International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2020): 7.803

Treatment and Strategy Plan for Chemotherapy: A Review

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Abstract: ***Chemotherapy uses anticancer drugs to stop rapidly developing cancerous cells. In the advanced stages of cancer, this form of therapy may be utilized to cure and try a patient to create palliative relief and symptomatic relaxation. Chemotherapy is often administered in a cyclic manner. Patients are given anticancer medication on a weekly or biweekly basis. After completing a certain cycle session, therapy is halted for a set length of time to allow the patient to rest for their body to recover from the harmful effects of anticancer drugs. In general, six or more chemotherapeutic cycles are required in cancer patients, and combination chemotherapy is typically preferable. Anticancer drugs are used to eliminate not just cancer cells but also normal cells that grow under normal conditions, such as those in the digestive system, bone marrow, and hair follicles. Traditional treatments, such as radiation, surgery, or other cytotoxic drugs, are always favoured over combination chemotherapy. Each treatment has a unique mode of action for suppressing cell division and proliferation in quickly developing cells. Each therapy has its specific set of adverse effects. There are several cancer treatment strategies available, depending on the severity and stage of the disease, the type of cancer, and the affected body parts. The study discusses various techniques that combine chemotherapy with other treatment strategies that have been investigated in order to increase treatment selectivity, minimize recurrence, and improve patient quality of life.***

Keywords: Chemotherapy; Radiotherapy; Dose - Dense Chemotherapy, Cancer immunotherapy; Cell proliferation; Hyperthermia

1. Introduction

Chemotherapy is the use of chemicals to suppress malignant cells or infectious agents of a disease, such as microorganisms, without significantly harming host cells (1). As a result, the treatment may be generally classified into two types: cancer chemotherapy and antimicrobial chemotherapy. These medicines vary from the others in that they are typically intended to kill or suppress the target organism while having no or minimal effect on host cells (2). Previously, it was thought that chemotherapy drugs were restricted to synthetic compounds; however, many more natural compounds are currently being promoted as possible chemotherapeutic agents or antibiotics. The current situation necessitates the inclusion of both synthetically and naturally or microbiologically produced drugs. All anticancer medicines used in conventional chemotherapy are cytotoxic to both cancer and normal cells (3). As a result, chemotherapy destroys cells that proliferate rapidly under normal conditions, such as those in the digestive system, bone marrow, and hair follicles. The following are the most common adverse effects seen after chemotherapy treatment: Mucositis (inflammation of the digestive system lining) alopecia (hair loss) and myelosuppression (decreased production of blood cells, hence also immunosuppression) (4). The majority of monoclonal antibodies are not indiscriminately toxic and work by targeting proteins that are overexpressed in cancer cells and are required for cell growth (5). This type of treatment, known as targeted therapy (in contrast to traditional chemotherapy), is always given in conjunction with traditional chemotherapeutic drugs in a cancer treatment regimen. Furthermore, in addition to combination and targeted chemotherapy, certain modern strategies, notably the utilization of light (phototherapy) and heat (hyperthermia), have been studied. Photochemotherapy or photodynamic treatment are terms used to describe various strategies in which medicines are transformed to cytotoxic agents only when exposed to light (6).

2. Treatment Strategies

Many techniques for administering chemotherapy medicines have now been developed. Chemotherapeutic medicines can be used to either cure or prolong life.

a) Combined chemotherapy is a form of cancer treatment approach in which more than one type of therapy, such as radiation therapy, surgery, and/or hyperthermia, can be used at the same time. Induction chemotherapy, on the other hand, is used to treat cancer for the first time with an anticancer medication (7) .
b) Consolidation chemotherapy is typically administered following remission to extend the disease - free duration and enhance overall survival (8) .
c) Intensification chemotherapy is the same as consolidation treatment, however it uses a different medication than induction therapy.
d) Various drugs in combination with chemotherapy have different mechanisms of action and adverse effects. The most significant advantage of combination chemotherapy is that it reduces the likelihood of developing resistance to any of the drugs. In addition, the medicines can be taken at lower doses with fewer side effects and toxicity
e) Neoadjuvant chemotherapy is used before a local treatment like surgery to reduce the main tumour (9) . It

is also used to describe a situation in which there is a high risk of micro metastatic disease.

f) This therapy (Neoadjuvant chemotherapy) can be utilized when there is a low likelihood of cancer present and a risk of recurrence. It is also advantageous to eliminate malignant cells that have spread to other parts of the body (10) .

g) Maintenance chemotherapy is used to prolong remission by administering a lowdose on a regular basis.

