Marmara Pharmaceutical Journal 21/3: 603-611, 2017
DOI: 10.12991/marupj.323286

RESEARCH PAPER

Influence of Pharmacist Recommendations for Chemotherapy-Related Problems in Diabetic Cancer Patients

Fikret V. Izzettin, Anmar Al-taie, Mesut Sancar, Mehmet Aliustaoğlu

ABSTRACT

Drug related-problems pose additional worse outcomes in cancer patients treated with chemotherapy. A vital role of the clinical pharmacist is the detection and prevention of drug-related problems. The provision of patient education is an important step to reduce and prevent drug-related problems during chemotherapy administration**.** The objective of this study was to assess the occurrence of drug-related problems and the importance of effective provision of patient education and appropriate recommendations by the clinical pharmacist in reducing and solving of these problems in diabetic patients suffering from cancer.

A prospective study carried out on 50 diabetic patients as a single group with new diagnosis of diverse cancer types eligible for chemotherapy adminitration recruited between September 2014 and April 2015 at the oncology unit in one of the Teaching and Research Hospital (Istanbul-Turkey). Drug-related problems were evaluated, and proper patient education alongside pharmacist recommendation regarding chemotherapy was provided during the required chemotherapy protocol schedule**.** (n=65) of the drug-related problems were contributed to inappropriate IV fluid selection; (n=33) were attributed to low drug dose prescribed, and (n=30) to high drug dose prescribed. Drug-related problems totally solved due to clinical pharmacist recommendations were 69.57% (n=80). There was a significant increase in the occurrence of paleness (P=0.0001); urinary frequency (P=0.003); loss of appetite (P=0.0001), nausea (P=0.0001), vomiting (P=0.0001); and numbness (P=0.0001). A significant decrease in the occurrence and severity of chemotherapy-related adverse effects was observed as a mild urinary frequency (P=0.0001) and mild vomiting (P=0.0001) after the clinical pharmacist recommendations and provision of patient education.

Results of this study revealed that diabetic cancer patients are definitly prone to the occurrence of drug-related problems and adverse drug reactions. Clinical pharmacist is expected to provide a well-defined education and care to those patients and the outcomes of pharmacist recommendations may diminish and prevent many drug-related problems and adverse drug reactions and by this, influence patients' desire to complete the course of chemotherapy.

Keywords: Clinical Pharmacist Recommendations, Diabetes Mellitus, Drug-Related Problems, Adverse Drug Effects

Introduction

Diabetes mellitus (DM) and cancer are considered to be the most common severe conditions with worse effects on general health (1). According to the Pharmaceutical Care Network Europe (PCNE) classification, drug related-problem is defined as 'an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes' (2). Drug related-problems (DRPs) include many issues such as adverse drug reactions (ADRs), unnecessary drug therapy, inappropriate choice of drugs, and untreated conditions. Drug related-problems are associated with a prolonged hospitalization, increased economic burden, and an almost 2-fold increased risk of substantial morbidity and mortality. It also affects the patient's recovery and is a major limitation in providing healthcare to the patient (3-5).

Fikret V.Izzettin, Anmar Al-taie, Mesut Sancar
Clinical Pharmacy Department, Faculty of Pharmacy, Marmara University, Istanbul, Turkey

Mehmet Aliustaoğlu
Oncology Center, Dr. Lütfi Kırdar Kartal Teaching and Research Hospital, Istanbul, Turkey

Corresponding Author:
Anmar Al-taie
E-mail: altaii1978@gmail.com

Submitted / Gönderilme: 18.01.2017 **Revised / Düzeltme:** 06.04.2017
Accepted / Kabul: 12.04.2017

Rational and safe drug use is greatly important since patient´s health is majorly influenced by the occurrence of adverse drug reactions. Adverse drug reactions are considered one of the main problems as they can increase the rate of morbidity and mortality. In addition, they can impose a remarkable financial burden on healthcare systems (6,7). Adverse drug reaction is defined as a response to a drug which is a noxious and unintended, and occurs at doses normally used for the prophylaxis, diagnosis, or therapy of disease (8). Cancer chemotherapies are associated with numerous adverse drug complications which often result in dose reductions or treatment delays leading to compromising clinical outcomes or even mortality (9). Despite these facts, ADRs still do not consider as a relevant problem by a large proportion of healthcare professionals (10). Patients and healthcare professionals should have a profound attention to prevent unnecessary drug treatment and subsequent ADRs (11). The most important step of the clinical pharmacist is a reduction and effective management of ADRs in cancer therapy. This is done by the provision of sufficient and essential pre-chemotherapy education including those about the possible occurrence of side effects and the proper ways for self-care management (12). Many studies indicate that patient education can decrease certain treatment-related issues, improve physical and psychosocial outcomes, influence patients' desire to complete the course of chemotherapy and finally improve patients´quality of life (12-14).

