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Evaluation of type I drug hypersensitivity reactions caused by chemotherapy in hospitalized children

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Abstract

Background and Objective: Type I drug hypersensitivity reactions causes immune responses that could endanger life. Therefore this study was designed with the aim of evaluation and register reactions that caused by chemotherapy in hospitalized children in Rasoul Akram Hospital in 2015.

Methods: This is a descriptive, cross sectional study. All statistical calculation was performed using the version 21 SPSS software. Significant level of tests was considered 0.05 ($p < 0.05$).

Results: the incidence of hypersensitivity reactions in the study population is estimated to be 4.9%. The results also showed that men have been experiencing more hypersensitivity reactions.

Cancers such as ALL (29%), retinoblastoma (22.6%) neuroblastoma (19.4%) and brain tumor (12.9%) have been the highest among all kinds of treated cancers. Based on the severity of the reaction, nausea and abdominal cramps (41.9%), skin changes, including flushing, hives and pruritus (35.5%), skin and lips angioedema (22.6%) had the highest prevalence.

Conclusion: The results showed that in more than half of the studied samples hypersensitivity reaction started in less than 10 minutes after drug administration. Most drug reaction is to vincristine, cisplatin, methotrexate, AraC (cytarabine) and carboplatinum and the majority of reactions have occurred after phase3 of chemotherapy that is comparable with previous studies.

Keywords: Drug hypersensitivity reactions, Chemotherapy, Children

Introduction

Cancer is the second most common factor of death in developed countries (1). Advances in medical sciences have a huge impact on the future of cancer patients (2). Cancer is one of the death factors worldwide and chemotherapy is the most common treatment for cancer (3).

Hypersensitivity reactions are inflammatory reactions that may cause extensive tissue damage or even death. There are four types of hypersensitivity reactions, which have distinct executive molecules and clinical protests.

Type-1 hypersensitivity reaction that immunoglobulin binds from Fc region to surface receptors of mast cells or basophils, mediated by IgE. IgE cross-linking lead to degranulation of mast cells or basophils and the release of the pharmacologically active agents. The main effects of these agents are smooth muscle contraction and vasodilation. Clinical features of type 1 reactions are including hay fever, asthma and even anaphylaxis that can be life threatening.

Chemotherapy drugs can have potentially great harm to recipients and nurses (1). Long-term exposure of these drugs can be carcinogenic effects, mutagenic and toxic effects on the genes. Exposure to chemotherapy drugs is related with serious side effects such as contact dermatitis, local skin reactions, abdominal pain, headache, dizziness, hair loss, liver damage, inflammation, sore throat, cough, allergic reactions, diarrhea, nausea, vomiting and eye damage (1-4).

Table 1. Distribution of samples with drug reaction by type of reaction

Reviewed items	Standard deviation	Mid	Mean	Max	Min
Age	3. 5	4.5	5.5	14 years	1 month
Duration of acute reactions (after taking the drug)	52	3. 5	29 min	180 min	1 min
During of acute reaction time	24. 4	10	20	180 min	1 min
The overall reaction time to full recovery	32	24	27	120 h	1 h

Chemotherapy drugs also may stimulate the immune system and cause hypersensitivity reaction. Hypersensitivity complications is usually type 1 reaction, but can also occur from other types (5-9).

Table 2. Distribution of samples with drug reaction by type of reaction

Description	Number	Percent
Nausea and vomiting	10	32.3
Rubefaction	6	19.4
Lips Redness	2	6.5
Diffuse redness	5	16.1
Swelling of the skin	3	9.7
Swelling of the face	2	6.5
Stomach ache	1	3.2
Fever	1	3.2
Cold sweat	1	3.2
Total	31	100

Table 3. Distribution of samples with drug reaction based on actions taken when sensitivity began

Description	Percent	Number
Not take any action	38.7	12
Use of Sedative drugs	3.2	1
Discontinuation of the drug	19.4	6
The antihistamine	3.2	1
MRI	3.2	1
Serum therapy	29	9
Cooling	3.2	1
Total	100	31

Table 4. Distribution of samples with drug reaction based on total response time

Description	Percent	Number
1 minutes	22.6	7
2 minutes	9.7	3
5 minutes	3.2	1
10 minutes	9.7	3
20 minutes	3.2	1
60 minutes	9.7	3
24 hours	29	9
48 hours	3.2	1
72 hours	3.2	1
120 hours	6.5	2
Total	100	31

Chemotherapy drugs have many complications some of them are common such as fatigue, confusion, hair loss and scalp sensitivity, mouth, gum and throat sores. Blood problems such as thrombocytopenia and increasing risk of infection are other complications (3-4).

This study aim was to evaluate and register drug hypersensitivity reactions caused by chemotherapy in hospitalized children in Rasoul Akram Hospital in 2015.

Methods

The population included all hospitalized children in Rasoul Akram hospital during 2015 that during treatment had hypersensitivity reactions. Sampling was census. Children at age eighteen or less were enrolled.

