

Full Length Research Paper

Monitoring report on 341 cases of adverse reactions caused by antitumor drugs

Hong-jun Guo, Fang Ren, Dongya Zhang and Mei Ji*

Department of Gynecology and Obstetrics, the First Affiliated Hospital of Zhengzhou University, Zhengzhou 410052 China.

Accepted 30 March, 2012

This study aimed to summarize the main adverse reactions caused by antitumor drugs in China's Henan Province and to provide reliable basis for strengthening drug administration in the future. This is a retrospective study conducted to analyze the monitoring of reports on 341 cases of adverse reactions caused by antitumor drugs collected from some AAA hospitals in Henan Province. Along with age increase and adverse drug reactions increase, the incidence of adverse reactions caused by cytarabine is the highest, infusion is the most prone to adverse reactions, and digestive system damage is the most common adverse reaction. Antitumor drugs have big toxic side effect on human body and cause many adverse reactions, and the supervision of clinical application of antitumor drugs must be strengthened.

Key words: Antitumor drug, adverse reaction, monitoring report, retrospective study.

INTRODUCTION

Along with the continuous increase in patients with tumor and continuous clinical application of antitumor drugs, the incidence of adverse reactions of antitumor drugs presents an increasing trend (Yang and Tang, 1889 to 1893). Most of antitumor drugs at therapeutic dose cannot avoid producing toxic side effects on normal tissues and organs of body. Therefore, the clinical monitoring of adverse reactions caused by antitumor drugs must be strengthened to provide necessary references for safe and rational drug use and to prevent adverse drug reactions.

DATA AND METHODS

Data

The reports of 341 cases of adverse reactions caused by antitumor drugs were collected from some AAA hospitals in China's Henan

Province.

Methods

A retrospective study was conducted to make statistical analysis on the distribution of ages, drug use, administration routes and involved systems – organs and the main clinical manifestations of the patients in the reports. As regards the drug classification method, the drug used was classified based on China's New Pharmacology. Adverse drug reaction causality assessment standard was applied and it contains 6 grades for ADR causality assessment specified in the adverse drug reaction monitoring management approach issued by the State Food and Drug Administration (SFDA).

RESULTS

Ages of the patients with adverse reactions

In the patients with adverse reactions, the youngest is 11 years old, the oldest is 86 years old and the incidence of adverse reactions in each age group is shown in Table 1.

*Corresponding author. E-mail: meiji2012@sohu.com.

Table 1. Relationship between patients with adverse reactions and ages.

Age group (years old)	Number of ADR cases (n)	Proportion (%)
<18	21	6.16
18-40	55	16.13
41-60	121	35.48
>60	144	42.23

Table 2. Distribution of antitumor drugs causing adverse reactions.

Drug variety	Number of cases (n)	Proportion (%)
Cytarabine	76	22.29
Fluorouracil	37	10.85
Methotrexate	35	10.26
Teniposide	23	6.74
Paclitaxel	21	6.16
Cisplatin	18	5.28
L-asparaginase	15	4.40
Oxaliplatin	11	3.23
Tretinoin	10	2.93
Gemcitabine hydrochloride	9	2.64
Floxuridine	8	2.35
Recombinant interferon α -1b	8	2.35
Docetaxel	7	2.05
Epirubicin hydrochloride	7	2.05
Imatinib	7	2.05
Bortezomib	6	1.76
Arsenic trioxide	6	1.76
Etoposide	6	1.76
Thalidomide	5	1.47
Recombinant human interleukin-2	5	1.47
Nedaplatin	4	1.17
Aidi	3	0.88
Vincristine sulphate	3	0.88
Daunorubicin	3	0.88
Rituximab	3	0.88
Cyclophosphamide	2	0.59
Gefitinib	1	0.29
Oxaliplatin	1	0.29
Meisoindigo	1	0.29

In which, 178 patients with adverse reactions are male, accounting for 52.20%, and 163 patients are female, accounting for 47.80%.

Distribution of drugs for patients with adverse reactions

In the collected 341 cases, 29 kinds of antitumor drugs are involved, and the situation of adverse reactions caused by each drug is shown in Table 2. Myelosuppression is the worst adverse reaction of

cytosine arabinoside (AraC). 10% of patient treated with large dose of AraC (2 ~ 3 g/m²) get Myelosuppression. The clinical manifestation is leucocytopenia and thrombocytopenia, 20% patients having the symptom of hemorrhage. The adverse reaction also includes allergic dermatitis, drug fever and enterogastric.

