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# Research Study on the Role of Clinical Pharmacists in Detecting the Side Effects of Chemotherapy Cytotoxicity in Cancer Departments

Dr Satish Kumar Sharma [1], Yassir Abubakar Fikak [2]

[1] Professor & Principal, Glocal School of Pharmacy, PVC, Glocal University, Saharanpur

[2] Research Scholar, Department of Pharmacy, Glocal University, Saharanpur, Uttar Pradesh, India

**ARTICLE DETAILS**

**Research Paper**

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**ABSTRACT**

So, the job of clinical pharmacist is to provide support medical plans and solutions to manage and limit the cytotoxic effects of chemotherapy, such as fatigue and hair loss. Easy bruising, bleeding, and infection. Anaemia (decreased red blood cell numbers) Nausea and vomiting. Appetite changes, constipation, diarrhoea. Mouth, tongue, and throat problems such as sores and swallowing difficulty, as well as improving cancer patients' quality of life, could considerably lower the death rate from these cancers.

## INTRODUCTION:

The National Cancer Institute estimates that over 40% of men and women will be diagnosed with some kind of cancer during their lives. A study of physicians, nurses, and physician assistants predicted a shortfall of qualified oncology and haematology practitioners in 2020. The job of a professional oncology pharmacist has also emerged as part of the interdisciplinary team that provides care to cancer patients. According to the extant literature, the duty of an oncology clinical pharmacist is primarily to identify, prevent, and manage any medication-related problems, such as drug selection, dosage, interactions, administration method, and adverse effects. Oncology pharmacists require particular knowledge, hence the subject has evolved into a separate pharmaceutical specialty with it. Currently, more than 1600 board-certified oncology pharmacists operate at various levels of cancer patient care around the world. ASHP-accredited cancer pharmacy residency programs can significantly enhance the knowledge, abilities, and practice of oncology pharmacists. It has been claimed that the oncology

clinical pharmacist plays an important role in cancer patient care by enhancing medication utilization, particularly chemotherapy and other high-risk medications. As part of a multidisciplinary team, clinical pharmacists play an important role in ensuring safe, effective, and cost-efficient medication therapy for cancer patients. hypersensitivity reactions, epidermal growth factors, skin toxicities, vascular endothelial growth factor and secondary hypertension, among other possible future roles reported by clinical pharmacist in the department . They can also serve as investigators in a number of research trials looking at the usage of pharmaceuticals in the treatment of cancer patients. According to current research, oncology clinical pharmacists are highly effective at improving medication usage and play a promising role in offering clinically essential medication use treatments. To guarantee that care plans are implemented effectively, oncology pharmacies could be established as part of research studies and integrated into disease management programs. Historically, general pharmacists have focused primarily on the operational role of dispensing accurate and safe medications; however, as cancer treatment becomes more complex and the population ages, the oncology drugs market is showing an increased need for more specialised knowledgeable health care practitioners.

**Serious adverse effects:**

Cytotoxic medicines primarily target quickly synthesized Cancers, particularly big tumors,
exhibit fractions (fewer cells in division phase) , anticancer can effects GIT produce NVD, alopecia , anemia , bone marrow damage which called myelosuppression, mucositis , gonadal dysfunction , teratogenicity, neuropathy , hepatotoxicity, nephrotoxicity, cardio toxicity cystitis and secondary cancer too and this can lead to death .

**1. Bone marrow depression**

| Drugs causing thrombocytopenia | Drugs causing aplastic anemia | Drugs causing bone marrow depression |
|---|---|---|
| Dacarbazine | Cisplatin | Carboplatin |
| Carboplatin | Docetaxel | Vinblastine |
| 5-flurouracil | Altretamine | Doxorubicin |
| Lomustine | Topotecan | Melphalan |
| Mitomycin | Paclitaxel | Paclitaxel |
| Thiotepa | Cytarabine | Cyclophosphamide |

**2. Toxicity of lymph reticular system:**

Lymphocytopenia and lymphocyte function inhibition reduce both cell-mediated and human oral immunity. Due to bone marrow depression, toxicity to the lymph reticular system, and epithelial surface injury, the host's defense systems (both specific and generic) are broken down, increasing susceptibility to all infections. Opportunistic infections caused by low-pathogenic organisms are particularly important. Anticancer medication can lead to infections with fungi (e.g. Candida), viruses (e.g. Herpes zoster, cytomegalic virus), fungus Pneumocystis jiroveci, and toxoplasma.