This study was a cross-sectional and prospective. For Data collection, all children were observed and any medical complications including local and systemic hypersensitivity reactions were observed and recorded. Then, patients' demographic characteristics registered and the type, dose and number of drugs, duration of drugs consumption and reactions type, including skin, cardiovascular, pulmonary and gastrointestinal, severity of drugs hypersensitivity reactions (type 1), response time and history of similar responses in the previous occasions were evaluated. Premedication and corticosteroid also were registered.

The severity of these reactions is graded from zero to four. In grade zero asymptomatic, grade 1 skin rash, grade 2 hives, grade 3 serum sickness, and grade 4 anaphylactic have been occurred. In grade 1 and 2 that have occurred in 3 patients, treatment regimen continued with steroid. In grade 3 and 4, regimen changed, although desensitization was performed (7-10).

Analysis

Collected information by researcher were presented at two levels of descriptive and inferential statistics. Chi-squre test for qualitative variables and t tests were used to compare quantitative variables.

Table 5. Distribution of samples with drug reaction based on type of drug

Drugs	Stage 2	Stage 3	Stage 4	Stage 5	Stage	Total	Percent
Vincristine		9	1	1	1	12	38.7
Carboplatinum			2			2	6.4
Cisplatin		3		1	1	5	16.2
IT MTA	3				1	4	12.9
Autopuzide		1	1		2	4	12.9
Ara-C	1	2		1		4	12.9
Total						31	100

Kolmogorov-Smirnov test was used to assess the normality of distribution parameters. All statistical calculation was performed using SPSS version 21. The significance of test level 0.05 ($p < 0.05$) was considered.

Results

In this study, 634 children were enrolled. Among them, 31 patients had hypersensitivity reactions. Therefore, the prevalence rate of hypersensitivity reactions is estimated to be 4.9%; among them, men's hypersensitivity reaction was more than women (58.1 vs 41.9%). About A X77.4% of patients had no history of allergic response.

Cancers such as ALL (29%), retinopathy blastuma (22.6%), neuroblastoma (19.4%) and brain tumor (12.9%) had the highest rates among treated cancers.

The presence of eosinophils in the first CBC in most samples (77.4%) were negative.

In more than half of the studied samples (53.9%) the hypersensitivity reaction started in less than 10 minutes after the drug administration.

Based on the severity of the reaction, nausea and abdominal cramps (41.9%), skin changes, including flushing, hives and pruritus (35.5%), skin and lips angioedema (22.6%) had the highest prevalence.

No treatment was performed in 38.7% of cases, but the most common were serum therapy (29%) and discontinuation of drugs (19.4%). 80.6% of patients had a history of pre-medication.

Discussion

The present study showed that men (58.1%) more than women (41.9%) have a hypersensitivity reaction. Age did not play a major role in the incidence of ADRs. Results of other studies were consistent with the results of this study (1-5).

The prevalence of hypersensitivity reactions in the study population was estimated to be 4.9%. The results of the Mariana and colleagues (2008) to investigate hypersensitivity reaction to chemotherapy in 413 patients showed that in 94% of cases there are no or mild hypersensitivity reactions (9). According to a study by Wisner hypersensitivity reactions in 7 of 10 children (78%) was observed (12). These differences can be explained by the fact that 80.6% of our patients had a history of pre-medication. It appears that premedication with glucocorticoids and H1 and H2 antagonists should routinely be administered to reduce the risk of hypersensitivity reactions (10-11).

Anaphylaxis reactions caused by antigen-antibody or antibody collection, is referring to immediate hypersensitivity, because its symptoms appears within a few minutes or a few hours after encounter sensitized receptor with the antigen. According to a study by Rashed and colleagues in several countries conducted on 1253 children with ADRs, the incidence of ADRs in children should be limited as much as possible. Concurrent prescription of several drugs may increase the risk of ADRs.

Most common symptoms at beginning were nausea and vomiting (32.3%), skin redness (19.4%), diffuse redness (16.1%) and swelling of the skin (9.7%), respectively. The results also showed that in more than half of the studied samples (53.9%) hypersensitivity reaction started in less than 10 minutes after the first drug delivery.

The results also showed that nausea and abdominal cramps (41.9%), skin changes, including flushing, hives and itching (35.5%), skin and lips Angioedema (22.6%) had the highest prevalence.

In our study, as seen in Table 5 most drug reaction is to vincristine, cisplatin, methotrexate, Ara-C (cytarabine) and carboplatinum and the majority of reactions after from phase 3 of chemotherapy have occurred that is comparable with previous studies.

According to a study on the 9 patients (6 females and 3 males) with mean age of 9.5 years that after the chemotherapy had immediate hypersensitivity reactions such as hives (4 of 9) and anaphylaxis (5 of 9), the used drugs were cyclophosphamide (1 of 9), carboplatin (2 of 9), Cyclosporine (2 of 9), mesna (1 of 9), and Wal-asparaginase (2 of 9). Three of the 5 patients with symptoms of anaphylaxis changed their drugs to other alternatives chemotherapy drugs. In 2 of these patients,

there was no viable alternative drugs but desensitization was performed successfully (3).

Conclusion

The high risk of allergic reactions to multiple courses of chemotherapy should be kept in mind. Premedication can reduce the risk of type 1 drug hypersensitivity reactions caused by chemotherapy.

Conflicts of interest: None declared.

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