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Safety Profile and Toxicity Amelioration Strategies of Common Adverse Effects Associated with Anticancer Medications

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Authors' contributions

This work was carried out in collaboration among all authors. Author MS conceptualized the idea of the manuscript, performed the initial literature review and wrote the initial draft of the manuscript in collaboration with author SP. Author PRS added few sections to the initial draft and revised the entire manuscript and author SS further performed literature review, made substantial changes in the initial draft, critically reviewed and revised the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

More than half the cancer patients undergoing cancer chemotherapy develop adverse drug reactions (ADRs). Cancer chemotherapeutic agents have a lower risk-benefit ratio than other drug therapy and kill cancerous as well as the normal rapidly dividing cells including bone marrow cells, gastrointestinal epithelium, hair follicles, etc. Their main ADRs are nausea and vomiting, mucositis, constipation, diarrhea, hematological toxicities, cardiac toxicity, alopecia, gonadal toxicity,

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pulmonary toxicity, neurotoxicity, nephrotoxicity, etc. The severity of the adverse effects may range from mild nausea to life-threatening neutropenia. Administering premedication and antidotes are very vital in these patients. Upon the occurrence of adverse effects, immediate steps should be taken to manage them. Though the ADRs due to anticancer medications are not avoidable, careful monitoring of the patients and modulating the drug schedules/dosages can help in minimizing them. Healthcare professionals should also develop strategies to minimize the occupational hazards associated with these drugs.

Keywords: Adverse drug reactions; alopecia; cancer chemotherapy; hematological toxicity; teratogenicity; toxicity; vomiting.

1. INTRODUCTION

Cancer is considered to occur as a result of a disturbance in mechanisms that control cell proliferation and differentiation [1]. Radiotherapy, chemotherapy and surgery are the major treatment modalities available for the treatment of cancer [2,3]. An ideal anticancer medicine should eradicate cancer cells without harming normal tissues. But the traditional medicines for cancer cause substantial toxicity and the use of these medicines must include careful consideration of benefits against toxicity [4]. In general, chemotherapy not only targets cancer cells but also other rapidly dividing normal cells of the human body [5,6]. The damage to the normal cells produce various adverse effects which are also known as chemotherapy-induced adverse drug reactions. In this article, the authors discuss the various toxicities caused by anticancer medications and provide various methods for prevention, early diagnosis and management of these toxicities.

2. NAUSEA AND VOMITING

One of the most common chemotherapy-induced adverse drug reactions (ADRs) are nausea and vomiting, and these can be broadly categorized as acute, delayed, or anticipatory [7,8] (Table 1). Majority of the patients experience this ADR during chemotherapy. The severity of nausea and vomiting strongly depends on the type of chemotherapy regime and the dosage of individual drugs. The response of each individual to a given chemotherapy schedule varies [8]. The use of newer antiemetic agents has considerably reduced the incidence of nausea and vomiting though they may not prevent these [9]. Anticipatory nausea and vomiting are experienced by around 0-44% of patients on chemotherapy [10].

2.1 Pathophysiology

Different anticancer agents act at different sites and a few of them act at more than one site [11]. These sites include the chemoreceptor trigger zone (CTZ), and the gastrointestinal tract. Vestibular and cortical mechanisms, altered taste and smell sensations may also contribute. The commonest mechanism is through the activation of CTZ. [12] Nausea and vomiting occurring within the first 24 hours of administration of chemotherapy are defined as acute, whereas those occurring after 24 hours are defined as delayed [13]. Anticipatory vomiting is a conditioned response typically occurring before the administration of chemotherapy [13,14].

2.2 Management of Chemotherapy-Induced Nausea and Vomiting

For this purpose, patients are classified into three levels, level I (patients receiving mildly emetogenic agent), level II (patients receiving moderately emetogenic agent or patients receiving a mildly emetogenic agent who have failed to respond to at least two of the level I drugs) and level III patients (patients receiving highly emetogenic agent, patients receiving 2 or more moderately emetogenic agents, patients who have failed a level II regimen) [16-18] (Table 2).

Corticosteroids are valuable antiemetics in preventing delayed emesis. Studies have shown an advantage for metoclopramide combined with steroids [11,17,19] Lorazepam, is known to have some antiemetic effects [11].

2.3 Delayed Emesis

Two randomized studies, one with ondansetron and another with granisetron, indicated the usefulness of the serotonin antagonists for delayed emesis in patients receiving chemotherapy with agents of intermediary emetogenicity [11,20].

