Review Article

Mini-review on impact of known drug-drug interactions in cancer patients

Simranjeet Kaur[1]*, Diksha Arora[1], Amandeep Singh[2]

[1]Department of Pharmacology, Faculty of Pharmaceutical Sciences, PCTE Group of Institutes, Ludhiana, Punjab, India, [2]Department of Pharmaceutics, ISF College of Pharmacy, Moga, Punjab, India

Correspondence:
Simranjeet Kaur, Faculty of Pharmaceutical Sciences, PCTE Group of Institutes, Baddowal - 141012, Ludhiana, Punjab, India. Mobile: +91-6280177913. E-mail: simranjstl@gmail.com

How to cite this article: Kaur S, Arora D, Singh A. Mini-review on impact of known drug-drug interactions in cancer patients. Pharmaspire 2020;12(2):114-116.

Source of Support: Nil,
Conflicts of Interest: None declared.

ABSTRACT

When a patient concomitantly uses two or more drugs, a drug-drug interaction (DDI) can possibly occur, potentially leading to an increased or decreased clinical effect of a given treatment. Cancer patients are at high risk of such interactions because they commonly receive multiple medications. Moreover, most cancer patients are elderly and require additional medications for comorbidities. Majorly, drugs with narrow therapeutics index cause more potential DDI. Severity of the interaction shows individual variability because of genetic polymorphism. Therefore, it is essential to properly detect DDI. The aim of this article is to study the different DDIs reviewed by several articles and a cohort of cancer outpatients undergoing multiple treatments.

Keywords: Drug-drug interaction, Narrow therapeutic index, New drug-dug interaction, Over-the-counter

INTRODUCTION

A drug-drug interaction (DDI) can be defined as the pharmacological or clinical event which is caused by coexposure of a drug with another drug or substance that modifies the patient's response to therapy.[1] DDIs result from a variety of processes which occur by pharmaceutical, pharmacokinetic, or pharmacodynamic mechanisms and have different outcomes which either increase or decrease the therapeutic efficacy, inducing adverse responses, or resulting in a unique response that does not occur when either agent is given alone.[2] The clinical effects of DDIs depend on multiple factors which includes the health status of a patient (age, underlying medical condition) and the narrow therapeutic index (NTI) of drugs involved (the smaller is NTI, the higher is the risk).[3]

Genetic polymorphisms underlying the individual variability that influences the response to a given treatment. Moreover, the interactions between drugs and over-the-counter or alternative medicines and herbs also occur[4] [Table 1]. In theory, patients with cancer are particularly susceptible to DDIs because they frequently take many medications – to treat their cancer, to treat treatment-induced toxicity and cancer-related syndromes, and to treat other underlying illnesses.[5] In addition, their pharmacokinetic parameters may be disturbed because of impaired absorption due to mucositis, increased volume of distribution resulting from edema and malnutrition, and altered excretion secondary to organ dysfunction also cancer patients usually fall between higher age groups which causes varied other problems, the pharmacological management of cancer patients is often hampered by an ineffective communication between specialists and/or patients[6] [Table 2]. This "open loop" management can potentially cause a late detection of DDIs and have detrimental effects[4] [Table 3].

The decision-making process for detection of DDI is complex and consists of a range of sources including adverse event database entries, spontaneous or case reports, *in vivo* and *in vitro* drug metabolism studies, and *in vivo* drug interaction studies in healthy subjects and patients.[7,8] In the absence of further rigorous studies to assess the clinical significance of DDIs, an evidence-based appraisal of the current literature is essential to guide practitioners involved in patient care. Two types of settings were studied. Under the first setting, different articles were studies to form a review on different DDIs, and under the second study, 64 adult patients in the ambulatory setting with malignant solid tumors who were

Access this article online	
Website: www.isfcppharmaspire.com	**P-ISSN:** 2321-4732 **E-ISSN:** XXXX-XXXX

Table 1: NDDIs described between general and over-the-counter medications

Interaction	No. of cases	Description	Severity
Warfarin × corticosteroids	1	Increased or decreased in anticoagulant effect of warfarin, unknown mechanism	Moderate
Proton-pump inhibitors × phenytoin	2	Increased dosage of anticonvulsant required	Minor
Ondansetron × Opioids	1	Severe constipation	Moderate
Acetylsalicylic acid × Warfarin	4	Increased anticoagulant effect of warfarin	Major
Acetylsalicylic acid × ACE inhibitors/beta-blockers	2	Lowering blood pressure effect of ACE inhibitors and beta-blockers may be reduced by prostaglandin synthesis inhibition	Minor

