Journal of
Cancer Science & Therapy

Sisay et al., J Cancer Sci Ther 2015, 7:2
DOI: 10.4172/1948-5956.1000325

Research Article Open Access

Drug Related Problems in Chemotherapy of Cancer Patients

Eskinder Ayalew Sisay[1], Ephrem Engidawork[2], Teshager Aklilu Yesuf[1] and Ezra Belay Ketema[3]*

[1]Department of Pharmacy, College of Health Sciences, Mekelle University, Mekelle, Ethiopia
[2]Department of Pharmacy, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia
[3]Department of Biochemistry, College of Health Sciences, Mekelle University, Mekelle, Ethiopia

Abstract

Background: Drug Related Problems (DRPs) in cancer chemotherapy can have severe consequences originating from the high toxicity and narrow therapeutic range of anticancer drugs.

Objective: This study was conducted to investigate drug-related problems and factors associated with it in hospitalized cancer patients at Tikur Anbessa Specialized Hospital.

Method: A cross-sectional study was conducted at Tikur Anbessa Specialized Hospital from January to June 2013. A total of 367 study participants were recruited by simple random sampling technique and data were collected by medical chart review using data abstraction format.

Results: Four hundred seventy four drug-related problems were identified in 274 patients among the 367 patients, which gave rise to a prevalence of 74.7%. The most prevalent drug-related problem was adverse drug reaction (45.5%) followed by dosing problem (37.9%). The risk factors for DRPs were number of medications, co-morbidity and length of hospital stay.

Conclusion: Drug related problems were common among cancer patients in our set up indicating a need for intervention like involvement of a pharmacist for better therapeutic outcome.

Keywords: Cancer; Chemotherapy; Drug related problems; Ethiopia

Introduction

The increase in number of available drugs and drug users as well as more complex drug regimens lead to more side effects and drug interactions, and complicate follow-up [1]. Drug related problems (DRPs), which includes adverse drug reactions (ADRs), unnecessary drug therapy, inappropriate choice of drugs, and untreated conditions, has been reported in up to 25% of hospitalized patients. DRPs can lead to substantial morbidity and mortality. Drug toxicity is also a major limitation in providing healthcare to patients at a global level. It affects the patient's recovery as well as the economy of healthcare [1,2].

In systemic cancer therapy, drug regimens are administered following established protocols which have been carefully evaluated in clinical trials. The more complex drug therapy is the higher the risk of experiencing DRPs such as adverse effects, interactions, medication errors, and non-adherence. The use of anticancer drugs often results in the use of other agents to reduce or prevent side-effects of the anticancer treatment, thereby increasing the interaction potential. Furthermore, cancer itself increases the need for more medications. Cytotoxic agents have a narrow therapeutic window and a complex pharmacologic profile. In oncology patients, pharmacokinetic parameters can be altered by the disease itself or due to malnutrition, reduced levels of serum-binding proteins, edema, or hepatic and/or renal dysfunction. Patients with cancer are therefore more at risk for drug interactions (DRP) [3]. Therefore it must be the goal of all health care providers to minimize treatment-associated risks as much as possible in these patients.

A more comprehensive study of DRPs in hospitalized patients would provide valuable insights for the healthcare professionals trying to reduce the incidence of DRPs [4]. However there is scarcity of data on comprehensive DRPs among hospitalized patients. So far, most studies published had addressed either the problem of drug-related admissions to hospitals or focused only on adverse drug reactions (ADRs) among hospitalized patients. Therefore, the aim of this study was to investigate the prevalence, type and risk factors of DRPs in cancer patients admitted to the Oncology clinic of Tikur Anbessa Specialized Hospital (TASH).

Methods and Materials

Study setting

A cross-sectional study was conducted from January to June 2013 at the Oncology unit of Tikur Anbessa Specialized Hospital (TASH), the biggest and oldest tertiary hospital in Ethiopia. A total of 367 study participants were recruited using minimum sample size calculation by simple random sampling technique. New or follow up cases were included in the study when they came to the clinic and their medical chart was reviewed [5-7].