Table 1. Emetogenic status of anticancer drugs [15]

Emetogenic status	Examples
Highly emetogenic drugs (causes vomiting in 75% or more of the cases)	Cisplatin, Cyclophosphamide, Cytosine arabinoside, Dacarbazine, Doxorubicin, Ifosfamide, Methotrexate, Mitomycin, Carmustine
Moderately emetogenic drugs (Causes vomiting in 50%-75% of the cases)	Carboplatin, Etoposide, Daunorubicin, Gemcitabine, Mitoxantrone, Topotecan, Cisplatin (< 40 mg/m^2), Doxorubicin (<60 mg/m^2), Cyclophosphamide (<1g)
Mildly emetogenic drugs (Causes vomiting in 25%-50% of the cases)	Asparaginase, Bleomycin, Busulfan, Chlorambucil, Cladribine, Docetaxel, Fludarabine, Fluorouracil, Hydroxyurea, Paclitaxel, Vincristine, Thiotepa, Melphalan

Table 2. Management of chemotherapy-induced nausea and vomiting

Levels	Management
Level I	1. Prochlorperazine 10 mg P.O. before chemotherapy followed by 10 mg P.O. 4-6th hourly after chemotherapy. 2. Dexamethasone 4 mg P.O. before chemotherapy 3. Lorazepam 1 mg P.O. 6th hourly.
Level II	1. Dolasetron 100 mg P.O. or IV. or Ondansetron 10mg IV or Granisetron 10 mg/kg I.V. before chemotherapy 2. Dexamethasone 8 mg P.O. or 10 mg I.V. before chemotherapy 3. Prochlorperazine 10 mg P.O. 4-6th hourly after chemotherapy. 4. Lorazepam 1mg P.O. 6th hourly.
Level III	1. Dolasetron 100 mg I.V. or Ondansetron 32 mg I.V. or Granisetron 10 mg/kg I.V. before chemotherapy 2. Dexamethasone 10-20 mg I.V. before chemotherapy 3. Lorazepam 1 mg P.O. before chemotherapy followed by 6th hourly after chemotherapy 4. Metoclopramide 40 mg P.O. 6th hourly x 4 days 5. Dexamethasone 4 mg P.O. 6th hourly followed by 4 mg 12th hourly for 1 day after chemotherapy

3. GASTROINTESTINAL TOXICITY

Several chemotherapeutic drugs damage rapidly dividing cells of the gastrointestinal tract and cause mucositis and diarrhea [21,22].

3.1 Mucositis

Oral mucositis is a known complication associated with cancer medicines [23]. Cells in the mouth are usually renewed every 7 to 14 days. Antimetabolites, hydroxyurea and procarbazine hydrochloride are commonly associated with this ADR [24]. Upon occurrence, patients experience epithelial hyperplasia, epithelial dysplasia and collagen and glandular degeneration [25,26]. Poor nutritional status is known to worsen this condition [27].

3.1.1 Non-pharmacological interventions

Non-pharmacological intervention includes consulting a dentist at least 2 weeks before starting chemotherapy, asking the dentist regarding brushing and flossing, use of soft toothbrush and gentle cleaning, brushing teeth and gums after every meal, avoiding irritating, acidic foods and juices, and spicy, salty and coarse foods [28].

3.1.2 Prophylactic measures and treatment

Chlorhexidine mouth wash, saline rinses, sodium bicarbonate rinses, betadine mouth wash, and ice are considered beneficial in preventing mucositis. Xylocaine, magnesium-based antacids, diphenhydramine, nystatin and sucralfate, allopurinol, vitamin E and beta-carotene are also found to be beneficial [28-30].

3.2 Diarrhea

Chemotherapy-induced diarrhea leads to alteration of patients' therapy, dose reductions and dose delays in patients and even complete

termination of treatment [31,32] Drugs that induce diarrhea include 5-Fluorouracil, methotrexate, cytosine arabinose, capecitabine, and irinotecan. It is hard to predict which patient may develop diarrhea. Management of diarrhea includes adequate fluid intake, oral rehydration solution in mild to moderate diarrhea and intravenous fluid administration in case of severe fluid loss. Diarrhea can be controlled by Diphenoxylate+ Scopolamine 1 or 2 tabs. 3 or 4 times a day or Loperamide 2 capsules followed by 1 capsule after every loose stool (up to 8 capsules per day can be taken).

