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A Pharmaceutical Care Plan to Minimize the Incidence of Potential Drug-Related Problems in Cancer Patients

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ABSTRACT

Background: Drug-related problems (DRPs) are frequent among cancer patients and can have a poor influence on the quality of life (QoL), and increase morbidity as well as mortality.

Aim of the work: This study aimed to assess the impact of clinical pharmacist-implemented prescriber's education on the prevalence of DRPs and patients' QoL.

Patients and Methods: A cross-sectional, 3 phases interventional study (pre-education phase, education phase, and post-education phase) was conducted between May 2018 and May 2020. Prescriptions and filled QoL questionnaires were collected for 500 patients in pre-education and 500 patients' post-education phases from Cairo University National Cancer Institute (Cairo, Egypt) and Assiut University Hospital (Assiut, Egypt). The QoL for each patient was assessed using the Arabic version of the European Organization for Research and Treatment of Cancer (EORTC) QLQ C30 QoL questionnaire.

Results: Following clinical pharmacist education, the total number of DRPs in the post-education phase significantly decreased by 43.14 % ($p<0.0001$) compared to the pre-education phase. The acceptance rate of prescribers was 88.6% to the recommendations done by the clinical pharmacist. Comparing EORTC QLQ C30 questionnaire scores in pre- and post-education phases, there was a statistically significant improvement with fewer problematic patients in the global health status, functional, and symptom scales in the post-education phase.

Conclusion: Pharmacist interventions can potentially minimize the incidence of DRPs and are associated with improvement of QoL scores which highlights the importance of the clinical pharmacist's role in cancer care.

Keywords: Drug-related problems, Clinical pharmacist, Quality of life, Cancer patients.

INTRODUCTION

A drug may play a crucial role in disease treatment or prevention, but if it is not administered properly, it can have negative effects on patients' health. [(1)]. Additionally, the accessibility of a variety of pharmacological products as well as the complexity of drug regimens, can lead to an increase in adverse drug events (ADE) and drug-drug interactions (DDIs), which can be challenging for patient management [(2)]. According to Pharmaceutical Care Network Europe (PCNE) Foundation, a DRP is an event or circumstance involving a drug that actually or potentially impacts desired treatment goal [(3)], including medication errors that may occur during the prescription, dispensing, or administration of a drug [(4)]. These problems significantly impact the therapeutic goal for patients [(1)].

Cancer is a major cause of mortality leading to nearly 10 million deaths in 2020 [(5)]. In Egypt, there is an increasing incidence of cancer [(6)]. Polypharmacy is a major issue for cancer patients, especially in the elderly and it is a key risk of occurrence of DRPs [(7)]. Cancer treatment is complex and could result in many DRPs such as adverse reactions, medication errors, DDIs, and non-adherence which may cause drug-related morbidity and mortality [(8)], that's why detecting and resolving them is critical to achieving the optimum therapeutic outcomes and minimize cost spent for emergency department visits, hospital admissions and additional visits that could be needed as a result of DRPs [(9)]. Cancer diagnosis, treatment, and DRPs could negatively impact patients' QoL, that's why there is a need for clinical pharmacist intervention that could minimize DRPs and improve QoL [(10)].

Fortunately, a significant fraction of DRPs can be avoided. As part of the standard pharmacy practice, hospitalized patients' prescriptions and clinical data are reviewed to increase the efficacy and safety of their care. It has been demonstrated that including hospital pharmacists in multidisciplinary teams improves the detection and resolution of DRPs [(11)]. There is a need for clinical pharmacist intervention that could minimize DRPs and improve QoL [(6,7)].

It is crucial to pinpoint the activities that can be taken to prevent DRPs because they are largely preventable. Pharmaceutical care is the responsible use of drug therapy to achieve treatment goals and to improve a patient's quality of life. Pharmaceutical care presents a

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systematic approach that ensures patients receive the correct medicines, at the right dose, for proper indications and pharmacists can achieve this in collaboration with physicians and patients [12].