Aim of the study

The objective of this study was to evaluate the occurrence of DRPs during chemotherapy administration and the importance of effective provision of patient education and appropriate reccommendations offered by the clinical pharmacist on the occurrence of these problems in diabetic patients suffering from cancer.

Methods

Study Design and Patients Selection

This was an observational prospective study recruited between September 2014 and April 2015. The study approved by the Ethical Committee (Date and No.: 27-06-2014-1-). It was conducted at the oncology unit in one of the Teaching and Research Hospital in Istanbul after a permission (Date: 17-07-2014/ No.: 35778018-770-) from the General Secretaries of the South Provincial Public Hospitals at Istanbul-Turkey.

A total of 50 out of 59 diabetic patients with new diagnosis of diverse types of cancers eligible for different chemotherapeutic protocols were recruited after meeting the inclusion criteria at the oncology unit. Inclusion criteria included patients over the age of 18 years, diabetic patients with new diagnosis of cancer eligible for chemotherapy. Patients who expressed willingness to take part and to abide by this study's rules. Were provided with additional written information and were asked to sign the study consent form. Exclusion criteria included patients with neoadjuvant chemotherapy, patients who were receiving radiotherapy concomitantly, and patients who expressed willingness to withdraw from the study.

Basically, patient data were collected from the medical records of the patients. Any further information requied for this study were collected by the researcher clinical pharmascist via face-to-face interview with the patients for reporting details involving patients' sociodemographic data, knowledge about medications being prescribed, and lifestyle manners. Diabetic cancer patients received regular patient counseling regarding chemotherapy administration. The patient counseling included of correct and proper medication use, how to overcome any problems regarding chemotherapy taking, possible occurrence of adverse reactions and their proper management. These advices were reinforced at regular appointments of the chemotherapy schedules. The clinical outcomes regarding DRPs and ADRs of chemotherapy were followed at the 1st reading (after the 2nd cycle of receiving the chemotherapeutic regimens), and the 2nd reading (at the end) of the required chemotherapy protocol schedule. The researcher clinical pharmacist collaborated with other healthcare professionals to augment the counseling and patients were referred to specialists when there was a need. The assessment of DRPs was based on Pharmaceutical Care Network Europe V6.2 which deals with nature, prevalence, and incidence of DRPs (2). The assessment of ADRs due to chemotherapy administration was evaluated through the provision of specific adverse effects questionnaire. Those adverse effects were categorized as mild, moderate, and severe (15).

Statistical Analyses

The SPSS 16.0 Package was used for statistical analysis. Continuous variables were expressed as mean ± SD and categorical variables were reported as number (frequency). Chi-Square Test or Fisher's Exact Test was performed on categorical variables. The results were assumed to be

significant when the $p< 0.05$ threshold was reached by all statistical analyses.

Results

The characteristics of the study population are presented in (Table 1). The mean age was 60.98±8.99 years old at a range of 34-77 years. Most of the patients were females (58%), had a previous family history of cancer (66%). Majority of patients were non cigarette smokers (82%), married (96%), with a waist circumference of (91.02±19.72 cm), and had a primary level of education (62%). All patients were suffering from type 2 DM (100 %). Breast carcinoma was the most common type of cancer (16%) followed by (14%) Non-Samll Cell Lung Carcinoma (NSCLC). Most of the participants recieved chemotherapy regimens every 21 days (66%).

Table 1. Demographic and Clinical Patients' Characteristics

Parameter	n= 50 (%)
Gender	
Males	21 (42%)
Females	29 (58%)
Mean Age (year)±SD	60.98±8.99 (34-77 yr)
Cancer Family History	
Yes	33 (66%)
No	17 (34%)
Marital State	
Married	48 (96%)
Single	2 (4%)
Waist Circumference (cm)	91.02±19.72
Cigaratte Smoking	
Yes	9 (18%)
No	41 (82%)
Education Level	
Yes (Primary)	31 (62%)
Yes (Secondary)	2 (4%)
No	17 (34%)
Type of DM	
Type 1	0 (0%)
Type 2	50(100%)
DM Length (year)±SD	6.46±5.18
Cancer Type	
Breast CA	8 (16%)
Pancreas CA	5 (10%)
NSCL CA	7 (14%)
Non-Hodgkin's Lymphoma	1 (2%)
Rectum CA	4 (8%)
Colon CA	3 (6%)
Stomach CA	0 (0%)
Others	22 (44%)
Previous Chemo-radiotherapy	
Yes	17 (34%)
No	33 (66%)
Cancer Therapy Schedule	
Every 7 days	11 (22%)
Every 14 days	6 (12%)
Every 21days	33 (66%)

