INTERNATIONAL JOURNAL OF CLINICAL PHARMACOKINETICS AND MEDICAL SCIENCES

Published by Pharma Springs Publication Journal Home Page: <https://pharmasprings.com/ijcpms/>

A Review on chemotherapy induced toxicities: Challenges in their management

Peruri Pavan kumar^{*1}, Dinesh Kumar Kukunuri², Palla Neelima³

¹Jagadguru Sri Shivarathreeswara University, Mysore, Karnataka, India

²H.K.E.S.S Mathoshree Taradevi Rampure Institute of Pharmaceutical Sciences, Gulbarga, Karnataka, India

³Research Scholar, Department of Pharmacology, AU College of Pharmaceutical Sciences, Andhra University, Andhra Pradesh, India

Article History:

Received on: 27 Jan 2021

Revised on: 07 Feb 2021

Accepted on: 08 Feb 2021

Keywords:

Chemotherapeutic drugs,
Toxic effects,
Tolerability,
Management of toxicities

ABSTRACT

One of the reasons behind the chemotherapeutic drugs that differentiate from other drugs is the toxic effects. Toxicity is the main concern for chemo drugs. These drugs usually have a narrow therapeutic range and responsible for unwanted toxic effects. These toxic effects constitute a considerable end-point for pharmacodynamic studies of cytotoxic drugs. Toxic effects may vary depending upon the dose, term of usage, and individual susceptibility. The management of these toxicities should be given the utmost importance to better their health and to improve their tolerability. By conscious of the toxicity of independent regimens assist the physicians to pick out patients requiring supportive therapy or reduced toxic regimens. Any measure that aid to lessen the phenomenon or seriousness of toxicities in patients going on chemotherapy, would be favorable and amplify the patient's standard of living. This article offers an overview of toxicities and their management of chemotherapeutic drugs.

*Corresponding Author

Name: Peruri Pavan kumar

Phone: 9908148124

Email: peruri72@gmail.com

eISSN: 2583-0953

DOI: <https://doi.org/10.26452/ijcpms.v1i1.178>

Production and Hosted by

Pharmasprings.com

© 2021 | All rights reserved.

INTRODUCTION

Carcinoma is a fatal disease which is bring about due to unrestricted proliferation of the cells that leads to the formation of extra mass tissue known as a tumor. Malignancies cells can also spread through in the bloodstream and lymph nodes [1]. Some of the tumors does not expand throughout the body but grow uncontrollably like benign tumor [2]. The normal cells control the cell cycle regulation [3]. In

some cases, normal cells affected by risk exposures mainly chronic viruses like hep-B and C, Epstein Barr Virus (EBV), and Human papillomaviruses (HPV), a mutation in the p53 gene increase the high risk of malignancies [4]. Malignancies are majorly classified as three types Carcinomas Lymphomas Sarcomas [5]. These malignancies were treated with using various intravenous neoplastic agents by individual or by combination, and as adjunctive with radiation therapy or surgery are make use of extensively in the management of a diversity of carcinomas [6]. At present chemotherapeutic agents have a part in the clinical trials like primary treatment for advanced medical conditions and localized malignancies [7]. Numerous restoring tissues own excessive growing capacity rivaling dangerous, this kind of tissues like bone marrow cells, sebaceous follicles, the GI tract mucosa, and on expose to chemotherapy persist the determined noxious effects due to chemotherapeutic agents [8]. So these toxicities minimized by adjusting the dosage using Body mass

surface (BSA mg/m²) [9]. Frequent noxious effects included are myelosuppression, GI tract, sebaceous follicle toxicity, neurotoxicity, local effects, hepatic & cardio-vascular toxicity, gonadal toxicity, nephrotoxicity etc. [10]. This review offers a general outlook of the noxious effects of neoplastic drugs and their managing options or treatment. It helps to select the appropriate treatment and lessen the intensity and potency of toxicities by the clinicians that reduce the financial burden rely on patients.

Hematological Toxicity

Myelosuppression complications frequently were seen in patients treated with chemotherapeutic agents [11]. Chemotherapeutic agents may destroy the action of rapid growing blood cells, resulting the retardation of formed elements and prevalence of dangerous hemorrhage risk & blood borne infections [12]. Chemotherapeutic drugs resulting hematological toxic effects are mentioned in Table 1.