Hence, this study aimed to assess the impact of clinical pharmacists' implemented education to prescribers on the incidence of DRPs and QoL in cancer patients.

PATIENTS AND METHODS

Ethical Approval:

Approval of the study was obtained from Cairo University National Cancer Institute (Cairo, Egypt) (5-6-2017) and Assiut University Hospital (Assiut, Egypt) (14-9-2017). This work was carried out following The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria:

Patients with a confirmed diagnosis of cancer, and are on cancer therapy (including chemotherapy, targeted therapy, and/or immunotherapy) at the time of data collection and have prescriptions containing at least 2 medications.

Exclusion criteria

Patients with cognition impairment.

Study design, population, and protocol:

A 3-phases interventional study (pre-education, education, and post-education phases) was conducted between May 2018 and May 2020. The pre-education phase was a cross-sectional phase where the prescriptions were collected for 500 eligible patients from Cairo University National Cancer Institute (Cairo, Egypt) and Assiut University Hospital (Assiut, Egypt). Patients' demographics (including age and gender), number of drugs per prescription, disease status (metastasis), and comorbidities were extracted from each prescription.

All prescriptions were analyzed for the presence of DRPs using Food and Drug Administration (FDA) prescribing information of the different drugs to review dose, duration, and precautions, published primary literature, and National Comprehensive Cancer Network (NCCN) guidelines. The detected DRPs were classified according to Pharmaceutical Care Network Europe (PCNE) version 8.2 [13]. It is a validated DRP classification that is well established and continuously updated [3]. It includes five domains: problems (P), causes (C), planned interventions (I), intervention acceptance (A), and outcome of the DRP (O) [13]. Only P and C domains were used in this study. In addition, all prescriptions were screened for DDIs using, Lexicomp®, textbooks (Stockley's Drug Interactions [14] and Drug Interactions in the Therapy of Malignant Diseases) [15].

In addition, The QoL for each patient was assessed using the Arabic version of the European Organization for Research and Treatment of Cancer (EORTC) QLQ C30 QoL questionnaire [16] to determine the level of symptomatology and evaluate the supportive care provided.

In the education phase, the clinical pharmacist held educational sessions based on detected DRPs for groups of 3-5 physicians. The educational sessions included the definition of DRPs, their impact on patient outcomes, and health-related costs. Moreover, examples of the most important captured DRPs in the pre-education phase were discussed with physicians and appropriate recommendations were suggested. At the end of each session, the acceptance of the physician regarding the provided material was assessed.

The post-education phase was a cross-sectional phase similar to the pre-education phase including 500 eligible patients. The data were collected in the same manner as the pre-education phase and were compared to the pre-education phase.

The EORTC QLQ-C30 questionnaire:

The EORTC Core QoL questionnaire (EORTC QLQ-C30) is structured to assess cancer patients' different functions. The questionnaire is composed of 5 multi-item scales (physical, role, social, emotional, and cognitive functioning) and 9 single items (pain, fatigue, financial impact, loss of appetite, nausea/ vomiting, diarrhea, constipation, sleep disturbance, and QoL) [17].

All scales' scores range from 0-100. A high score on the functioning scale or global health scale represents a good level of functioning and better QoL, while a high score on a symptom scale represents a high level of symptom and problematic QoL [18].

The relevant descriptive statistics for the questionnaire items in both study groups were calculated. Patients were divided into three groups according to their scores: <33.3, 33.3-66.7, and >66.7. The patients whose scores are <33.3 for the functional scales and the global health status were considered problematic, and the patients who scored >66.7 were considered good in terms of QoL. For symptom scales, the score is reversed, meaning that the patients who scored <33.3 were considered good and the patients who scored >66.7 were considered problematic [19].

Statistical analysis:

Prism® (version 8.4.0, GraphPad Software Inc., La Jolla, CA, USA) was used to assemble and analyze the data. Qualitative data was represented using frequencies and percentages. The qualitative variables were compared using Fisher exact and Chi-square tests. The variation between quantitative variables in two groups was calculated using the Mann–Whitney U test. A p-value at < 0.05 was considered significant.