**3. Gastrointestinal toxicity:**

Diarrhea, mucositis, mucosa shedding, and hemorrhages . Drugs responsible for gastrointestinal toxicity are Constipation can be a major issue for caused discomfort

| **Drugs causing diarrhea / mucositis** |
|---|
| Bleomycin |
| Methotrexate |
| Paclitaxel |
| Irinotecan |
| Nitrosourea |

Nausea and vomiting are comment when we use chemotherapy, This is due to direct stimulation of chemoreceptor trigger zone (CTZ) The emetogenic potential of cytotoxic drugs given below:

| **Mild** | **Moderate** | **High** |
|---|---|---|
| Hydroxyurea | Cytarabine | Mustine |
| 6-Thioguanine | Carboplatin | Cisplatin |
| Fluorouracil | Procarbazine | Cyclophosphamide |
| Busulfan | Vinblastine | Actinomycin D |
| Bleomycin | Doxorubicin | Dacarbazine |
| Chlorambucil | Daunorubicin | Lomustine |

**4. Oral toxicity:**

vulnerable to cytotoxic medicines due to rapid epithelial cell turnover. Stomatitis is a common complication associated with anticancer therapy. Cytotoxic treatment decreases salivary flow, lowers amylase and IgA levels, and increases opportunistic infections.

| Drugs causing stomatitis |
|---|
| Methotrexate |
| Irinotecan |
| Cytarabine |
| 5- Flurouracil |
| Vincristine |
| Vinblastine |
| Etoposide |

**5. Hair follicle toxicity:**

Chemotherapy-induced alopecia (CIA), a mucocutaneous side effect of cancer therapy, is frequently regarded by patients as the most emotionally unpleasant component of treatment. The CIA prominently announces the sickness state, which reduces quality of life for those who are already dealing with the physical and mental consequences of cancer. Currently, CIA is one of the most significant unmet challenges in cancer management, as preventative therapeutic options are limited. Drugs that cause hair follicle poisoning

| Drugs causing hair follicle toxicity |
|---|
| Daunorubicin |
| Doxorubicin |
| Methotrexate |
| Ifosfamide |
| Cyclophosphamide |
| Vincristine |

**6. Renal toxicity:**

Abnormal renal function has a significant impact on the clinical care of cancer patients. While the tumor may induce renal impairment on its own, chemotherapeutic treatment may worsen it. Many chemotherapeutic drugs are processed and eliminated through the kidneys, hence their usage may pose a significant risk for the development of renal abnormalities. Furthermore, when renal impairment is evident prior to chemotherapy treatment, several medicines require dose changes or are not recommended. Careful monitoring of renal function during chemotherapy is thus required.

| Drugs causing renal toxicity |
|---|
| Cisplatin |
| Ifosfamide |
| Mitomycin |
| Plicamycin |
| Streptozotocin |

**7.Pulmonary toxicity:**

Antineoplastic drug-induced pulmonary toxicity is becoming more widely known, and the number of medications suspected of causing it is continuously increasing. Initially, patients may exhibit malaise, fever, and respiratory symptoms.

| Drugs causing Acute pneumonitis | Drugs causing Hypersensitivity pneumonitis | Drugs causing Non cardiogenic pulmonary edema |
|---|---|---|
| Bleomycin | Bleomycin | Mitomycin |
| Methotrexate | Methotrexate | Methotrexate |
| Mitomycin | Procarbazine | Cyclophosphamide |
| Procarbazine | Azathioprine | Cytarabine |
| Carmustine | | |

