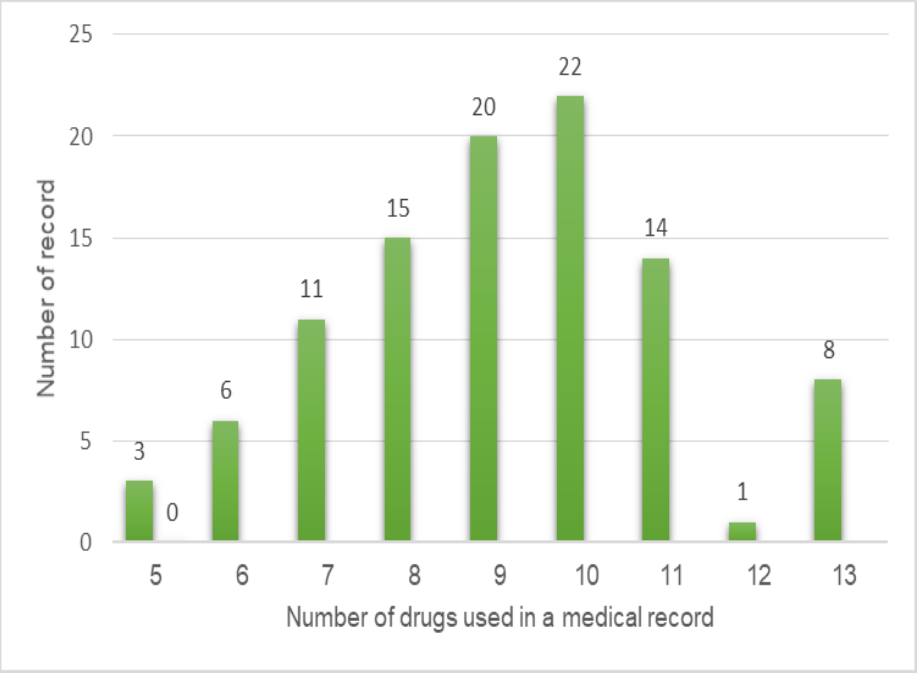


**Figure 1.** Distribution of drugs used in a medical record

Total number of medical records surveyed was 100. Number of Drug interaction facts recorded 80 and number of MIMs interaction facts recorded 91. Incidence of drug interactions, at all levels detected, by Drug Interaction Facts and Mims Interaction software are very high (80-91%). There were 31% clinically significant drug interactions for Drug Interaction Facts and 68% for Mims Interaction. The rate of drug interactions increases with the number of drugs used, consistent with the description of the domestic and international literature. about drug interactions that we refer to. When using 5 drugs in a prescription, only one over three of the medical records have interactions and only one interaction pair in a medical record. However, when adding 1 drug (using 6 drugs in one prescription), 4 out of 6 cases of drug interactions were found and the number of interaction pairs increased to 8 pairs. In particular, with the medical history of using 9 drugs, up to 7 pairs of interactions were encountered and with the history of using 11 drugs, up to 10 pairs of interactions were encountered. Research results on the relationship between the

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number of drugs used and drug interactions according to Drug Interaction Facts are presented (Figure 2).

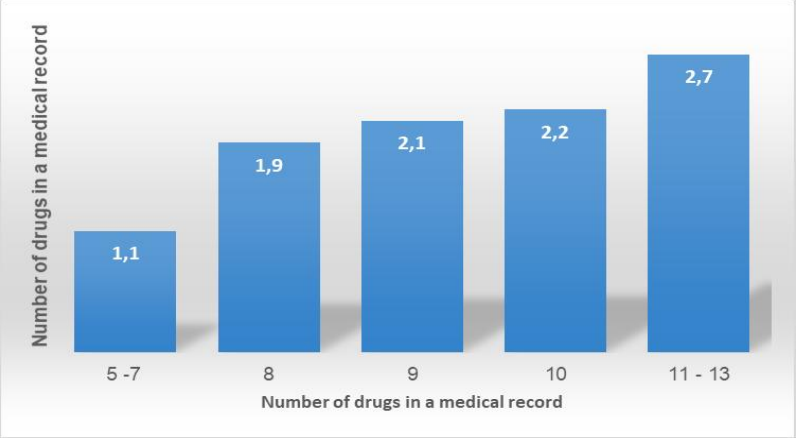


**Figure 2**. Relationship between number of drugs used and drug interactions according to Drug Interaction Facts

The rate of drug interaction increases with the number of drugs used, consistent with the description of the world literature and on drug interactions. When using 5 drugs in a single application, only one-third of the interaction history and only encountered a pair of interactions in a medical record. When using 6 drugs, there were 4/6 cases of interaction and the number of interaction pairs increased to 8 pairs. In particular, there are records of using 9 drugs met up to 7 interaction pairs and records of using 11 drugs met up to 10 interaction pairs.
Research results on the relationship between the number of drugs used and drug interactions according to Mims Interaction (Figure 3).

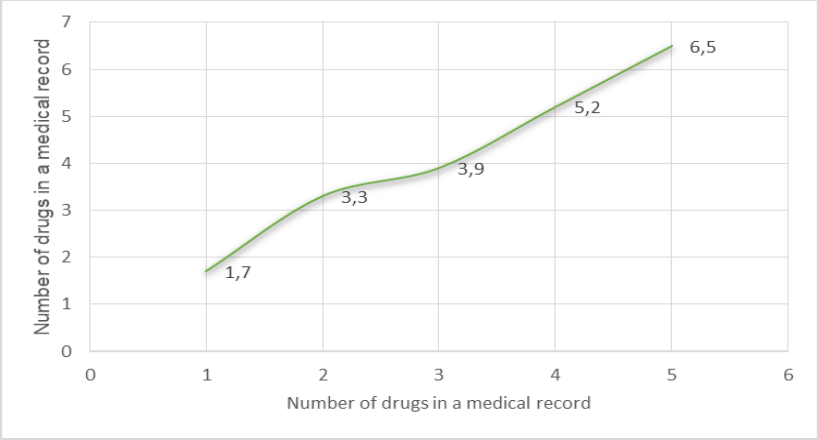


**Figure 3.** Relationship between number of drugs used and drug interactions according to Mims Interaction

The level of drug interaction is similar to that of Drug Interaction Facts. The rate of drug interaction increases according to the number of drugs in the prescription, in accordance with the description of domestic and international medical literature on drug interactions.