Table (2) presents the assessment of DRPs during chemotherapy administration. At the drug selection level, the results of our study showed that (n=65) of the DRPs were contributed to inappropriate IV fluid selection, amount of IV fluid administration, and IV incombatibility; DRPs (n=33) was attributed to low drug dose prescribed, and (n=30) to high drug dose prescribed. At the drugs use process level, (n=15) of DRPs were related to a wrong drug use. At the patient level, (n=15) of DRPs were reported as patients' forgetting to use the medicines.

Table 2. Drug-Related Problems Assessment During Chemotherapy Administration

Domain	Cause	Number of occurrence (n=)
Drug selection The cause of the DRP is related to the selection of the drug	Inappropriate drug selection (mainly IV incombatibility, amount of IV fluid administration, IV fluid selection)	**65**
	Inappropriate combination of drugs, or drugs and food	**1**
	Drug dose too low	**33**
	Drug dose too high	**30**
Drug use process The cause of the DRP can be related to the way the patient uses the drug inspite of proper dosage instructions (on the label)	Wrong drug taken/administered	**15**
Patient The cause of the DRP can be related to the personality or behaviour of the patient.	Patient forgets to use/take drug	**15**

Table (3) shows the effect of clinical pharmacist recommendations on the outcomes of DRPs during chemotherapy administration. At the prescriber level, (n=91) of the recommendations were approved by the prescriber. At the patient/ career level, patient counseling provided by the researcher clinical pharmacist represented (n=50) of the recommendations, (n=31) of the recommendations reported as patient referred to prescriber, and (n=12) of the recommendations provided as oral education given to family member/caregiver of the patient. At drug level, (n=70) of the recommendations were observed as dosage changed. DRPs totally solved due to recommendations by the clinical pharmacist were 69.57% (n=80).

Table 3. Clinical Pharmacist Reccommendations on Drug-Related Problems During Chemotherapy Administration

Domain	Recommendations	Number of occurrence (n=)
At patient/carer level	Patient (medication) counselling	**50**
	Patient referred to prescriber	**31**
	Spoken to family member/caregiver	**12**
At drug level (Recommendations proposed, approved by prescriber)	Drug changed (mainly antiemetics, IV fluid)	**10**
	Dosage changed	**70**
	Drug stopped (mainly antiemetics, IV fluid)	**11**
Domain	**Outcome of recommendations**	**Number of occurrence (n=)**
Solved	Problem totally solved	**80**
Not solved	Problem not solved, lack of cooperation of patient	**20**
	Problem not solved	**15**

Generally, there was a significant ($p<0.05$) increase in the occurrence of some ADRs during chemotherapy administration as presented in Figures (1 to 4), including paleness (P=0.0001), urinary frequency (P=0.003), loss of appetite (P=0.0001), nausea (P=0.0001), vomiting (P=0.0001), numbness (P=0.0001), ear ringing (P=0.021), and fatigue (P=0.0001). After clinical pharmacist recommendations and provision of patient education, a significant decrease in the occurrence (1st vs. 2nd readings) and severity (mild vs. moderate) of adverse drug effects was observed as a mild urinary frequency (P=0.0001) and a mild vomiting (P=0.0001). Although statistically non-significant, there was also a decrease in the occurrence and severity of the following adverse drug effects, including mild urine burning, mild mouth ulcers, moderate constipation and moderate diarrhea.