***Drugs causing Pulmonary fibrosis….(** Bleomycin **)**

**8.Cardiac toxicity:**

Cytotoxic and targeted medicines used to treat cancer, such as traditional chemotherapeutic agents, monoclonal antibodies that target tyrosine kinase receptors, small molecule tyrosine kinase inhibitors, and even antiangiogenic medications, all have an effect on the cardiovascular system. Combination medicines frequently increase cardiac toxicity. prevalent cardiac toxicity associated with chemotherapy , pericarditis, arrhythmias, ECG abnormalities, and angina are less common.

| Drugs causing Left Ventricular dysfunction | Drugs causing Cardiac ischemia | Drugs causing QT prolongation |
|---|---|---|
| Doxorubicin | Capecitabine | Arsenic trioxide |
| Paclitaxel | Docetaxel | Paclitaxel |

| | | |
|---|---|---|
| Docetaxel | Fluorouracil | |
| Idarubicin | | |
| Epirubicin | | |

**9. Nervous system toxicity:**

Anticancer medications cause toxic effects on the central nervous system via a variety of pathways, resulting in reversible or irreversible neurologic impairment. To guarantee patient safety, it's important to be aware of neurotoxic side effects due to limited therapy options. Discontinuing chemotherapy is the only way to prevent future CNS damage.

| **Drugs causing encephalopathy** | **Drugs causing Seizures** | **Drugs causing Aseptic meningitis** | **Drugs causing Cerebral infarctions** |
|---|---|---|---|
| Methotrexate | Methotrexate | Methotrexate | Methotrexate |
| Cis-platinum | Etoposide | Cytosinarabinoside | Cyclosporine |
| 5-fluorouracil | Vincristine | | Platinum derivatives |
| Procarbazine | Dacarbazine | | |
| Etoposide | Cyclosporine | | |

**10. Ocular toxicity:**

Ophthalmic problems caused by cytotoxic chemotherapy are frequently underestimated and underreported due to the focus given to other life-threatening illnesses. The use of more harsh regimens, novel drugs, and combination chemotherapies has resulted in a large increase in documented occurrences of chemotherapy-induced ocular adverse effects.

| **Drugs causing Blurred vision** | **Drugs causing Photophobia** | **Drugs causing Cataract** |
|---|---|---|
| Cisplatin | 5-Florouracil | Tamoxifen |
| Cyclophosphamide | Methotrexate | Anastrazole |
| Methotrexate | Fludarabine | Busulfan |
| Imatinib | Cytosine | |
| Tamoxifen | Arabinoside | |
| Mitomycin-C | Pentostatin | |

| Drugs causing Optic neuropathy | Drugs causing Keratitis | Drugs causing Conjunctivitis |
|---|---|---|
| Cisplatin | 5-Florouracil | Oxaliplatin |
| Carboplatin | Chlorambucil | Cyclophosphamide |
| Methotrexate | Erlotinib | Methotrexate |
| Paclitaxel | Capecitabine | 5-Florouracil |
| Vincristine | Cetuximab | Docetaxel |

**11. Skin toxicity**:

The dermatological complications of cancer chemotherapy have become an increasingly significant subject in the management of cancer patients as the development of new antineoplastic drugs has continued to add to the arsenal of oncological treatment. Hyperpigmentation is a common cutaneous toxicity. Urticaria is the second most common Chemotherapy induced adverse drug reaction. Pruritus and other hypersensitivity reaction are also noticed in patients undergoing cancer chemotherapy.

| Drugs causing nail changes | Drugs causing hyperpigmentation | Drugs causing hypersensitivity. |
|---|---|---|
| Bleomycin | Bleomycin | Docetaxel |
| Cyclophosphamide | Cyclophosphamide | Cyclophosphamide |
| Doxorubicin | Busulfan | Carboplatin |
| 5-Flurouracil | Carmustine | Cytarabine |
| Hydroxyurea | Dactinomycin | Doxorubicin |
| Paclitaxel | Methotrexate | L-asparginase |

**12.Hepatic toxicity:**

Collateral injury to the liver during cancer treatment is not uncommon. Hepatotoxicity from chemotherapy happens frequently in an unpredictable or idiosyncratic manner, and previous liver

disease enhances the risk. The pattern of presentation might range from inflammatory hepatitis to cholestasis, steatosis, and finally a vascular manifestation as hepatic veno-occlusive disease. The severity ranges from asymptomatic elevated liver function tests, acute liver failure, to gradual fibrosis ending in end-stage liver disease.

