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Adverts Drug Events on Outpatients Treated in the Nuclear Medicine and Oncology Center of Bach Mai Hospital via Clinical Pharmacist's Active Surveillance

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Abstract

Background: Despite significant advances in malignant neoplasms treatment and an increase of the survival in patients as a result of the chemotherapy using, a significant number of side effects, both immediate and delayed, significantly worsen the quality of life and often contribute to the development complications. Timely detection, monitoring, and control of the chemotherapy side effects are important in the algorithm for successful treatment and prevention of severe reactions in the human. ***The purpose*** of the study is to make survey of clinical characteristics of cancer patients treated by chemotherapy and adverse drug events (ADE) analysis via active surveillance of clinical pharmacist in the Nuclear medicine and oncology center.

Materials and Methods: We have analyzed data on the objective condition of patients and their medical files in August 2018. This is a discreptive cross-sectional study, ADE active surveillance without intervention.

Results: Ha been identified total 3.273 ADEs, in which 326/332 (98.2%), 259/332 (78.0%) patients had ADEs via interviewed and reviewed lab results, respectively. The most common ADEs were fatigue, appetite loss, anemia, leukopenia/neutropenia and ALAT/ASAT increased. The incidence and severity of ADE on each grades from 1 through 5 were 77.4%; 15.8%, 5.0%, 1.9% and 0%, respectively. The present study showed that the incidence of ADEs related to chemotherapy is very high.

Conclusions: Have been proved that active surveillance by clinical pharmacists in the Nuclear medicine and oncology center could effectively improve the quantity of ADEs. These active surveillance programs should be implemented usually in Nuclear medicine and Oncology hospitals to ensure patient safety.

Keywords: adverse drug events, out patients, Nuclear medicine and Oncology center, active surveillance, clinical pharmacist.

1. Introduction

Despite the proven efficacy of chemotherapeutic anti-cancer drugs in improving remission rates and patient survival, this type of therapy is receiving considerable attention from both doctors and patients. Even improved modern chemotherapy is capable of causing a significant number of side effects that offset the improvement in the clinical picture due to a strong deterioration in the patient's well-being and the development of resistance to the prescribed drugs [1-3].

The most common side effects of chemotherapy are nausea and vomiting. These gastrointestinal symptoms can also have a delayed, more difficult to recognize and treat, effect. Inadequate monitoring and treatment of nausea and vomiting can lead to a number of serious complications that can lead to life-threatening consequences, such as electrolyte balance due to dehydration, acute surgical conditions such as tears in the esophagus and bleeding [4-6].

In addition to the above, there are a number of other potentially fatal gastrointestinal (GI) complications of chemotherapy. Mucositis of the oral cavity and other parts of the digestive system manifests itself as systemic ulceration and causes pain, which as a result can lead to anorexia, cybophobia, maldigestion and malabsorption syndrome, severe dehydration, and anemia. Despite numerous studies on mucositis, effective preventive measures have not yet been developed [7-9].

A common side effect of chemotherapy is also peripheral neuropathy, manifested by impaired sensory function, abnormalities in gastrointestinal motility. Also, neuropathy is manifested by chronic fatigue syndrome, depression, ataxia, and sleep disorders [10-12].

Neuropathic pain (ND) is one of the most impairing quality of life complications of chemotherapy-induced peripheral neuropathy. NB often leads to decreased patient compliance and discontinuation of treatment [13]. The consequences of the central neurotoxic effect of chemotherapy may be persistent cognitive impairments, the development of which is associated with the redistribution of the components of the cerebrospinal fluid, as well as with genetic polymorphisms [14-16].

Cytopenia is a common side effect of chemotherapy, described as a result of different regimens and combinations of chemotherapy drugs [17, 18]. A side effect and consequence of chemotherapy is thrombocytopenia, which manifests itself as a critical decrease in the number of platelets and requires the administration of prophylactic thrombopoietic agents [19, 20]. A number of prospective studies have also shown an association between leukopenia as a side effect of cancer chemotherapy and patient survival rates. It has been shown that immunosuppression, associated with a decrease in the number of leukocytes in the blood, can contribute to the resistance of cancer to used chemotherapeutic drugs and reduce the response of tumor cells to treatment [21].