Data collections

Two Pharmacists and one Nurse were recruited for data collection. Appropriate orientation was given for them on the data abstraction tool. The quality of data was checked by the principal investigator for appropriateness on a daily basis.

Data was collected from patients' medical chart using data

***Corresponding author:** Ezra Belay Ketema, Department of Biochemistry, College of Health Sciences, Mekelle University, Mekelle, Tigray 231, Ethiopia, Tel: 251(344)404005; E-mail: aga.bely@gmail.com

Received December 04, 2014; **Accepted** February 25, 2015; **Published** February 27, 2015

Citation: Sisay EA, Engidawork E, Yesuf TA, Ketema EB (2015) Drug Related Problems in Chemotherapy of Cancer Patients. J Cancer Sci Ther 7: 055-059. doi:10.4172/1948-5956.1000325

abstraction format which was prepared by review of literature for relevant variables in DRPs, review of treatment protocols and referring Pharmacy Guide to Chemotherapy-Clinical Assessment of British Colombia Cancer Agency (BCCA) [8]. A pre-test of the data abstraction format was done and the components of the format were modified accordingly. The format consists of variables like patient's age, sex, weight, height, diagnosis/cancer type, co-morbidity, medications and dosage, length of hospital stay, laboratory results.

DRPs were identified by cross-checking the collected data with the local treatment protocol, other protocols like BCCA, using Pharmacy Guide to Chemotherapy-Clinical Assessment and Review of BCCA, chemotherapy drug monographs and drug interaction database.

Equations like Cockcroft-Gault equation for creatinine clearance calculation in assessment of renal function, Du Bois method for Body Surface Area (BSA) calculation, Calvert formula for carboplatin dose calculation were used. Drug interaction was checked using Micromedex 2.0 and Medscape.com online drug interaction checker.

DRPs were classified as adverse drug reaction, dosing problem, need for additional drug therapy, unnecessary drug therapy, potential drug-drug interaction and inappropriate drug chart based on classification systems developed by other authors with modification [1,9-11].

Inclusion and exclusion criteria

All charts of patients who were admitted to the oncology unit and who had taken chemotherapy were included in the study. Charts of patients who had not taken chemotherapy like who came for blood transfusion were excluded from the study population.

Statistical analysis

Data was entered using Epi Info Version 3.5.1. The independent variables were tested for statistical association with the chance of DRPs using binary logistic regression analysis with Statistical Package for the Social Sciences (SPSS) version 16.0 software to investigate for risk factors of DRPs. Statistical association was considered to be significant at $P<0.05$.

Ethical consideration

Ethical clearance was obtained from the Institutional Review Board of College of Health Sciences, Addis Ababa University. Official letter was written to the Oncology Department of TASH where the data was collected.

Results

Characteristics of the study population

A total of 367 patients were included in this study of which 186 (50.7%) were female. The mean age ± standard deviation was 42.7 ± 1.4 years (range 12 to 78 years) (Table 1).

The most prevalent cancer type was Gastrointestinal, diagnosed in 108 (29.4%) patients, followed by Head/Neck cancer [69 (18.8%)] and Genitourinary cancer [60 (16.3%)]. About one-fifth (21.8%) of patients had co-morbidities. The common co-morbid diseases recorded include Type 2 diabetes, hypertension and HIV/AIDS. Metastasis stage was determined in 184 (50.1%) patients; of which metastasis stage IV cancer was recorded in 68 (18.5%) patients. A total of 2,325 drugs were prescribed considering the recent chemotherapy cycle of each patient. The median number of medications prescribed per cycle was 6.0. The median length of Hospital stay was 2 days (Table 1).

Drug types

Majority of patients were on Cisplatin + Fluorouracil regimen (103 patients) followed by Fluorouracil + Leucovorin (65 patients) (Table 2).

