

## **Treatment Related Adverse Events in Chemotherapy and Their Intervention**

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Received: October 23, 2021

Published: November 23, 2021

### **Abstract**

**Objective:** Patient who are receiving chemotherapy are highly complaining from adverse effects. These adverse effects are common in general and some of them may be related to the type of chemotherapy. Drugs as ant metabolic will not differentiate between cancerous cells and normal cells of body. That is why adverse effects are common. Now there are a lot of intervention to fight these adverse effects according to its nature may be pharmacological or even non pharmacological.

**Method:** A systemic electronic literature search of 5 data bases: web of science, Scopus, google scholar, EMBASE/EXCERPTA medica and pumped.

**Results:** 51 studies include in this review with emphasis on unwanted effect of chemotherapy and possible overcome solution to each effect.

**Conclusion:** Chemotherapy is a weapon with double-edged. If we do not know how to use it then it will Herat us. The chemotherapy is also a boondocks without it, the simple disease can kill us as in the past, so what we should do with this boondock is using it in right way to get the benefit and avoid the harm.

### **Introduction**

Chemotherapy is the process of using chemicals to kill microorganisms or prevent their multiplication. These compounds can act against organisms like bacteria, viruses, fungi, protozoa, helminthes, cancer cells and prions in order to eliminate these infecting organism and invading elements from the host [1]. The ideal chemotherapeutic agent -the chemical used in chemotherapy- should inhibit the infecting organism growth, or kill the organism /invading elements, without damaging the cells of the host at low concentrations [1].

Patient who are receiving chemotherapy are highly complaining from adverse effects. These adverse effects are common in general and some of them may be related to the type of chemotherapy. Drugs as ant metabolic will not differentiate between cancerous cells and normal cells of body. That is why adverse effects are common. Now there are a lot of intervention to fight these adverse effects according to its nature may be pharmacological or even non pharmacological [2,3].

The chemotherapeutic agents' selective toxicity is relative, not absolute, requiring that the drug concentration be carefully controlled to attack the microorganism while still being tolerated by the host. Because Patients receiving chemotherapy treatment can experience a number of potential side effects and reactions and each person reacts to chemotherapy and its potential side effects differently, clinicians should be aware of these adverse events that can result from administration of cer-

tain agents. Fortunately, medicine now have ways to reduce and even prevent these adverse effects [4-7]. In this study I talked about the treatment-related adverse events in chemotherapy and their intervention.

### **Complications of chemotherapeutic**

The complications of chemotherapeutic treatment with anti-cancer agents occur due to, Unfortunately, most of these drugs cannot tell the difference between fast-growing cancer cells and a healthy cell that are fast-growing too such as, hair follicles, blood-forming cells in the bone marrow, and cells in the mouth, digestive tract, and reproductive system. The adverse effects are mostly seen on tissues that are consistently renewed like bone marrow (effecting blood cells), hair, and mucous membrane. The severity of the side effects depends on the type of drug being used, dosage, and body response to therapy [8,9]. Chemotherapy adverse effects can be limited by using multi-drug therapy in which several drugs are used in low doses, this reduces the side effects and the emergence of cellular resistance to the drug [10]. Multidrug therapy is effective because different drugs work by different mechanism that will kill or inhibit the growth of the cell [10-13]. Most of the adverse effects occurs over the course of chemotherapy treatment but some cytotoxic drugs can cause long term adverse effects by damaging the heart , lung , kidney [12] .

Fatigue is one of the most famous complain from cancer pa-

tients and even sometimes they will decide to discontinue the chemotherapy because of this severe fatigue. To fight this complaint we must now find the real reason of fatigue and deal with it [14,15].

Several causes can result in fatigue. Anemia is very common in cancer patients who are receiving chemotherapy because of hemolytic, hemorrhage, nutritional deficiency and anemia related to chemotherapy itself. Treatment of anemia with drugs as erythropoietin alpha or darbepoetin alpha has approved to improve the cases of fatigue in a lot of clinical trials [16]. Exercise can also improve fatigue and also improve the quality of life. Patient with fatigue will prefer to stay with any additional efforts. Special types of the exercise such as walking and cycle ergometers must be prescribed in advance before even starting the cycles of chemotherapies. It was reported that exercise also have good effects on the functional capacity following chemotherapy. On the other hand, the evidence of efficacy of exercising in people with advanced diseases is still poor [17]. Psychosocial interventions were been reported to have good impact on the chemotherapy related fatigue in patients with cancer. This psychosocial program includes health education, enhancement of problem-solving skills, stress treatment and psychological support [18,19]. Pharmacological interventions by giving drugs as psychostimulants, pregestational agents, and corticosteroid. studies approved the effect of methylphenidate for improving chemotherapy related fatigue even in patients with advanced cancer. modafinil was reported to improve fatigue in some studies but with patient who having multiple sclerosis. Cortisones also decrease depression, increase appetite and increase daily activities especially with orally methylprednisolone in advanced cancer patients who receiving chemotherapy finally no pharmacological interventions show benefits more than the psychostimulant in fighting fatigue related chemotherapy [20-23].