h) Salvage chemotherapy is helpful for basically reducing tumour burden and increasing life expectancy (11) . (**Table 1).**

Table 1: Common combination chemotherapeutic regimen [1]

Cancer Type	Drugs
Hodgkin's Disease	Mustine, Vincristine, Procarbazine, Prednisolone
	Doxorubicine, Bleomycine, Vinblastine, Dacarbazine
Bladder Cancer	Epirubicine, Cisplatin, 5 - Fluorouracil
	Methotraxate, Vincristine, Doxorubicine, Cisplatin
Germ Cell Tumour	Bleomycin, Etopside, Cisplatin
Stomach Cancer	Epirubicine, Capecetabine, Cisplatin
Breast Cancer	Cyclophsphamide, Methotraxate, 5 – Fluorouracil
	Doxorubicine, Cyclophsphamide
Non - Hodgkin's Lymphoma	Cyclophsphamide, Doxorubicine, Vincristine, Prednisolone
Lung Cancer	Cyclophsphamide, Doxorubicine, Vincristine
Colorectal Cancer	5 - Fluorouracil, Folonic acid, Oxaliplatin

All of the chemotherapy regimens listed above are administered to patients who may be able to resist the treatment. A patient's performance status is always utilized as a measure to determine if the chemotherapy can be continued or whether a dosage adjustment is required. Because each treatment results in less cell death in the tumour, dosage repetitions are necessary to reduce the tumour's growth. Current chemotherapy regimens are used to treat patients in a cyclic manner, with the duration and frequency of treatments limited by patient toxicity (12).

Cytotoxic agents and targeted therapy

Targeted treatments are a relatively recent method of cancer treatment that has considerably overcome many of the issues observed with standard anticancer medicines (13). The cytotoxic agent that targets non - specific cells is responsible for the high toxicity reported with the administration of anticancer medicines. They can inhibit or kill whatever growing or developing cell, tumour, or normal. Targeted treatments work directly on cellular proteins, which are responsible for abnormal cell growth (14). This demonstrates the necessity for a high dosage to cancer cells with relatively low exposure to other normal cells. Different types of cancer can be treated with specific proteins or even on a specific basis through targeted treatments. Furthermore, as compared to standard anticancer medicines, the reported adverse effects are relatively low. Initially, it was thought that target treatments would only be selected for one protein. However, it is now well established that a single medication may bind to a specific range of protein targets (15). A protein generated by the Philadelphia chromosome, a genetic lesion common in chronic myelomonocytic leukemia, provides an example of a target for targeted treatment. Imatinib, a small molecule drug, can decrease the enzyme activity of this fusion protein (16).

Chemotherapy Treatment Strategy Using Hyperthermia

The lack of selectivity in standard chemotherapy is a key disadvantage, resulting in a variety of adverse effects such as alopecia (hair loss), a blood disorder, tiredness, nausea, and vomiting. As a result, there is a need to investigate new therapeutic strategies in which heat (Hyperthermia) is used in combination with other chemotherapies to increase treatment selectivity, reduce recurrence, and improve patient quality of life. It has been observed that surgical removal of solid tumours generally fails to achieve entire remission, and so a combined therapy with anticancer medicines, radiation, hyperthermia, targeted therapy, and so on is needed. One new strategy that may achieve these goals is to combine hyperthermia with other forms of chemotherapy. A fractionated or continuous dose is administered to the target site throughout the hyperthermia process, which might improve the tumour's susceptibility to chemotherapy, radiation, immunotherapy, and immune - based therapies (17). However, this new approach, in which hyperthermia (heat applied only to the tumour site) was successfully combined with other chemotherapeutics, has renewed interest in the field of modern chemotherapy. The primary goal of hyperthermia is to increase tumour cell sensitivity to therapeutic agents and facilitate drug release from thermoresponsive nanocarriers (usually below 43°C, referred to as mild hyperthermia) Alternatively, at higher temperatures, inducing necrosis directly (over 43°C, referred to as thermal ablation) (18). Furthermore, between 42 - 45°C, cancer cells are more susceptible to a thermal environment than normal tissues, with a directly proportional link between tissue death and temperature or exposure duration. Hyperthermia's mechanism of action is accompanied by numerous ways where the cells or tissues lead to increased antitumor response. Hyperthermia, in general, inhibits cell activities, increases permeability and fluidity, disrupts the stability and structure of the cell membrane, and affects transmembrane transport proteins and cell surface receptors (19). The transfer of heat away from tumour cells is directly proportional to the rate and volume of tumour perfusion (20), and the mechanism is more effective in malignant tissue than in healthy tissue (21), suggesting that hyperthermia is selective. However, the major effects of hyperthermia are thought to be on protein, which denatures and precipitates at temperatures over 40°C. Although the effects on lipids are generally reversible, the effect on DNA, when a double - strand break occurs and an effect is generated, is significant and irreversible. This essentially affects many cellular activities such as cell cycle arrest, replication, and DNA synthesis, as well as altering protein synthesis, resulting in cell proliferation and death suppression (22) (23). Oncologists can utilize a variety of different techniques to regulate chemotherapy.