Management of hematological toxicities

Management varies from dose reduction if in case persistent myelosuppression occurs than changing to the regimen. Patients who had to develop grade-IV toxicity require hospitalization, treatment of infection, or bleeding manifestation. CSF factors such as erythropoietin, Granulocyte-Colony stimulating factor, Granulocyte Macrophage-Colony stimulating factor, Darbopoietin alpha, and various cytokines, etc are helpful in treating the condition of myelosuppression [13].

Anemia

Anemia is the frequent and tenacious blood disorder in carcinoma patients. According to the National Cancer Institute (NCI), Anemia scale was classified as Grade 0, 1, 2, 3, 4, 5 depending on the seriousness level [14]. Chemo drugs causing anemia listed in Table 2.

Management

1. Blood transfusion
2. Recombinant human erythropoietin, darbepoetin alfa and epoetin alfa & beta
3. Identifying and resolving underlying causes.

Neutropenia

Chemotherapeutic agents induced neutropenia is a life threatening toxicity and listed in Table 3. Neutropenia is nothing but reduced neutrophil cells. Absolute neutrophil count (ANC) <1500 cells/mm³ and can be graded based on the severity as [15].

1. Mild or acute

2. Moderate
3. Sever (<500cells/mm³)

Management

Mild neutropenia should be given with antibiotics listed in Table 4 and severe neutropenia (>20% risk) should be managed with the transfusion of colony stimulating factors such as G-CSF and GM-CSF [16]. The recommended dosage of G-CSF is 5 mcg/kg/day, and for GM-CSF, 250 mcg/m²/day administered through the subcutaneous or intravenous route along with the antibiotic drug regimen [17].

Thrombocytopenia

Thrombocytopenia can be caused by myelosuppressive due to different types of cancer treatment agents listed in Table 5. In adequate chances of bleeding, platelets or thrombocyte cell count falls below the level of 50,000cells/mm³ and if the platelet count would be less than 20,000cells/mm³ considered as severe [18].

Management

Initial and middle stage of thrombocytopenia is treated by the blood platelet transfusion at the rate of 4 to 6 units if a random donor and 1 unit in individual donor aphaeresis [19].

Gastrointestinal toxicities

GI toxicity is also one of the commonly a raised obstacle of cancer therapy that can lead to the different kind of unwanted effects like diarrhea, constipation, nausea & vomiting, weight loss, pain, and infections causing remarkably trouble to the patients' improvement due to dose adjustments and interrupting the therapy [20].

Oral mucositis

Among the frequent toxicities of chemotherapeutic agents, induced oral mucositis is listed in Table 6 [21] and characterized by the infiltration of inflammatory cells leading to epithelial disruption and ulceration. Habitually the oral mucositis occurs within 4-7 days following the administration of a elevated dose regimen and subsided 2-4 weeks following the treatment is succeeded [22]. Oral mucositis severity is graded into Grade 1,2,3,4,5 based on the seriousness according to the using National Cancer Institute CTCAE [23].

Management

Oral mucositis was managed by reducing the dose of certain chemotherapeutic agents, it maintains dental hygiene and early detection mandatory [24]. During chemotherapy, saprophytic bacteria, these

Table 1: Drugs induced bone marrow depression

High risk	Moderate risk	Mild risk	Lower risk
Carbolpatin	Dactinomycin	Vinblastine	Doxorubicin
Chlorambucil	Mitomycin	Melphelan	Gemcitabine
Oxaliplatin	Procarbazine	Oxaliplatin	Daunorubicin
Cyclophosphamide	Fludarabine	Idarubicin	Paclitaxel
Cytarabine	Mustine	Irinotecan	Hydroxyurea
Vinorelbine	Topotecan	Rituximab	
Ifosamide	Mitoxantrone	Transtuzumab	

Table 2: Chemotherapeutic agents induced anemia

High risk	Moderate risk	Lower risk
Cisplatin	Altretamine	Topotecan
Docetaxel	Cytarabine	Paclitaxel

