Parallel Assessment of Chemotherapy Adherence and Supportive Therapy Adherence on Occurrence and Minimization of Adverse Drug Reactions Among Cancer Patients: A Clinical-Based Observational Study

Jyoti Kumar, PharmD¹, Manjula Gudhoor, MPharm¹ ,
and Madiwalayya Shivakantayya Ganachari, PhD¹

Abstract

Background: Cancer is a disease that is inevitably treated using chemotherapy, but the cytotoxic drugs used in the treatment have the potency to cause adverse drug reactions (ADRs). Thus, supportive therapy plays an essential role in managing the untoward effects of the cancer drugs in patients. This highlights the importance of medication adherence in managing the disease, mitigating and preventing the occurrence of chemotherapy-induced ADR without compromising the health status of the cancer population. **Objective:** To assess the adherence to chemotherapy and supportive therapy and to evaluate type and degree of causality of ADRs observed in cancer patients. **Methods:** On ethics committee approval, a 6-month observational study was conducted among recruited cancer patients undergoing chemotherapy in a tertiary care hospital. Morisky Medication Adherence Measurement Scale–8 was employed to assess the medication adherence, and ADR causality was determined using Naranjo ADR Probability Scale. **Results:** Ninety cancer patients participated in the study, out of which females were 61.11%. Chemotherapy adherence in comparison to supportive drugs was observed to be more (21.11%). Twelve different combination of ADR were reported in the subjects with variability in the degree of causality assessment. **Conclusion and Relevance:** The distinction of adherence to the medication used in cancer management with marked level of ADR was well depicted in the study, implicating the necessity of prudent symbiotic practice of an oncology pharmacist, patient, and physician relationship in optimizing the quality of life of cancer patients by imparting vigilant efforts in medication adherence.

Keywords

chemotherapy, supportive care, adverse drug reactions, adherence, cancer, pharmaceutical care

Background

The increased accessibility of potent medications and advancement in the technology used in the biomedical sector has shown remarkable improvement in the quality of life of cancer patients.¹ Although there is a rapid evolution of cancer treatment,² medication adherence is overlooked in cancer patients. Studies related to medication adherence to chemotherapy and non-chemotherapeutic supportive care therapy seems underutilized in daily oncology practice. Moreover, due to rise of uncontrolled adverse drug reactions (ADRs), the recovery rate of cancer patients has been reduced in the geriatric population.³ Imbalance in the medication-taking behavior and occurrence of ADRs has resulted

in intensive clinical and economic consequences.² Thus, it is necessary to gain insight into the factors influencing the nonadherence to chemotherapy and supportive drugs, such that the ADR occurrence is controlled wisely and the patient's disease condition is managed thoroughly. This will, in turn, generate an evidence to prove the effective use of chemotherapy and supportive therapy in fulfilling the gap in

¹KLE College of Pharmacy, KAHER, Belagavi, Karnataka, India

Corresponding Author:

Manjula Gudhoor, Department of Pharmacy Practice, KLE College of Pharmacy, KLE Academy of Higher Education, Belagavi 590010, Karnataka, India.
Email: g.manjula273@gmail.com

Figure 1. Methodology.

cancer management. Additionally, it will help in treatment decision-making to improve medication adherence in cancer patients.

Objective

The primary goal of the study was to assess the adherence to chemotherapeutic and non-chemotherapeutic drugs along with the evaluation of the type of ADRs and the causality level of the ADRs observed in cancer patients receiving chemotherapy.

Methods

On institutional ethics committee approval, a 6-month observational study was conducted in cancer patients admitted in the Oncology Department of KLE Dr. Prabhakar Kore Hospital and Research Centre, Belagavi, Karnataka, India (Figure 1).

The role of an oncology pharmacist in our institution is to do medication reconciliation, drug wastage minimization, check the admixture form and medicines sent by the oncologist for its appropriateness, and simultaneously preform reconstitution, which is further delivered to the nursing unit for administration, postdischarge patient counseling, medication adherence assessment, ADR and toxicity monitoring through routine laboratory tests, ADR management through patient education, and training to health care professionals on safe handling practices to reduce exposure to hazardous drugs. This indicates the collaborative approach toward the pharmaceutical care to optimize the therapeutic outcome in oncology clinical settings.

Table 1. Demographic Details: Age and Gender Distribution.