| Drugs causing hepatotoxicity |
|---|
| Cyclophosphamide |
| 5-Flurouracil |
| 6-Mercaptopurine |
| Methotrexate |

**13.Local toxicity:**

Extravasation is an acute reaction caused by the release a medication into subcutaneous tissues. especially vulnerable to drug extravasation because to numerous punctures, phlebitis, lymphedema from previous surgery, and overall debilitation. Vesicant medications cause tissue necrosis or sloughing, while irritant drugs . These substances cause the release of free radicals, which are harmful to the tissues.

| drugs causing extravasations |
|---|
| Doxorubicin |
| Dacarbazine |
| Mitomycin |
| Mechlorethamine |
| Carmustine |
| Vinblastine |
| Paclitaxel |

**14. Carcinogenicity:**

Chemotherapy is far more potent in inducing secondary leukemia , Many of the chemicals used in cancer treatment are known carcinogens. Studies have linked alkylating chemicals to leukemia and cyclophosphamide to bladder cancer. The risk of leukemia increases 5-10 years after the start of chemotherapy and gradually diminishes when it ends. Other tumors observed with increased incidence are non-Hodgkin's lymphoma and lung cancer.

**Metabolic abnormalities:**

The acute tumor lysis syndrome (ATLS) is characterized by the rapid development of hyperuricemia (i.e. high level of uric acid in the blood), hyperkalemia (i.e. high level of potassium in the blood), hyperphosphatemia (i.e. high level of phosphate in the blood), and acute renal failure , The majority of ATLS cases are due to hematologic malignancies. Controlling hyperuricemia and achieving a high urine flow are the cornerstones of prevention. At some point throughout their cancer treatment, 10% to 20% of people develop hypercalcemia. The most prevalent electrolyte anomaly in cancer patients is hyponatremia, which is characterized by an increase in total body salt and water content and manifests as edema and/or ascites. Patients who receive cisplatin may develop hyponatremia due to salt loss.

**Teratogenicity:**

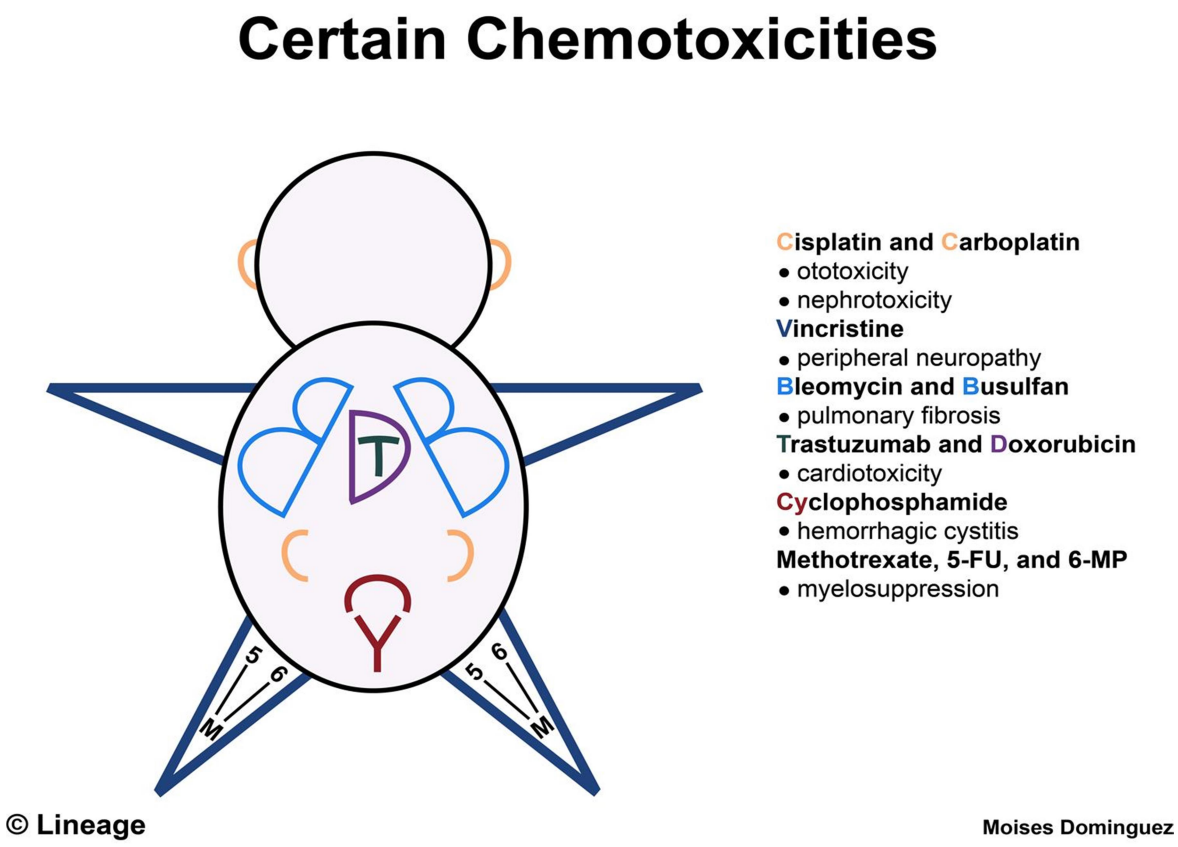
Almost all cytotoxic medications administered to pregnant women severely harm the developing baby, resulting in abortion, fetal death, and teratogenesis.Almost all chemotherapeutic drugs cause teratogenic effects in animals. For some medications, only experimental data are available. Women who have been diagnosed with cancer during their childbearing years should be made aware of the hazards connected with using cancer chemotherapy while pregnant.