Table 3: Chemotherapeutic agents induced neutropenia

S.NO	Agents
1.	Alkylating agents
2.	Anthracyclines
3.	Antimetabolites
4.	Camptothecins
5.	Epipodophyllotoxins
6.	Hydroxyurea
7.	Taxanes

Table 4: Broad spectrum antibiotics management of neutropenia

S.NO	Antibiotic	Route of Administration	Dose	Frequency
1.	Amoxicillin/clavulanate	PO	500/125mg	q8hrly
2.	Cefepime	IV	2g	q8hrly
3.	Ceftazidime	IV	2g	q8hrly
4.	Ciprofloxacin	IV/PO	400mg/750mg(PO)	q8-12hrly
5.	Clindamycin	PO	600mg	q8hrly
6.	Gentamycin or tobramycin	IV(if Crcl>60ml/min)	6-7mg/kg	q24hrly
7.	Imipenem	IV	500mg	q6hrly
8.	Meropenem	IV	1gm	q8hrly
9.	Piperacillin/Tazobactam	IV	4.5mg	q6hrly
10.	Ticarcillin/clavulanate	IV	3.1gm	q4-6hrly
11.	Vancomycin	IV	25mg/kg loading dose , f/b 15mg/kg	q12hrly
12.	Metronidazole	IV	500mg	q12hrly

Table 5: Chemotherapeutic agents induced thrombocytopenia

S.NO	Agents
1.	Dacarbazine
2.	Carboplatin
3.	5-fluorouracil
4.	Lomustine
5.	Mitomycin
6.	Thiotepa

Table 6: Chemotherapeutic agents induced Oral mucositis

Alkylating agents	Athracyclines	Antimetabolites
Busulfan, procarbazine Cyclophosphamide, Thiotepa	Doxorubicin Epirubicin daunorubin	5-Fluorouracil, Hydroxyurea Methotrexate
Antitumor antibiotics Actinomycin D Mitomycin	Taxanes Paclitaxel	Vinca alkaloids Vinblastin Vincristine

Table 7: Risk of emesis with chemotherapeutic agents

Emetic Risk	Chemotherapeutic agents
High	Cisplatin, Streptozotocin, Dacarbazine, Carmustine, Dactinomycin Cyclophosphamide Mechlorethamine.
Moderate risk (30 to 90%)	Oxaliplatin, Cytarabine (> 1000 mg/m ²), Carboplatin, Ifosfamide, Doxorubicin, Daunorubicin, Epirubicin, Idarubicin, Irinotecan.
Low risk (10% to 30%)	Paclitaxel, Docetaxel, Mitoxantrone, Topotecan, Etoposide, cetuximab, Pemetrexed, Methotrexate, Mitomycin, Gemcitabine.
Minimal risk	Bevacizumab, Bleomycin, Busulfan, Fludarabine, Vincristine, Vinorelbine, Vinblastine, 2-Chlorodeoxyadenosine, Rituximab.

Table 8: Neurotoxicity inducing chemotherapeutic drugs

Acute myelopathy	Encephalopathy	Cranial nerve toxicity
Intrathecal administration of: cytarabine methotrexate thiotepa	Carmustine Cisplatin Ifosamide	Carmustine Vinblastine Cisplatin Vincristine
Autonomic neuropathy Vindesine Paclitaxel Vinblastine Procarbazine Cisplatin	Cerebellar syndrome 5-Fluorouracil Oxaliplatin Cytarabine	Peripheral Neuropathy Vincristine Carboplatin Vindesine Procarbazine Oxaliplatin Paclitaxel

Table 9: Chemotherapeutic agents induced peripheral Neuropathy Toxicities WHO scale Grading

Gading Scale	Description
Grade 0	-
Grade 1	Paraesthesia- tingling/ pricking sensation
Grade 2	Progression of grade 1 condition, weakness
Grade 3	Progression of grade 2 condition, numbness, unbearable weakness.
Grade 4	Paralyzing of body

Table 10: Management of chemotherapeutic agents induced peripheral neuropathy

Drug	Dosage
Anti depressants	Amitriptyline 10mg daily with dose. Venlafaxine 50mg 1hr before to Oxaliplatin infusion.
Antiepileptic	Gabapentin 300 mg. Lamotrigine 25 mg at bed time
Topical	Baclofen + Amitriptyline and Ketamine gel Amitriptyline and Ketamone Cream

