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REVIEW ARTICLE

ON CLINICAL ADVERSE DRUG REACTION OF ANTI-NEOPLASTIC AGENTS

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ABSTRACT

Adverse drug reaction (ADR) is an unintended and unexpected effect can be caused by many drugs; this definition is differing by the side effect. It is fourth leading cause of death in developed western countries and sixth leading cause of death in the world. An adverse drug reaction (ADRs) shows an important public health problem in animals, human beings and the environment which include less efficacy of drug, sensitivity like reactions. Pharmacovigilance is associated in the field of ADRs study. At present Cancer is the second leading cause of death globally, and was responsible for 8.8 million deaths in 2015. Globally, nearly 1 in 6 deaths is due to cancer uncontrolled growth of cells is called cancer. Cancer cells are also referred to as tumours or neoplasms. It is a heterogeneous group of diseases caused by the impairment of normal functioning of genes, which leads to genetic damage. Many treatment options for cancer exist with the primary ones including surgery, chemotherapy, radiation therapy and palliative care. These treatments are used depending upon the type, location and grade of the cancer. The most common medications affect mainly the fast-dividing cells of the body, such as blood cells and the cells lining the mouth, stomach, and intestines. Along with other oncology clinicians, intervention played by Clinical Pharmacist is vital and can therapeutically minimize, assess, monitor and manage ADRs of ANAs. Clinical Pharmacist should inform the clinicians about these adverse reactions during each administration time.

INTRODUCTION

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Chemotherapeutic techniques have a range of side-effects that depend on the type of medications used. Commonly the causality caused by adverse drug reactions is unknown and uncertain, making it more accurate to refer to suspected adverse drug reactions. The most common medications affect mainly the fast-dividing cells of the body, such as blood cells and the cells lining the mouth, stomach, and intestines. Clinical Pharmacist should inform the clinician about these adverse reactions during each administration time.

MECHANISMS

.Mechanisms of unpredictable adverse drug reactions. (Rieder MJ.)

There are mainly two types of ADRs. Type A and type B, mostly are Type a and fewer ADRs are Type B and Common mechanisms are:

1. Abnormal pharmacokinetics due to genetic factors and comorbid disease states
2. Synergistic effects between either a drug and a disease or two drugs

ADVERSE EFFECTS OF ANTINEOPLASTHETIC DRUGS

IMMUNOSUPPRESSION AND MYELOSUPPRESSION

This occurs by paralyzing the bone marrow and leading to a decrease of white blood cells, red blood cells, and platelets. Anemia and thrombocytopenia, when they occur, are improved with blood transfusion. Neutropenia (a decrease of the neutrophil granulocyte count below 0.5 x 109/liter) can be improved with synthetic G-CSF (granulocyte-colony-stimulating factor, e.g., filgrastim, lenograstim).

In severe myelo suppression, almost all the bone marrow stem cells (cells that produce white and red blood cells) are destroyed, meaning allogeneic or autologous bone marrow cell transplants are necessary. (In autologous BMTs, cells are removed from the patient before the treatment, multiplied and then re-injected afterward; in allogeneic BMTs, the source is a donor.) However, some patients still develop diseases because of this interference with bone marrow.

TYPHLITIS

"Typhlitis is an intestinal infection which may manifest itself through symptoms including nausea, vomiting, diarrheal, a distended abdomen, fever, chills, or abdominal pain and tenderness. It has a very poor prognosis and is often fatal unless promptly recognized and aggressively treated. Successful treatment hinges on early

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diagnosis provided by a high index of suspicion and the use of CT scanning, no operative treatment for uncomplicated cases, and sometimes elective right hemi colectomy to prevent recurrence.

GASTROINTESTINAL DISTRESS

Nausea, vomiting, anorexia, diarrhea, abdominal cramps, and constipation are common side-effects of chemotherapeutic medications that kill fast-dividing cells. Malnutrition and dehydration can result when the patient does not eat or drink enough, or when the patient vomits frequently, because of gastrointestinal damage. This can result in rapid weight loss, or occasionally in weight gain, if the patient eats too much in an effort to allay nausea or heartburn. Weight gain can also be caused by some steroid medications. These side-effects can frequently be reduced or eliminated with antiemetic drugs. Self-care measures, such as eating frequent small meals and drinking clear liquids or ginger tea, should recommend by clinical pharmacist while patient counselling.

ANEMIA

Anemia in cancer patients can be a combined outcome caused by myelo-suppressive chemotherapy, and possible cancer-related causes such as bleeding, blood cell destruction (hemolysis), hereditary disease, kidney dysfunction, nutritional deficiencies and/or anemia of chronic disease. Treatments to mitigate anemia include hormones to boost blood production (erythropoietin), iron supplements, and blood transfusions. Myelo-suppressive therapy can cause a tendency to bleed easily, leading to anemia.

FATIGUE

Fatigue may be a consequence of the cancer or its treatment, and can last for months to years after treatment. One physiological cause of fatigue is anemia, which can be caused by chemotherapy, surgery, radiotherapy, primary and metastatic disease and/or nutritional depletion. Anaerobic exercise has been found to be beneficial in reducing fatigue in people with solid tumours.

CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING

Nausea and vomiting are two of the most feared cancer treatment-related side effects for cancer patients and their families. Chemotherapy-induced nausea and vomiting (CINV) are common with many treatments and some forms of cancer. Effective mediation of these unpleasant and sometimes-crippling symptoms results in increased quality of life for the patient and

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more efficient treatment cycles, due to less stoppage of treatment due to better tolerance by the patient, and due to better overall health of the patient.

HAIR LOSS

Hair loss (Alopecia) can be caused by chemotherapy that kills rapidly dividing cells; other medications may cause hair to thin. "Severe hair loss occurs most often with drugs such as doxorubicin, daunorubicin, paclitaxel, docetaxel, cyclophosphamide, ifhosfamide and etoposide. Permanent thinning or hair loss can result from some standard chemotherapy regimens. Chemotherapy induced hair loss occurs by a non-androgenic mechanism, and can manifest as alopecia totalis, telogen effluvium, or less often alopecia areata. Chemotherapy induces hair loss in women more often than men. Scalp cooling offers a means of preventing both permanent and temporary hair loss; however, concerns about this method have been raised.

INFERTILITY

Some types of chemotherapy are gonadotoxic and may cause infertility. Chemotherapies with high risk include procarbazine and other alkylating drugs such as cyclophosphamide, ifhosfamide, busulfan, melphalan, chlorambucil, and chloromethane. Drugs with medium risk include doxorubicin and platinum analogs such as cisplatin and carboplatin. On the other hand, therapies with low risk of gonado toxicity include plant derivatives such as vincristine and vinblastine, antibiotics such as bleomycin and dactinomycin, and antimetabolites such as methotrexate, mercaptopurine, and 5-pfluorouracil.

Female infertility by chemotherapy appears to be secondary to premature ovarian failure by loss of primordial follicles. This loss is not necessarily a direct effect of the chemotherapeutic agents, but could be due to an increased rate of growth initiation to replace damaged developing follicles.

TERATOGENICITY

Chemotherapy is teratogenic during pregnancy, especially during the first trimester, to the extent that abortion usually is recommended if pregnancy in this period is found during chemotherapy. Second- and third-trimester exposure does not usually increase the teratogenic risk and adverse effects on cognitive development, but it may increase the risk of various complications of pregnancy and fetal myelosuppression. In males previously having undergone chemotherapy or radiotherapy, there appears to be no increase in genetic defects or

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congenital malformations in their children conceived after therapy.

CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY

Between 30 and 40 percent of patients undergoing chemotherapy experience chemotherapy-induced peripheral neuropathy (CIPN), a progressive, enduring, and often irreversible condition, causing pain, tingling, numbness and sensitivity to cold, beginning in the hands and feet and sometimes progressing to the arms and legs. Chemotherapy drugs associated with CIPN include thalidomide, epothilones, vinca alkaloids, taxanes, proteasome inhibitors, and the platinum-based drugs should be verify during medication history interview. Though the symptoms are mainly sensory, in some cases motor nerves and the autonomic nervous system are affected. CIPN often follows the first chemotherapy dose and increases in severity as treatment continues.

COGNITIVE IMPAIRMENT

Some patients report fatigue or non-specific Neuro cognitive problems, such as an inability to concentrate; this is sometimes called post-chemotherapy cognitive impairment, referred to as "chemo brain" by patients' groups.

ORGAN DAMAGE

Cardio toxicity (heart damage) is especially prominent with the use of anthracycline drugs (doxorubicin, epirubicin, idarubicin, and liposomal doxorubicin). The cause of this is most likely due to the production of free radicals in the cell and subsequent DNA damage. Other chemotherapeutic agents that cause cardio toxicity, but at a lower incidence, are cyclophosphamide, docetaxel and clofarabine.

Hepatotoxicity (liver damage) can be caused by many cytotoxic drugs. The susceptibility of an individual to liver damage can be altered by other factors such as the cancer itself, viral, immunosuppression and nutritional deficiency. The liver damage can consist of damage to liver cells, hepatic sinusoidal syndrome (obstruction of the veins in the liver), cholestasis (where bile does not flow from the liver to the intestine) and liver fibrosis.

Nephrotoxicity (kidney damage) can be caused by tumor lysis syndrome and also due direct effects of drug clearance by the kidneys. Different drugs will affect different parts of the kidney and the toxicity may be asymptomatic (only seen on blood or urine tests) or may cause acute renal failure. Ototoxicity (damage to the inner ear) is a common side effect of platinum based drugs

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that can produce symptoms such as dizziness and vertigo.

OTHER ADVERSE EFFECTS

Less common adverse-effects include red skin (erythema), dry skin, damaged fingernails, a dry mouth (xerostomia), water retention, and sexual impotence. Some medications can trigger allergic or pseudo allergic reactions. Specific chemotherapeutic agents are associated with organ-specific toxicities, including cardiovascular disease (e.g., doxorubicin), interstitial lung disease (e.g., bleomycin) and occasionally secondary neoplasm (e.g., MOPP therapy for Hodgkin's disease).

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