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**Severity of drug interactions**

Findings of the present study showed that the patterns of incidence of DDI are positively associated with patients' age, gender, number of drugs prescribed and length of hospital stay. A higher rate of DDI was present in women and patients who were more than 60 years of age [20-21]. The severity of DDI may vary from non-significant interactions to serious or life threatening interactions.

Research results on the severity of drug interactions encountered according to Drug Interaction Facts and MIMs interaction are presented in Table 1 and Table 2.

**Table 1.** Severity of drug interactions encountered according to Drug Interaction Facts

| Interaction level | Number of pairs Interactive | Frequency | |
|---|---|---|---|
| | | Interactively | % |
| Grade 5 | 11 | 67 | 33.0 |
| Grade 4 | 12 | 51 | 25.1 |
| Grade 3 | 5 | 48 | 23.6 |
| Grade 2 | 11 | 19 | 9.4 |
| Grade 1 | 7 | 18 | 8.9 |
| Total | 46 | 203 | 100 |

**Table 2.** Severity of drug interactions encountered according to Mims Interaction

| Interaction level | Number of pairs Interactive | Frequency | |
|---|---|---|---|
| | | Interactively | % |
| Grade 5 | 9 | 35 | 8.2 |
| Grade 4 | 22 | 65 | 15.2 |
| Grade 3 | 23 | 89 | 20.7 |
| Grade 2 | 62 | 193 | 45.0 |
| Grade 1 | 17 | 47 | 10.9 |
| Total | **133** | **429** | **100** |

The rate of drug interactions is most moderate and mild (91-92%). Severe drug interactions are still encountered with the rate of 8.2-8.9%.

The research on the serious drug interactions that are currently encountered in clinical practice according to Drug Interaction Facts and MIMs interactions was provided.

**Table 3.** Severe interaction pairs are encountered in clinical practice according to Drug Interaction Facts

| | **Medicine 1** | **Medicine 2** |
|---|---|---|
| 1 | Digoxin | Furocemide |
| 2 | Enalapril | Spironolactone |
| 3 | Potassium chloride | Spironolactone |
| 4 | Lisinopril | Spironolactone |
| 5 | Digoxin | Hydrochlothiazide |
| 6 | Digoxin | Indapamide |
| 7 | Amoxycycllin | Doxycycline |

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There were 7 pairs of serious interactions encountered in the use of drugs at the Heart Institute according to Drug Interaction Facts and 9 pairs of serious interactions according to MIMs interaction (Table 3 and Table 4).

**Table 4.** Severe interaction pairs are encountered in clinical practice according to MIMs interaction

| | **Medicine 1** | **Medicine 2** |
|---|---|---|
| 1 | Clarithromycine | Metoclopramide |
| 2 | Enalapril | Potassium aspartate |
| 3 | Enalapril | Potassium chloride |
| 4 | Lisinopril | Potassium aspartate |
| 5 | Lisinopril | Potassium chloride |
| 6 | Perindopril | Potassium aspartate |
| 7 | Perindopril | Potassium chloride |
| 8 | Spironolactone | Potassium aspartate |
| 9 | Spironolactone | Potassium chcloride |

In clinical practice, drug-drug interactions occur for two primary reasons: (1) the clinician is unaware of the effects of the combination of the 2 drugs due to lack of personal knowledge and (2) it is sometimes necessary to endure the effects of a drug-drug interaction because the benefit of therapy outweighs the risk of the potential adverse event [22]. Few other studies also suggest that cardiac patients are at higher risk of DDI as a number of cardiac drugs are associated with DDI as these patients are more vulnerable to DDI due to complexity of disease and multiple drug therapy [23-24]. Proper therapeutic planning, routine monitoring of cardiac in-patients and usage of online DDI database will avoid potentially hazardous consequences in cardiac in-patients [25]. The research results also show that, the problem of drug interactions encountered in clinical practice at the Heart Institute is relatively common and also shows that, if reducing the number of drugs used in a prescription, it will significantly reduce the number of correlations. drug effects encountered. The rate of drug interactions increases with the number of drugs used in the medical record. Drug interactions are encountered at all levels (Severe: 8-9%; Moderate: 34-56%; Mild: 36-56%). Several pairs of serious interactions are still being encountered in clinical practice, such as: ACE inhibitors with a potassium-sparing diuretic or loop diuretics, furosemide with digoxin, cephalosporin with an N-metylthiotetrazole ring. The absence of severe drug interactions and the restriction of mild and moderate drug interactions should be taken into account in prescription practice aimed at safe and effective use of drugs.

## Conclusions

The rate of drug interactions encountered increases with the number of drugs used in the medical record. Pairs of serious interactions seen are: ACE inhibitors with a potassium-sparing diuretic or loop diuretics, furosemide with digoxin, cephalosporin with an N-metylthiotetrazole ring. We suggest to limit to the maximum number of drugs used in a medical record, control the risk of drug interactions between expected drugs to be administered to the patient before prescribing, do not appoint drugs with an interaction of a dangerous level, enhance clinical performance and support measures to control safe prescription**.**

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