NDDIs: New drug-drug interactions

Table 2: Real drug-drug interactions

Drug combination	Clinical event	Mechanism of interaction
Phenytoin + warfarin	Deep venous thrombosis	Phenytoin induces warfarin hepatic metabolism with consequent reduction in its anticoagulant effect
Warfarin + omeprazole	Upper digestive hemorrhage	Omeprazole inhibits hepatic metabolism of warfarin, enhancing its anticoagulant effect
Diclofenac + enoxaparin	Post-surgical bleeding	Additive anticoagulant effect

Table 3: NDDIs between antineoplastic drugs and other medications[2]

Interaction	No. of cases	Description	Severity
Warfarin × Capecitabine/Paclitaxel	1 (head-neck)	Decreased dosage of warfarin required owing to an increased risk of hemorrhage	Moderate
Quinolones × Cyclophosphamide	2 (breast)	Mucositis induced by anticancer agents might alter the absorption of kinolon	Minor
Ondansetron × Cisplatin	1 (colorectal)	Increased dosage of cisplatin required	Moderate
Warfarin × Tamoxifen	4 (breast)	Increased risk of hemorrhage probably due to decreased metabolism of warfarin	Major
Phenytoin × Cisplatin	2 (colorectal)	Increased dosage of phenytoin required	Major
Hydrochlorothiazide × 5-FU/cyclophosphamide	1 (bladder)	Hydrochlorothiazide may prolong chemotherapy-induced neutropenia	Moderate
Furosemide × Cisplatin	1 (colorectal)	Ototoxicity augmentation, unknown mechanism	Minor

Table 4: Detail of settings 1 and 2

Process	Setting 1	Setting 2
Materials and method	PubMed was searched for epidemiology articles related to DDI, that is, articles describing the frequency of potential DDIs, of real DDIs and/or risk factors for DDIs among cancer patients. The search was complemented with abstracts presented at the American Society of Clinical Oncology meetings from 2005 to 2008. Descriptive statistics were used to describe the results, separated by potential versus real DDIs	Sixty-four adults were eligible patients in the ambulatory setting with malignant solid tumors treated with systemic anticancer therapies from January 2013 to June 2013. All patients recruited in the study had a performance status less than or equal to 2. Anamnestic and clinical data were collected on age, sex, diagnosis, and cancer treatment, comorbidity. Patients also declared any medication prescribed or self-taken in the 2 weeks previous to study enrolment

DDI: Drug-drug interaction

receiving systemic anticancer treatment were studied, as shown in Table 4.

DISCUSSION

For setting 1, studies of potential DDIs found that approximately one-third of patients are exposed to dangerous drug doublets, with the most common ones involving warfarin and anticonvulsants. One study of real DDIs found that 2% of hospitalized cancer patients had a DDI as the cause of admission. For setting 2, about 34 % of cancer outpatients within the cohort were prescribed/assumed interacting drug combinations. The most frequent major NDDIs involved the anticoagulant warfarin (33% of total NDDIs) that, in association with tamoxifen, or capecitabine and paclitaxel, increased the risk of hemorrhage. About 60% of NDDIs involved acetylsalicylic acid.

CONCLUSION

DDIs were studies for two settings wherein the first one involved reviewing the articles and compiling the information and the second one involved tests on 64 adult eligible patients and different results were recorded in both the cases but all in all drug interactions comprise an important issue in oncology, with approximately one-third of ambulatory cancer patients being at risk of DDIs. Data are limited on the clinical consequences of drug interactions among cancer patients.

REFERENCES

1. Moghaddas A, Adib-Majlesi M, Sabzghabaee AM, Hajigholami A, Riechelmann R. Potential drug-drug Interactions in hospitalized cancer patients: A report from the Middle-East. J Oncol Pharm Pract 2020;17:1078155220910209.
2. Assiri A, Noor A. A computational approach to predict multi-pathway drug-drug interactions: A case study of irinotecan, a colon cancer medication. Saudi Pharm J 2020;29:17.
3. Roberts AG, Gibbs ME. Mechanisms and the clinical relevance of complex drug-drug interactions. Clin Pharmacol 2018;10:123-34.
4. Ussai S, Petelin R, Giordano A, Malinconico M, Cirillo D, Pentimalli F. A pilot

study on the impact of known drug-drug interactions in cancer patients. J Exp Clin Cancer Res 2015;34:89.

5. Kaur V, Kaur K, Singh A. Development and characterization of probiotic loaded suppositories for cervical cancer management. Development 2020;1:48-53.
6. O'brien SN, Blijlevens N, Mahfouz TH, Anaissie EJ. Infections in patients with hematological cancer: Recent developments. Hematology 2003;1:438-72.
7. Lorberbaum T, Sampson KJ, Woosley RL, Kass RS, Tatonetti NP. An integrative data science pipeline to identify novel drug interactions that prolong the QT interval. Drug Saf 2016;39:433-41.
8. Singh A, Kaur K, Mandal UK, Narang RK. Nanoparticles as budding trends in colon drug delivery for the management of ulcerative colitis. Curr Nanomed 2020;10:225-47.