**Conclusion**

Advances in chemotherapy have clearly demonstrated that anticancer medications can cure cancer when combined with other treatment choices such as radiation therapy and surgical therapy. The fundamental barrier to chemotherapy's therapeutic success has been its toxicity to the body's natural tissues. Acute toxicity is most prevalent in tissues that reproduce rapidly, such as bone marrow, oral mucosal lining, gastrointestinal system, and hair follicles. In addition, anticancer medicines may cause persistent and cumulative toxicities. It covers hazards associated with the management of cytotoxic medications and their interactions with other drugs. These toxicity to patients has an impact on their overall quality of life. This study outlines the severe side effects of anticancer medications and common antineoplastic agents that cause them.

**Summary**

In summary the anticancer side effects are a significant concern for cancer patients undergoing treatment. These side effects can impact various parts of the body and manifest in a range of symptoms, affecting the patient's quality of life and overall well-being. Healthcare providers must be aware of the potential side effects of anticancer treatments and work closely with patients to manage and alleviate these symptoms to improve outcomes and ensure a successful treatment experience.




**References**

1)K.V.R.S.S. Gopal R, Lakshmi AV, Kumar R. Anticancer herbs in Ayurveda: A review. Int J Res Ayurveda Pharm 2013; 4(2):284-87.

2)Chorawala MR, Oza PM, Shah GB. Mechanisms of Anticancer Drugs Resistance: An Overview. Int J of Pharmaceutical Sci and Drug Research 2012; 4(1): 01-09

3)Tripathi KD. Anticancer Drugs. In: Essentials of Medical Pharmacology. 7th edition. Jaypee brother's medical publishers Ltd; 2013.p 857-77.

4)Chemotherapy. [Internet] National cancer institute [Updated:29 Apr 2015; Cited: 13 Sep 2017] Available from: https://www.cancer.gov/about-cancer/treatment/types/chemotherapy

5)Tripodo G, Mandracchia D, Collina S, Rui M, Rossi D. New Perspectives in Cancer Therapy: The Biotin-Antitumor Molecule Conjugates. Med chem. 2014;S1(4):1-8. doi:10.4172/2161-0444.S1-004

6)Ramesh A. Toxicities of anticancer drugs and its management. Int J Basic Clin Pharmacol. 2012;1(1):2-12

7)Sivak LA, Maidanevich NN, Lyalkin SA, Aleksik EM, Askolskiy AV, Klimanov MY, et al. The toxic effects of chemotherapy on the gastrointestinal tract. Lik Sprava. 2015;(1-2):108-12.

