

Brief Communication

Prescribing Pattern and Prescription-writing Quality of Antineoplastic Agents in the Capital City of a Middle-income Developing Country

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INTRODUCTION

Cancer is a global health concern and the third cause of death in Iran.^[1,2] Chemotherapy is the cornerstone of treatment in most of the malignancies.^[3] With respect to increased number of patients who are treated in outpatient and chemotherapy clinics, the continuity of care is especially important.

In Iran, antineoplastic medications are dispensed mainly by authorized community-dwelling pharmacies. Patients should get the antineoplastic medications from these pharmacies and then return to the physician office or clinic for administration. Lack of national health information network in addition to inadequate communication between health-care providers involved in this hospital-community interface could negatively

affect the efficacy and safety of chemotherapy.^[4] The prescription plays a specifically important role in this setting as the main link between prescriber, dispenser, and the patient.

To the best of our knowledge, antineoplastic use and prescribing pattern have not been studied in Iran. Moreover, no report was published about antineoplastic prescription-writing quality in our country. This study aimed at evaluation of prescribing pattern and prescription-writing quality in the capital city of Iran.

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ABSTRACT

Objective: Cancer is a global health concern with growing incidence worldwide. Chemotherapy is the main treatment modality in many malignancies. This study aimed at evaluation of antineoplastic prescribing pattern and prescription-writing quality in the capital city of Iran. **Methods:** All dispensed chemotherapy prescriptions by four main authorized pharmacies in Tehran during 1 month were targeted. Prescriptions with no antineoplastic medications or written by specialties other than oncology-related fields were excluded from the study. From the total 10,944 eligible prescriptions, 2736 (25%) prescriptions were selected randomly for data extraction. **Findings:** Total 5784 antineoplastic medications were written by 239 physicians; most of them were adult hematologist–oncologist (69.0%) and male (86.6%). Each prescription contained an average of 1.8 (± 0.9) antineoplastic medications. The most widely prescribed antineoplastic agents were cyclophosphamide (16.2%), fluorouracil (15.2%), doxorubicin (12.8%), and oxaliplatin (11.0%). The quality of prescription writing was poor; diagnosis, drug dosing, treatment schedule, and instructions were mostly absent. Sixty percent of drugs were written in brand names. **Conclusion:** The prescribing writing quality was poor and patients were at great risk of medication errors. Prompt action including policies and educational strategies should be taken to assure effective and safe patient treatment with antineoplastic medications.

KEYWORDS: *Antineoplastic agent, oncology, prescribing pattern, prescription*

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METHODS

All dispensed chemotherapy prescriptions by four authorized community pharmacies in Tehran from August 22, 2014, to September 22, 2014, were targeted. Prescriptions contained at least one antineoplastic medication based on the AHFS Pharmacologic-Therapeutic Classification (AHFS Drug Information 2015) were included in the study. We excluded prescriptions that were written by the physician with specialties other than oncology, hematology–oncology, radiotherapy, gynecology–oncology, and urology–oncology.

Of the 10,944 eligible prescriptions, 2736 (25%) were selected randomly. Sampling was performed using a random number list to select 25% of each day's prescriptions, filled in each pharmacy. For each prescription, data including prescription requirements, prescribed medication(s), physician and patient characteristics, and dispensed medication(s) were recorded. The prescription-writing quality was evaluated considering the frequency of recording prescription requirements that were determined based on the WHO guide to good prescribing and Iran medical council law.^[5]

Chemotherapy combinations in the prescriptions were identified, and the major indication of each combination was determined based on the Physicians' Cancer Chemotherapy Drug Manual 2015^[6] and opinions of expert oncologist and clinical pharmacist (Cancer Institute, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences).

Descriptive statistics were applied to explore the data. Mean (standard deviation [SD]) and frequency (percentage) were reported to describe quantitative and qualitative data. Categorical data were analyzed using Pearson's Chi-square test; $P < 0.05$ was defined as a statistically significant difference. All statistical analyses were performed using SPSS version 21 (IBM SPSS Statistics, IBM Corporation, Armonk, NY, USA).

RESULTS

The selected prescriptions were written by 239 physicians and contained 5784 antineoplastic medications. Physicians' characteristics are described in Table 1. Thirty physicians wrote approximately 50% of the prescriptions. The mean (SD) age of patients was 53.6 (16.91) years and 41.2% of them were male.