Table 11: Drugs Induced Pulmonary Toxicities

S.NO	Agents
1.	Procarbazine
2.	Azathioprine
3.	Bleomycin
4.	Methotrexate
5.	Vinca alkaloids
6.	Methotrexate
7.	Procarbazine
8.	Carmustine
9.	Mitomycin
10.	Cyclophosphamide

Table 12: Drugs induced cardiac Toxicities

S. NO	Agent
1.	Cyclophosphamide
2.	Ifosfamide
3.	5- fluorouracil
4.	Paclitaxel
5.	Carmustine
6.	Docetaxel
7.	Epirubicin

Table 13: Chemotherapeutic agents induced Renal Toxicities agents

Alkylating & Platinating agents	Antimetabolites	Miscellaneous
Chlorethyl nitrosoureas	Azacitidine	Diaziquone
Carmustine	Gemcitabine	Interferon -Alpha
Semustine	Methotrexate	Mitomycin
Cisplatin	Pentostatin	
Carboplatin		
Ifosfamide		

Table 14: Causes of Hemorrhagic cystitis Agents

S. NO	Agents
1.	Ifosfamide
2.	Cyclophosphamide
3.	Busulphan
4.	Thiotepa
5.	Temozolomide
6.	9-Nitrocampthothecin

type of infections should resolved by the administration of penicillin in combination with metronidazole, is an appropriate oral mucositis treatment. Secondary oral mucositis infection should be managed with anti fungal therapy either topical or systemic drug therapy, antifungal treatment for oral candidiasis, included fluconazole with the dose of 100 mg/day, or ketoconazole with the dose of 200 mg/day. If in case the infection resistance to the above drugs, the use of itraconazole with the dose of 200-400 mg/day is highly recommended [24].

Nausea & Vomiting

Nausea & vomiting are the commonest toxicities that occur by receiving chemotherapeutic agents listed in Table 7 [25]. Pathophysiology of CINV Cytotoxic agents can damage the GI tract initially, principal neurotransmitter (substance P) involved in delayed CINV. Anti cancer drugs triggers the principal neurotransmitter release that bind to NK-1 receptors that results in nausea and vomiting [26]. CINV is predominantly classified as [27].

1. Acute
2. Delayed
3. Anticipatory
4. Breakthrough/refractory

CINV Management

Nausea and Vomiting were managed by reducing the dose of certain chemotherapeutic agents, or by utilizing the antiemetic drugs. Dopamine receptor antagonists like Prochlorperazine and chlorpromazine which are frequently consumed antiemetic drugs given as dose of 5 to 10 mg TID / day or QID / day orally to a maximum of 40 mg/ day through intramuscular route and dose of 10 to 25 mg every 4 to 6 hours through oral route respectively [28]. One more class of drugs Selective 5HT₃ receptor antagonists drugs like ondansetron and granisetron are also recommended with dose of ondansetron is 4–8 mg given OD/BD/day and granisetron, 200 mg once a day orally [29].

Nervous System Toxicity

Chemotherapeutic agents induced peripheral neuropathy is one of the most persistent toxicities caused by anti-neoplastic listed in Table 8 [30, 31] and WHO grading scale mentioned in Table 9. The management of peripheral neuropathy listed in Table 10 [32, 33].

Pulmonary Toxicities

Chemotherapeutic agents may effects either of epithelial or endothelial cells of the lung tissue as unmediated or secondarily [34] and drugs for reason was listed in Table 11 [35].

Clinical manifestations of this toxicity includes the effects like lung fibrosis, non-cardiogenic pneumonitis and edema of lung etc. Numerous patients have characteristics of clinical features and pathological findings related to greater than one kind of toxicity. Anti cancer drugs which resulting the pulmonary toxicities are given.

Management of pulmonary fibrosis

Bleomycin induced pulmonary fibrosis, they initially treated by using prednisone at 0.75 to 1 mg/kg. Followed by 4 - 8 weeks, the dose would be tapered unceasingly over a supplementary of 4 - 6 months, following the patient's clinical state and response [36].