Distribution of administration routes for patients with adverse reactions

In the 341 patients with adverse reactions, there are

Table 3. Distribution of administration routes causing adverse reactions.

Administration routes	Number of cases (n)	Proportion (%)
Intravenous infusion	236	69.21
Intrathecal administration	90	26.39
Oral administration	15	4.40

mainly three administration routes: intravenous infusion, intrathecal administration and oral administration, as shown in Table 3.

Distribution of systems – organs involved by adverse reactions and the main clinical manifestations

In the 341 patients with adverse reactions, the statistics is made on the involved systems / organs and the clinical manifestations according to the “world health organization (WHO) adverse drug reaction term set”, as shown in Table 4.

DISCUSSION

Relationship between ages and adverse reactions

It can be seen from Table 1 that the incidence of adverse reactions increases with age increase (Wang and Zhou, 2007). Possible reasons are that: the function of the tissues and organs of the elders reduces by varying extent with age increase (Xiang et al., 2011; Wang et al., 2009), liver blood flow keeps reducing, liver drug enzyme activity gradually decreases, so the detoxification capacity reduces and drug metabolism slows down; renal function decreases, glomerular filtration rate and tubular secretion reduce, renal blood flow reduces significantly, and drug excretion slows down; plasma protein content in blood reduces, blood concentration increases, drug accumulation is easy to occur, and the incidence of adverse drug reactions increases (Wenhua, 2006).

Relationship between drug use and adverse reactions

A total number of 341 cases of ADR reports involve totally 29 kinds of antitumor drugs, in which, cytarabine causes 76 cases of ADR, accounting for 22.29% of the total number reported; cytarabine is massively and widely used in some AAA hospitals in our province, so the incidence of its adverse reactions is relatively higher. Meanwhile, the adverse reactions caused by cytarabine are mainly manifested as the symptoms in digestive system and nervous system, such as fever, headache, nausea, etc, and they mostly occur during drug use and

the relevance of adverse reactions is easy to determine, so the reporting rate of the adverse reactions of this drug is relatively higher (Wang and Zuxin, 2006; Li, 2008; Chunshuang, 2009; Zhehui et al., 2008).

Relationship between administration routes and adverse reactions

It can be seen from Table 3 that intravenous infusion is easier to cause ADR than other administration routes (Zeng et al., 2010) (236 cases, accounting for 69.21% of the total). For reason analysis, this administration route directly send drugs into blood, without hepatic first-pass effect, so its pharmacological effects and adverse reactions are faster and stronger than other administration routes; meanwhile, drug pH value, particulate, endotoxin, excipient, infusion operation process and other factors are likely to cause adverse reactions. In addition, drug treatment for inpatients must be made in hospital and is mainly for intravenous drug use, and medical staff pays more attention to the monitoring of adverse reactions, so the reporting rate of ADR caused by intravenous infusion is higher. Compared with inpatients, intravenous infusion for outpatients is relatively less, and drugs are taken outside hospital, so the adverse reactions can not be effectively and accurately monitored. Moreover, patients and their family members have insufficient knowledge on adverse drug reactions, so the number of reported ADR is less than the number of actual occurrences, and there might be a big deviation between the two (Nian and Minghua, 2010). Therefore, the incidence of adverse reactions caused by intravenous infusion is the highest.

Relationship between distribution of involved systems – organs and adverse reactions

Adverse reactions in digestive system are the most common in the treatment of malignant tumor (Liu and Yancai, 2011), the incidence is high and it can be seen from Table 4 that there are totally 202 cases, with the incidence of 59.24%. The adverse reactions are mainly manifested as nausea, vomiting (Prestayko et al., 1979), abdominal pain and diarrhea, as well as constipation, acute gastritis and peptic ulcer, and even gastrointestinal bleeding, intestinal obstruction and intestinal necrosis in

Table 4. Distribution of systems – organs involved by adverse reactions and the main clinical manifestations.