Each prescription contained an average (SD) of 4.7 (2.3) and 1.8 (0.9), total items, and antineoplastic medications, respectively. The most widely prescribed antineoplastic medications were cyclophosphamide ($n = 443$, 16.2%), fluorouracil ($n = 417$, 15.2%),

Table 1: Physicians' characteristics

	No. (%)
Specialty	
Adult hematologist-oncologist	1887 (69.0)
Radiotherapist	723 (26.4)
Pediatric hematologist-oncologist	88 (3.2)
Other	38 (1.4)
Academic degree	
Specialist	613 (22.4)
Post-graduate medical resident	23 (0.8)
Post-graduate medical fellow	83 (3.0)
Sub-specialist	2017 (73.7)
Sex	
Male	2370 (86.6)
Female	366 (13.4)

doxorubicin ($n = 350$, 12.8%), and oxaliplatin ($n = 302$, 11.0%). The most frequent prescribed antineoplastic medications in patients younger than 18 years old were vincristine and methotrexate with a frequency (%) of 41 (47.1) and 24 (27.6), respectively.

Table 2 summarizes frequently prescribed ($\geq 1\%$) chemotherapy combination regimens. Based on expert opinion, 14 of the 22 frequent chemotherapy regimens are mainly used in the treatment of different stages of colorectal and breast cancers.

In 41.4% of the prescriptions, R/superscription was not recorded. Diagnosis was not recorded in 92% of the prescriptions. No physician mentioned patient's weight and/or body surface area (BSA) in the prescription. Dosing instruction was only mentioned for 9.3% of the 5780 prescribed antineoplastic items. Among them, only one dosing was written accurately (i.e., in mg/kg or mg/m²). Route of administration was only written for 1.6% of the antineoplastic medications. For >99% of the written antineoplastic medications, the number and duration of the cycle were not mentioned in the prescription.

The abbreviation was detected for names of the 16 antineoplastic medications and used in writing of 11.5% of the total prescribed antineoplastic items. Fluorouracil was the most frequent abbreviated item (453 of the 665 abbreviations). About 40.5% of the prescribed antineoplastic medications were written in the generic name. Furthermore, writing antineoplastic names in generic or brand was independent of the academic degree ($P = 0.245$) and specialty ($P = 0.596$) of the physician.

Among prescribed antineoplastic medications that were written in brand names, data regarding dispensed medication by the pharmacies were available for 2645 items. Nearly 69.9% of the dispensed medications by the pharmacies were in accordance with the prescribed brand

Table 2: Chemotherapy combination regimens with frequency of $\geq 1\%$ in the prescriptions

(%)	Chemotherapy combination	Assumed Diagnosis
9.0	Fluorouracil + Oxaliplatin	Metastatic colorectal/colorectal cancer
8.6	Doxorubicin + Cyclophosphamide	Breast cancer
4.5	Carboplatin + Paclitaxel	Metastatic breast cancer
4.1	Cisplatin + Fluorouracil + Docetaxel	Head and neck cancer
3.8	Capecitabine + Oxaliplatin	Colorectal cancer
2.7	Doxorubicin + Cyclophosphamide + Vincristine + Rituximab	Gastric cancer/DLBCL
2.3	Bleomycin + Dacarbazine + Vinblastin + Doxorubicin	Hodgkin lymphoma
2.0	Docetaxel + Cyclophosphamide	Breast cancer
1.8	Epirubicin + Cyclophosphamide	Breast cancer
1.8	Gemcitabine + Oxaliplatin	Biliary tract/Hepatocellular cancer
1.8	Docetaxel + Cyclophosphamide + Doxorubicin	Breast cancer
1.7	Fluorouracil + Methotrexate + Cyclophosphamide	Breast cancer
1.6	gemcitabine + Vinorelbine	NSCLC
1.6	Tamoxifen + Triptorelin	Breast cancer
1.3	Carboplatin + Docetaxel	Advanced NSCLC
1.2	Bevacizumab + Irinotecan + Fluorouracil	Metastatic colorectal cancer
1.2	Carboplatin + Gemcitabine	Metastatic NSCLC/bladder cancer
1.1	Fluorouracil + Irinotecan	Metastatic colorectal
1.1	Epirubicin + Cyclophosphamide + Fluorouracil	Breast cancer
1.0	Bevacizumab + Oxaliplatin + Fluorouracil	Advanced colorectal cancer
1.0	Bortezomib + Cyclophosphamide	Multiple myeloma
1.0	Cetuximab + Oxaliplatin + Fluorouracil	Metastatic colorectal cancer

DLBCL=Diffuse Large B-Cell Lymphoma, NSCLC=Non-small-cell lung carcinoma

of medication. The prescribed brands and dispensed medications matched in most of the cases in three of the pharmacies, but one of the pharmacies had less matching than the rest (Pearson's Chi-square = 399.41, $P < 0.001$).