Cardiac toxicities

Cardiomyopathy is the most frequent Chemotherapeutic Agents induced cardiac toxicity that causes epigenetic changes resulting abnormal cell signaling that finally leads to CV dysfunction, cardiomyocyte apoptosis and cardiomyopathy and so on [37] and the agents listed in Table 12.

Management of cardiac toxicities

The initial plan of action for the management cardiac toxicity is through the early detection of the condition and rather immediate treatment with ACE inhibitors like enalapril 2.5–20 mg per day and or Beta blocker carvedilol 12.5–50 mg per day and also using anti-oxidants like Probuco and vitamin E will benefit [38].

Renal Toxicities

Chemotherapeutic agents-induced nephrotoxicity is the crucial object of morbidity and mortality among cancer victims listed in Table 13 [39]. Chemotherapy damages the structures and blood vessels of kidney resulting the toxic effect due to their active metabolites [40].

Management of Renal Toxicities

Chemotherapy induced renal toxicities are managed by Thiophosphate Cytoprotectants like Amifostine and monitor the creatinine clearance frequently [41].

Urinary Tract Toxicity

Chemotherapeutic agents induced urinary bladder hemorrhagic cystitis it ranges from renal tubular damage by cisplatin and ifosfamide (Table 14) [42] pathogenesis of this toxicity was followed by the formation of active metabolite of chemotherapeutic drug, that too main element was acrolein. Acrolein was a urotoxic metabolite that acts on the urinary bladder epithelial layer it leads to hemorrhagic cystitis [43].

Management of Hemorrhagic cystitis

Management of hemorrhagic cystitis using Acrolein conjugator, MESNA and the use of MESNA and hydration therapy considerably lessen the risk of bladder toxicity with Ifosamide or Cyclophosphamide and if it is severe, cystectomy is recommended. While radiation induced hemorrhagic cystitis treated with aminocaproic acid and prostaglandin and if it is severe, surgery is recommended [42].

CONCLUSION

Even though many advance treatment choices are accessible to treat carcinoma, the toxic effects of cytotoxic drugs worsen the effectiveness of treatment. Rapidly proliferating tissue sites are the main sites affected with toxicities such as Bone marrow, GI tract and sebaceous follicles. In addition to the effective treatment, the management of toxicities should also be focused because they not only effect the patient treatment but also the quality of life. Finally, there is a need to improve tolerability and reduce sequelae. It is an essential need for more discoveries of newer chemotherapeutic drugs which combat these general toxicities and improves patient's wellbeing.

Funding Support

The authors declare that they have no funding support for this study.

Conflict of Interest

The authors declare that there is no conflict of interest.

REFERENCES

- [1] Sunny Y. Wong and Richard O. Hynes. Lymphatic or Hematogenous Dissemination: How Does a Metastatic Tumor Cell Decide? *Cell Cycle*, 5(8):812–817, 2006.
- [2] Ashima Bali, Mohit Pal Singh, Padmavathi P, Manisha Khorate, and Junaid Ahmed. Malignant Fibrous Histiocytoma - An Unusual Transformation from Benign to Malignant. *Journal of Cancer Science & Therapy*, 02(02):53–57, 2010.
- [3] Michael B. Kastan and Jiri Bartek. Cell-cycle checkpoints and cancer. *Nature*, 432(7015):316–323, 2004.
- [4] W C Mcbee, A S Gardiner, R P Edwards, J L Lesnock, and R Bhargava. MicroRNA analysis in human papillomavirus (HPV)-associated cervical neoplasia and cancer. *J Carcinogene Mutagene*, 1(1), 2011.
- [5] Cancer Prevention Guide. Cancer Classifications Lymphoma, Carcinoma, Sarcoma and Leukemia, 2020. Accessed on: 25 Jan 2021.
- [6] Isabelle Ray-Coquard, Claire Cropet, Martine Van Glabbeke, Catherine Sebban, Axel Le Cesne, Ian Judson, Olivier Tredan, Jaap Verweij, Pierre Biron, Inthidar Labidi, Jean-Paul Guastalla, Thomas Bachelot, David Perol, Sylvie Chabaud, Pancras C.W. Hogendoorn, Philippe Cassier, Armelle Dufresne, and Jean-Yves Blay. Lymphopenia as a Prognostic Factor for Overall Survival in Advanced Carcinomas, Sarcomas, and Lymphomas. *Cancer Research*, 69(13):5383–5391, 2009.
- [7] Vincent T. DeVita Jr., Samuel Hellman, and Steven A Rosenberg. Cancer: Principles and Practice of Oncology. 6th edition, Lippincott Williams and Wilkins, ISBN: 9780781728072.
- [8] H P Rang, M M Dale, J M Ritter, and P K Moore. Text book of Pharmacology. UK: Churchill Livingstone.
- [9] S. A. Kaestner and G. J. Sewell. Chemotherapy Dosing Part I: Scientific Basis for Current Practice and Use of Body Surface Area. *Clinical Oncology*, 19(1):23–37, 2007.
- [10] N Srivastava, A Majumder, and S Rastogi. Adverse Drug Reactions of Anti-Cancer Drugs and its Management: A Review. *International Journal of Advanced Research in Medicinal Chemistry*, 1(1):19–27, 2019.