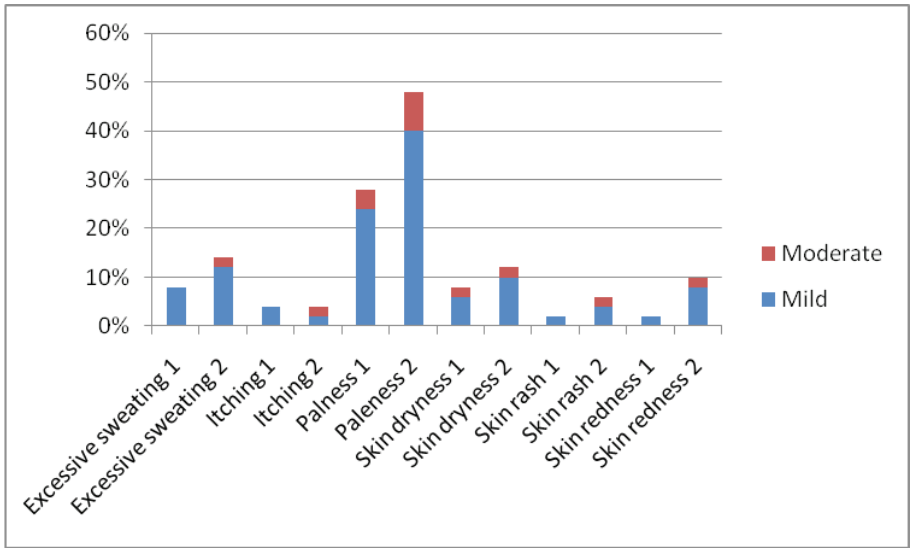

Figure 1. Adverse Drug Effects During Chemotherapy Administration Regarding Skin

1=the first reading after the 2nd cycle of receiving the chemotherapeutic regimens
2 =the second reading at the end of the requied chemotherapy protocol schedule

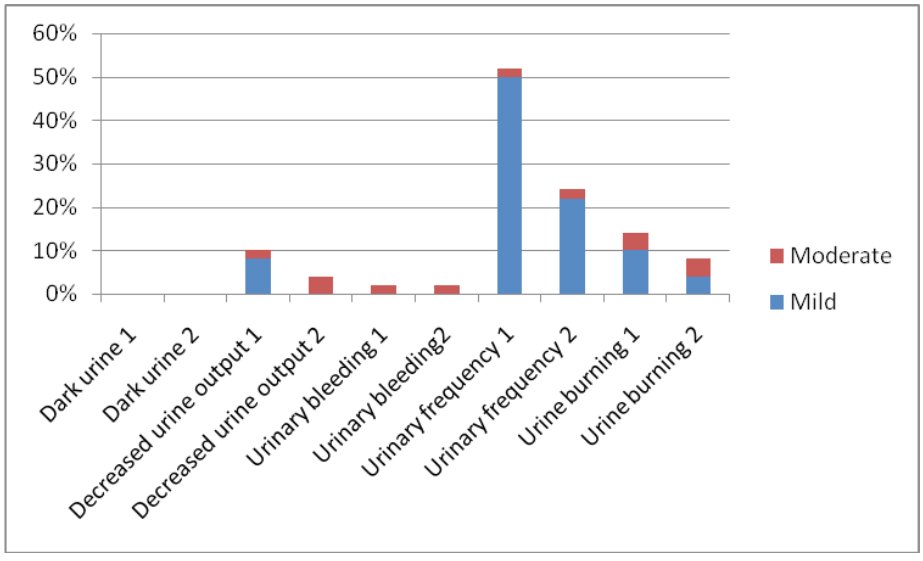

Figure 2. Adverse Drug Effects During Chemotherapy Administration Regarding Urinary System

1=the first reading after the 2nd cycle of receiving the chemotherapeutic regimens
2 =the second reading at the end of the requied chemotherapy protocol schedule

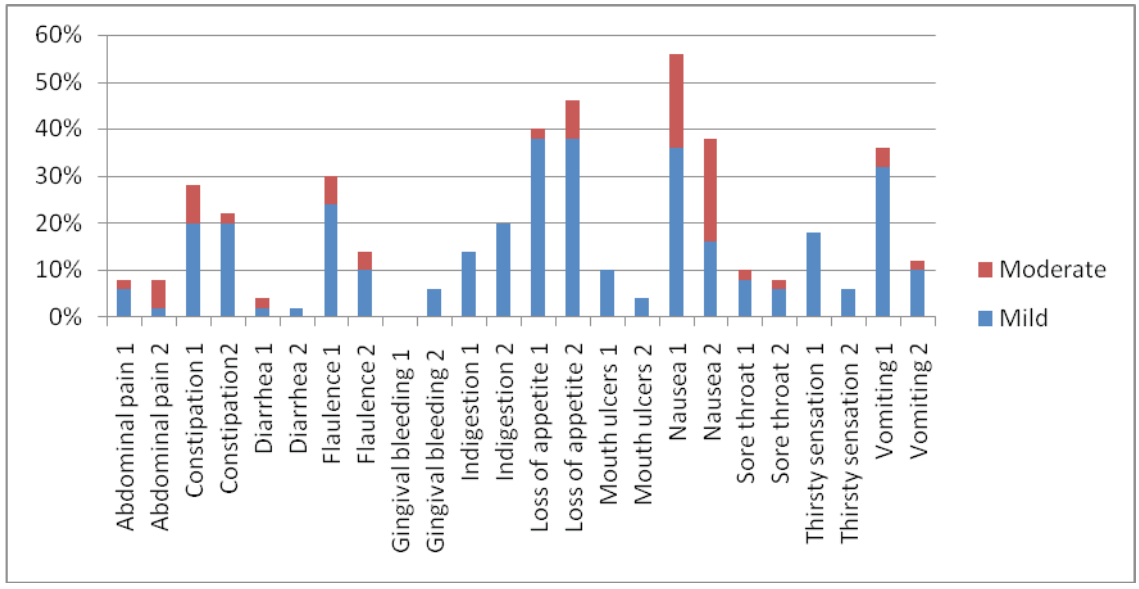

Figure 3. Adverse Drug Effects During Chemotherapy Administration Regarding Gastrointestinal System

