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Evaluation Of Adverse Drug Reaction On Different Body Organs In The Center Of Nuclear Medicine & Oncology – Bach Mai Hospital

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Abstract

Background: Combination chemotherapy is the gold standard in the treatment of advanced malignant neoplasms. Side effects of chemotherapy necessitate a deeper study of clinical manifestations in patients receiving chemotherapeutic agents. And the algorithms for systemic assessment and correction of emerging side effects must be created.
The **main aim.** To evaluate the monitoring, supervising, and reporting activities for adverse drug reaction (ADR) events in Bach Mai hospital.

Materials and Methods: The retrospective study on ADR reports is presenteted. Data exploration steps included: assessing the situation of monitoring, monitoring and reporting ADR at Bach Mai Hospital. The classification ADR was made by the age group, route of injection and drugs using, clinical manifestations, affected body organs.

Results: Bach Mai hospital has introduced the activities of monitoring, supervising, and reporting for ADR events in common. All units of the Bach Mai Hospital have carried out these activities with a total of 2074 ADR reports (0,58%). According to the reports, ADR occurs in all patient age groups. ADR met at all the route of drug administration, the ratio is the highest for oral introduction (32.08-37.24%). Each organ can be affected by ADR, in which disorders of the skin and

subcutaneous tissue are the most commonly reported (53.18-58.03%). Almost ADR can recover completely (96.68-98.44%). There were no fixed deaths due to ADR.

Conclusion: The number of ADR reports was inadequate compared to the large scale and potential of the hospital. ADR monitoring, detection, and reporting had been unsteady, the involvement of clinical pharmacists was still limited.

Keywords: malignant neoplasm, treatment, chemiotherapy, adverse drug reaction (ADR).

1. Introduction

Chemotherapy is an effective method of treating malignant neoplasms, either alone or in combination with other treatments [1,2]. Chemotherapy drugs are characterized by a powerful damaging effect on cells not only of tumor tissue, but also of nearby structures. At the same time, there is an increase in the frequency of development of undesirable side effects, including those associated with inhibition of hematopoietic germs. Despite an increase in the number of complications, multi-chemotherapy combination therapy is increasingly being used instead of isolated chemotherapy [3-5]. There are prerequisites that such therapy, especially in combination with radiation therapy, may become the standard of treatment for patients with inoperable forms of lung cancer for the next decade [6, 7]. In this regard, the assessment of the nature, frequency of development and severity of undesirable side effects during anticancer therapy for predicting their occurrence and timely relief is relevant [8, 9].

Chemotherapy has several advantages over screening radiation therapy in patients with stage IV cancer, as proven in several studies. Based on data from meta-analyzes and clinical studies, multi-chemotherapy drugs are of crucial interest to oncologists, but their significant disadvantages are considered to be toxicity, inherent resistance, and multi-organ side effects [10].

The toxic effect of chemotherapy on hematopoiesis is the most common side effect of the use of chemotherapeutic agents and is manifested by the suppression of all hematopoietic germs. Especially often the progenitor cells of leukocytes and platelets are damaged, and less often the cells responsible for the development of erythrocytes [11]. The risk factors for the development of toxic effects of chemotherapy drugs on the bone marrow include: previous chemotherapy and radiation therapy, the age of patients over 60 years old and younger than 1 year, the general condition of the patient, exhaustion. Inhibition of hematopoiesis is usually observed in the coming days after the appointment of chemotherapy (7-12 days). Some drugs have a delayed toxic effect. A sharp and prolonged decrease in the number of leukocytes can lead to an increased incidence of infectious complications. In the past 20 years, there has been an increase in the incidence of fungal and viral infections. With a significant decrease in the number of platelets, nosebleeds, gastrointestinal bleeding, cerebral hemorrhages, etc [12, 13] .

Cardiotoxicity is most often as a side effect when using anthracyclines, cyclophosphamide, 5-fluorouracil, etoposide. Development of cardiotoxicity is more often observed in people over 60 years old, with heart disease, with irradiation of the lungs or mediastinum, with previously performed chemotherapy with drugs that have cardiotoxicity. Early manifestations of cardiotoxicity include: tachycardia, hypotension, tachycardia, arrhythmias. Later symptoms of cardiotoxicity include arrhythmias and conduction disturbances, ischemic changes. Serious complications of chemotherapy as manifestations of cardiotoxicity are myocarditis, cardiomegaly, and heart failure [14].

