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A retrospective study on potential drug interactions: A single center experience

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ABSTRACT

Background: In this study, it is aimed to explain the type and frequency of potential drug-drug interactions (pDDI) in patients a Medical oncology service.
Methods: This study retrospective descriptive design. pDDIs were identified using the checker programme (Medscape®). Interactions were classified according to their clinical relevance as minor, moderate and major as appropriate.
Results: The prevalence of pDDIs was 71.3% and median age was 61 years-old (interquartile range 54–68) and female to male ratio was 116/211. The median number of drugs per patient was 8 (interquartile range 5–10). A total of 1102 pDDIs of 327 hospitalized cancer patients were identified. Of those, 16.7% were major and 61.8% moderate, respectively. Concomitant use of opioids was the most common interaction in our study.
Conclusions: Drug interactions were common in hospitalized cancer patients. In order to prevent potential hazardous effect of pDDI, awareness of the physicians should be increased about this issue.

1. Introduction

Drug-drug interaction (DDI) is defined as a situation in which a drug modify the action or effects of another drug, lead to alter the patient's response to therapy.[1–3] It is a common problem[4,5] and the rate of adverse drug reaction is 20–30% in routine clinical practice.[6,7] In addition, the mortality rate related to DDI is approximately 4%.[7,8] DDIs have various levels of severity ranging from mild to severe fatal events.[4] Drug interactions can categorized into 2 groups; potential drug drug interaction and real drug interaction. PDDI is defined as the occurrence of a potentially harmful combination. Real drug interaction can be demonstrated in clinical practice.[5,9] Pharmacologically, drug interactions are separated into three classes: a. Pharmaceutical interactions occurs when mixing chemically incompatible drugs outside the body; b. Pharmacodynamic interactions synergistic, additive, antagonistic and sequence-dependent effects may occurs when two drug are used concomitantly; c. Pharmacokinetic interactions occurs when a drug interferes with the absorption, distribution, metabolism and/or excretion of another drug.[1,9,10] DDIs have three possible consequences as altered the effectiveness or increased adverse events of the drugs or unexpected response.[1,5] The severity of fatal events related to DDIs may correlate with the polypharmacy[11,12] in hospitalized patients.[10] Not only polypharmacy, but also disease burden, length of stay and demographic and clinical characteristics of the patient also effect this potential hazardous event.

Patients with cancer are at high risk of DDIs as chemotherapeutic drugs are used in multi-drug combination regimens. These patients also use medications for cancer-related syndromes such as pain, emesis and infection. However, an additional problem is that cancer incidence increases with aging. Also elderly patients usually have multiple comorbidities and receive multiple drugs to treat these comorbidities.[1,12,13] Unfortunately, the patients receiving medical treatment for cancer is at high risk for potential drug

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interactions. This polypharmacy increases the risk DDIs in oncology practice. In our study, we aimed to assess the frequency and severity of pDDI in hospitalized cancer patients.

2. Methods

Data collection were started after Trakya University Ethics Committee approved the study.

2.1. Patients

This retrospective study was conducted between January and April 2017 in our medical oncology service. A total of 327 patients who were hospitalized more than 24 h were analyzed. Patients who received drugs in a clinical trial programme were excluded.

2.2. Study design

Drugs were categorized into two groups as chemotherapy and other drugs (drugs used for supportive treatment and drugs used in treatment of comorbidities). When a drug formulation included two or more active pharmaceutical ingredients like piperacillin/tazobactam each drug was counted separately in the analysis. However, when a patient who receiving the same medication in more than one formulation (e.g. intravenous and oral tramadol) was counted only once. Drug interactions were identified by using the checker programme (reference.medscape.com/drug-interactionchecker). PDDI was classified into three categories according to a level of severity as minor, moderate and major. “Minor” DDIs were defined as drug combinations likely to have no significant clinical relevance; “moderate” as drug combinations where a drug may modify the effect of the another drug and need to be monitored closely; “major” as drug combinations that should be usually avoided or may potentially lead to serious clinical consequences.

