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The Role of the Pharmacist in the Management of the Side Effects of Chemotherapy Treatment: Evaluation of Practices at the Onco-Hematology Service Level of Avicenna Marrakech Hospital

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ABSTRACT

The efficiency and safety of anti-cancer treatments are conditioned by the quality of the information delivered to the patient himself. In this situation, the pharmacist has a key role in managing patients under anticancer treatments. His expertise in drug therapy and counseling are essential for the implementation of measures to prevent certain undesirable effects, as well as understanding the modalities of their early detection and the behavior to be taken in case of their appearance. For this purpose, a study was carried out on 30 patients in the onco-hematology department of the Avicenna Marrakech Hospital, The survey used as a method of data collection a standardized questionnaire completed by the pharmacist during an interview with the patients. The side effects of chemotherapy in our patients varied depending on the drugs used, dosages, and the condition of the patient, then the appearance of these side effects requires management. Furthermore, the management of anticancer adverse reactions is often monitored closely by a designated doctor or nurse instead of the pharmacist. So our goal is that each professional must be refocused on his / her field of expertise. Among other things, the pharmacist must have a comprehensive approach to the patient, manage his eating disorders, his Social problems, his psychological problems, and pursue any delivery of advice, prevention messages, to help the proper use of the medicine.

1. INTRODUCTION

According to the WHO definition: "Cancer is a term used to describe the autonomous and anarchic malignant proliferation of cells. Such proliferation results in the formation of tumors that can invade nearby or distant organs, destroying normal tissue and competing for the use of oxygen and nutrients "[1].

On the biological level, all the cells of the body are subjected to a constant and programmed renewal: the cells of the same type are organized to form tissue or an organ; this regulation is under control that is initiated from the chromosomes that contain the genetic information [2]. Under the influence of certain factors (chemicals: tobacco, asbestos, insecticides ...- radiation, radiation: UVA, UVB, ionizing radiation- virus-bacteria, -stress-food habits ...) the genetic information contained can be modified [2].

In Morocco, cancer is a major public health problem. It is the second leading cause of death in our country after cardiovascular disease which is 11.3% [3]. The international agency for research on cancer (2010) published in its report, that Morocco experienced 27,600 new cases of cancer with a slight predominance of female cancer of_ 54.35%, and a mortality rate of 19 700 for both sexes, including 5 1.77% in men [4].

The cancer treatment consists in eradicating the tumor cells; it is adapted according to each situation. Indeed, each patient with cancer is a special case and requires appropriate care. The choice of a treatment or a combination of treatments depends on several factors, the most important of which are: the type of cancer, the degree of extension of cancer, the presence of possible other diseases, the age of the person, the general condition of the person.

There is different cancer treatments used alone or together, surgery-radiotherapy-chemotherapy-hormone therapy-immunotherapy -new "targeted" treatments. The choice of these treatments and the order in which they are administered should be made by a multidisciplinary medical team, and depending on the case, the treatments may have different objectives: Remove the tumor or metastases; reduce the risk of recurrence; slow down the tumor development or metastasis; improving the comfort and quality of life of the sick person by treating symptoms caused by the disease. During treatment, one control, on the one hand, the tolerance and on the other hand the evolution of cancer. Surveillance of medical treatments mainly concerns the hematological situation and radiotherapy mucocutaneous tolerance. For chemotherapy, the risk of infection dominates, and for radiotherapy, the risk of

radionuclide dominates with according to the seat of the irradiated region dysphagia, diarrhea, cystitis, and proctitis. The most common immediate risk being the dehydration and undernutrition. Monitoring makes it possible to adapt the treatment to tolerance.

The effectiveness and the safety of the cancer treatment are conditioned by the quality of the information delivered to the patient himself, but also by the health professionals practicing near his home or within the hospital.

Any problem of medication adherence should be detected as soon as possible by health professionals surrounding the patient. If not it can become dangerous for the patient himself and jeopardize the success of the treatment. Faced with this situation, the pharmacist has a key role in the care of patients with cancer, his expertise in drug therapy and counseling is essential for the implementation of measures to prevent certain adverse effects, the terms of their early detection and what to do in case of proven toxicity.

Supportive care includes all care that supports the consequences of cancer and its treatments such as pain, eating disorders, and socio-psychological issues.