Targeted Therapy

Targeted treatments are those that specifically target a protein or other molecules, and they offer the advantage of minimizing chemo adverse effects.

Hormone Therapy
Hormone receptor activation changes the way a gene is expressed. That is, these receptors change the way the gene functions, frequently promoting cell development. Extra hormone receptors are seen in hormone - sensitive cancer cells (24) .

Dose - Dense Chemotherapy
In chemotherapy, dose intensity is calculated as the total dose received by a given patient per unit of time. It is possible to increase the intensity by increasing the dose per cycle or decreasing the interval between cycles, which is known as dose density. Dose - dense chemotherapy refers to treatments that are planned to take place close together. If traditional chemotherapy treatments are administered every three weeks, the dose - dense regimen may be administered every two weeks. Dose - dense chemotherapy does not appear to increase adverse effects and appears to be the most effective in higher - risk individuals with hormone receptor - negative tumours. According to the Gompertzian model, the more benefit that can be expected from dose - dense therapy, the smaller the tumours are and the faster they grow. This approach is utilized for more advanced tumours that are spread (25) (26).

Combined Modality Chemotherapy
Using more than one form of therapy to treat cancer is referred to as a combined modality. The sequential or simultaneous use of several cancer treatment modalities, such as surgery, radiation, and chemotherapy, is known as combined modality therapy. Adjuvant and induction chemotherapy are included in sequential combination modality treatment. Concomitant chemoradiotherapy is the administration of both modalities at the same time, each approach has unique theoretical and practical advantages (27).

Palliative Chemotherapy
Palliative therapy, a distinct medical specialty that is frequently included within the continuum of comprehensive cancer care, is defined as "specialized medical care for people with serious illnesses, focused on providing patients with relief from the symptoms, pain, and stress of a serious illness"—regardless of the diagnosis or prognosis. "The goal is to improve the patient's and family's quality of life. "The American Society of Clinical Oncology (ASCO), the European Society for Medical Oncology, the National Comprehensive Cancer Network (NCCN), and the Society for Surgical Oncology all support palliative care as part of best practice in oncology. Many oncologists feel that including palliative care when a patient is diagnosed with advanced cancer improves patient care and complements their practice (28).

Photodynamic therapy (PDT)
Photodynamic therapy (PDT) is presently being utilized as an alternative treatment for the management of cancer. PDT can be used to treat basal cell carcinoma (BCC) or lung cancer; it can also be utilized to remove traces of malignant tissue following surgical excision of large tumours. It is based on the uptake of a photosensitizer (PS) molecule, which, when activated by light of a certain wavelength, combines with oxygen to produce oxidant species (radicals, singlet oxygen, and triplet species) in target tissues, resulting in cell death. PDT cytotoxicity has recently been established to be related to the oxidation of a wide variety of biomolecules in cells, including nucleic acids, lipids, and proteins, resulting in significant changes in cell signalling cascades or gene expression regulation. It can also be utilized to remove traces of malignant tissue following surgical excision of large tumours (29) (30).

Cancer immunotherapy
Cancer immunotherapy is a new clinical approach that incorporates targeted antibodies, cancer vaccines, adoptive cell transfer, tumour - infecting viruses, checkpoint inhibitors, and cytokines to target and destroy cancer cells. Immunotherapies are regarded as a type of biotherapy since they are generated from living organisms to fight cancer. Many immunotherapy treatments for cancer prevention, management, or treatment can be used in conjunction with surgery, chemotherapy, radiation, or targeted therapies to improve their efficacy. Cancer immunotherapy may not have the same side effects as chemotherapy and radiation, which can vary depending on the procedure performed. Cancer immunotherapy targets the immune system and is frequently more effective than chemotherapy or radiation, chemotherapy and radiation both destroy healthy cells. Frequently resulting in hair loss and nausea/vomiting, adverse effects Immunotherapy may have fewer side effects. Cancer immunotherapy has been utilized successfully in haematological malignancies as well as certain solid tumours. Several new monoclonal antibodies have been developed against cell cycle checkpoint targets, most notably cytotoxic T - lymphocyte - associatedprotein 4CTLA4 and PD1PDL1. As a result, the FDA approved Ipilimumab (against CTLA4), Nivolumab and Pembrolizumab (against PD1), and Atezolizumab, Avelumab, and Durvalumab (against PDL1) as treatment alternatives in certain advanced malignancies. These and other ongoing checkpoint inhibitors, such as novel CTLA4, PD1, and PDL1 inhibitors, are being developed to treat patients with various cancers (31).