Age (Years)	Gender		Total (%)
	Male, n (%)	Female, n (%)	
11-20	1 (1.11)	0 (0)	1.11
21-30	4 (4.44)	2 (2.22)	6.66
31-40	4 (4.44)	6 (6.66)	11.11
41-50	3 (3.33)	5 (5.55)	8.88
51-60	5 (5.55)	22 (5.55)	30
61-70	13 (14.44)	17 (18.88)	33.33
71-80	5 (5.55)	3 (3.33)	8.88
Total	35 (38.88)	55 (61.11)	100

Results

Patient Demographics

The demographic details signify that among 90 recruited patients, 61.11% were females and 38.88% were males. A total of 33.33% are in the age group of 61 to 70 years, and 30% are from 51 to 60 years of age. Around 11.11% were in the age group of 31 to 40, whereas 8.88% of the recruited patients were in the age group of 41 to 50 and 71 to 80 years. And only 1.11% was found between 11 and 20 years of age (Table 1).

Therapeutic Regimen

The cancer distribution was done into 11 different groups. These groups were further classified using mostly prescribed oral and intravenous (IV) chemotherapy and supportive therapy (Table 2).

Chemotherapy and Supportive Therapy Adherence

To check the adherence of the patients to chemotherapy as well as supportive therapy, Morisky Medication Adherence Scale-8 Questionnaire was utilized. In case of chemotherapy adherence, it was observed that 57.8% of patients showed high adherence, 26.7% showed intermediate adherence, and the remaining 15.6% exhibited low adherence. Apparently, there was minute difference observed in case of adherence to supportive therapy to about 45.6% patients with highest adherence followed by 28.9% at intermediate level and 25.6% low adherence (Table 3).

Factors of Medication Nonadherence

Out of 90 patients, 69 patients were prescribed with both IV and oral chemotherapy. Among these 69 patients, 40 patients were affected by these factors resulting in nonadherence (Table 3). But patients who received IV chemotherapy were affected to minimal level by factors influencing

Table 2. Type of Cancer Distribution Among 90 Patients With Regard to Common Therapeutic Regimen.

	Diagnosis	Number of Patients	Intravenous Chemotherapy	Oral Chemotherapy	Supportive Therapy
1	Breast cancer	32	Paclitaxel, Doxorubicin, 5-fluorouracil, Daunorubicin, cyclophosphamide, 2-sulphanylethanesulphonate, trastuzumab	Capecitabine, vinorelbine	Palonosetron HCl, calcitonin salmon nasal solution, zoledronic acid, tigecycline
2	Esophagus cancer	3	Irinotecan, 5-fluorouracil	Tegafur + uracil	Leucovorin calcium, amphotericin B, dexamethasone
3	Lung cancer	6	Paclitaxel, carboplatin, pemetrexed	Vinorelbine	Aprepitant, zoledronic acid, tigecycline, netmicin, Cerebrolysin
4	Germ cell tumor	6	Gemcitabine, bleomycin, etoposide, cisplatin	Etoposide	Palonosetron HCl, aprepitant, alprostadil, Cerebrolysin
5	Rectum cancer	4	Oxaliplatin, paclitaxel	Capecitabine	Aprepitant, tigecycline, amoxicillin + potassium clavulanate
6	Colon cancer	4	Oxaliplatin, daunorubicin	Tegafur + uracil	Palonosetron HCl, amphotericin B
7	Multiple myeloma	5	Bortezomib	Melphalan, etoposide	Netmicin, zoledronic acid, caspofungin acetate, dexamethasone
8	Ovary cancer	3	Paclitaxel, carboplatin	Etoposide	Tigecycline, dexamethasone, cerebrolysin
9	Pancreas cancer	4	Paclitaxel	Fluorouracil	Aprepitant, octreotide acetate, tigecycline
10	Follicular lymphoma	5	Cyclophosphamide, doxorubicin	Cyclophosphamide, fludarabine	Tigecycline, caspofungin acetate, dexamethasone
11	Others	18	Rituximab, cyclophosphamide, doxorubicin, vincristine, epirubicin	Procarbazine, Abiraterone, Capecitabine, Letrozole	Aprepitant, pegfilgrastim, netmicin, zoledronic acid, tigecycline, dexamethasone
Total		90			

Table 3. Morisky Medication Adherence Scale on Chemotherapy and Supportive Therapy, and Factors Affecting Medication Nonadherence in Patients Receiving Oral Chemotherapy.