Multi-chemotherapy drugs and their combinations promote cancer treatment with the lowest number of detected side effects, which is explained by the synergism of pharmacological drugs in combination and overcoming the resistance of malignant cells to therapy, which improves patient survival [23, 24]. The need for early detection and control of side effects of chemotherapy is an urgent and obvious problem in modern oncology. Many of the above clinical manifestations are life-threatening and significantly worsen the quality of life of patients, increase the number of readmissions and mortality.The purpose of the study is to make survey of clinical characteristics of cancer patients treated by chemotherapy and adverse drug events (ADE) analysis via active surveillance of clinical pharmacist in the Nuclear medicine and oncology center.

2. Materials and Methods

The experiment was as observation research to register and characterize adverse drug events (ADE) caused by cancer chemotherapy.

2.1. Selection criteria

Patients and medical records of patients who come for medical examination and treatment at an outpatient clinic of the Center for Nuclear Medicine & Oncology during the study period are prescribed, from August 1, 2018, using cancer treatment chemicals.

2.2. Exclusion criteria

Patients with radiation therapy.

2.3. Study design

It is descriptive, cross-sectional study and active monitoring of non-intervention ADE. Patients who satisfy the selection and exclusion criteria are actively monitored for ADE through activities, including:

- Interview patients (or patients' relatives), health workers according to the designed questionnaire, record the related ADE.
- Retrospective review: review and analysis of biochemical blood and hematological tests of interviewed patients.

ADE is classified according to standards of the US National Cancer Institute (Common Terminology Criteria for Adverse Events v4.0 - CTCAE) [25], including 5 levels: level 1 - mild; degree 2 - medium; grade 3 - heavy; level 4 - life threatening; degree 5 – death.

Cancer chemicals are classified into pharmacological groups according to the ATC code, including:

L01A – Alkylating agents
L01B – Metabolic resistance drugs
L01C – Alkaloids from plants and other naturally occurring medicines
L01D – Antibiotics that are cytotoxic and related
L01X – Other anticancer drugs
L02A – Hormones and related substances
L02B – Hormone antagonists and related substances
L04A – Immune modulators

The study was conducted in accordance with ethical standards approved by the Bioethical Review Commission of Bach Mai Hospital. All patients signed voluntary informed consent to participate in the publication of the study results. Participants could withdraw from the study at any time.

The data obtained were analyzed statistically to determine the significance of various parameters using the SPSS program (v. 14.0). The normal distribution of variables was assessed using the Kolmogorov-Smirnov test. Values between groups are compared using one-way ANOVA. Nonparametric Mann-Whitney tests were used for quantitative variables that were not normally distributed. A p value < 0.05 was considered statistically significant. Regression analysis was used to examine the relationship between parameters.

3. Results

3.1. Research results on general characteristics of the sample

3.1.1. General characteristics of the patient

During the study, we selected 332 patients who met the criteria of selection and exclusion. The research results show that patients in the research sample belong to many age groups. However, it is mainly distributed among elderly people (58, 6 years on average). Different gender distributions do not make sense. Characteristics of patients in the sample are shown in Table 1.

Patients in the sample are distributed in many different types of cancer, the most common of which is lung cancer. The characteristics of patient distribution in the sample based on diagnosis are shown in Figure 1.

3.2. Characteristics of cancer treatment chemicals used in the research sample

The results showed that the cancer treatment chemicals used in the research sample belong to 8 different pharmacological groups according to the ATC code, of which the most used pharmaceutical group is L01X, followed by L01B and L01C.

The results of the research on cancer treatment chemical characteristics in the research sample are presented in Table 2.

3.3. Research results on ADE through active monitoring of DSLS

The obtained data show that patients using cancer treatment chemicals encounter ADE with a high rate: interview results show that patients encounter 7.0 [4.0-12.0] expressions ADE current; The corresponding result obtained by screening is 1.0 [1.0-2.0]. Research results on ADE recorded through interviews and test screening are detailed in Table 3.