Involved system – organs	Number of cases (n)	Proportion (%)	Main clinical manifestations
Digestive system	202	59.24	Nausea, vomiting, diarrhea, abdominal pain, abdominal distension, abnormal liver function, oral ulcer, constipation, acute pancreatitis, dry mouth
Blood system	48	14.08	Bone marrow suppression, thrombocytopenia, neutropenia, abnormal hemorrhage and blood coagulation
Local and phlebitis	22	6.45	Local swelling and pain, blood vessel swelling
Nervous system	20	5.87	Fever, chill, headache, dizziness, extremity numbness, lower limb pain
Skin and subcutaneous tissue	16	4.69	Rash, skin itch, red papule, erythema, facial flushing, whole body edema, facial edema, lip swelling, skin pigmentation
Cardiovascular system	13	3.81	Chest tightness, palpitation, tachycardia, hypertension, abnormal ECG
Respiratory system	7	2.05	Difficult breathing, shortness of breath, throat discomfort, lip cyanosis, cough
Urinary system	5	1.47	Abnormal renal function, ketoacidosis
Musculoskeletal system	3	0.88	Myalgia, arthralgia, bone pain, low back pain
Eye	2	0.59	Blurred vision, eye pain, eye discomfort, conjunctival hemorrhage, photophobia, lacrimation
Allergic shock	2	0.59	Confusion, blood pressure / heart rate unmeasured, difficult breathing, lip cyanosis
Dysbolism and dystrophy	1	0.29	High blood sugar

severe cases. In which, vomiting is most common. Vomiting caused by chemotherapy can be classified as acute vomiting, delayed vomiting and anticipatory vomiting (Zhong and Zheng, 2008).

Centralized monitoring of adverse reactions caused by antitumor drugs is an important part of rational and safe clinical application of antitumor drugs. Centralized monitoring of adverse reactions in clinical and safety evaluation of clinical application of antitumor drugs have important significance on the guiding of clinical drug use scientificity, especially the use of antitumor drugs with bigger toxic side effects.

REFERENCES

- Chunshuang D (2009). An Analysis of 112 Articles of Adverse Reaction Caused by Anticancer Drug. *J. China Pharm.*, 2(8): 617.
- Li J (2008). Using Principles of Anticancer drug by UK related department[J]. *Progress Pharm. Sci.*, 32(9): 429.
- Li Z, Wang X, Li B (2008). Analysis of 95 Adverse Drug Reaction Reports of Antineoplastics. *Chinese J. Pharmacol. vigilance*, 5(2):104.
- Liu L, Yancai Y (2011). Retrospective analysis on reports of 661 cases of adverse reactions caused by antitumor drugs [J]. *Chinese J. Pharmacoepidemiol.*, 20 (5): 229-233.
- Nian H, Minghua M (2010). Analysis on reports of 72 cases of adverse reactions caused by antitumor drugs [J]. *Chinese J. New Drugs Clini. Remedies*, 29 (9): 704-707.
- Prestayko AW, Daoust JC, Issell BF (1979). Cisplatin(cis-diamminedichloroplatinum II) *J. Cancer Treat. Rev.*, 6(1): 17-39.
- Wang A, Xuxin Y (2006). An Analysis of 15903 Inpatient with Cancer in Shanxi Province. *J. Chinese J. Oncol.*, 15(5):307-308.
- Wang L, Zhou X (2007). Analysis on 405 cases of adverse drug reaction reports in our hospital. *J. China Pharm.*, 18 (2): 137.
- Wang L, Wang S, Liang C (2009). Reduction of adverse reactions caused by antitumor drugs and precautions Hebei. *J. Traditl. Chinese Med.*, 31 (7): 1064-1065.
- Xiang, Cao G, Ye Xi (2011). Retrospective analysis on 134 cases of adverse reactions caused by antitumor drugs [J]. *Chinese J. Clin. Pharm.*, 20 (2): 116-118.
- Yang M, Tang Z (1889-1893). Adverse reactions caused by antitumor drugs and preventive measures [J]. *Chinese J. New Drugs*, 17 (21):
- Zeng Yi, Xie W, Liang H (2010). Analysis on 586 cases of adverse drug reaction reports [J]. *Chinese J. Pharmacoepidemiol.*, 19(12): 681-683.
- Zhong H, Zheng Z (2008). Adverse reactions caused by antitumor drugs needing concern by pharmacists in ward round and preventive measures. *China Modern Doc.*, 46(36): 43-44.