Neurotoxicity as a complication of chemotherapy can manifest itself in various parts of the nervous system. In most cases, it is a side effect of the appointment of vincristine, etoposide, prospidin, natulan, platinum preparations, taxol, etc. Central neurotoxicity is most often manifested in the form of cognitive impairment of attention, memory, emotional disorders, and a decrease in general tone [15, 16]. Hallucinogenic syndrome and agitation are considered serious and difficult to treat complications. Peripheral neurotoxicity manifests itself in the form of paresthesia, Raynaud's syndrome, dysfunction of the upper and lower extremities, flatulence, impairment of vision and hearing. Neurotoxicity predominantly develops with the introduction of chemotherapy drugs into the spinal canal or the use of high doses. In this case, patients may experience headaches, dizziness, nausea, vomiting, disorientation and consciousness disorders [17].

Side effects of chemotherapy are also manifested in dysfunction of the gastrointestinal tract in the form of nausea, vomiting, stomatitis, enteritis and diarrhea, mucositis as a result of damage to the mucous membranes of the oral cavity and intestines, toxic liver damage. Nausea and vomiting are not the most dangerous, but the most common and most painful manifestations of the toxic effect of chemotherapy drugs. In some cases, these reactions can even lead to refusal of treatment.

The multiorganism and polymorphism of side effects of chemotherapy necessitate a deeper study of clinical manifestations in patients receiving chemotherapeutic agents and the development of algorithms for systemic assessment and correction of emerging side effects [18].

2. Materials and Methods

2.1. Research Subject

The study was conducted on ADR reports, ADR records and medical records of units of Bach Mai Hospital in the period of three years. Exclude cases of drug poisoning (overdose). Selection criteria: Patients and medical records of patients who come for medical examination and treatment at an outpatient clinic of the Bach Mai Hospital using cancer treatment chemicals. Exclusion criteria: Patients with radiation therapy.

2.2. Study design

It is retrospective study on ADR reports, ADR records and medical records from 2015 to 2017. Data exploration steps included:

1. Assessing the situation of monitoring, monitoring and reporting ADR at Bach Mai Hospital in period of 2015-2017.
2. Classify ADR collected in three years observation by: Age group, route of administration, use of drugs, clinical manifestations, affected body organs, management and consequences to again of ADR.

The study was conducted accoding 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

The study results showed that 2074 ADRs were recorded in the period of 2015-2017, accounting for 0.58% of the total number of patients hospitalized and treated during this period (Table 1).

So, all units have reported ADR and these are reports of ADR appeared due to drug use during treatment in the hospital. The number of reports by the Center for Allergy - Clinical Immunity accounted for the highest percentage (8.59-14.16%), followed by the Center for Medical Medicine (4.11-10.36%) and the Center for toxic (4.11-7.52%) (Table 2).

We have divided the patient's age according to the national ADR track into 15-year classifications. The research results are presented in Table 3.

Patients experiencing ADR are divided into 5 age classes and ADR occurs in all age classes. The age groups: 16-30, 31-45 and over 60 years old all meet ADR with a relatively high rate (12.7-27.15%).

Research results show that, there are 4 routes to bring drugs to meet ADR the most: oral (32.08-37.24%), intravenous (33.5-34.5%), intravenous infusion (15.37-20.96%) and intramuscular (4.11-13.3%) (Table 4).

The study results showed that all groups of drugs can cause ADR. However, the prevalence of ADR was highest among antibiotics (2015: 51.3%; 2016: 45.81% and 2017: 47.82%). In particular, in those 3 years, there were 13 patients experiencing ADR due to using Oriental medicine (Table 5).

Among 10 antibiotic groups reviewed, betalactam is still the group of drugs with the highest ADR rate (Table 6).

The most common ADRs are skin and subcutaneous tissue disorders (53.18-58.03 or 5%) and general disorders (12.08-14.74%) (Table 7).

Results of summary and classification of reports by ADR consequences were summarised. So, the biggest number of the ADRs has be treated (85.84-96.1%), and the shot fully recovers after being treated (96.68-98.44%). Out of a total of 2074 ADR reports collected, 51 reports (2,46%) did not record the consequences of ADR.

4. Discussion

Research results show that there are 2074 ADR cases recorded, accounting for 0.58% of the total number of medical records treated in the period. This result is much higher than the period 2006-2008 (813 cases) [19]. The above results show that the ADR reporting rate of that Bach Mai Hospital increased significantly in comparison with the number of reports obtained in the period 2006-2008. In particular, the ADR reports collected from the Center for Nuclear Medicine and oncology increased markedly. This result is in agreement with the fact that the medicine considers that the group of cancer treatment drugs is one of the groups of drugs with a high rate of ADR. On the other hand, this result also reflected that the hospital's monitoring, misdemeanor and adversity that the hospital's ADR was concerned and strengthened. However, these rates are still very low and consistent with the research results of Tran Hong Linh [20]. The low ADR prevalence at Bach Mai Hospital may be due to the fact that this is only the result obtained mainly from voluntary ADR reports. Research results also show: In the period 2015-2017, all All units of BVBM have ADR reports. These are the ADRs that arise from drug use during hospital treatment. In particular, the number of reports of the Center for Clinical Immunallergy accounts for the highest percentage (8.59-14.16%), followed by the Center for Medical Medicine (4.11-10.36%) and the Center anti-poison (4.11-7.52%).