However, the stool should be investigated to rule out infective pathology especially during the nadir period (10-14 days after administration of chemotherapy). Infective diarrhea is managed with appropriate antibiotics or antimicrobials. For diarrhea caused due to irinotecan, atropine is given if diarrhea occurs within 24 hours of drug infusion. If diarrhea occurs after 24 hrs. it is managed by Loperamide 2mg once every 2hrs up to 12 hrs. after diarrhea subsides [32,33].

3.3 Constipation

Constipation is often an underestimated complication in patients with advanced cancer [34]**.** Constipation can be caused by vinca alkaloids like vincristine, vinblastine, vinorelbine and drugs used in supportive care such as narcotic analgesics and calcium-containing antacids. Vinca alkaloids cause constipation within 7 days from the day of administration [32].

3.3.1 Management

Constipation can be managed by a diet high in bulk fiber, fresh fruits, vegetables, adequate fluid intake and laxatives such as senna or bisacodyl. Senokot is given as 2 tablets twice daily until regular bowel functioning followed by 1 tab per day. Bisacodyl is given as 1 to 2 tablets per day if senna is ineffective. Lactulose 30 ml 2 to 3 times daily or milk of magnesia 30ml at bedtime can be added. Other alternatives include cisapride 10 to 20 mg 6^{th} hourly, magnesium citrate, bisacodyl suppository, and enema [32].

4. HEMATOLOGICAL TOXICITY

4.1 Toxicity to White Blood Cells (WBCs)

White blood cells (WBCs) are affected rapidly, due to their short life span resulting in neutropenia. The cells recover 3-4 weeks after chemotherapy. An absolute neutrophil count <1500/cmm will increase the risk of infections [35,36]. To increase the WBC count, Granulocyte Colony Stimulating Factor (G-CSF) and Granulocyte-macrophage colony-stimulating factor (GM-CSF) are used frequently. G-CSF is administered subcutaneously at a dose of 300 mcg if the patient weighs less than 75 kg and 480 mcg if the patient's weight is 75kg or more. It causes adverse effects such as nausea, fever, and bone pain which can be managed symptomatically. GM-CSF is administered intravenously or subcutaneously at a dose of 250 mcg/m^2. It causes adverse effects such as fever, flushing, rigors and bone pain [37]. Febrile neutropenia is managed with appropriate drugs according to the treatment guidelines [38,39].

4.1.1 Preventive measures to reduce the threat of infection

Patients should be informed when their neutrophil count is low. The patient should be aware of the signs and symptoms of infection and report to the physician if he/she has any symptoms. When the neutrophil count is low, an infection can be prevented by avoiding crowds and persons with a cold, flu, or other infections. Keeping the body clean by bathing each day and washing hands after using the bathroom are recommended. Hands should be washed thoroughly before eating.

4.2 Toxicity to Platelets

Platelets are also affected due to chemotherapy resulting in thrombocytopenia. The usual time for the occurrence of thrombocytopenia is 10 to 21 days after the administration of chemotherapy [40]. Thrombocytopenia is managed with platelet transfusion when indicated. The usual indications for platelet transfusion include any evidence of bleeding, platelet count less than 10,000/cmm, and platelet count less than 20,000/cmm with fever [40,41].

4.3 Toxicity to Red Blood Cells (RBCs)

RBCs are also affected during chemotherapy. Anemia due to chemotherapy-induced myelosuppression typically happens 2 to 3 weeks subsequent to the administration of chemotherapy. This toxicity can be managed by transfusion of blood and erythropoietin 40,000 units per week subcutaneously [42,43].

5. HAIR LOSS

Body hair loss (alopecia) is common with chemotherapy and the degree of loss in patients is dependent both on anti-cancer medicines used and dose. Long-term treatment may cause loss of pubic, axillary, and facial hair in addition to scalp hair [44-46].

Alopecia due to cancer chemotherapy is not irreversible and re-growth of hair occurs 1-2 months after treatment termination. Alterations in color and texture of hair may happen: hair shade may lighten or darken and often the hair curls as it regrows. Doxorubicin and cyclophosphamide are common anticancer drugs known to cause epilation (loss of hair). Alopecia may be expected with single-agent antibiotics, alkylating agents, nitrosoureas, and especially their combinations [47,48]. Temporary vasoconstriction can reduce blood circulation in the scalp and can be beneficial in preventing hair loss by reducing access to anticancer medicines to the hair follicles [49].