The initial hypothesis is that the presence of a pharmacist in the context of a care service contributes to improving the quality of life of the patient, in particular by monitoring the correct use of medicines, managing their side effects and the quality of the administered board.

Our study was carried out on the level of onco-hematology services of the Avicenna Military Hospital of Marrakech (HMAM) on patients undergoing chemotherapy, in order to evaluate the necessity of the presence of the pharmacist within these services.

The aim of the study:

In our country, no study has been published on this subject. The specific objective of this work is to try to answer the following question: What is the pharmacist's role in cancer patients?

2. METHODS

Study design and Setting:

This is a perspective and descriptive study spread over 4 months, activities occupied by pharmacists in the context of control of pain and adverse effects induced by anticancer drugs in patients hospitalized or followed within the Military Hospital Avicenna Marrakech.

Study participants:

The patients in our study included 30 adults (military and their families) hospitalized or consultants or having a chemotherapy session at the HMA or civilian patients referred to hospitals Mohamed VI University Hospital.

The selected patients were those with solid cancer or hematological malignancy whether hospitalized, consulting or having a chemotherapy session at HMAM. In this study were excluded patients who did not give a favorable opinion to participate and be part of the study. Patients having difficulty answering questions and patients receiving their first course of chemotherapy.

Data collection:

To carry out our study, a plug was developed to document the different levels of pharmacist interventions in onco-hematology; it was also to collect proposals to develop a tool or tools that can meet their needs and expectations. In the first part, the collection of information was done from the files of hospitalized patients or consultants at the HMA as well as from the interview conducted by the pharmacist.

These records of operations included: 1- General patient information: last name, first name, age 2-Service 3-Diagnosis 4-Chemotherapy protocol and dosage 5-Co-medications and interactions 6-Undesirable effects and their uptake charge 7-General advice to patients 8-Adherence to treatment for patients on oral anticancer drugs (AKPO).

Data analysis:

The data entry was done on the software used SPSS (Statistical Package for the Social Sciences), version 16.0.

Essentially descriptive statistical analyzes have used:

• Calculation of numbers and percentages for qualitative variables

• Calculation of central (mean and median) trends and dispersion (standard deviation) measures for quantitative variables.

The statistical threshold (α) was set at 0.05. P values below 0.05 were considered significant.

Ethical aspects:

Prior consent of the patient for participation in the requested study. Respect for the anonymity and the confidentiality of the files.

3. RESULTS :

The average age of our patients was 61 years old with extremes ranging from 31 to 80 years old. Our 30 patients were divided into 9 women (30%) and 21 men (70%), with a male / female sex ratio of 2.3 (Table I).

The vast majority (73%) answered that they had received information about their cancers, treatments and side effects, 27% of patients were unaware of their cancer or had no explanation for the treatment and its side effects. Patients informed about their illnesses and the side effects of treatment received only these data from their referring physicians.

Of the 30 cases that were informed, 6 patients had received advice on their treatment and management of side effects, while 24 patients had not received anything.

Patients treated with intravenous injection were the first to be compared with those treated with the 2-partnered or those treated with the oral route alone (Figure 1). Of our 13 patients receiving oral chemotherapy, 12 were prescribed the time and the recommendations of the treating physician when only one patient sometimes forgot his treatment.

Hormone-dependent cancers (breast, ovarian, and prostate cancer) ranked highest in our HMA-treated patients (21%); followed second by lung cancer; lymphoma and multiple myeloma. Colon cancer and myeloproliferative syndromes were ranked last. For men, the most common cancers were successively lung cancer (24%), multiple myeloma (19%), liver cancer (14%), and lastly prostate cancer (5%). For women, breast cancer occurred first

(56%), followed by myeloproliferative syndromes (22%) and then leukemia and myeloma (11%) (Figure 2).

In the HMA hemato-oncology department, 47% of patients were treated with conventional chemotherapy, 33% with conventional chemotherapy combined with immunotherapy, and 20% with immunotherapy alone (Table II). Conventional chemotherapy remained the treatment leading to more adverse effects than immunotherapy or mixed treatments.

