Original Article

Clinical drug-drug interactions of cardiovascular drugs and their case report

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ABSTRACT

This article deals with multifarious range of drug-drug interactions of all types of cardiovascular drugs (e.g., anti-anginal drugs, antihypertensive drugs, etc.) and their severity therein. This piece of work has been formulated after extensive research among various pharmacy-related literatures and contains inputs from all those works therein. DDI in patients receiving multidrug therapy is a major concern. The aim of the present study was to assess the incidence and risk factors of DDIs in patients admitted in the cardiology unit of a teaching hospital. Heparin and aspirin were the most common drugs responsible for DDIs. Bleeding was the most common clinical consequence found in the population. On assessment of severity of DDIs, the majority of the cases were classified as moderate in severity. Aging, female gender, and increase in concurrent medications were found to be associated with increased DDIs. Patients having these risk factors can be actively monitored during their stay in the cardiology department to identify DDIs.

Keywords: Cardiovascular drugs, drug-drug interactions, adverse drug reactions

INTRODUCTION

In general terms, drug-drug interactions of drugs can be explained as undesired or unexpected effects (mostly detrimental but sometimes minimalistic too) in addition to its normal known effect after administration of the drug due to its reaction or interaction with a coadministered drug.[1] Research has also shown that DDIs are associated with increased health-care use.[2] According to a recently published study, 1% of all hospital admissions are caused by DDIs, and 0.05% emergency department visits, 0.6% of the hospital admissions, and 0.1% of rehospitalizations are caused by adverse drug reactions (ADRs) due to DDIs.[3-5] Patients with cardiovascular diseases are particularly vulnerable to DDIs due to their advanced age, polypharmacy, and the influence of heart disease on drug metabolism.[4] The DDI potential for a particular cardiovascular drug varies with the individual, the disease being treated, and the extent of exposure to other drugs.[6]

A drug interaction is a result of PD and/or PK mechanisms. A PD interaction occurs due to additive or synergistic effect of two agents with similar molecular targets, which results in excessive clinical response or toxicity. A PK interaction involves one drug or substance changing the absorption, distribution, metabolism, or elimination of another drug or substance. The most common PK interactions involve the cytochrome P450 (CYP450) enzymes and the P-glycoprotein. The CYP enzymes lead to metabolism within the gastrointestinal (GI) tract. A drug-drug interaction occurs when an orally administered CYP3A substrate is given simultaneously with an inhibitor or inducer of intestinal CYP activity. For example, atorvastatin is metabolized through CYP3A4, and when given along with ceritinib (CYP3A4 inhibitor), elimination of atorvastatin decreases, which results in increased plasma concentrations and pharmacologic effect. Dose reduction or another statin (with a different metabolic enzyme pathway) may be vital in such cases.[7]

Objective drug	Precipitant drug	Clinical consequence[6-10]
Heparin	Aspirin	Bleeding
Heparin	Streptokinase	Bleeding
Heparin	Warfarin	Bleeding
Aspirin	Diltiazem	Bleeding
Aspirin	Eptifibatide	Bleeding
Aspirin	Insulin	Hypoglycemia
Aspirin	Captopril	Reduces captopril action

The above table showcases the clinical consequences of ample of cardiovascular drugs when coadministered. The table highlights the

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fact that in majority of the cases, bleeding has remained a major clinical consequence. Most of the interactions are shown by common drugs such as antiplatelets and anticoagulants. In the present study, heparin and aspirin coded for major interactions followed by drugs such as warfarin, diltiazem, and captopril.

One of the similar studies in 2006 known as NPSA assessment performed risk assessment of the prescription habits and found that prescription of anticoagulants with NSAIDs is one of the high risk involving coprescription. In case of such kind of practice, for instance, 7–26% of warfarin taking patients can face bleeding issues; in categories of minor, major, and fatal. There has been a linear relation in the interactions and the number of drugs prescribed.

Organ system	Affect	% Age
Platelet, bleeding	Increased bleeding	76
Whole body	Drug toxicity	11
Heart rate and rhythms	Bradycardia	9
Urinary tract	Acute renal failure	5

In the above table, various negative interactions have been showcased along with the site of occurrence and the probability as well. The first case of bleeding strikingly codes toward a PTT and indicates that it's level must be balanced in all cases, and even a little increase or decrease of its level in blood may have far reaching consequences and that situation in quite probable due to intake of majority of cardiovascular drugs. So, the caution while prescription must be taken. The second case refers to toxicity in the entire body of the individual, this can induce dysfunctional aspects to many cells in the body leading to wear and tear or termination of their activity altogether, though the chances of incidence are somewhat lower than the case of bleeding, but still it can prove fatal for many individuals, especially the elderly.

Another case of arrhythmia is no exception to cardiovascular drugs, as heart is the main target site of cardiovascular drugs. In many of the studies, bradycardia is seen as a probable interaction mainly in the elderly or mainly the cardiac patients. Acute renal failure is also one of the clinical consequences associated with the cardiovascular drugs but they have a lower probability as compared to the cases of bleeding, toxicity, and bradycardia. However, caution is required during prescription of drugs with thorough analysis of patient's epidemiology.

DISCUSSION

DDIs were reported from the cardiology department.[11] Concurrent use of many drugs and frequent addition of new drugs makes this group of patients vulnerable to DDIs. Despite all this, there is a need to increase the awareness of possible DDIs in all hospital departments, as a sizable number of DDIs have been recorded in all of them.[12] The age, gender, number of drugs taken, and multiple disease states were identified as the risk factors for developing DDIs.[4,13] There was an extremely significant linear relationship between the number of drugs prescribed and the DDIs in patients. Similarly, a significant linear relationship was observed between length of stay and DDIs. These results are in accordance with previous reports available in the literature.[12] Consistent with previous research, it was observed in this study that the use of multiple medications was associated with significantly increased risk of being prescribed potentially harmful drug-drug combinations .

CONCLUSION

This study reports the incidence of DDIs in the cardiology department in a hospital setting. This study also examined patient, drug characteristics, causality, and severity of DDIs. This study shows that DDIs are frequent among hospitalized cardiac patients. The factors influencing DDIs are age, gender, number of prescribed drugs, and length of hospital stay and cost. Thus, development and implementation of cautionary guidelines and computer-based screening might help to prevent potentially harmful drug interactions.

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