Morisky Medication Adherence Scale for Chemotherapy and Supportive Therapy ^a			
Morisky Medication Adherence Scale	Chemotherapy Adherence, n (%)	Supportive Therapy Adherence, n (%)	Average Adherence
Low adherence	14 (57.8)	23 (45.6)	19
Intermediate adherence	24 (26.7)	26 (28.9)	25
High adherence	52 (15.6)	41 (25.6)	46
Factors Influencing Medication Nonadherence ^b			
Factors	Percentage of patients (N = 69)		
Skipping due to occurrence of ADR	30.44%		
Less tolerability to medication	5.79%		
Absence of caretaker, ignorance, negligence, and cost burden	13.04%		
Polypharmacy, lack of knowledge about therapy	8.69%		

Abbreviation: ADR, adverse drug reaction.

^aScore: 3-4 = low adherence; 1-2 = intermediate adherence; 0 = high adherence.

^bForty were affected by nonadherence factors, and remaining 29 were unaffected.

nonadherence because IV chemotherapy was given under supervision of health care professionals.

Assessment of Adverse Drug Reactions

Almost 12 types of reactions were observed among the 90 patients receiving chemotherapy. Causality for majority of

the ADRs was assessed using a standard tool, that is, the Adverse Drug Reaction Probability Scale, also termed as Naranjo Scale, which consists of 10 questionnaires. These combination of reactions were dominantly related to alopecia and nausea (9); alopecia and generalized weakness (6); gastrointestinal upset, nausea, and loss of appetite (11); alopecia and skin allergic reactions (7); alopecia, nausea, loss

Table 4. Parallel Assessment of ADR and Medication Adherence.

Type of ADR	Doubtful ADR ^a	Probable ADR ^a	Possible ADR ^a	Total
Alopecia	1	4	1	6
Alopecia and nausea	2	6	1	9
Alopecia and generalized weakness	0	3	3	6
Gastrointestinal upset, nausea, and loss of appetite	0	10	1	11
Alopecia and skin allergic reactions	0	6	1	7
Alopecia, nausea, loss of appetite, and generalized weakness	0	6	2	8
Alopecia, tastelessness, and loss of appetite	2	8	4	14
Skin allergic reactions	2	2	0	4
Alopecia, nausea, and loss of appetite	0	6	2	8
Gastrointestinal upset, nausea, loss of appetite, and generalized weakness	0	2	6	8
Others reactions	9	0	0	9
Total number of patients	16	53	21	90
Degree of adherence (chemotherapy and supportive therapy)				
Low adherence	4	9	6	19
Intermediate adherence	8	12	5	25
High adherence	4	32	10	46

Abbreviation: ADR, adverse drug reaction.

^aNaranjo ADR score: 0 = doubtful ADR; 1-4 = probable ADR; 5-9 = possible; >9 = definite ADR.

of appetite, and generalized weakness (8); alopecia, tastelessness, and loss of appetite (9); skin allergic reactions (4); alopecia, nausea, and loss of appetite (8); alopecia, tastelessness, and loss of appetite (5); gastrointestinal upset, nausea, loss of appetite, and generalized weakness (8); and other reactions (9). But only alopecia was observed in 6 patients. Around 53 cases were reported under probable ADR, 21 under possible ADR, and 16 cases were with doubtful ADR (Table 4).

Parallel Assessment of ADR and Assessment

Four out of 16 patients with doubtful ADR showed high medication adherence; similarly, 8 patients showed intermediate adherence, and low adherence was observed in 4 patients. Additionally, out of 53 patients with probable ADR manifested, 32 showed high adherence, 12 showed intermediate adherence, and 9 showed low adherence. Also, 10 showed high adherence, 5 intermediate adherence, and 6 low adherence in 21 patients with possible ADR (Table 4).

Discussion

We examined level of adherence and occurrence of ADRs in 90 patients, out of which 61.11% females were diagnosed with cancer in higher proportion in comparison to males (38.88%). It was because most of the patients recruited in the study suffered from breast cancer. Hence, in the present study, females were more than males (Table 1).

For the current research, the study population recruited was inpatients receiving IV chemotherapy under the supervision of health care professional, so this became the direct

measurable component to assess the chemotherapy medication adherence. Thus, medications were prescribed based on the patient condition (chemotherapy) and sensitivity and tolerability to the chemotherapy-induced complications (supportive therapy; Table 2).