The side effects of chemotherapy varied according to the drugs used, the dosages and the people. The most common side effects of anticancer drugs are presented below (Table III). All patients received a parenteral antiemetic before the chemotherapy session, 13 patients still had vomiting and nausea after the session of which only 5 patients (38%) were treated. The 10 patients with gastric pain were treated according to the recommendations in force. Patients who had constipation or diarrhea following chemotherapy were 9 patients. Two (22%) of these patients had received treatments to regulate their intestinal transit while the other 7 patients (78%) did not require it. Twenty-five patients in our series had asthenia and/or vertigo, of which 5 cases (20%) were treated, while the others required no treatment. Of the 30 cases treated, 3 patients had fever or chills, 1 of which required treatment. Patients who had adverse biological effects following chemotherapy were 5 patients.

All these patients were treated according to the recommendations in force. Sixteen patients had other undesirable effects than those mentioned (ascites, blackish nasal discharge, loss of consciousness ...), 10 patients (38%) among these 16 were treated, and the other 6 patients (63%) received no cure.

4. DISCUSSION:

In our study, the average age at diagnosis was 60 years for women and 62 years for men. We can conclude that cancer is a pathology that affects all ages, with a predilection in the elderly population. In Algeria [5], the average age for all cancers is 54 years old. This age is low compared to the median age of cancers in developed countries (62 years on average). In Canada [6], cancer affects mostly old people; about 64% of women and 75% of men are at least 60 years old at the time of diagnosis. In France, the median age at diagnosis in 2015 is 68 years for men and 67 years for women [7].

In our series, there was a male predominance with a sex ratio of 2.3 which is not consistent with the data from the studies cited above. These results can be explained by the fact that our study was conducted in a military environment where the staff is predominantly male. It could, therefore, be a recruitment bias [6, 8, 9].

Regarding knowledge about cancer, the results of our study are similar to the results of other studies. Santucci Raoul et al [10] shows that 82% of patients are satisfied or very satisfied, and Carretier et al [11] shows that 86% of patients report having received, during their treatment, information that is "totally" or "rather sufficient" from the doctors and the health care team. In our study, patients who were aware of their diseases and side effects received only these data from their referring physicians; these results are consistent with literature data [10, 11].

When it comes to informing patients, the doctors have an obligation of means. Jurisprudence requires free, informed and informed consent of the patient. Since the Hedreul judgment (Cass Civ, 1st February 25, 1997), the "doctor has a special obligation to inform his patient and he has to prove that he has performed this obligation "(Durand-Zaleski, 1999). In Morocco, there is no text specifying the rights and duties of patients. The obligation to inform the patient, therefore, exists on the ethical level. In practice, the majority of physicians inform their patients to participate actively in the medical treatment decision. Patients must have adequate information to play a significant role in making decisions that reflect their own choices.

In our study, the majority of our patients were treated with intravenous treatment, which is comparable to the results of a French study [12]. As part of oral outpatient treatment, the responsibility of the patients and/or their entourage is engaged, both in taking the treatment and in the management of side effects. This is why the prescription and dispensing of oral anticancer agents are not intended for all patients. In particular, they target patients who are able to take care of themselves, are valid, voluntary, informed, observing and benefiting from a suitable family environment. It should not be imposed but proposed and informed (accompanied by adequate information). In our series, lung cancer (for men) and breast cancer (for women) are in the first place what is similar to other studies whereas the frequency of appearance of other hematologic cancers is totally different from other studies [13], who show colorectal cancer, prostate cancer, and that, cervix. Our study was conducted

in the hemato-oncology department of the military hospital, which explains the frequency of hematological cancers as well.

According to a study by Cooreman M et al, today, chemotherapy is automatically associated with targeted immunotherapy, recent studies have also concluded that the addition of immunotherapy to this chemotherapy gives better results in treating leukemia. Chronic lymphoid [14]. In America, the annual conference of the American Society of Oncology (ASCO) held in 2015 [15], shows that Nivolumab would be more effective, but also better tolerated than standard treatment, for the second-line management of cancer non-squamous non-small cell epidermoid In our study, immunotherapy remained the treatment inducing fewer adverse effects, which is similar with the studies cited.

An adverse effect is "a harmful and unwanted reaction to a drug, occurring at doses normally used in humans for the prophylaxis, diagnosis or treatment of a disease or for the restoration, correction or modification of a disease. a physiological function, or resulting from misuse of the drug or product " [16].