3. Conclusion

Because there are so many different types of therapies available to oncologists, this is not a full list of all the chemotherapy techniques available to them. New therapies and new techniques for employing current treatments are being developed as a result of ongoing research. More effective anticancer drugs will probably be developed in the future to improve this therapy method. The method described below, which is based on altering clinically approved drugs, appears to be promising. However, further validation of all of these approaches is still required because authentic strategies also display relevant therapeutic properties under normal conditions and to determine whether it has advantages over the well - established use of chemotherapeutics, some of which are currently in clinical trials.

4. Acknowledgement

The authors are thankful to teaching and non - teaching staff of Department of clinical pharmacy, Poona College of

Pharmacy, Bharati Vidyapeeth (Deemed to be University) Pune (Maharashtra) India.

References

[1] Knoepfler PS. Deconstructing Stem Cell Tumorigenicity: A Roadmap to Safe Regenerative Medicine. Stem Cells Dayt Ohio.2009 May; 27 (5): 1050.
[2] Drusano GL. Antimicrobial pharmacodynamics: critical interactions of "bug and drug. " Nat Rev Microbiol.2004 Apr; 2 (4): 289–300.
[3] Ferrara N, Kerbel RS. Angiogenesis as a therapeutic target. Nature.2005 Dec 15; 438 (7070): 967–74.
[4] Conklin KA. Dietary antioxidants during cancer chemotherapy: impact on chemotherapeutic effectiveness and development of side effects. Nutr Cancer.2000; 37 (1): 1–18.
[5] Wang S, Placzek WJ, Stebbins JL, Mitra S, Noberini R, Koolpe M, et al. Novel targeted system to deliver chemotherapeutic drugs to EphA2 - expressing cancer cells. J Med Chem.2012 Mar 8; 55 (5): 2427–36.
[6] Sanchez - Barcelo EJ, Mediavilla MD. Recent patents on light based therapies: photodynamic therapy, photothermal therapy and photoimmunotherapy. Recent Pat Endocr Metab Immune Drug Discov.2014 Jan; 8 (1): 1–8.
[7] Adam R, Pascal G, Castaing D, Azoulay D, Delvart V, Paule B, et al. Tumor progression while on chemotherapy: a contraindication to liver resection for multiple colorectal metastases? Ann Surg.2004 Dec; 240 (6): 1052–61; discussion 1061 - 1064.
[8] Einhorn LH, Crawford J, Birch R, Omura G, Johnson DH, Greco FA. Cisplatin plus etoposide consolidation following cyclophosphamide, doxorubicin, and vincristine in limited small - cell lung cancer. J Clin Oncol Off J Am Soc Clin Oncol.1988 Mar; 6 (3): 451–6.
[9] Buzdar AU, Singletary SE, Theriault RL, Booser DJ, Valero V, Ibrahim N, et al. Prospective evaluation of paclitaxel versus combination chemotherapy with fluorouracil, doxorubicin, and cyclophosphamide as neoadjuvant therapy in patients with operable breast cancer. J Clin Oncol Off J Am Soc Clin Oncol.1999 Nov; 17 (11): 3412–7.
[10] Peters WA, Liu PY, Barrett RJ, Stock RJ, Monk BJ, Berek JS, et al. Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high - risk early - stage cancer of the cervix. J Clin Oncol Off J Am Soc Clin Oncol.2000 Apr; 18 (8): 1606–13.
[11] Fishman PN, Pond GR, Moore MJ, Oza A, Burkes RL, Siu LL, et al. Natural history and chemotherapy effectiveness for advanced adenocarcinoma of the small bowel: a retrospective review of 113 cases. Am J Clin Oncol.2006 Jun; 29 (3): 225–31.
[12] Green MR, Manikhas GM, Orlov S, Afanasyev B, Makhson AM, Bhar P, et al. Abraxane, a novel Cremophor - free, albumin - bound particle form of paclitaxel for the treatment of advanced non - small - cell lung cancer. Ann Oncol Off J Eur Soc Med Oncol.2006 Aug; 17 (8): 1263–8.