RESULTS

Patients' demographic characteristics:

Participants in the study's pre- and post-educational stages ranged in age from 18 to 76, and 55.2% of them

were men. Median number of drugs per prescription in pre-education phase and post-education phase were 5 and 6 drugs/prescription respectively, with a statistically significant difference (p<0.0001). Also, 34.8% of the study population had metastatic disease and 25.9% of them had comorbidities. The most common comorbidity, reported by 12.4% of the participants, was cardiovascular disease and 10% reported to have diabetes. Other comorbidities reported in the study included gout, osteoarthritis, hepatitis, bronchial asthma, and renal failure. There were significant differences between pre-education phase and post-education phase regarding cardiovascular comorbidities (p=0.0436) and the presence of metastases (p=0.0065) **(Table 1).**

Table (1): Patients' demographic characteristics in pre-and post-education phases.

	Pre-education phase (n=500)	Post-education phase (n=500)	p-value
Age (year)			
Median (range)	58 (18-76)	56 (18-74)	0.29
Sex (n and %)			
Male	267 (53.4%)	285 (57%)	0.2797
Female	233 (46.6%)	215 (43%)	
Number of drugs per prescription			
Number of patients with metastatic cancer (n and %)			
Yes	153 (30.6%)	195 (39%)	0.0065[b]
No	347 (69.4%)	305 (61%)	
Comorbidities (n and %)			
Yes	140 (28%)	119 (23.8%)	0.1487
No	360 (72%)	381 (76.2%)	
Type of comorbidities (n and %)			
Cardiovascular disease	73 (14.6%)	51 (10.2%)	0.0436[b]
Diabetes	55 (11.0%)	45 (9.0%)	0.4328
Other	24 (4.8%)	28 (5.6%)	0.6696

p-value < 0.05 is considered significant
[a] Mann-Whitney test
[b] Fisher's exact test

Incidence and classification of DRPs:

A total of 2276 DRPs were detected, 1451 DRPs in pre-education and 825 DRPs in post-education phases. Compared to the pre-education phase, the total number of DRPs decreased by 43.14 % in the post-education phase. There was a statistically significant difference between the pre-education phase mean number of DRPs/prescription (2.9) and the post-education phase (1.65) (p<0.0001) **(Figure 1).**

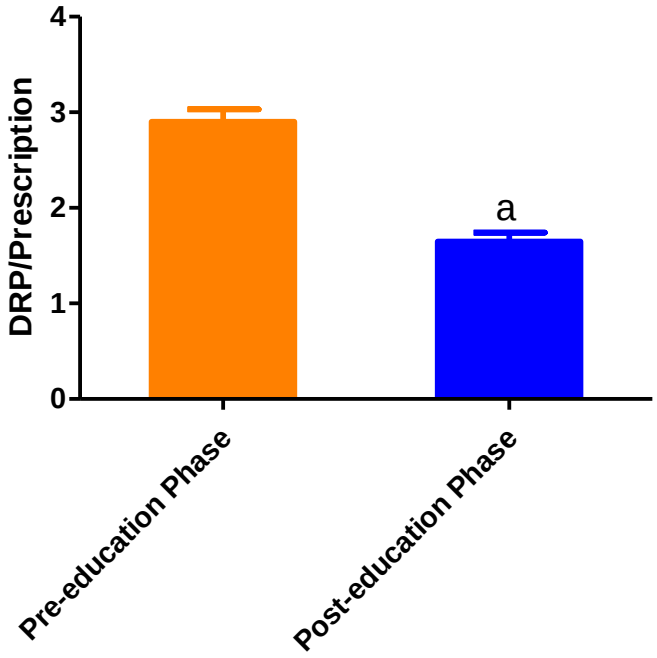

Figure (1): DRPs per prescription in pre-and post-education phases. Data were presented as mean ± SE. p-value < 0.05 is considered significant. [a]Mann-Whitney test