Drug-related problems (DRPs)

Altogether, 474 DRPs were identified in 274 patients, giving the prevalence rate of 74.7%. The most prevalent DRP was ADR (45.5%) followed by dosing problem (37.9%) (Table 3). Among the ADRs, Nausea and vomiting was the most prevalent which was recorded in 161 patients.

Dosing problem was occurred in 139 patients (high or low doses). Some of the problems seen were related to use of un-updated body surface area, exceeding appropriate cumulative doses or missing dose adjustment in abnormal laboratory results, such as low creatinine clearance.

In this study, about 62 patients (16.9%) encountered unnecessary drug therapy such as duplication of therapy while 8.2% of the study participants were in need for additional drug therapy. The specific cases we found in this study include the patients' need for additional premedication before the chemotherapy regimen was given and the need for initiation of treatment of medical conditions like chronic atopic dermatitis and dyslipidemia.

Characteristics	Corresponding value
Age (years)	
Mean ± SD Median	42.7 ± 1.4
Distribution n (%)	45
10-19	27 (7.4%)
20-29	53 (14.4%)
30-39	68 (18.5%)
40-49	66 (18%)
50-59	111 (30.2%)
60-69	37 (10.1%)
70-79	5 (1.4%)
Sex	
Female (n [%])	186 (50.7%)
Male (n [%])	181 (49.3%)
Cancer Type (n [%])	
Gastro-intestinal	108 (29.4%)
Head and Neck	69 (18.8%)
Genitourinary	60 (16.3%)
Sarcoma	46 (12.5%)
Others	84 (22.9%)
Metastasis stage determined (n [%])	184 (50.1%)
Metastasis stage IV cancer (n [%])	68 (18.5%)
Co-morbidity exist (n [%]	80 (21.8%)
Number of medications	
Mean + SD	6.4 + 0.97
Median	6.0
Minimum	4
Maximum	10
Length of Hospital stay (days)	
Mean + SD	2.6 ± 2.4
Median	2
1-2 days (n [%])	209 (56.9%)
3-5 days (n [%])	150 (40.9%)
6 days (n [%])	8 (2.2%)

Table 1: Clinical and demographic characteristic of cancer in-patients at TASH.

Chemotherapy Regimen	Number of patients (%)
Cisplatin + Fluorouracil	103 (28%)
Fluorouracil + Leucovorin	65 (17.7%)
Paclitaxel + Cisplatin (Carboplatin)	55 (15%)
VAC	36 (9.8%)
CHOP	22 (6%)
FOLFOX	15 (4.1%)
Cisplatin + Doxorubicin	10 (2.7%)
BEP	10 (2.7%)
AFP	8 (2.2%)
Cisplatin + Cyclophosphamide	7 (1.9%)
Cisplatin only	6 (1.6%)
Paclitaxel only	6 (1.6%)
Vinblastin + Cisplatin	6 (1.6%)
Others (each given in less than 5 patients)	18 (4.9%)

* VAC: Vincristine, Adriamycin and Cyclophosphamide; CHOP: Cyclophosphamide, Adriamycin, Vincristine and Prednisolone; FOLFOX: Oxaliplatin, Fluorouracil and Leucovorin; BEP: Bleomycin, Etoposide and Cisplatin and AFP: Adriamycin, Fluorouracil and Cisplatin

Table 2: Types of Chemotherapy regimens given in TASH.

	Number of Occurrences	Proportion / Sample* [N = 367]	Proportion / Total DRPs [N = 474]
Adverse drug reaction	167	45.5	35.2
Dosing problem	139	37.9	29.3
Inappropriate drug chart	65	17.7	13.7
Unnecessary drug therapy	62	16.9	13.1
Needs additional therapy	30	8.2	6.3
Drug-drug interaction	11	3	2.3

*Total does not add up to 100% as some patients had >1 reported DRP.

Table 3: Classification of Drug-related problems in cancer in-patients at TASH.