1=the first reading after the 2nd cycle of receiving the chemotherapeutic regimens
2 =the second reading at the end of the requied chemotherapy protocol schedule

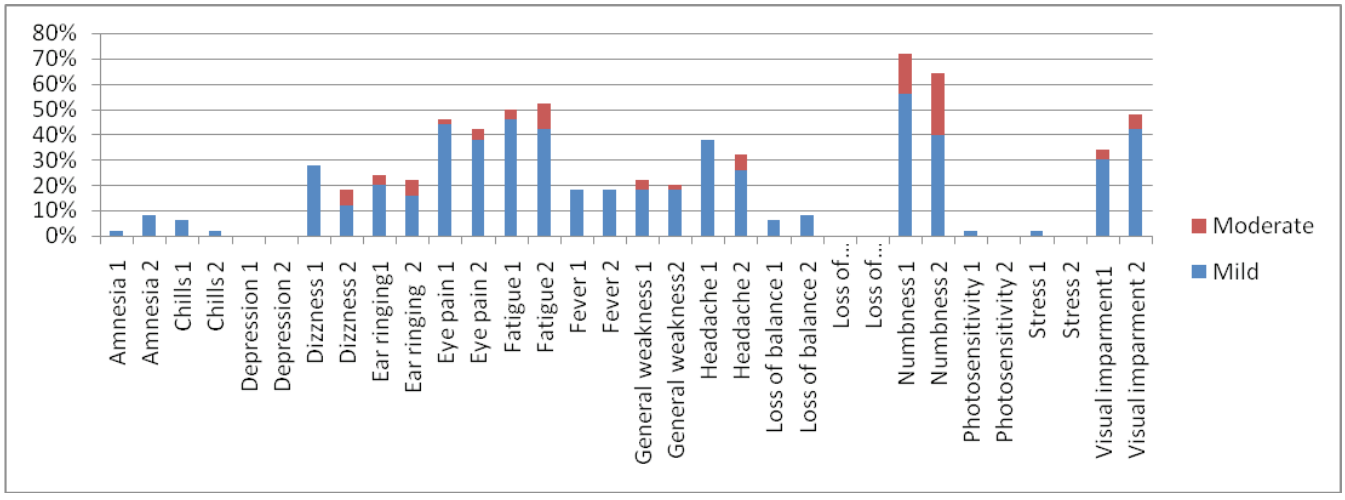

Figure 4. Adverse Drug Effects During Chemotherapy Administration Regarding Central Nervous System

1=the first reading after the 2nd cycle of receiving the chemotherapeutic regimens
2 =the second reading at the end of the requied chemotherapy protocol schedule

Discussion

Drug-related problems in cancer chemotherapy are associated with severe and undesirable consequences resulting from the administration of anticancer agents that are highly toxic and most of them have narrow therapeutic index. Furthermore, diabetic patients are known to be at risk of drug-related problems since those patients commonly receive multiple medications due to co-morbid diseases associated with the condition (16,17).

As presented in Table (2), a high occurrence of DRPs were related to inappropriate IV fluid selection and administration. DRPs were also related to to either high or low drug dose. A study by Nouran Ameen Hamza et al. supported our findings and reported that wrong dose error (n=134), missed dose

(n=74), errors in the calculation of the chemotherapy dose and protocol breach (n=96) were the most frequent types of prescribing errors (18). After the recommendations of clinical pharmacist as shown in Table (3), DRPs totally solved were 69.57% (n=80). A comparable study showed that 89% of clinical pharmacist recommendations were accepted by the prescribers (19).