6. CARDIAC TOXICITY

Anthracyclines, taxanes, cyclophosphamide, ifosfamide, vinca alkaloids, 5-fluorouracil, mitomycin-c, cisplatin, trastuzumab (Herceptin) are known to cause cardiac toxicity. Cardiomyopathy caused by the anthracyclines has three clinical presentations: acute, subacute, and late. The acute toxicity presents as myopericarditis, pericardial effusion, and myocardial dysfunction, sometimes leading to cardiac failure and occasionally death, within a few days of administration of the drug. The subacute presentation has an insidious onset and appears up to 200 days after the administration of the last dose. The late presentation occurs 5 or more years after completion of therapy [50-53]. Incidence of late abnormalities depends upon the cumulative dose of anthracycline received [54-56].

6.1 Methods for Preventing Cardiomyopathy

Monitoring cardiac status, modification of drug delivery and use of cardioprotective agents are considered beneficial. Cardiac evaluation before anthracyclines and monitoring before each alternate treatment course until an aggregate dose of 300 mg/m^2 and reducing the peak dose of anthracycline is known to be beneficial [56-58]. Cardioprotective agents such as vitamin E, ascorbic acid, n-acetyl-cysteine, coenzyme Q10 and amifostine may be useful in minimizing cardiotoxicity [59]. Cardiomyopathy caused by anthracyclines can be managed with inotropic support and afterload reduction, angiotensin-converting enzyme inhibitors and selective beta-receptor blockers, such as metoprolol and carvedilol [60,61].

7. NEUROTOXICITY

Chemotherapy may have detrimental effects on either the central or peripheral nervous system. Drugs causing neurotoxicity include vinca alkaloids, cisplatin, oxaliplatin, cytosine arabinose, ifosfamide, 5-fluorouracil, methotrexate, paclitaxel, docetaxel, procarbazine, fludarabine, cladribine, pentostatin, etc [61].

Vinca alkaloids are among the commonest group of drugs causing neurotoxicity. For vincristine, neurotoxicity is the main dose-limiting toxicity. The common signs caused by vincristine include depression of the deep tendon reflexes, paresthesias of the distal extremities, motor dysfunction manifested as lower extremity weakness, cranial nerve involvement causing ophthalmoplegia and facial palsy, autonomic neuropathy causing orthostatic hypotension and erection/ejaculatory dysfunction [62-64]. Cisplatin and oxaliplatin-induced neuropathy can be manifested as sensory peripheral neuropathy, Lhermitte's sign, autonomic neuropathy, grand mal or focal seizures, encephalopathy, transient cortical blindness, retrobulbar neuritis, and retinal injury [65]. Manifestations of cytosine arabinose induced neuropathy include cerebellar dysfunction, seizures, generalized encephalopathy, peripheral neuropathy, necrotizing leukoencephalopathy, spinal myelopathy, basal ganglia necrosis, and pseudobulbar palsy [66]. Neurotoxicity from methotrexate can manifest as meningeal irritation, transient paraparesis, or encephalopathy. When the drug is administered intrathecally (IT), it can cause headaches, nausea and vomiting, lethargy, nuchal rigidity, and other features of meningeal irritation [67,68].

7.1 Management

The mainstay of treatment involves the cessation of cancer chemotherapy and waiting for neurologic recovery. After cessation of therapy, neuropathy symptoms may continue for 3 to 4 years. Vitamin therapy may not be very effective.

Intestinal dysfunction from autonomic neuropathy may be improved by metoclopramide therapy. Neurotoxic symptoms may last for months after cisplatin therapy is discontinued. Recovery from the neurologic effects usually occurs within a few days after discontinuing cytarabine therapy [69].

8. NEPHROTOXICITY

Cisplatin, cyclophosphamide, ifosfamide, methotrexate, mitomycin, carmustine, lomustine and streptozocin are known to cause renal toxicity [70]. The pathologic lesion of cisplatin nephrotoxicity is seen primarily in the proximal and distal tubules but may also involve the collecting ducts, whereas the glomeruli are unaffected. The hemolytic uremic syndrome has been reported in patients treated with cisplatin [70,71].

8.1 Management

Higher doses of cisplatin require aggressive hydration. Mannitol is also used to enhance diuresis, Amifostine demonstrated significant protection against cisplatin-induced nephrotoxicity [72,73]. Twenty-four-hour creatinine clearance value less than 70 mL/min, particularly in patients 60 years old or older is considered a contraindication for cisplatin therapy [74]. Treatment for mitomycin induced nephrotoxicity include hemodialysis and plasmapheresis [75]. Methotrexate-induced renal insufficiency can be largely prevented by hydration and urine alkalinization. Sequential hemodialysis and charcoal hemofiltration have been used as a treatment of acute nephrotoxicity from methotrexate [71].