Regarding drug interaction, cimetidine had shown most of the drug interactions which was the routinely prescribed drug for any in-patients coming for chemotherapy.

Factors associated with DRPs

Two patient data were excluded from the analysis since they were outliers in their length of hospital stay with 21 and 31 days. The following variables were tested for their association with DRPs: number of medications, sex, presence of co-morbidity, age, length of hospital stay, regimen deviation, use of inappropriate body surface area (BSA), undetermined metastasis stage and inappropriate use of laboratory result. Presence of Co-morbidity (p=0.002), number of medications (p=0.02) and length of hospital stay (3-10 days) (p=0.001) were positively and significantly associated with incidence of DRPs (Table 4).

Multivariate logistic regression analysis also revealed that presence of co-morbidity (AOR: 3.1; p<0.003), length of hospital stay (AOR: 2.6; P<0.000) and number of medications (AOR: 1.4; p<0.028) were positively associated with the occurrence of DRPs (Table 5).

Regimen deviation from local protocol accounted for 155 cases (42.2%). Of these, 155 patients, DRP was identified in 118 (76.1%) patients.

Discussion

Drug-related morbidities are a significant healthcare problem, and great proportions are preventable. Increasingly, there have been numerous reports of the incidence, prevalence, and preventability of medication error-related deaths, drug-related hospital admissions, and adverse drug events in the inpatient and outpatient setting [2,12-14].

We identified 474 DRP in 367 patients which was much lower as compared with the prospective study done in Netherland that showed 952 DRP in 546 patients [6]. But a higher number of DRP was detected in this study when compared with another retrospective study done in Portugal that detected 43 DRP in 56 patients although it focused mainly on intervened DRPs (avoidable) which do not account for unavoidable DRPs like ADR [5]. This variation indicates that as such comparisons are hampered by different settings, measurement methods and classification systems.

In cancer chemotherapy ADRs are strongly connected to the treatment itself. Because of the fact that most cytotoxic agents cannot distinguish between normal and neoplastic cells, most ADRs seem to be unavoidable. They are often accepted not only by patients but also by health care providers. The most prevalent DRP in this study was ADR which occurred in 45.5% of the population (34.4% of the total number of DRPs). The study done in Florida among elderly patients found an actual or potential ADR in 56.3% of the study participants [12]. Similarly a study done in Thailand showed that ADR was the most common DRPs which was seen in 44 of 68 cancer patients (64.70%) both in inpatient and outpatient setting. The ADRs detected were nausea, vomiting, alopecia, and diarrhea which were also recorded in our study except diarrhea [7].

Another study done in Portugal where the team of oncology pharmacists monitored 56 patients between showed that interventions related to adverse effects such as emesis protocol optimization and other supportive treatment accounted for about 11.6%. This indicates the presence of ADR as a DRP but the percentage is low compared to

Variables		DRP		Crude OR (95% CI)	p-value
		Yes	No		
Regimen deviation		118 (76.1%)	37 (23.9%)	1.16 (0.72-1.87)	0.545
Inappropriate BSA		28 (100%)	0 (0%)		0.998
* undetermined metastasis stage		136 (74.3%)	47 (25.7%)	1 (0.64-1.64)	0.929
Use of in appropriate lab results		17 (94.4%)	1 (5.6%)	6.133 (0.805-46.74)	0.08
Sex	Male	139 (77.2%)	41 (22.8%)	1	
	Female	133 (71.9%)	52 (28.1%)	1.326 (0.83-2.13)	0.243
Age	70-79	4 (80%)	1 (20%)	1.4 (0.15-12.9)	0.769
	60-69	31 (83.8%)	6 (16.2%)	1.8 (0.697-4.65)	0.224
	50-59	80 (72.1%)	31 (27.9%)	0.9 (0.52-1.57)	0.709
	40-49	48 (73.8%)	17 (26.2%)	0.98 (0.51-1.9)	0.963
	< 40	109 (74.1%)	38 (25.9%)	1	0.722
Co-morbidity	Yes	69 (88.5%)	9 (11.5%)	3.2 (1.514-6.65)	0.002
Hospital stay	1-2	142 (67.9%)	67 (32.1%)	1	
(days)	3-10	130 (83.3%)	26 (16.7%)	2.36 (1.414-3.94)	0.001
No. of Meds				1.4 (1.0-1.85)	0.02