According to a study conducted in Canada [17], by a group of 5 pharmacists at the Tom Baker Cancer Center for a period of more than 6 weeks out of 56 patients. The activities of these pharmacists are as follows: Dose change, diet modification, management of side effects, organization and refilling of prescriptions, interactions with other health professionals, assessments of recalls, providing advice on current medications. Pharmacists followed up with patients they found necessary and also documented their activities and interventions. In these patients, there is the appearance of certain adverse effects induced by chemotherapy (Table IV).

The following results indicate that the frequency of adverse events in Canadian patients is at least similar to our results.

After the intervention of the pharmacists, the majority of the patients indicated that the follow-up service was allowed to get the help they needed and even exceeded their expectations. This included questions about drug information, providing patient updates, and providing advice on the patient's drug alteration [17, 18].

More importantly, the majority of patients surveyed were more confident about managing their own medications and monitoring themselves for side effects indicating that pharmacists

have been successful in their initiatives to educate patients about the appropriate use of drugs. medications and the management of side effects if they occur.

Pharmacists have also contributed to the safety and effective use of drugs for pain by addressing the occurrence of adverse effects. They addressed 41 adverse effects (32 of these required drug modifications were included in the 126 interactions previously discussed).

All who responded confirmed that the pharmacy follow-up service was beneficial, improved patient outcomes and experiences, and was a valuable part of the clinic. 84% of health professionals surveyed indicated that pharmacists were available to answer their drug-related questions outside of the clinic. While some indicated that they were not able to comment, the majority indicated that they felt that the pain and symptom control clinic was more effective with the pharmacists' follow-up service and allowed to see more patients in the clinic [19].

The aim is to enable the rapid identification of adverse effects, in order to propose adapted and validated solutions to patients. An undesirable side effect, even minor medically unsupported can be a great source of discomfort (physical and/or psychological), and cause a change in compliance, and stop taking of treatment.

In our study, patients with nausea and vomiting were 13 of whom only 5 were cared for; as all our patients were treated with antiemetic prophylaxis such as metoclopramide and ondansetron. They may be due to the disease itself or else to the treatments administered. Beside these treatments, there are to be associated with hygienic and dietary rules that the pharmacist can state to the patient [20].

The drugs with the highest risk of causing diarrhea are capecitabine, hydroxycarbamide, gefitinib, imatinib. It is important to never underestimate diarrhea because it can quickly lead to the loss of water, nutrients, and weight. Undernutrition can occur with lassitude and asthenia. Treatments are often recommended: loperamide, racecadotril, diosmectite [21]. In addition to these treatments, there is a combination of dietary and hygiene rules that the pharmacist can give to the patient.

Constipation may be due to some anticancer drugs such as vinorelbine. It can also be linked to the use of morphine helping to fight against pain. Laxatives or enemas may be prescribed [22].

Undernutrition not only affects the survival of patients, causing death in 5 to 25% of cancers but also their quality of life and generates high costs of treatment. The diet of a patient with cancer must follow 5 important rules: it must be regular, balanced, appetizing, friendly and adapted. Several measures are recommended to increase dietary intakes [23].

5. CONCLUSION:

The pharmacist is first in line for detecting unwanted effects occurring during processing. It is then important to provide advice and information to help the patient in the life of every day to better withstand the treatment, in some cases, recommendations can be provided for prevention of the occurrence of these adverse effects expected. It is in this context that this work whose overall objective is to help improve the management of patients treated with anticancer, specifically to identify the role of the pharmacist directly from their patient (tips and monitoring). The pharmaceutical advice and psychological support will prevent complications; improve patient quality of life and minimize the severity of adverse effects.

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Table I: Patient distribution by age and sex.