8)Dewan P, Singhal S, Harit D. Management of Chemotherapy-Induced Nausea and Vomiting. Indian Pediatrics. 2010; 47:149-155.

9)Vigarios E, Epstein JB, Sibaud B. Oral mucosal changes induced by anticancer targeted therapies and immune checkpoint inhibitors. Support care cancer 2017; 25:1713-39.

10) Villasante AC, Herskovitz I, Mauro LM, Jimenez JJ. Chemotherapy-Induced Alopecia. J Clin Investigat Dermatol. 2014; 2(2): 8.

11) Di Vito R, Sirolli V, Amoroso L, Bonomini M. Nephrotoxicity induced by chemotherapy. G Ital Nefrol. 2011; 28(3):296-304.

12) Byrd RP. Drug induced pulmonary toxicity. [Internet] Medscape [Updated:31 Dec 2015; Cited: 13 Sep 2017] Available from: http://emedicine.medscape.com/article/1343451-overview

13) Albini A, Pennesi G, Donatelli F, Cammarota R, Flora SD, Noonan DM. Cardiotoxicity of Anticancer Drugs: The Need for Cardio-Oncology and Cardio-Oncological Prevention. J Natl Cancer Inst 2010; 102:14–25

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14) Schlegel U. Central Nervous System Toxicity of Chemotherapy. Eur Assoc Neurooncol Mag 2011;1(1):25–9.

15) Singh P, Singh A. Ocular adverse effects of anti-cancer chemotherapy and targeted therapy. Journal of Cancer Therapeutics & Research 2012. p.1-7. DOI:

http://dx.doi.org/10.7243/2049-7962-1-5

16) Kamil N, Kamil S, Ahmed SP, Ashraf R, Khurram M, Ali MO. Toxic effects of multiple anticancer drugs on skin. Pak. J. Pharm. Sci. 2010;23(1):7-14.

17) Grigorian A and Brien CBO. Hepatotoxicity Secondary to Chemotherapy. J of Clin and Translational Hepatology 2014;2:95–102.

18) Thakur A, Thakur JS. Extravasational toxicity of anticancer chemotherapy and its management. OA Case Reports 2013; 2(3):26.

19) Martin A, Schneiderman J, Helenowski IB, Morgan E, Dilley K, Danner-Koptik K, et al. Secondary malignant neoplasms after high-dose chemotherapy and autologous stem cell rescue for high-risk neuroblastoma Pediatr Blood Cancer 2014;61:1350-56.

20) Ikeda AK. Tumor lysis syndrome. [Internet] Medscape [Updated:17 Aug 2017; Cited: 14 Sep 2017] Available from: http://emedicine.medscape.com/article/282171-overview

21) Meistrich ML. Effects of chemotherapy and radiotherapy on spermatogenesis in humans. Fertility and Sterility. 2013;100(5):1180-86.

22) Gutierrez K, Glanzner W, O Chemeris R, Gonçalves PBD. Gonadotoxic effects of busulfan in two strains of mice. Repro toxic. 2015;59. DOI: 10.1016/j.reprotox.2015.09.002.

23) Koren G, Carey N, Gagnon R, Maxwell C, Nulman I, Senikas V. Cancer Chemotherapy and Pregnancy. J Obstet Gynaecol Can 2013;35(3):263–278

24) Ho L., Akada K., Messner H., Kuruvilla J., Wright J., Seki J.T. Pharmacist's role in improving medication safety for patients in an allogeneic hematopoietic cell transplant ambulatory clinic. Can. J. Hosp. Pharm. 2013;66:110–117. doi: 10.4212/cjhp.v66i2.1233. , McKee M., Frei B.L., Garcia A., Fike D., Soefje S.A. Impact of clinical pharmacy services on patients in an outpatient chemo- therapy academic clinic. J. Oncol. Pharm. Pract. 2011;17:387–394. doi: 10.1177/1078155210389217.