The classification of DRPs by PCNE for all study participants showed that the majority of them (78.13%) were connected to treatment safety while only 20.42% of them were related to treatment effectiveness. There was a reduction in the number of DRPs impacting treatment effectiveness by 53.3% and a drop in those affecting treatment safety by 40.1% when comparing the post-education period to the pre-education phase **(Table 2).**

Table (2): Classification of DRPs in pre-and post-education phases

	Pre-education phase	Post-education phase	p-value
Total potential drug-related problems	**1451 (100%)**	**825 (100%)**	
[*]P1 Treatment effectiveness	**317 (21.85%)**	**148 (17.94%)**	**0.0751**
[*]P2 Treatment safety	**1112 (76.63%)**	**666 (80.73%)**	
[*]P3 Others	**22 (1.52%)**	**11 (1.33%)**	
Comparisons between groups were performed by Chi-square test. [*]Indicated problem			

Incidence and classification of DDIs:

Based on the detected DRPs, 99.3% are related to inappropriate drug combinations, most of which were related to non-cancer therapy in both phases **(Figure 2).**

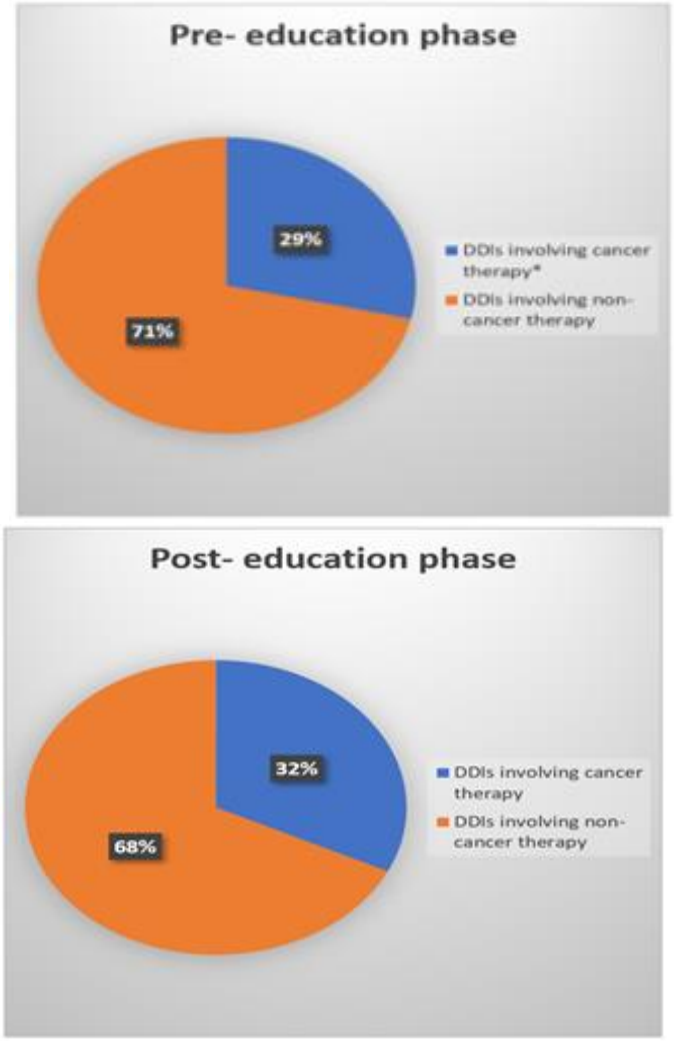

Figure (2): Drug-drug interactions (DDIs) in pre-and post-education phases. *Indicted that cancer therapy included chemotherapy, immunotherapy, and targeted therapy.

