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STUDY ON THE USE OF ANTIEMETIC DRUGS IN BREAST CANCER PATIENTS UNDERGOING CHEMOTHERAPY

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ABSTRACT

Breast cancer is a malignant disease that most commonly attacks women. Therapies used in the treatment of breast cancer are divided into local and systemic therapies. Local therapy, namely surgical therapy and radiotherapy, for systemic therapy, namely hormone therapy, chemotherapy. Chemotherapy is a treatment option for breast cancer that has metastasized or is at an advanced stage. The most common side effect of chemotherapy is nausea, vomiting, so to prevent nausea and vomiting due to chemotherapy, do antiemetic therapy before and after chemotherapy. The design of this research is non-experimental research, namely descriptive quantitative, the population in this study was 150 and the sample in this study was 39 patients**.** From the results of data analysis, it was found that the most widely used class of premedication drugs before chemotherapy was a combination of ondansetron injection 4 mg, ranitidine injection 100 mg and dexamethasone injection 15 mg. Meanwhile, the use of post-medication medication after chemotherapy uses a single therapy of 8mg ondansetron injection, and for oral medication taken home by the patient uses a single therapy of 4mg ondansetron, The use of antiemetic drugs to treat nausea and vomiting is given pre-chemotherapy and post-chemotherapy drugs.

INTRODUCTION

Cancer is the abnormal growth of new cells that grow beyond normal limits and are metastatic, that is, they attack parts of the body and spread to other organs. Metastasis is the first cause of death from cancer (WHO, 2017). *Mammary carcinoma*or breast cancer is a malignant disease that most often attacks women. This disease is caused by irregular division of body cells so that cell growth cannot be controlled and will grow into tumor lumps (Effendi & Anggun, 2019). Based on data from *World Health Organization* (WHO)The number of cancer sufferers worldwide has reached 14 million cases with a death rate of 8.2 million every year (WHO, 2017).Data *Global Cancer Burden Study* (Globocan) In 2020 the number of new cases of breast cancer reached 68,858 cases (16.6%) out of a total of 396,914 new cases of breast cancer in Indonesia. Meanwhile, in East Java,

according to the results of basic health research in 2018, the prevalence of cancer in East Java reached 2.2 per 1,000 population. Therapies used in the treatment of breast cancer can be divided into local therapy and systemic therapy. Local therapy given is surgical therapy and radiotherapy, while systemic therapy is hormone therapy, chemotherapy, immune, complementary and genetic therapy (Giovani et al., 2020). Chemotherapy is a treatment option for breast cancer that has metastasized or is at an advanced stage. Side effects caused by chemotherapy vary from mild to severe, side effects that often occur are gastrointestinal symptoms in the form of nausea, vomiting, diarrhea, constipation, *alopecia.*According to research conducted by Dian Anjasari et al (2017) stated that the side effects caused by chemotherapy were alopecia (94.1%), nausea (84.3%) and vomiting (58.8%). Nausea, vomiting is a frightening side effect for sufferers and their families (Shinta & Surarso, 2016). This condition gives rise to the patient's desire not to continue chemotherapy, if nausea and vomiting due to chemotherapy is not treated immediately it will have a negative impact on the patient's quality of life such as decreased appetite, dehydration, weight loss, insomnia, and feelings of anxiety (Juartika et al., 2020) .

Chemotherapy-induced nausea and vomiting is classified into 3 types, among others *acute, delayed,* And *anticipatory*. Nauseous vomit*acute*namely, nausea and vomiting occur in the first 24 hours after administration of chemotherapy. Patients in this phase usually experience severe nausea and vomiting. Nauseous vomit *late* are nausea and vomiting that occurs 24 hours to 6 days after chemotherapy and nausea and vomiting *anticipatory* are symptoms of nausea and vomiting before administration of chemotherapy (Society & Institute, 2016). One way to prevent nausea and vomiting due to chemotherapy is to carry out antiemetic therapy before chemotherapy or administer premedication drugs. Antiemetic therapy should also be continued for a period equal to the duration of the emetic activity of the chemotherapeutic agent used. *Chemotherapy causes nausea and vomiting*(Acute CINV) occurs within 1-2 hours of administration of chemotherapy and can last up to 24 hours, delayed CINV occurs more than 24 hours to 120 hours after administration of chemotherapy. Antiemetic premedication has reduced the prevalence of vomiting significantly, but evaluation shows that approximately 60.7% of patients still experience acute or delayed nausea after chemotherapy (Rahmadi et al., 2020).