The occurrence of DRPs is of major concern in cancer as many studies reported that patients are disposed to alter in pharmacokinetic parameters by the disease itself, malnutrition, reduced serum-binding proteins levels, edema, hepatic and/or renal dysfunction (20). In our study, patients were not only supposed to suffer from DRPs due to chemotherapy administration, but also they were considered as diabetic which is regarded as an additional risk factor for the high occurrence of DRPs (17). The occurrence of DRPs might also be related either to polypharmacy and/or a decrease in cognitive memory function as the majority of patients in this study were elders. Many studies showed a high occurrence of DRPs, a French study delete this word by Slama C. *et al.* revealed there were more than 300 medication errors out of 1262 prescriptions in oncology department (21). A study by Chan DC*et al*. reported a higher percentage (35%) of DRPs occurrence in the geriatric population (22). Study by Bob W and Ines K. showed that 5.9% of the diabetic patients had dosing problems (23). Viktil KK *et al.* found a proportional relationship between the number of medications being used and the occurrence of DRPs (24).

The results of our study reflect the important role of clinical pharmacist in reducing the occurrence of DRPs. Many literatures indicate that pharmacist recommendations is important to prevent DRPs and produce improved impact on their outcomes (25,26). In our study after clinical pharmacist recommendations and provision of patient education, a significant decrease in the occurrence and severity were observed for urinary frequency, and vomiting. There was also a decrease (statistically non-significant) for mild mouth ulcers, moderate constipation and moderate diarrhea. As the duration of cancer and hence the chemotherapy cycles increases, the occurrence of some adverse drug effects also increases (27). The occurrence of ADRs may be related to patients' characteristics such as age, gender (females), polypharmacy, and co-morbidities.

Many literatures reported that ADRs occur more commonly in the elder females, age-related problems, multiple comorbidities, polypharmacy, and previous ADRs (28-30). A study by Huan-Keat Chan and Sabrina Ismail assessed the most common adverse effects occurred by chemotherapy administartion and reported that patients experienced (83.3%) nausea, (78.9%) vomiting, (23.3%) loss of appetite and (6.7%) peripheral neuropathies (31). The findings of a study by Muhammad Shahbaz Aslam showed that after chemotherapy administartion, the majority of patients were suffering from weakness (95%), fatigue (90%) nausea (77%), vomiting (75%) and numbness (49%) (27).

These results support the evidence that a cornerstone of a clinical pharmacist in oncology practice is to identify ADRs, record their frequencies, report factors that may increase their risks, solving and preventing of drug-related problems, and provision of information to the medical team to prevent future ADRs (32). A study by Huan-Keat Chan and Sabrina Ismail reported that majority of patients had a desire to receive more information about chemotherapy-related adverse effects from the clinical pharmacists through oral conversation before chemotherapy treatment (27). Therefore, effective management of chemotherapy-related adverse effects is important to improve quality of life of patients, which may eventually influence their willingness to complete the treatment (14,33).

Limitations of the study

A main weak of this study was a limited number of the participants recruited as they were selected to be diabetic patients with new diagnosis of cancer alongside a shortened timescale of the study. Further extension of the study duration would be required to support more clinical pharmacist recommendations even after completion of the required chemotherapeutic schedules.

Conclusion

Our study was one of those few that evaluted the role of clinical pharmacist in diabetic patients with cancer and the results clearly pointed out the vital role of clinical pharmacist in reducing and resolving drug-related problems of chemotherapy and also revealed that provision of patient education offered by the clinical pharmacist is of great importance to improve the outcomes of these problems in diabetic cancer patients.

Conflict of interest: We declare that we have no conflict of interest.

Funding: The authors did not receive any financial support

ÖZET

Diyabetli Kanser Hastalarında Kemoterapiyle İlişkili Problemler Üzerine Eczacı Önerilerinin Etkisi