3.4. The results of research on 10 ADE were most recorded through interviews

Fatigue is the highest rate of ADE (60, 2%) of the ten ADE manifestations recorded. Next is anorexia, tingling numbness in the feet/hands, dry mouth, muscle weakness or muscle aches, vision

loss, dizziness, nausea, alopecia, constipation. Among the ADE obtained from interviewing activities, the 10 most common manifestations are described in detail in Table 4.

3.5. Research results on ADE through screening of test results

According to the getted results, the decrease in Hb and increase in ALAT/ASAT are the ADEs recorded with the highest rate (57.2% and 28.9%). This is followed by neutropenia and neutropenia. Hypercalcemia and hypokalemia are less common ADEs. The general characteristics of ADEs recorded through screening results have been detailed in Table 5.

The results showed that ADE was mainly recorded at level 1.2 (77.4%; 15.8%). only a small percentage of ADEs at level 3 (5.0%) and grade 4 (1.9%). no ADE was recorded at grade 5 in the sample.The ADE ratios at various levels. obtained through screening of biochemical and hematological test results.

4. Discussion

4.1. The results obtained are consistent with the data of previous epidemiological studies

The lung cancer has remained the leading cause of death in cancer patients for many years. The difference in smoking prevalence determines the epidemiological situation in different countries regarding mortality from lung cancer. The decline in smoking rates, the discovery of a number of new risk factors in developed countries, and the emergence of new screening methods and data on molecular profiling of tumors have led to changes in the geography of the prevalence of lung cancer, which dominates mainly in developing countries [26, 27].

The use of group L01X is pathogenetically substantiated and has an extensive evidence base. The anticancer effects of the group are associated with inhibition of the expression of tumor cyclooxygenase-2, which leads to inhibition of the mechanisms of apoptosis and inhibition of oxidative phosphorylation with the formation of free damaging radicals. Combinations of drugs in this group are used in the treatment of osteosarcoma, melanoma, glioblastoma, pancreatic cancer and small cell lung cancer.The least commonly used pharmacological group is L02A [28].

Fatigue as a side effect of cancer treatment is defined as chronic because it is present for a long period of time, systemically affects the body, and does not decrease after sleep and rest. Fatigue due to chemotherapy usually decreases after the end of therapy, but its effects can persist even for several months or even years after the end of treatment [29].

Antitumor therapy, as a rule, leads to the occurrence of severe hepatotoxic reactions, since the liver is one of the main links in the biotransformation of cytostatics. The leading mechanism of drug-induced liver damage is the dose-dependent direct toxic effect of the drug and its metabolites on hepatocytes, followed by their necrosis, disruption of bilirubin metabolism, dilatation of sinusoids, or vein occlusion. The main role in the metabolism of drugs is played by liver monooxygenases, which simultaneously activate and detoxify functions. An important place in the development of cytostatic liver damage is occupied by the activation of the processes of free lipid peroxidation, which leads to a decrease in antioxidant protection and an increase in the activity of lysosomal enzymes [30, 31].

5. Conclusions

The present study showed that the incidence of ADEs related to chemotherapy is very high. Our data also proved that active surveillance by clinical pharmacist in the Nuclear medicine and oncology center could effectively improve the quantity of ADEs. This active surveillance programs should be implemented usually in the Nuclear medicine and Oncology and other clinical wards of hospital to ensure patient safety.

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Table 1. *Patient characteristics in the study*

Research targets	Results
Patient (n)	332
Age (X ± SD)	58.6 ± 12.0
Male (n (%))	183 (55.1)

Table 2. *General characteristics of cancer treatment chemicals in the research samples*

Pharmaceutical group	Pharmaceutical group	Prescription number	(%)
L01X	cisplatin, carboplatin, oxaliplatin, rituximab, trastuzumab, bevacizumab, imatinib, gefitinib, erlotinib, sorafenib, irinotecan	193	41.2
L01B	pemetrexed, 5FU, gemcitabin, capecitabin, tegafur (dạng phối hợp)	148	31.5