Regarding the evaluation of ADR reports: In total 2074 ADR divided into 5 age classes shows: ADR occurs in all age classes. In which, the age groups: 16 to 30; 31 to 45 years old and over 60 years old have the highest rate of ADR (12.7-27.15%). This result is quite similar to the research results of some other authors [19-21].

The study results also showed that, there are 4 routes to bring drugs to meet ADR the most: oral (32.08-37.24%), intravenous (33.5-34.5%), intravenous infusion (15.37-20.96%) and intramuscularly (4.11-13.3%). The oral use of drugs has the highest proportion of ADR possible

because, oral is the simplest route of administration and is used the most, so ADR will also account for a high proportion in the ADR reports received. On the other hand, with inpatients treated at BVBM, most of them are critically ill and when on therapy, many injectable drugs (intravenous, intravenous or intramuscular) are often indicated.

Research results also show that all groups of drugs can cause ADR and the most prevalence of ADR in antibiotics group (2015: 51.3%; 2016: 45.81% and 2017: 47.82%). All groups of antibiotics can cause ADR and of the 10 antibiotic groups reviewed, betalactams remained the group with the highest ADR rate (2015: 47.81%; 2016 42.58% and 45.31% with 2017). This result is similar to the results of some studies in other hospitals and reports sent to the national ADR center. Other studies have also confirmed that the group of antibiotics is the group of drugs with the highest ADR rate [19, 21]. In particular, in those 3 years, there were 13 patients experiencing ADR due to using Oriental medicine.

In terms of manifestations, the most common ADRs are skin and subcutaneous tissue disorders (53.18-58.03 or 5%) and ADR on general disorders (12.08-14.74%). Most ADRs have to be managed (85.84-96.1%) and can fully recover after being treated (accounting for 96.68-98.44%). No deaths have been reported from ADR. However, it cannot be concluded that there is no death due to ADR because many critically ill patients are often asked to take their patients home in critical stages. On the other hand, this is mainly the result of voluntary ADR reports collected from agencies. Moreover, of a total of 2074 ADR reports collected 51 shots (2.46%) failed to record the consequences of ADR. This situation is consistent with the appraisal results of ADR report of the National ADR Center (15.1% did not report enough information) and the results of some other studies [22, 23]. And yet, the result of no case of using drugs to die from ADR in the period 2015-2017 is not really objective. We can still confirm that the consequences of the adverse drug reactions beyond the mild to severe clinical manifestations on the dog's body organs can be dangerous to human life result research in the period 2006-2008 that owl 6 cases of deaths due to ADR [20].

5. Conclusion

The number of ADR reports was inadequate compared to the large scale and potential of the hospital. ADR monitoring, detection and reporting had been unsteady, the involvement of clinical pharmacists was still limited. Therefore, more effective solutions should be taken to enhance ADR surveillance activities, particularly through clinical pharmacology.

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Table 1. Number of ADR reports at Bach Mai Hospital in the observed period

Targets	2015	2016	2017	Total
Number of ADR reports	579	692	803	2.074
Number of medical records	104,625	118,148	135,897	358,670
ADR incidence, %	0.55	0.58	0.59	0.58

Table 2. The amount of ADR of the departments in the observed period

Department	2015		2016		2017	
	ADR reports number	Ratio, %	ADR reports number	Ratio, %	ADR reports number	Ratio, %
Endocrinology	11	1.89	25	3.61	58	7.22
Allergy Center	63	10.88	98	14.16	69	8.59
Poison control center	38	6.56	52	7.52	33	4.11
Neurology	16	2.76	36	5.20	49	6.10
Osteoarthritis	22	3.80	37	5.35	25	3.11
Dermatology	6	1.03	20	2.89	29	3.61
Cardiovascular Institute	31	5.36	47	6.79	53	6.60
Obstetrics & Gynecology	37	6.39	42	6.07	51	6.35
Respiratory	39	6.74	23	3.32	44	5.48
Urology	25	4.32	19	2.74	39	4.86
Surgery	16	2.76	32	4.62	28	3.49
Dentistry	8	1.38	12	1.73	16	1.99
Intensive care	35	6.05	37	5.35	42	5.23
Pediatrics	31	5.36	25	3.61	16	2.00
Anesthesia	9	1.56	15	2.16	12	1.50
Hematology	44	7.60	27	3.90	37	4.61
Nuclear medicine	60	10.36	49	7.08	33	4.11