DISCUSSION

The evaluation of prescribing pattern revealed that antineoplastic medications are mainly prescribed by hematologist–oncologists, and the type of mostly prescribed medications is compatible with the prevalent cancer types in our country.^[7]

An average of 1.8 antineoplastic medications was written in the prescriptions. Similarly, an average number of 1.97 and 1.78 cytotoxic medications per prescription was reported in the institutional studies in India and Nepal, respectively.^[8,9]

Sixty-three percent of the detected chemotherapy regimens are mainly used in the treatment of different stages of the breast and colorectal cancers. It is in agreement with the GLOBOCAN report that mentioned breast cancer to have the highest age-adjusted incidence in Iran.^[7] Moreover, institutional studies in India also reported fluorouracil and platinum combination as the most frequently used chemotherapy.^[9] Similarly, pyrimidine analogs (for example, cytarabine, fluorouracil, gemcitabine, capecitabine, and tegafur) were also the

most frequently used antineoplastic medications in Taiwan.^[10]

The quality of prescription writing in the studied antineoplastic prescriptions was unacceptable. Diagnosis was written only in 8% of the prescriptions. Weight and/or BSA of the patient were not written in any prescription. The dosing instruction and route of administration of antineoplastic medication were mentioned for <10% of the prescribed items, and nearly, all of them had no information regarding the treatment cycle duration and intervals.

We could not find any published study regarding antineoplastic medication prescribing quality and pattern in Iran. Scant data are available about commitment to prescription-writing principles in Iran. In a study in Kashan, dosing instructions were written in 47% of the prescribed items and weight of the patient was available in 0.6% of prescriptions.^[11]

The physicians might assume it unnecessary to write instructions for antineoplastic agents when the patient should return for administration after filling the prescription. However, lack of dosing and administration instruction in the prescriptions could easily result in medication error that would be fatal for antineoplastic medications. Moreover, the clinical verification of the antineoplastic prescription by the pharmacist could not be performed when no data are

recorded regarding diagnosis, patient weight or BSA, dosing, administration instruction, and treatment schedule. This is while the verification is a main recommended strategy to prevent chemotherapy prescription errors.^[12] In addition, writing dosing and use instructions and chemotherapy schedule is especially important for oral antineoplastic medications.^[4] In our country, the prescription sheets of insurance companies do not have a specified part for recording patient's weight and/or BSA. The prescription sheets of most of the insurance companies have a section for writing the diagnosis. However, there is no obligation prohibits filling prescriptions that do not contain the diagnosis.

In spite of recommendations to use generic names (not brand names) and avoiding abbreviations in prescribing,^[12] more than half of the antineoplastic medications were written in brand names in our study. In addition, writing fluorouracil in abbreviation occurred frequently in studied prescriptions. Specific notifications have been released to avoid writing fluorouracil in abbreviation, considering reported incidents and medication errors. Physicians usually emphasize on getting a specific brand medication, concerning efficacy and safety of the less popular brand and generic medications. Nearly 70% of the written and dispensed brand antineoplastic medications were compatible in our study.

One of the study limitations is restriction of prescription inclusion to the main pharmacies in Tehran. However, pharmacies with major share of antineoplastic medication dispensing in Tehran were considered as the study setting while distribution of cancer treatment services in the country is discriminate, and chemotherapy facilities are concentrated in the capital city.^[2] Another limitation is short duration of study that could affect the comprehensiveness of the observation.

This study could provide a snapshot about antineoplastic prescribing pattern in Iran. The prescription-writing quality was unacceptable that puts patients at risk of medication errors. Prompt action including policies and educational strategies should be taken to assure effective and safe patient treatment with antineoplastic medications.

AUTHORS' CONTRIBUTION

Concept: Molouk Hadjibabaie, Design: Molouk Hadjibabaie, Maryam Taghizadeh-Ghehi, Definition of intellectual content: Molouk Hadjibabaie, Maryam Taghizadeh-Ghehi, Ava Mansouri, Literature search: Maryam Taghizadeh-Ghehi, Data acquisition: Asiyeh

Amouei, Data analysis: Maryam Taghizadeh-Ghehi, Ava Mansouri, Asiyeh Amouei, Statistical analysis: Arefeh Jafarzadeh Kohneeloo, Manuscript preparation: Maryam Taghizadeh-Ghehi, Asiyeh Amouei, Manuscript editing and manuscript review: Ava Mansouri, Arefeh Jafarzadeh Kohneeloo.

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Conflicts of interest

There are no conflicts of interest.

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