Age class	Sex		Total
	Men	women	
<50	1	1	2
50-60	7	3	10
60-70	9	3	12
70-80	4	2	6

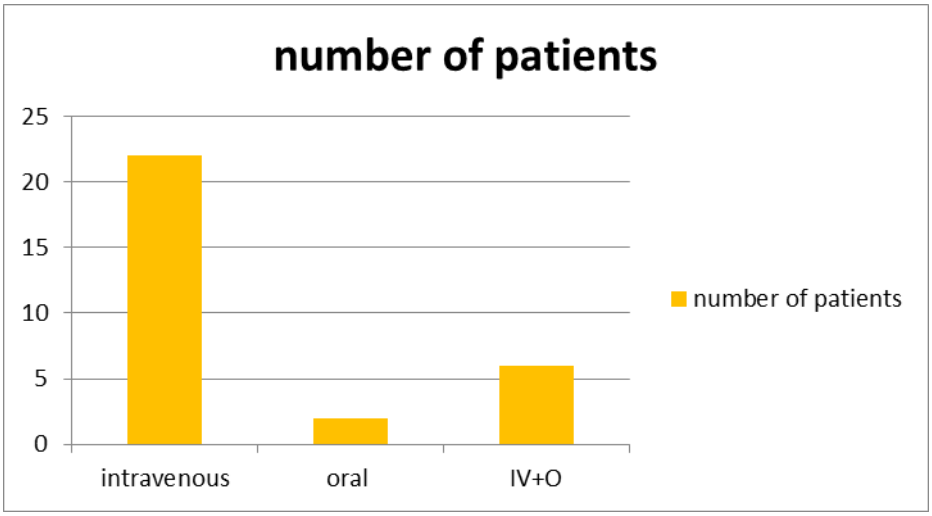

Figure 1: Representation of patients according to the route of administration of their treatment

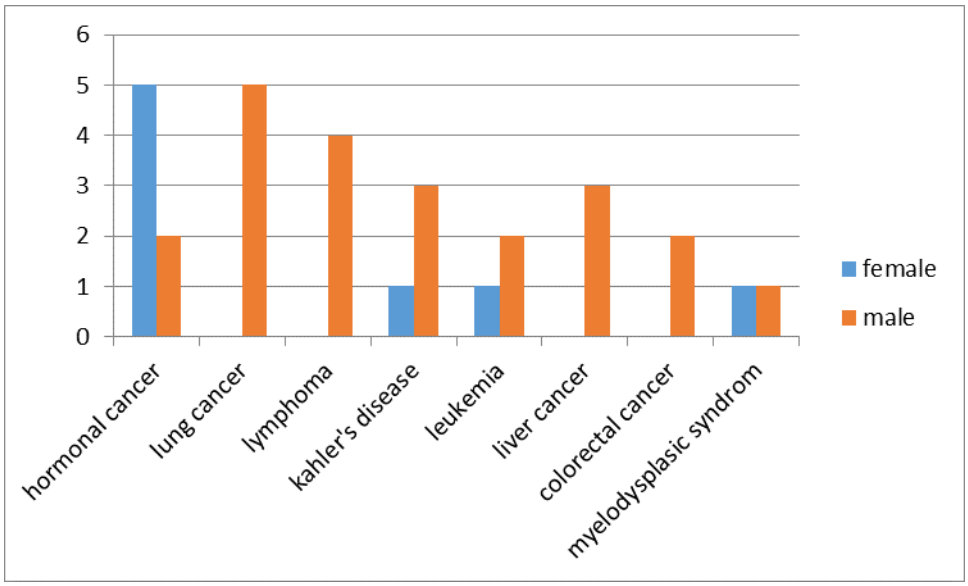

Figure 2: Patient representation by sex and type of cancer

Table II: Distribution of patients according to the treatment used

Type of chemotherapy used	Number of patients treated by type of chemotherapy
Classic chemotherapy	1 6
Classic chemotherapy+ Immunotherapy	10
Immunotherapy alone	4

Table III: Adverse effects and their frequencies

	Side effects	Frequency of side effects
Digestive toxicity	Nausea and vomiting	13
	Constipation/ diarrhea	9
	Canker sores and mucositis	2
	Malnutrition	6
Cutaneous toxicity	Alopecia	13
	Brown spots of milk	4
	Hyperpigmentation	5
hematological Toxicity	Neutropenia	5
	Anemia	5
General toxicity	Dizziness	10
	Tiredness	24
	tingling of the lower limbs	7
	Fever	2
	others	16

Table IV: comparison of adverse effects in our patients and patients in the Canadian study

Side effect	Number of Canadian patients	Number of patients in our study
Nausea and vomiting	8	13
Constipation	10	9
Diarrhea	3	9
Anorexia	11	6
Tiredness	3	24
Drowsiness	6	-
Others	15	16