Chemotherapy is also related with CNS problems that can affect the quality of life of the cancer patient who is receiving chemotherapy it is called chemotherapy induced neuropathy. It doses controlled neuropathy. Chemotherapy used to manage breast, ovarian, and prostatic cancer has this serious side effect which called CIPN. The symptoms are sensory problems and also can spread to motor functions and the autonomic nervous system. Tingling, numbness, cramps, and aching or burning sensation is also symptoms of chemotherapy induced neuropathy. The patient will suffer with normal activities such as holding something, opening a jar a lot of problems with standing, walking or climbing stairs [24,26]. The degree of severity of the symptoms is related to the type of the chemotherapy that he is receiving the duration of receiving and of course the dose the condition of the person before begins the chemotherapy. The good thing that the neuropathy resolves in a lot of patient after stopping the chemotherapy. Unfortunately, a lot of studies done to prove any drugs can be used to prevent this side effect but without benefit. Still need a lot of studies to clarify this point because using chemotherapy is essential in treating cancer [24-27].

When a chemotherapeutic agent enters the body, sensors in the brain and digestive system detect its presence as a foreign substance. In a complex series of signals between the brain and the mouth, stomach, small intestine and bloodstream, the drug stimulates the vomiting center that is present in the brain [28]. Therefore, several chemicals, including ones called substance

P and serotonin, are released then trigger the nausea and vomiting reflex in order the body to get rid of the foreign substance [29].

The intervention: anti-nausea medications with different routes of administration based on the type of used chemotherapy and how much nausea and vomiting may be expected [30,31]. For examples:

Serotonin antagonists to stop serotonin (a naturally occurring substance in the brain) from sending signals that cause vomiting. These drugs are usually administered intravenously before starting the chemotherapy [32], another option corticosteroid, especially to prevent delayed nausea and vomiting, dopamine antagonists. They are usually prescribed for "breakthrough" nausea and vomiting when symptoms not already controlled with other types of medications. Also, NK-1 inhibitors. They block the action of substance P. It is taken before a chemotherapy session and for two days afterward [30-32].

Chemotherapeutic agents have the potential to cause sores in the mouth and on the mucus that lines the throat and digestive tract. These sores can be an annoying problem because they cause pain and infections, making it difficult to eat, drink and swallow [33-35].

The intervention for Pain control topical mouth rinses. Some contain an anesthetic such as 2% viscous lidocaine that may be mixed with diphenhydramine and a soothing covering agent such as Maalox in equal volumes. Using of topical anesthetic agents has the advantage to provide short-term relief [36-38]. Other option Ice chips (cryotherapy), they are placed in the mouth, starting 5 minutes before chemotherapy administration and replenished if needed for up to 30 minutes [39]. Systemic analgesics (opioids), required for patients with severe mucositis, especially who will undergo hematopoietic cell transplantation[40]. Nutritional Support, A soft diet and liquid diet supplements. Gastrostomy tube, it is placed prophylactically in patients expected to develop severe mucositis. Oral Decontamination, It can decrease infection of the oral cavity by opportunistic pathogens, which in turn reduce the risk of systemic sepsis from resident opportunistic pathogens in the mouth, especially in patients with immunosuppressed immune system because of the chemotherapy [37-40]. Oral decontamination can be done by using Gargling solutions, drinking plenty of fluids, and Caring of oral hygiene and teeth in general.

Hyposalivation can further aggravate the tissues inflammation and then increase the risk of local infection leading to difficult chewing. This problem can be solved by frequent drinking of water, chewing sugarless gum to stimulate salivary flow, and Using cholinergic agents if necessary [41-43].

Patients with oral mucositis have a potential to experience bleeding from the oral mucositis ulcerations, especially in patients who are thrombocytopenic because of high-dose chemotherapy. This local intraoral bleeding can usually be controlled by using topical hemostatic agents such as gelatin sponge and fibrin glue. It is thought that the pathogenesis of mucositis occurs due to reduction oral epithelial cells proliferation, so growth factors that can increase the proliferation of epithelial cells. Examples: IV recombinant human keratinocyte growth factor-1 [44].

Glutamine can decrease mucosal injury by decreasing of the proinflammatory cytokines production and cytokine-related apoptosis. In addition, it may enhance healing by increasing collagen and fibroblast synthesis [45].

INH-induced peripheral neuropathy occur due to the combination of INH and Pyridoxine (Vitamin B6) to form a Hydrazone which is excreted in the urine, resulting in Pyridoxine deficiency. Peripheral neuropathy is characterized by peripheral neuritis, insomnia, urinary retention, and psychotic episodes [46]. To overcome this issue, we need to concurrent administration of Pyridoxine.

Nephrotoxicity induced by Cidofovir and it can be detected by proteinuria, AKI, or a Fanconi-type syndrome with proximal tubular dysfunction. This can be reduced with pre-hydration using NORMAL SALINE and blocks active tubular secretion by high dose of probenecid [47,48].

Thrombophlebitis is an inflammatory process that causes a blood clot to form and block one or more veins, usually in the legs. To overcome by applying heat on pain site, elevating the affected leg, using NSADs and injection of an anticoagulant medication, such as Heparin if needed [49,50].

Superinfection is a second infection superimposed on a first infection. It occurs after using broad spectrum antibiotic, this antibiotic alters the normal bacterial flora and causes an imbalance of the flora. Examples of superinfections: Pseudomembranous colitis. Treatment with Vancomycin or Metronidazole to overcome [51].

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