9. HEPATOTOXICITY

Several antitumor agents cause hepatic toxicity. The hepatotoxicity caused by chemotherapeutic drugs is manifested in three forms, which are chemical hepatitis, venoocclusive disease and chronic fibrosis. The antitumor drugs known to produce hepatotoxicity include l- asparaginase, carmustine, cytarabine, dactinomycin, etoposide, levamisole in combination with 5-fluorouracil, 6-mercaptopurine, and methotrexate in high doses, streptozocin, vincristine, busulfan and cyclophosphamide [76,77].

10. HYPERSENSITIVITY REACTIONS

Most antitumor agents can produce hypersensitivity reactions especially taxanes, which cause reactions severe enough to stop the treatment. Paclitaxel and Docetaxel produce hypersensitivity reactions including bronchospasm, angioedema, hypotension and pneumonitis [78]. Antianaphylaxis medication must be readily available and the patient should be observed after the drug is administered to avoid these reactions. Paclitaxel and docetaxel are administered slowly over 1 to 3 hrs along with premedication using corticosteroids [78,79].

11. GONADAL DYSFUNCTION AND TERATOGENICITY

Infertility is an important problem for young adults treated with chemotherapy drugs [80]. In males, chemotherapy drugs result in loss of germinal cells leading to germinal aplasia. During the first 2 to 3 months of cytotoxic therapy, sperm counts may remain normal or be only moderately reduced. Some regimens cause azoospermia [81,82]. When sperm count recovers after cytotoxic therapy, fertility is generally restored. Drugs causing azoospermia include cisplatin, chlorambucil, cyclophosphamide, carmustine, and lomustine [83-85]. Methods to preserve fertility include semen cryopreservation, which is extremely important for men who want to preserve their fertility after cytotoxic treatment, and restoration of spermatogenesis is also possible using cryopreserved cells [86,87]. In vitro fertilization (IVF), with artificial insemination, is important in achieving pregnancies from stored semen after the completion of cytotoxic therapy [88]. Ovulation may be temporarily stimulated by gonadotropin treatment and steroid hormone replacement therapy [89].

12. CUTANEOUS EFFECTS

Mucocutaneous surfaces are particularly susceptible to the adverse effects of anti-cancer medicines, as they are composed of rapidly dividing cells [90].

12.1 Nail Complications

Nail involvement is dose-dependent and may range from mild formation of multiple Beau's lines to severe onychomadesis, onycholysis and onychodystrophy. The big toe is the commonest nail to be affected. Nail pigmentation may be either diffuse or limited to the lunula or horizontal or vertical bands of pigmentation may occur. Anthracyclines (doxorubicin, daunorubicin) and taxanes (paclitaxel, docetaxel) commonly produce severe nail dystrophy and pigmentation in up to 40% of cases [91].

12.2 Sweat Gland Abnormalities

Neutrophilic hidradenitis may occur in response to a range of anti-cancer medicines, the commonest being cytarabine and bleomycin. Clinically erythematous papules, plaques and nodules are seen, mainly on acral areas. Syringosquamous metaplasia is closely related to neutrophilic hidradenitis and is due to the direct toxicity of anti-cancer medicines on the sweat ducts. Erythematous weals are seen, which resolve weeks after cessation of therapy [92,93].

12.3 Epidermal Complications

The epidermal complications include toxic erythema and acral erythema.

a. Chemotherapy-induced toxic erythema: This is usually caused by busulfan, cytarabine, etoposide and methotrexate. There is a prodrome of tingling pain, followed by tender erythema and edema. Severe cases may resemble toxic epidermal necrolysis [94,95].

b. Chemotherapy-induced acral erythema: This is due to the concentration of drugs in sweat glands of palms and soles. It is most common with cytarabine and doxorubicin and develops in 1-3 weeks as sharply demarcated erythema of palms and soles [96-98].

12.4 Keratoses

Multiple actinic and seborrheic keratoses may occur especially with fluorouracil and cytarabine [99].

12.5 Hyperpigmentation

Bleomycin causes a peculiar flagellate hyperpigmentation in 8-66% of cases [100]. Serpentine supravenous hyperpigmentation is caused by IV drugs like fluorouracil and vinorelbine. Daunorubicin causes polycyclic bands of scalp hyperpigmentation. Generalized hyperpigmentation is a common adverse effect of many cytotoxic agents, increased drug deposits due to increased blood flow, an increase in melanocyte-stimulating hormone (MSH) secretion and drug-induced depletion of tyrosinase inhibitors [101,102].