Pharmaceutical group	Pharmaceutical group	Prescription number	(%)
L01C	vincristin, vinorelbin, etoposid, paclitaxel, docetaxel	59	12.6
L01D	doxorubicin, epirubicin, mitroxantron	20	4.3
L01A	cyclophosphamid, temozolomid	19	4.1
L02B	tamoxifen, bicalutamid, anastrozol, letrozol	18	3.8
L04A	Thalidomide	10	2.1
L02A	Goserelin	2	0.4
Total		469	100.0

Table 3. *Characteristics of ADE recorded through interviewing and screening*

Research targets	ADE recorded from interview activities (n = 332)	ADE recorded via screening test (n = 332)
Patients count with ADE (n (%))	326 (98.2)	259 (78.0)
Total ADE (n)	2792	481
ADE / BN number (median [quartile])	7.0 [4.0-12.0]	1.0 [1.0-2.0]

Table 4. *Ten ADEs most recorded through interviews*

ADE expression	Number of patients with ADE (n=332)	Ratio (%)
Tired	200	60.2
Anorexia	162	48.8
Tingling/numbness in hands / feet	148	44.6
Dry mouth	138	41.6
Muscle weakness or muscle aches	130	39.2
Decreased vision	119	35.8
Dizzy	114	34.3
Nausea	114	34.3
Alopecia	114	34.3
Constipation	106	31.9

Table 5. *ADE records through screening of test results*

ADE expression	Number of patients with ADE (n = 332)	Ratio (%)
Blood chemistry		
Increased ALAT/ASAT	96	28.9
Increased serum calcium	10	3.0
Decreased serum potassium	10	3.0
Hematology		
Decreased Hb	190	57.2
Leukopenia	48	14.5
Neutropenia	48	14.5
Thrombocytopenia	29	8.7

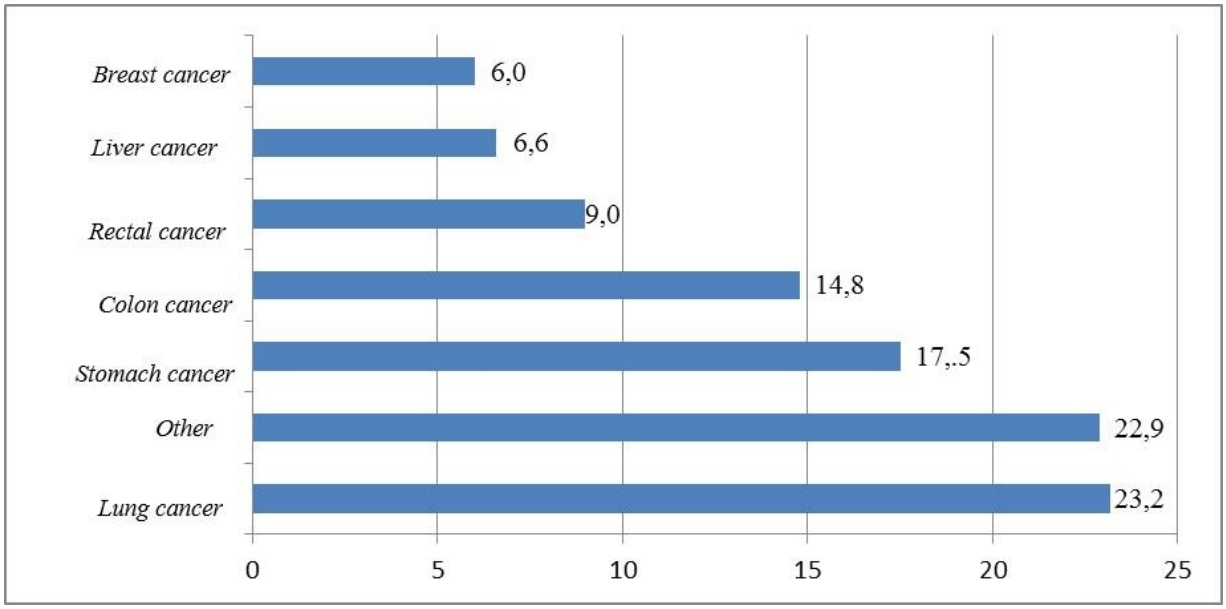

Figure 1. *Distribution of patients by disease diagnosis (%)*