Kemoterapi alan kanser hastalarında ilaç kaynaklı problemler, normalden daha şiddetli sonuçlar gösterir. Klinik eczacının en önemli rollerinden biri ilaç kaynaklı problemlerin belirlenmesi ve önlenmesidir. Hasta eğitiminin sağlanması, kemoterapi uygulanırken ortaya çıkabilecek ilaç kaynaklı problemlerin önlenmesi veya şiddetlerinin azaltılması adına önemli bir adımdır. Bu çalışmanın amacı, diyabetli kanser hastalarına ait bu problemlerin azaltılması ve çözülmesinde klinik eczacı tarafından verilen etkili hasta eğitimi ve yapılan uygun önerilerin öneminin anlaşılması ve ilaç kaynaklı problemlerin ortaya çıkış sıklığının belirlenmesidir. Çeşitli kanser tiplerine ait yeni teşhis konmuş ve kemoterapi alması uygun görülmüş olan 50 diyabetli hasta üzerinde prospektif ve tek grup olarak yürütülen çalışma, Eylül 2014 ve Nisan 2015 tarihleri arasında İstanbul, Türkiye'deki bir eğitim ve araştırma hastanesinde gerçekleştirilmiştir. Uygun görülen kemoterapi protokol takvimi sırasında, ilaç kaynaklı problemler değerlendirilmiş ve kemoterapiye dair eczacı önerileriyle, hastalara uygun eğitim verilmiştir. İlaç kaynaklı problemlerin n=65'i uygunsuz IV sıvı seçiminden, n=33'ü reçete edilen ilacın dozunun düşük olmasından, n=30'u da reçete edilen ilacın dozunun yüksek olmasından dolayı ortaya çıkmıştır. Klinik eczacı önerileriyle tamamen çözülen ilaç kaynaklı problem yüzdesi %69.57'dir (n=80). Solgunluk (p=0,0001), idrar sıklığı (p=0,003), iştahta azalma (p=0,0001), bulantı (p=0,0001), kusma (p=0,0001) ve uyuşukluk (p=0,0001) belirtilerinde anlamlı bir artış görülmüştür. Klinik eczacı önerilerinden ve hasta eğitiminden sonra kemoterapiye bağlı yan etkilerden idrar sıklığı (p=0,0001) ve kusmanın (p=0,0001) şiddeti ve sıklığında anlamlı azalma gözlenmiştir. Bu çalışma, diyabetli kanser hastalarının ilaç kaynaklı problemlere ve ilaç yan etkilerine açık olduklarını ortaya koymuştur. Klinik eczacının bu tür hastalara anlaşılabilir bir eğitim ve bakım sağlaması beklenir. Eczacı önerilerinin sonucunda birçok ilaç kaynaklı problemin ve yan etkinin önlenmesi ve ortadan kaldırılması sağlanarak hastaların kemoterapi kürlerine devam etme isteği artırılabilir.

Anahtar kelimeler: Klinik eczacı önerileri, diabetes mellitus, ilaç kaynaklı problemler, ilaç yan etkileri.

References

1. Vigneri P, Frasca F, Sciacca L, Pandini G, Vigneri R. Diabetes and cancer. Endocr Relat Cancer 2009;16:1103-23.
2. Pharmaceutical Care Network Europe. DRP-Classification V6.2. 2010. http://www.pcne.org/upload/files/11_PCNE_classification_V6.2.pdf. Accessed date: 8 March 2017.
3. Ruths S, Viktil KK, Blix HS. Classification of drug-related problems. Tidsskr Nor Laegeforen 2007; 127: 3073-6.
4. Leendertse AJ, Egberts AC, Stoker LJ, van den Bemt PM; HARM Study Group. Frequency of and risk factors for preventable medication-related hospital admissions in the Netherlands. Arch Intern Med 2008;168:1890-6.
5. Stafford AC, Tenni PC, Peterson GM, Jackson SL, Hejlesen A, Villesen C, Rasmussen M. Drug-related problems identified in medication reviews by Australian pharmacists. Pharm World Sci 2009 ;31:216-23.
6. Molokhia M, Tanna S, Bell D. Improving reporting of adverse drug reactions: Systematic review. Clin Epidemiol 2009;1:75-92.
7. Routledge PA, O'Mahony MS, Woodhouse KW. Adverse drug reactions in elderly patients. Br J Clin Pharmacol 2004;57:121-6.
8. Jamali AN, Aqil M, Alam MS, Pillai KK, Kapur P. A pharmacovigilance study on patients of bronchial asthma in a teaching hospital. J Pharm Bioallied Sci 2010;2:333-6.
9. Ouyang Z, Peng D, Dhakal DP. Risk factors for hematological toxicity of chemotherapy for bone and soft tissue sarcoma. Oncol Lett 2013;5:1736-1740.
10. Cosentino M, Leoni O, Oria C, Michielotto D, Massimo E, Lecchini S, Frigo G. Hospital-based survey of doctors' attitudes to adverse drug reactions and perception of drug-related risk for adverse reaction occurrence. Pharmacoepidemiol Drug Saf 1999;8 Suppl 1:S27-35.
11. van Grootheest K, de Jong-van den Berg L. Patients' role in reporting adverse drug reactions. Expert Opin Drug Saf 2004;3:363-8.
12. Aranda S, Jefford M, Yates P, Gough K, Seymour J, Francis P, Baravelli C, Breen S, Schofield P. Impact of a novel nurse-led prechemotherapy education intervention (ChemoEd) on patient distress, symptom burden, and treatment-related information and support needs: results from a randomised, controlled trial. Ann Oncol 2012;23:222-31.
13. Carelle N, Piotto E, Bellanger A, Germanaud J, Thuillier A, Khayat D. Changing patient perceptions of the side effects of cancer chemotherapy. Cancer 2002;95:155-63.
14. Kayl AE, Meyers CA. Side-effects of chemotherapy and quality of life in ovarian and breast cancer patients. Curr Opin Obstet Gynecol 2006;18: 24-8.
15. Hadder Akram AbdulRazzaq. Prediction of uncontrolled dyslipidemia of cardiac patients and the adverse effect od pharmaceutical excipients. Universiti Sains Malaysia (USM), doctor of Philosophy (PhD) Thesis, 2013, Penang, Malaysia (Supervisor; Syed Azhar Syed Sulaiman).
16. Sisay EA, Engidawork E, Yesuf TA, Ketema EB. Drug Related Problems in Chemotherapy of Cancer Patients. J Cancer Sci Ther 2015; 7: 055-9.
17. Ogbonna BO, Ezenduka CC, Opara CA, Ahara LG. Drug therapy problems in patients with Type-2 Diabetes in a tertiary hospital in Nigeria. IJIRD 2014; 3: 494-502.
18. Hamza NA, Abdou Sallam S, El-Nimr NA. Rates and types of prescribing errors and related ınterventions in oncology. Int J Curr Microbiol App Sci 2013; 2: 435-45.