12.6 Photosensitivity

Phototoxic reactions simulating sunburns are common. Photoallergic reactions are seen as papulovesicular, mainly over photo exposed areas. Radiation enhancement reaction is a synergistic reaction between antineoplastic drugs (Vinca alkaloids) and radiation [103].

12.7 Dermal Adverse Effects

These include local injury due to extravasation leading to chemical cellulitis manifesting as erythema, induration and pain at IV infusion sites, or even ulcers and severe necrosis attributable to drugs like doxorubicin. Cisplatin and Asparaginase are well known to cause urticaria and angioedema (65% incidence). Sclerotic dermal reactions mimicking morphea are well known with bleomycin, docetaxel and melphalan. Raynaud's phenomenon may occur secondary to bleomycin and cisplatin [104].

13. CARCINOGENIC EFFECTS

Busulfan may also be leukemogenic [105]. Several cases of acute leukemia have been reported in patients who developed pancytopenia 5 to 8 years earlier secondary to the use of busulfan. In an evaluation of 439 children with acute lymphoblastic leukemia (ALL), an increased risk for the development of secondary myelodysplasia (MDS) or acute myeloid leukemia (AML) was demonstrated when mercaptopurine was administered in patients with low thiopurine methyltransferase (TPMT) activity or excessively high intracellular levels of thioguanine nucleotides and methylated mercaptopurine metabolites [106-108].

14. MISCELLANEOUS ADVERSE EFFECTS

Some of the other adverse effects due to anticancer drugs are mentioned below.

14.1 Tumor Lysis Syndrome

This syndrome occurs from the rapid destruction of chemotherapy-sensitive cells resulting in the release of intracellular phosphate, urates, and other cell contents. Burkitt's and similar fast-growing lymphomas, and less frequently small cell lung cancer, breast cancer, and seminoma may show the syndrome [109,110]. Administration of IV fluids, allopurinol and calcium gluconate are the usual methods of management.

14.2 Sepsis

In cancer patients undergoing combination chemotherapy, sepsis is a life-threatening

condition [111]. A high incidence of streptococcal septicemia has been reported in patients with acute myelogenous leukemia following high-dose cytarabine therapy for remission induction or post-remission intensive consolidation. Prophylactic regimens, including cotrimoxazole, were ineffective in preventing this complication. More studies are required to confirm these findings [112,113].

14.3 Injection Site Extravasation

Leakage of vincristine into the adjacent tissue during intravenous administration may cause significant irritation; avoid extravasation. Dactinomycin is very corrosive, and extravasation for the duration of IV administration can result in cellulitis and injury to soft tissues and contracture of the arms [114,115]. It can be managed by stopping the infusion, injecting hydrocortisone around the site and use of ice pack. It can be minimized by administering the drugs using central lines [115].

15. SAFE HANDLING AND TOXICITY OF CANCER CHEMOTHERAPEUTIC AGENTS TO HEALTHCARE WORKERS

Since cancer chemotherapeutic agents are a highly toxic group of drugs, they can also cause an occupational hazard to the health workers handling these medications. For example, health workers involved in preparing IV mixtures of cancer chemotherapeutic agents are likely to be exposed to these medications and can get affected. Often the chemotherapeutic agents may affect these health workers through contaminated clothing, medical equipment, patient excreta, etc. The magnitude of the risk depends on the quantity of the exposure and the toxicity profile of the agent involved. These agents are known to enter the human body through direct skin contact, inhalation, skin surface, ingestion, or injection. Reconstituting powdered or lyophilized drugs can be another condition leading to exposure. Handling and disposal of unused chemotherapeutic agents can be also an associated issue [116].

16. CONCLUSION

The prevalence of cancer is increasing. Chemotherapy is an important treatment modality. A thorough investigation of the health status of the patient should be done before starting chemotherapy. Appropriate premedication and antidotes can be of great help in minimizing the toxicity. On the occurrence of toxicity, immediate management measures should be taken. Though the toxicity profile of anticancer medications is unfavorable and some of the toxicities are not preventable, initiating appropriate steps can minimize these toxicities to a great extent. Apart from the adverse effects caused to the patients, these drugs can also cause serious hazards to the healthcare professionals getting exposed to them. Hence all healthcare professionals should take adequate preventive measures to minimize the exposure to the cancer chemotherapeutic agents as far as possible.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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