DDIs with risk ratings C, D, and X dropped by 41.3%, 78.2%, and 70.3%, respectively, suggesting a statistically significant difference (p<0.0001) between the post-education phase and the pre-education phase **(Table 3).**

Table (3): Classification of DDIs according to risk rating in pre-and post-education phases

	Number of DDIs		
Risk rating	**Pre-education phase**	**Post-education phase**	**p-value**
C	803	471	<0.0001[a]
D	229	50	
X	27	8	

p-value < 0.05 is considered significant
[a] Chi-square test
Action required for these risk rating for the DRP is, C; monitor therapy, D; Consider therapy modification, and X; avoid combination

Most DDIs were moderate in terms of severity, and their moderate and major risks dropped by 32.5% and 66.6%, respectively, in the post-education phase compared to the pre-education phase, with statistically significant differences (p=0.0175) **(Table 4).**

Table (4): Classification of DDIs according to the degree of severity in pre-and post-education phases

The QoL outcomes in pre-and post-education phases:

Analysis of EORTC QLQ C30 questionnaires showed that the most common global health status/QoL and functional impairment (scoring<33.3%) in the pre-education phase were related to financial difficulties, followed by social functioning and role functioning, representing 86.6%, 50.2%, and 26.6% respectively. Post-education, there was a significant reduction in the number of patients with global health status/QoL and functional impairment across the different scales. The most common symptom impairment (scoring >66.7%) in the pre-education phase was related to dyspnea, followed by loss of appetite and insomnia representing 45%, 39%, and 36.6% respectively. Post-education, there was a significant reduction in the number of patients with symptom impairment across the different scales except for constipation. Across the different score categories (<33.3%, 33.3-66.7, >66.7) there was a statistically significant difference achieved in the post- versus pre-education phase except for constipation **(Table 5).**

Table (5): Comparison of frequency of patients in the different QoL score groups between pre-and post-education phases

Scale	Score	Pre-education phase (n and %)	Post-education phase (n and %)	p-value
Global health status				
	<33.3 33.3-66.7 >66.7	30(6) 132(26.4) 338(67.6)	0(0) 248(49.6) 252(50.4)	0.0001[a]
Functional scales				
Physical functioning	<33.3 33.3-66.7 >66.7	48(9.6) 206(41.2) 246(49.2)	6(1.2) 243(48.6) 251(50.2)	0.0001[a]
Role functioning	<33.3 33.3-66.7 >66.7	133(26.6) 34(6.8) 333(66.6)	58(11.6) 239(47.8) 203(40.6)	0.0001[a]
Emotional functioning	<33.3 33.3-66.7 >66.7	120(24) 182(36.4) 198(39.6)	9(1.8) 319(63.8) 172(34.4)	0.0001[a]
Cognitive functioning	<33.3 33.3-66.7 >66.7	126(25.2) 14(2.8) 360(72)	52(10.4) 255(51) 193(38.6)	0.0001[a]
Social functioning	<33.3 33.3-66.7 >66.7	251(50.2) 5(1) 244(48.8)	47 (9.4) 255(51) 198(39.6)	0.0001[a]
Symptom scales				
Fatigue	<33.3 33.3-66.7 >66.7	299(59.8) 125(25) 76(15.2)	279(55.8) 179(35.8) 42(8.4)	0.0001[a]
Nausea and vomiting	<33.3 33.3-66.7 >66.7	343(68.6) 55(11) 102(20.4)	262(52.4) 191(38.2) 47(9.4)	0.0001[a]
Pain	<33.3 33.3-66.7 >66.7	293(58.6) 83(16.6) 124(24.8)	270(54) 184(36.8) 46(9.2)	0.0001[a]
Dyspnea	<33.3 33.3-66.7 >66.7	275(55) 0(0) 225(45)	194(38.8) 295(59) 11(2.2)	0.0001 [a]
Insomnia	<33.3 33.3-66.7 >66.7	317(63.4) 0(0) 183(36.6)	76(15.2) 398(79.6) 26(5.2)	0.0001[a]
Appetite loss	<33.3 33.3-66.7 >66.7	305(61) 0(0) 195(39)	146(29.2) 312(62.4) 42(8.4)	0.0001[a]
Constipation	<33.3 33.3-66.7 >66.7	367(73.4) 0(0) 133(26.6)	370(74) 0(0) 130(26)	1.0000
Diarrhea	<33.3 33.3-66.7 >66.7	423(84.6) 0(0) 77(15.4)	214(42.8) 285(57) 1(0.2)	0.0001[a]
Financial difficulties	<33.3 33.3-66.7 >66.7	433(86.6) 0(0) 67(13.4)	330(66) 164(32.8) 6(1.2)	0.0001[a]