Treatment adherence in cancer patients is associated with improved health outcome and decreased health care cost.⁴ In present study, Morisky Medication Adherence Scale-8 Questionnaire was used to assess the adherence of antineoplastic and supportive drugs. Around 57.8% patients showed high adherence to oral as well as IV chemotherapy (Table 3). A retrospective analysis conducted by Seal et al⁵ claims fairly high adherence of IV chemotherapy with mean medication possession ratio ranging between 0.84 and 0.88. In current study, we examined the supportive therapy adherence that accounted for 45.6% (high adherence), which gives strength to the present study for measuring the level of adherence for supportive therapy, because there are hardly any research studies conducted to assess supportive therapy adherence in cancer patients.

Higher adherence was observed with chemotherapy in comparison to supportive therapy (Table 3) because patients had knowledge of importance of administration of cancer drugs for their own betterment. Despite awareness, 57.96% of patients showed nonadherence to cancer therapy (antineoplastic and supportive drugs) because of several factors leading to critical clinical consequences. Factors corresponding to nonadherence were due to occurrence of ADRs as reported by 30.44% subjects, 5.79% participants reported less tolerance as one of the factor, 13.04% patients who had ignorant attitude, negligence toward therapy due to absence of caretaker or financial constraints, and 8.69% patients

skipped medications due to polypharmacy as well as lack of knowledge to distinguish between cancer and noncancer drugs (Table 3). Bouwman et al⁶ conducted a cross-sectional study where almost 50% hematological adult cancer participants claimed factors like lower age group, staying alone, and false perception of lack of social support as reasons for nonadherence to medication. Besides, an open-label randomized controlled trial conducted by Krikorian et al⁷ on outpatients receiving antineoplastic drugs reports nonadherence due to falling asleep, feeling depressed, forgetfulness, and to avoid adverse effects.

Behera et al⁸ conducted a study in a tertiary care hospital in India, claiming that 21.8% of ADRs were due to antineoplastic agents. However, in present research work, patients were observed with significant doubtful, probable, and possible ADRs. A total of 12.1% of the patients suffered from a combination of various reactions like gastrointestinal upset, nausea, and loss of appetite, and 8% to 10% had experienced concoction of alopecia, skin allergy, generalized weakness, and gastrointestinal disturbances. Hardly any definite ADRs were reported in such a short span. In addition, only 4% to 6% of the patients have reported mono or dual reactions of alopecia and skin allergy during the chemotherapy cycle. These types of ADRs can be managed through supportive therapy, but lack of adherence or discontinuation of medication led to clinical repercussions (Table 4). A similar study by Lau et al⁹ had identified 10 common ADRs in patients diagnosed with cancer, who reported skin allergy, anorexia, alopecia, mucositis, constipation, fatigue, drowsiness, diarrhea, nausea, myelosuppression, and vomiting. Yet the current study focused on highlighting the significance of medication adherence in relation to ADRs. Furthermore, the study of Leporini et al¹ has reported the use of supportive care in an effective manner that shows an importance in controlling ADRs in elderly cancer patients. Thus, a vigilant approach through usage of supportive drugs will help manage ADR rationally in cancer patients undergoing chemotherapy.

The duration and sample size of study population are limiting factors in this study. According to inclusion criteria, we recruited patients with different types of cancer, because of variable cancer disease distribution, so a standard medication adherence (Morisky Medication Adherence Scale-8 Questionnaire) scale was used. But with regard to specific cancer types, selection of adherence scale will change (eg, usage of Brief Adherence Rating Scale [BARS] to assess the adherence in cancer patients).

Conclusion and Relevance

Disease condition in cancer patients worsens due to impaired medication adherence leading to the latency in maintaining the longitudinality of care. This depicts that there is an

obligatory demand to make a move toward judiciously identified factors affecting nonadherence of chemotherapy and supportive therapy; thus, in future research we must consider mentioning offending determinants to overcome nonadherence and to improve medication adherence level. This helps in minimizing the occurrence of ADR in cancer patients. This reveals the prominence of supportive therapy in cancer management. Thus, there is an implicit need for a collaborative role of oncology pharmacists and physicians to tailor the treatment plan shrewdly based on patient needs and satisfaction so that the subjects abide with the therapy and are able to cope up with cancer cautiously.

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ORCID iD

Manjula Gudhoor <https://orcid.org/0000-0002-7173-6408>

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