*undetermined metastasis stage indicates metastasis stage is unknown or not described in patient chart

Table 4: Univariate Logistic Regression results for individual risk factors.

Variables		DRP		Adjusted OR (95% CI)	p-value
		Yes	No		
Use of inappropriate Laboratory result		17 (94.4%)	1 (5.6%)	7.67 (0.98-60)	0.052
Co-morbidity	Yes	69 (88.5%)	9 (11.5%)	3.1 (1.47-6.72)	0.003
Hospital stay (in days)	1-2	142 (67.9%)	67 (32.1%)	1	
	3-10	130 (83.3%)	26 (16.7%)	2.6 (1.55-4.45)	0
No. of Meds				1.4 (1-1.92)	0.028

Table 5: Multivariate Logistic Regression results.

this study and it could possibly be due to the study sample differences and this study recorded all ADRs not the interventions made to ADRs [5].

In this study, nausea and vomiting occurred in 161 (43.9%) patients of which about 134 patients (83%) needed aprepitant when they took highly emetic chemotherapy. But unavailability of antiemetic like aprepitant is one major problem in our case. The second more prevalent DRP in this study was dosing problem (low dose or high dose) that occurred in 37.9% of the participants accounting 28.7% of the total number of DRPs. Low dose was also the second more prevalent DRP in the Thailand study which occurred in 34.24% of the study population. The study indicated only low dose as a dosing problem while our study included high dose with low dose as a dosing problem [7]. The Portugal study also showed that the majority of interventions were related to the need to adjust dosages (53.5%) which is much higher than this study. This could be because oncology pharmacists were involved in the follow-up and small sample size was included in the study [5]. Relatively low dose per body surface area is given in the oncology unit of TASH and this is to avoid life threatening complications which are supposed to be difficult to manage in this Hospital.

Inappropriate drug chart recorded in 17.7% of the participants (13.4% of the total number of DRPs) while Thailand study showed incomplete patient's data in 21 cases (30.88%) [7]. These findings indicate as presence of patient chart registration problem could possibly affect therapeutic outcome. If the drug chart is written as "premedication" then the nurse will encounter a problem in administering appropriate chemotherapy, since the chemotherapy drugs need a different kind of premedication according to the regimen selected, some may be mild emetic or highly emetic or some might need prophylaxis for infusion reaction like in paclitaxel. Unnecessary drug therapy is one of DRPs which occurs when there is duplication of therapy (multiple drug products are being used for a condition that requires single drug therapy), contraindication or when the drug is given in the absence of a medical condition (or when not it is needed). In this study, duplication of the antiemetics was found. Antiemetics were given while they were not important in the low and moderately emetic chemotherapy regimens. A contraindicated drug was also used while there was a renal dysfunction.

The study in Florida identified number of medications, presence/absence of dementia, and age as risk factors for the presence of DRPs. The factor having the strong association with incidence of DRPs was the number of medications (AOR: 4.17) [12]. Our study also showed a statistically significant association between numbers of medications and presence of co-morbidity with occurrence of DRPs but it did not show significant association between age and presence of DRPs.

A study done in Norway indicated that the number of DRPs per patient increased approximately linearly with the increase in number of drugs used; one unit increase in number of drugs yielded an 8.6% increase in the number of DRPs (95% CI 1.07, 1.100 [15]. Our logistic regression analysis also showed that one unit increase in the number of drugs increases the presence of DRP by 1.4 odds. This study also found that the length of hospital stay to be a risk factor for DRPs in addition to the presence of co-morbidity and number of medications.