25.McKee M., Frei B.L., Garcia A., Fike D., Soefje S.A. Impact of clinical pharmacy services on patients in an outpatient chemo- therapy academic clinic. J. Oncol. Pharm. Pract. 2011;17:387–394. doi: 10.1177/1078155210389217, Lam M.S., Cheung N. Impact of oncology pharmacist- managed oral anticancer therapy in patients with chronic myelogenous leukemia. J. Oncol. Pharm. Pract. 2016;22:741–748. doi: 10.1177/1078155215608523.

26. Randolph L.A., Walker C.K., Nguyen A.T., Zachariah S.R. Impact of pharmacist interventions on cost avoidance in an ambulatory cancer center. J. Oncol. Pharm. Pract. 2016;24:3–8. doi: 10.1177/1078155216671189. - DOI - PubMed

Holle L.M., Puri S., Clement J.M. Physician-pharmacist collaboration for oral chemotherapy monitoring: Insights from an academic genitourinary oncology practice. J. Oncol. Pharm. Pract. 2016;22:511–516. doi: 10.1177/1078155215581524. - DOI - PubMed Chung C., Collins A., Cui N. Development and implementation of an interdisciplinary oncology program in a community hospital. Am. J. Health-Syst. Pharm. 2011;68:1740–1747. doi: 10.2146/ajhp100626.

27. . Association of American Medical Colleges Center for Workforce Studies. Forecasting the Supply of and Demand for Oncologists: A Report to the American Society of Clinical Oncology (ASCO) From the AAMC Center for WorkforceStudies. http://www.asco.org/ASCO/Downloads/Cancer%20Research/Onocology%20Workforce%20Report%20FINAL.pdf. Erikson C, Salsberg E, Forte G, et al.

28. Gralla RJ, Raftopoulos H. Progress in the control of chemotherapy-induced emesis: new agents and new studies. J Oncol Pract 2009;5:130-3.

29. Grunberg SM, Warr D, Gralla RJ, et al. Evaluationof new antiemetic agents and definition of antineoplastic

agent emetogenicity: state of the art. Support Care Cancer 2010;19:S43-47.

30. Herrstedt J, Dombernowsky P. Anti-emetic therapy in cancer chemotherapy: current status. Basic Clin Pharmacol Toxicol 2007;101:143-50.

31. Hesketh PJ, Kris MG, Basch E, et al. Antiemetics: ASCO guideline update. J Clin Oncol 2020. 38(24): 2782-2797

32. Hesketh PJ, Kris MG, Grunberg SM, et al. Proposal for classifying the acute emetogenicity of cancer chemotherapy. J Clin Oncol 1997;15:103-9.

33. Multinational Association for Supportive Care in Cancer. MASCC/ESMO Antiemetic Guideline 2016

with 2019 updates. Available at www.mascc.org.

34. Naeim A, Dy SM, Lorenz KA, et al. Evidencebased recommendations for cancer nausea and vomiting. J Clin Oncol 2008;26:3903-10.

35. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology:

Antiemesis, version 2, 2022. Available at https:// www.nccn.org/professionals/physician_gls/pdf/ antiemesis.pdf.

36. Navari RM, Gray SE, Kerr AC. Olanzapine versus aprepitant for the prevention of chemotherapy induced nausea and vomiting: a randomized phase III trial. J Support Oncol 2011;9:188-95.

37. Navari RM, Nagy CK, Gray SE. Olanzapine versus metoclopramide for the treatment of breakthrough

chemotherapy-induced nausea and vomiting in patients receiving highly emetogenic chemotherapy. Support Care Cancer 2013;21:1655-63.

38. Navari RM, Qin R, Ruddy KJ. Olanzapine for the prevention of chemotherapy-induced nausea and vomiting. N Engl J Med 2016;375:134-42.

39. Anderson K, Ismaila N, Flynn PJ, et al. Role of bone-modifying agents in multiple myeloma: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 2018;36:812-8.

40. Anghelescu DL, Ehrentraut JH, Faughnan LG, et al. Opioid misuse and abuse: risk assessment and management in patients with cancer pain. J Natl Compr Canc Netw 2013;11:1023-31.