p-value < 0.05 is considered significant

[a] Chi-square test

The patients who scored ≤33.3 for the functional scales and the global QoL were considered problematic

The patients who scored >66.7% on the symptom scales were considered problematic

Physician acceptance of the education sessions' suggested recommendations:

Different DRPs' actions were consolidated by the clinical pharmacists and were shared with the prescribers to improve their knowledge about the DRPs' risks and potential recommendations to solve these problems. The acceptance rate of the recommendations proposed to prescribers is 88.6%.

DISCUSSION

Previously published evidence has shown that clinical pharmacists significantly contributed to DRPs solving in collaboration with physicians [20]. The current study focused on the role of clinical pharmacists implemented education for prescribers and its impact on DRPs related to prescribing errors and QoL scores. Prescribing errors prevalence is around 36- 50% [21,22] and are reported to be even higher in cancer patients presenting with a prevalence of 65-91% [23,24]. The chemotherapy prescribing errors can cause serious consequences in this patient group [25].

In the pre-education phase of our study, the rate of DRPs detected was 2.9 DRPs/ patient. This rate was higher than that found in cancer patients in a hospital in Ethiopia (1.72 DRP/ Patient) [26] and as well as the rate reported for cancer patients in a French study (0.12 DRP/ patient) [27]. Similar to our study, it is reported in studies that the treatment safety class of DRPs was the most frequent [28], while treatment effectiveness was the major in another study [29]. Similar to the current study results, the most frequently detected type of DRPs was caused by inappropriate drug selection, while other studies showed that drug selection is the second most frequent cause after dose selection [30].

Our findings demonstrated that clinical pharmacy education for prescribers might reduce the frequency of DRPs, particularly DDIs, since there was a notable decrease of 43.14% in the rate of DRPs in the post-education phase.

The acceptance rate in our study is consistent with previous results; almost 89% were accepted by prescribers. The acceptance rate of clinical pharmacist education varies; it was 41% in a study for older cancer patients with polypharmacy [31] and 81.9-99% among hospitalized cancer pain patients [32].

Cancer patients usually have unmet needs. This could be attributed to the high level of untreated symptoms that is indirectly related to cancer; usually, these symptoms are underestimated by physicians [33]. Examples of untreated symptoms reported in studies on cancer patients are a lot. In one of the studies, 66% of the patients suffered from severe pain [34]. It was also reported in a study for non-small cell lung cancer (NSCLC) that more than 90% of the patients reported fatigue, cough, loss of appetite, shortness of breath in addition to pain which negatively impacted QoL [35].

In the present study, we assessed cancer patient QoL using the EORTC QLQ C30 questionnaire. In the pre-education phase, there were at least 433 patients (scoring <33.3%) have a problem at least in one domain in the functional scales, this number decreased by 23% in the post-education phase meaning fewer problematic patients. Similarly in symptom scales, there was a statistically significant improvement after education because patients achieving >66.7% decreased significantly in most of the domains. In the pre-education phase there were at least 225 patients have a problem (scoring >66.7%) at least in one domain on the symptom scale, this number decreased by 42% in the post-education phase. This highlights the impact of clinical pharmacy education on the improvement of QoL which can review and give consultation to physicians leading to control of prescribing errors.

CONCLUSION

The clinical pharmacist role is very crucial in cancer care working with the multidisciplinary team having a potential impact on minimizing the incidence of DRPs through prescriber-implemented education and is also associated with improvement of QoL scores which is very important for cancer patients.

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