[13] Cho K, Wang X, Nie S, Chen ZG, Shin DM. Therapeutic nanoparticles for drug delivery in cancer. Clin Cancer Res Off J Am Assoc Cancer Res.2008 Mar 1; 14 (5): 1310–6.
[14] Peer D, Karp JM, Hong S, Farokhzad OC, Margalit R, Langer R. Nanocarriers as an Emerging Platform for Cancer Therapy. In: Nano - Enabled Medical Applications. Jenny Stanford Publishing; 2020.
[15] Higueruelo AP, Jubb H, Blundell TL. Protein - protein interactions as druggable targets: recent technological advances. Curr Opin Pharmacol.2013 Oct; 13 (5): 791–6.
[16] Fabian MA, Biggs WH, Treiber DK, Atteridge CE, Azimioara MD, Benedetti MG, et al. A small molecule - kinase interaction map for clinical kinase inhibitors. Nat Biotechnol.2005 Mar; 23 (3): 329–36.
[17] Needham D, Dewhirst MW. The development and testing of a new temperature - sensitive drug delivery system for the treatment of solid tumors. Adv Drug Deliv Rev.2001 Dec 31; 53 (3): 285–305.
[18] Zhang Z, Wang J, Nie X, Wen T, Ji Y, Wu X, et al. Near Infrared Laser - Induced Targeted Cancer Therapy Using Thermoresponsive Polymer Encapsulated Gold Nanorods. J Am Chem Soc.2014 May 21; 136 (20): 7317–26.
[19] Alvarez - Berríos MP, Castillo A, Mendéz J, Soto O, Rinaldi C, Torres - Lugo M. Hyperthermic potentiation of cisplatin by magnetic nanoparticle heaters is correlated with an increase in cell membrane fluidity. Int J Nanomedicine.2013; 8: 1003–13.
[20] Khaled A - RA, Vafai K. The role of porous media in modeling flow and heat transfer in biological tissues. Int J Heat Mass Transf.2003 Dec 1; 46: 4989–5003.
[21] Jori G. Tumour photosensitizers: approaches to enhance the selectivity and efficiency of photodynamic therapy. J Photochem Photobiol B.1996 Nov; 36 (2): 87–93.
[22] Evan GI, Vousden KH. Proliferation, cell cycle and apoptosis in cancer. Nature.2001 May 17; 411 (6835): 342–8.
[23] Clavel CM, Nowak - Sliwinska P, Păunescu E, Dyson PJ. Thermoresponsive fluorinated small - molecule drugs: a new concept for efficient localized chemotherapy. MedChemComm.2015 Dec 3; 6 (12): 2054–62.
[24] Feldman BJ, Feldman D. The development of androgen - independent prostate cancer. Nat Rev Cancer.2001 Oct; 1 (1): 34–45.
[25] Del Mastro L, De Placido S, Bruzzi P, De Laurentiis M, Boni C, Cavazzini G, et al. Fluorouracil and dose - dense chemotherapy in adjuvant treatment of patients with early - stage breast cancer: an open - label, 2 × 2 factorial, randomised phase 3 trial. Lancet Lond Engl.2015 May 9; 385 (9980): 1863–72.
[26] Almeida FK de, Rosa DD. Adjuvant Dose - Dense Chemotherapy for Breast Cancer: Available Evidence and Recent Updates. Breast Care.2018; 13 (6): 447–52.
[27] Vokes EE. Combined modality therapy of solid tumours. The Lancet.1997 May 1; 349: S4–6.
[28] Rangachari D, Smith TJ. Integrating Palliative Care in Oncology: The Oncologist as a Primary Palliative Care Provider. Cancer J Sudbury Mass.2013 Oct; 19 (5): 373.

[29] Brown SB, Brown EA, Walker I. The present and future role of photodynamic therapy in cancer treatment. Lancet Oncol.2004 Aug; 5 (8): 497–508.
[30] Photodynamic therapy in cancer treatment - an update review [Internet]. [cited 2021 Nov 23]. Available from: https: //jcmtjournal. com/article/view/3026
[31] Dhar. Cancer immunotherapy: Recent advances and challenges [Internet]. [cited 2021 Nov 23]. Available from: https: //www.cancerjournal. net/article. asp?issn=0973 - 1482; year=2021; volume=17; issue=4; spage=834; epage=844; aulast=Dhar

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