center						
Otorhinolaryngology	15	2.59	14	2.02	23	2.87
Rehabilitation center	2	0.34	5	0.72	11	1.37
Psychiatric hospotals	9	1.55	4	0.58	12	1.50
Artificial kidney surgery	7	1.21	14	2.02	27	3.36
Gastroenterology	13	2.25	28	4.05	32	3.99
Ophthalmology	10	1.73	6	0.87	9	1.12
Infection	21	3.63	12	1.74	31	3.86
Radiology	7	1.21	11	1.60	13	1.61
Oriental Medicine	4	0.69	2	0.29	11	1.36
Total	579	100.0	692	100.0	803	100.0

Table 3. Classification of ADR reports by age

Age	2015		2016		2017	
	ADR reports number	Ratio, %	ADR reports number	Ratio, %	ADR reports number	Ratio, %
0 – 15	62	10.70	77	11.13	92	11.46
16 – 30	111	19.17	147	21.24	183	22.79
31 – 45	109	18.83	150	21.68	218	27.15
46 – 60	124	21.42	164	23.70	201	25.03
> 60	140	24.18	139	20.08	102	12.70
Others	33	5.70	15	2.17	7	0.87
Total	579	100	692	100	803	100

Table 4. Classification of ADR reports by route of administration

Dosing route	2015		2016		2017	
	ADR reports number	Ratio, %	ADR reports number	Ratio, %	ADR reports number	Ratio, %
Oral	186	32.12	222	32.08	299	37.24
Intramuscular	77	13.30	62	8.96	33	4.11

Intravenous	194	33.50	234	33.82	277	34.50
Truyền TM	89	15.37	145	20.96	160	19.93
Subcutaneously	6	1.04	9	1.30	8	0.99
Topical	4	0.69	11	1.59	19	2.37
Others	7	1.22	3	0.43	4	0.49
No data	16	2.76	6	0.86	3	0.37
Total	579	100.0	692	100.0	803	100.0

Table 5. Classification of ADR reports by group of drugs causing ADR

Drug Class	2015		2016		2017	
	ADR reports number	Ratio, %	ADR reports number	Ratio, %	ADR reports number	Ratio, %
Antibiotics	297	51.30	317	45.81	384	47.82
NSAIDs	134	23.14	150	21.67	161	20.05
Drugs in neurology	86	14.85	125	18.07	122	15.19
Traditional medicines	2	0.35	2	0.29	9	1.12
Corticoid	4	0.69	26	3.76	34	4.24
Others	52	8.98	63	9.10	88	10.96
No data	4	0.69	9	1.30	5	0.62
Total	579	100	692	100	803	100

Table 6. Classification of ADR reports by group of antibiotics causing ADR

Antimicrobial preparates	2015		2016		2017	
	ADR reports number	Ratio, %	ADR reports number	Ratio, %	ADR reports number	Ratio, %
Beta-lactam	142	47.81	135	42.58	174	45.31
Quinolone	47	15.83	72	22.71	85	22.14
Aminoside	41	13.81	44	13.88	55	14.32
Macrolide	8	2.69	11	3.47	19	4.94
Sulfamide	11	3.70	4	1.26	0	0.00
Vancomycine	14	4.71	9	2.84	13	3.39
Cycline	21	7.07	12	3.79	7	1.83
Imidazole	9	3.03	10	3.15	22	5.73

Phenicole	0	0.00	3	0.95	0	0.00
Lincosamide	4	1.35	17	5.37	9	2.34
Total	297	100	317	100	384	100

Table 7. Classification of ADR reports by affected organ system

Affected Organ System	2015		2016		2017	
	ADR reports number	Ratio, %	ADR reports number	Ratio, %	ADR reports number	Ratio, %
Skin and subcutaneous tissue	336	58.03	368	53.18	431	53.67
Systemic disorders	76	13.13	102	14.74	97	12.08
Digestive system	42	7.25	58	8.38	46	5.73
Respiratory system	12	2.07	29	4.19	27	3.36
Nerve system	22	3.80	27	3.90	46	5.73
Cardiovascular system	26	4.49	35	5.06	41	5.11
Mental	31	5.35	28	4.05	49	6.10
Blood	20	3.46	26	3.76	32	3.99
Others	14	2.42	19	2.74	34	4.23
Total	579	100	692	100	803	100