Conclusion

This study showed that DRPs were common at TASH Oncology clinic. The risk factors associated with DRPs were the presence of co-morbidity, number of medications and length of hospital stay. Our findings indicated that cancer patients are one of the groups who are most at risk of developing DRPs. This calls for interventions which could include involvement of a pharmacist in management of cancer patient to detect and intervene DRPs to ensure a better therapeutic outcome.

Acknowledgments

The authors would like to thank all the staffs of Tikur Anbesa Hospital oncology clinic, and data collectors and study participants involved in the study.

Authors Contributions

Conceived and designed the experiments: EA EE TA EB. Performed the experiments: EA EE TA EB. Analyzed the data: EA EE TA EB. Contributed to reagents/materials/analysis tools: EA EE TA EB. Wrote the paper: EA EE TA EB. Prepare and wrote the manuscript: EA TA EB.

References

1. Ruths S, Viktil KK, Blix HS (2007) [Classification of drug-related problems]. Tidsskr Nor Laegeforen 127: 3073-3076.
2. Leendertse AJ, Egberts AC, Stoker LJ, van den Bemt PM; HARM Study Group (2008) Frequency of and risk factors for preventable medication-related hospital admissions in the Netherlands. Arch Intern Med 168: 1890-1896.
3. Jaehde U, Liekweg A, Simons S, Westfeld M (2008) Minimising treatment-associated risks in systemic cancer therapy. Pharm World Sci 30: 161-168.
4. Koh Y, Kutty FB, Li SC (2005) Drug-related problems in hospitalized patients on polypharmacy: the influence of age and gender. Ther Clin Risk Manag 1: 39-48.
5. Cavaco P, Dias S Ornelas S, Ribeiro N, Falcao F (2012) Pharmacotherapeutic Follow-Up in Oncology. Eur J Hosp Pharm: 19: 225.
6. Bulsink A, Imholz AL, Brouwers JR, Jansman FG (2013) Characteristics of potential drug-related problems among oncology patients. Int J Clin Pharm 35: 401-407.
7. Itchipruchyabun A (2008) Drug related problems in chemotherapy patients. Medical journal of srisaaket surin buriram hospitals 23: 333-340.
8. British Columbia Cancer Agency (2011) Pharmacy Guide to Chemotherapy: Clinical Assessment and Review, 3rd Edition, 2011.
9. Cipolle RJ, Strand LM, Morley PC (2012) Pharmaceutical Care Practice: The Clinician's Guide. 2nd ed. New York: McGraw Hill, 2004.
10. Gómez MA, Villafaina A, Hernández J, Salgado RM, González MA, et al. (2009) Promoting appropriate drug use through the application of the Spanish drug-related problem classification system in the primary care setting. Ann Pharmacother 43: 339-346.
11. Pharmaceutical Care Network Europe (2006) PCNE Classification for Drug Related Problems V5.01. PCNE classification.
12. Bain KT, Weschules DJ, Tillotson P (2006) Prevalence and Predictors of Medication-related Problems. Medicare Patient Management 2006: 14-27.
13. Rahmawati F, Pramantara DP, Rohmah W, Sulaiman SAS (2009) Polypharmacy and Unnecessary Drug Therapy On Geriatric Hospitalized Patients In Yogyakarta Hospitals, Indonesia. International Journal of Pharmacy and Pharmaceutical Sciences: 1: 6-11.
14. Singh H, Kumar BN, Sinha T, Dulhani N (2011) The incidence and nature of

drug-related hospital admission: A 6-month observational study in a tertiary health care hospital. J Pharmacol Pharmacother 2: 17-20.

15. Viktil KK, Blix HS, Moger TA, Reikvam A (2007) Polypharmacy as commonly defined is an indicator of limited value in the assessment of drug-related problems. Br J Clin Pharmacol 63: 187-195.