19. Kuo G, Touchette D, Marinac J. Drug errors and related interventions reported by United States clinical pharmacists: The American college of clinical pharmacy practice-based research network medication error detection, amelioration and prevention study. Pharmacother 2013;33: 253-65.
20. Jaehde U, Liekweg A, Simons S, Westfeld M. Minimising treatment-associated risks in systemic cancer therapy. Pharm World Sci 2008;30:161-8.
21. Slama C, Jerome J, Jacquot C, Bonan B. Prescription errors with cytotoxic drugs and the inadequacy of existing classifications. Pharm World Sci 2005 ;27:339-43.
22. Chan DC, Chen JH, Kuo HK, We CJ, Lu IS, Chiu LS, Wu SC. Drug-related problems (DRPs) identified from geriatric medication safety review clinics. Arch Gerontol Geriatr 2012;54:168-74.
23. Bob W, Ines K. Development of an evidence-based checklist for the detection of drug-related problems in type 2 diabetes mellitus. Pharm World Sci 2009; 31:580–95.
24. Viktil KK, Blix HS, Moger TA, Reikvam A.Polypharmacy as commonly defined is an indicator of limited value in the assessment of drug-related problems. Br J Clin Pharmacol 2007; 63:187-95.
25. Feyer P, Kleeberg UR, Steingräber M, Günther W, Behrens M.Frequency of side effects in outpatient cancer care and their influence on patient satisfaction—a prospective survey using the PASQOC questionnaire. Support Care Cancer 2008; 16:567–75.
26. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M; Medical Research Council Guidance. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ 2008;337:a1655.
27. Aslam MS, Naveed S, Ahmed A, Abbas Z, Gull I, Athar MA. Side effects of chemotherapy in cancer patients and evaluation of patients opinion about starvation based differential chemotherapy. J Cancer Ther 2014; 5: 817-22.
28. Atkin PA, Veitch PC, Veitch EM, Ogle SJ. The epidemiology of serious adverse drug reactions among the elderly. Drugs Aging 1999;14:141-52.
29. Roughead EE, Barratt JD, Gilbert AL. Medication-related problems commonly occurring in an Australian community setting. Pharmacoepidemiol Drug Saf 2004; 13: 83-7.
30. Steinman MA, Landefeld CS, Rosenthal GE, Berthenthal D, Sen S, Kaboli PJ. Polypharmacy and prescribing quality in older people. J Am Geriatr Soc 2006;54:1516-23.
31. Chan H-K, Ismail S. Side effects of chemotherapy among cancer patients in a Malaysian General Hospital: Experiences, perceptions and ınformational needs from clinical pharmacists. Asian Pac J Cancer Prev 2014; 15: 5305-9.
32. Baniasadi S, Habibi M, Haghgoo R, Karimi Gamishan M, Dabaghzadeh F, Farasatinasab M, Farsaei S, Gharekhani A, Kafi H, Karimzadeh I, Kharazmkia A, Najmeddin F, Nikvarz N, Oghazian MB, Rezaee H, Sadeghi K, Tafazzoli A, Shahsavari N, Fahimi F. Increasing the number of adverse drug reactions reporting: the role of clinical pharmacy residents. Iran J Pharm Res 2014;13:291-7.
33. Carelle N, Piotto E, Bellanger A, Germanaud J, Thuillier A, Khayat D. Changing patient perceptions of the side effects of cancer chemotherapy. Cancer 2002;95:155-63.