- [11] David C. Bodensteiner and Gary C. Doolittle. Adverse Haematological Complications of Anticancer Drugs. *Drug Safety*, 8(3):213–224, 1993.
- [12] S. Gupta, R. Tannous, and M. Fridman. Incidence of anemia in CHOP-treated intermediate-grade non-Hodgkin's lymphoma (IGNHL). *European Journal of Cancer*, 37:S94, 2001.
- [13] D C Dale. Colony-stimulating factors for the management of neutropenia in cancer patients. *Drugs*, 62(1):1–5, 2002.
- [14] NCCN. Clinical Practice Guidelines in Oncology. Cancer and Chemotherapy Induced Anemia, 2018. National Comprehensive Cancer Network. Version 2, Accessed on: 25 Jan 2021.
- [15] L S Schwartzberg. Neutropenia: etiology and pathogenesis. *Clinical cornerstone*, 8:5–11, 2006.
- [16] D C Dale. How I diagnose and treat neutropenia. *Current opinion in hematology*, 23(1):1, 2016.
- [17] L Risk. Empiric treatment of febrile neutropenia. *Cancer*, 71(11):3640–3646, 1993.
- [18] S Jayachandran, Khushboo Singh, and L Kayal. Idiopathic thrombocytopenic purpura. *Contemporary Clinical Dentistry*, 5(3):410, 2014.
- [19] RajeshChand Arya, G S Wander, and Pankaj Gupta. Blood component therapy: Which, when and how much. *Journal of Anaesthesiology Clinical Pharmacology*, 27(2):278, 2011.
- [20] S Boussios, G Pentheroudakis, K Katsanos, and N Pavlidis. Systemic treatment-induced gastrointestinal toxicity: incidence, clinical presentation and management. *Annals of gastroenterology*, 25(2):106, 2012.
- [21] Maddireddy Umameshwar Rao Naidu, Gogula Venkat Ramana, Pingali Usha Rani, Iyyapu Krishna Mohan, Avula Suman, and Priyadarshni Roy. Chemotherapy-Induced and/or Radiation Therapy-Induced Oral Mucositis-Complicating the Treatment of Cancer. *Neoplasia*, 6(5):423–431, 2004.
- [22] Athanasios Pouloupoulos, Petros Papadopoulos, and Dimitrios Andreadis. Chemotherapy: oral side effects and dental interventions. A review of the literature. *Stomatological Disease and Science*, 1(2):2573–2575, 2017.
- [23] NCI. Common Terminology Criteria for Adverse Events (CTCAE) Version 3.0 , 2020. National Cancer Institute, Accessed on: 25 Jan 2021.
- [24] D D Mosel, R L Bauer, D P Lynch, and S T Hwang. Oral complications in the treatment of cancer patients. *Oral Diseases*, 17(6):550–559, 2011.
- [25] K Feeny, M Cain, and A Nowak. Chemotherapy induced nausea and vomiting. Prevention and treatment. *Australian Family Physician*, 36(9):2–5, 2007.
- [26] Matti Aapro. CINV: still troubling patients after all these years. *Supportive Care in Cancer*, 26(1):5–9, 2018.
- [27] T Chang. Nausea and Vomiting. pages 159–175, 2015. In *Supportive Care in Pediatric Oncology*, Springer, Berlin, Heidelberg.
- [28] Stephen J Peroutka and Solomon H Snyder. Antiemetics: Neurotransmitter Receptor Binding Predicts Therapeutic Actions. *The Lancet*, 319(8273):658–659, 1982.
- [29] William D. Figg, George E. Dukes, J. Fred Pritchard, David J. Hermann, Henry R. Lesesne, Stanley W. Carson, Stephen S. Songer, J. Robert Powell, and Lawrence J. Hak. Pharmacokinetics of Ondansetron in Patients with Hepatic Insufficiency. *The Journal of Clinical Pharmacology*, 36(3):206–215, 1996.
- [30] W. Grisold, G. Cavaletti, and A. J. Windebank. Peripheral neuropathies from chemotherapeutics and targeted agents: diagnosis, treatment, and prevention. *Neuro-Oncology*, 14(Suppl_4):iv45–iv54, 2012.
- [31] Jacqueline B. Stone and Lisa M. DeAngelis. Cancer-treatment-induced neurotoxicity—focus on newer treatments. *Nature Reviews Clinical Oncology*, 13(2):92–105, 2016.
- [32] A. B. Miller, B. Hoogstraten, M. Staquet, and A. Winkler. Reporting results of cancer treatment. *Cancer*, 47(1):207–214, 1981.
- [33] M S Trivedi, D L Hershman, and K D Crew. Management of chemotherapy-induced peripheral neuropathy. *American Journal of Hematology/Oncology®*, 11(1), 2015.
- [34] M S Wilson and T A Wynn. Pulmonary fibrosis: pathogenesis, etiology and regulation. *Mucosal Immunology*, 2(2):103–121, 2009.
- [35] Anna M Sadowska, Pol Specenier, Paul Geronpre, and Marc Peeters. Antineoplastic therapy-induced pulmonary toxicity. *Expert Review of Anticancer Therapy*, 13(8):997–1006, 2013.
- [36] Dorothy A. White and Diane E. Stover. Severe Bleomycin-Induced Pneumonitis. *Chest*, 86(5):723–728, 1984.
- [37] D K Shakir and K I Rasul. Chemotherapy induced cardiomyopathy: pathogenesis, mon-