2.3. Statistical analysis

Descriptive statistics (mean, median) were applied to characterize all study sample with regard to demographics, cancer type, treatment objective, type of anticancer agents, comorbidities, number of drugs per patient and interaction characteristics. The difference between the groups was compared using Chi-square or Fisher's Exact tests. All data were analyzed using the Statistical Package for the Social (SPSS) version 16.0 (SPSS Inc. Chicago, IL) computer programme and a value of $p < 0.05$ was considered statistically significant.

3. Results

3.1. General characteristics

Table 1 showed the demographic and clinical characteristics of the patients. The median age was 61 years (interquartile range 54–68) and female to male ratio was 211/116. The most common underlying diseases were gastrointestinal cancer (30.9%), followed by lung (25.0%) and genitourinary (13.5%) cancer. Two hundred-three (80.4%) patients had metastasis and 39.1% of these (n = 128) had at least one comorbid disease. The majority of patients had hypertension (73.4%), diabetes mellitus (25.7%). In addition, the median length of hospital stay of patients was 5 days (interquartile range 2–10) and fifty patients (15.3%) died during hospitalization. Ninety-eight patients received chemotherapy during admission. Approximately three quarters (76.2%) of the patients were hospitalized for palliative care. Thirty-four patients (10.4%) did not take any medication for the treatment of their primary disease.

Table 1
Characteristics of patients, N = 327.

Characteristic	n	%
Age (years)		
Median (Interquartile range)	61 (54–68)	–
Gender		
Male/Female	211/116	64.5/35.5
Chemotherapy ratio	98	30.0
Underlying disease		
Gastrointestinal cancer	101	30.9
Lung cancer	82	25.0
Genitourinary cancer	44	13.5
Head and neck cancer	31	9.5
Hepatobiliary cancer	26	7.9
Breast cancer	19	5.8
Others	24	7.4
Patients with comorbidity	128	39.1
Hypertension	94	73.4
Diabetes Mellitus	33	25.7
Hypothyroidism	5	3.9
Coronary arterial disease	4	3.1
Length of stay (days)		
Median (Interquartile range)	5 (2–10)	–
Death		
Yes/No	50/277	15.3/84.7
Metastatic stage	263	80.4
Reason for admission		
Chemotherapy	78	23.8
Palliative care	249	76.2
Cancer treatment		
Chemotherapy	214	65.4
None	34	10.4
Chemotherapy + Antibody	31	9.5
Supportive Care	23	7.0
TKI/mTORs	14	4.3
Antihormonal therapy	8	2.5
Chemotherapy + antihormonal therapy	2	0.6
Antibody	1	0.3

3.2. Drug-drug interactions

PDDI was detected in 233 patients (71.3%) who had at least one interaction, while 94 patients did not show any interaction. The median number of drugs per patient was 8 (interquartile range 5–10). The maximum number of drug used during the admission was 22. Table 2 showed that a total of 1102 potential drug-drug interactions were detected among the patients who received 2 or more medications. Only 21 (1.9%) of these were with chemotherapy drugs. Most of the interactions (n = 1081, 98.1%) were together with supportive care medications. Major and moderate pDDIs were detected as 16.7% and 61.9%, respectively.

Table 3 demonstrated the common pDDIs in patients who received the multiple medications. The most frequent agents included at pDDIs were opioids, SSRIs, corticosteroids, nonsteroidal

Table 2
Drug-drug interactions.

pDDI	n	%
pDDI		
Yes/No	233/94	71.3/28.7
Number of drugs per patient		
Median (Interquartile range)	8 (5–10)	–
Minimum-Maximum	1–22	
Total	1102	100
Chemotherapy-related	21	1.9
Other drugs related	1081	98.1
Level of severity		
Major	184	16.7
Moderate	682	61.9
Minor	236	21.4

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