- itoring and management. *Journal of clinical medicine research*, 1(1):8, 2009.
- [38] Brent Reed and Carla Sueta. A Practical Guide for the Treatment of Symptomatic Heart Failure with Reduced Ejection Fraction (HFrEF). *Current Cardiology Reviews*, 11(1):23–32, 2014.
- [39] Fatemeh Ghane Sharbaf, Hamid Farhangi, and Farahnak Assadi. Prevention of chemotherapy-induced nephrotoxicity in children with cancer. *International Journal of Preventive Medicine*, 8:76, 2017.
- [40] M. Kleber, M. Cybulla, K. Bauchmüller, G. Ihorst, B. Koch, and M. Engelhardt. Monitoring of renal function in cancer patients: an ongoing challenge for clinical practice. *Annals of Oncology*, 18(5):950–958, 2007.
- [41] Valeria Santini. Amifostine: chemotherapeutic and radiotherapeutic protective effects. *Expert Opinion on Pharmacotherapy*, 2(3):479–489, 2001.
- [42] Lalgudi N Dorairajan, R Manikandan, and Santosh Kumar. Hemorrhagic cystitis: A challenge to the urologist. *Indian Journal of Urology*, 26(2):159, 2010.
- [43] Bhavana Ravindra Doshi, Vijaya Veeranna Sajjan, and B S Manjunathswamy. Managing a side effect: Cyclophosphamide-induced hemorrhagic cystitis. *Indian Journal of Drugs in Dermatology*, 5(1):66, 2019.

Copyright: This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

Cite this article: Peruri Pavan kumar, Dinesh Kumar Kukunuri, Palla Neelima. A Review on chemotherapy induced toxicities: Challenges in their management. *Int. J. of Clin. Pharm. Med. Sci.* 2021; 1(1): 1-9.

© 2021 Pharma Springs Publication.