Nausea and vomiting in post-chemotherapy breast cancer patients are usually given class drugs Serotonin antagonist(5HT3), dopamine antagonists, antihistamines, and corticosteroids (Arisanti et al., 2020). Treatment of nausea and vomiting *delayed* usually use a class of dopamine antagonist drugsworks by inhibiting peripheral dopamine receptors and increasing esophageal peristalsis, gastric motility thereby facilitating gastric emptying and reducing small intestinal transit time, while nausea and vomiting *acute* usually use a class of serotonin antagonist (5HT3) drugs which have a mechanism of action on the 5HT3 receptor which is located on the vagus nerve terminal, the vagus nerve can sense triggers for nausea and vomiting in the digestive tract such as stomach irritation. According to presearch conducted by (Ariyani et al., 2017) stated that as many as 23 out of 30 (76.7%) research subjects experienced nausea and vomiting after chemotherapy so they had to be

treated using nausea and vomiting drugs. Due to the large number of side effects in the direction of nausea and vomiting, where nausea and vomiting greatly affect the patient's quality of life, this study aims to look at the profile of the use of nausea and vomiting drugs in chemotherapy patients, so that the hope regarding the administration of nausea and vomiting drugs in chemotherapy patients can decrease and the patient's quality of life increases.

MATERIALS AND METHODS

The design of this research is non-experimental research, namely descriptive quantitative, the population in this study was 150 and the sample in this study was 39 patients. Researchers analyzed the use of antiemetic drugs using univariate analysis which was displayed in the form of frequencies and percentages.

RESULTS AND DISCUSSION

From the results of research conducted on 39 patients who used pre-chemotherapy antiemetic drugs to treat nausea and vomiting for breast cancer, 39 patients (100%) used a combination of 4mg ondansetron injection, 100mg ranitidine, and 15mg dexamethasone injection.

According to research conducted by Dian Anjasari et al (2017), the side effects caused by chemotherapy were alopecia (94.1%), nausea (84.3%), and vomiting (58.8%). Nausea, vomiting is a frightening side effect for sufferers and their families (Shinta & Surarso, 2016). Giving premedication nausea and vomiting medication aims to reduce the side effects of high doses of chemotherapy drugs such as cisplatin, carboplatin which have a high potential for nausea and vomiting. For high risk of vomiting, Aprepitant + Dexamethasone, or Serotonin antagonist + Dexamethasone or Metoclopramide can be given. In patients with the new protocol they receive pre-medication in the form of administering antiemetics before chemotherapy. These antiemetics can help prevent vomiting after the patient undergoes chemotherapy. In the acute type of vomiting, for chemotherapy regimens that usually pose a moderate to high risk of vomiting, such as carboplatin. Carboplatin is a drug class classification *alkylating agent* The mechanism of action of carboplatin is intracellular activation to form a reactive platinum complex which can inhibit DNA synthesis by forming crosslinking of DNA molecules (Giovani et al., 2020).

Table 1.1 Patient characteristics based on age at Baladhika Husada Hospital, Jember Regency, 2022 period

Patient age (years)	Number of patients	Percentage (%)
20-30 years	9	23,1%
31-40 years old	30	76,9%
Total	39	100%

Carboplatin is recommended for combined antiemetic use such as a combination of serotonin antagonist + Dexamethasone + Aprepitant for high risk of vomiting. The use of Aprepitant when combined with dexamethasone, causes an interaction, where AUC *(Area Under the Curve)* dexamethasone increased on days 1 and 5. The same dose of Aprepitant is given with a reduced dose of dexamethasone therefore, the AUC of dexamethasone is the same as the standard regimen without Aprepitant. The mechanism that occurs is because Aprepitant is an intermediate inhibitor of the cytochrome P450 isoenzyme CYP 3A4, and can increase the level of this corticosteroid in a short time by inhibiting its metabolism via CYP 3A4 (Fidinillah & Karuniawati, 2021).

Table 1.2 Patient characteristics based on gender at Baladhika Husada Hospital, Jember Regency, 2022 period

Gender	Amount	Percentage (%)
Woman	39	100%
Man	0	0
Total	39	100%

Antiemetic premedication from the 2017 version of the NCCN guidelines for cancer patients receiving highly emetogenic chemotherapy, namely 5-HT3 ondansetron 8–16 mg intravenously, and dexamethasone 15 mg intravenously or orally, but the NK-1 antagonist (aprepitant) is not widely available in Indonesia. therefore the protocol was modified by adding ranitidine and diphenhydramine. Ranitidine blocks H2 receptors and minimizes gastric acid secretion thereby preventing nausea and vomiting. A single pre-chemotherapy dose combination of 5-HT3 Antagonists and Dexamethasone is usually used as therapy to prevent emesis in patients receiving chemotherapy with a high risk of vomiting. The addition of Aprepitant can increase the prevention of vomiting (Putri, 2022).

Ondansetron is an anti-emetic of the serotonin receptor type 3 (5-HT3) group. This drug is effective for treating the level of therapy that causes vomiting. Antiemetic drugs are often combined with the aim of increasing effectiveness and reducing toxicity. Corticosteroids such as Dexamethasone work by increasing antiemetic activity when given together with 5-HT3 receptor antagonists (Arisanti et al., 2020). According to research conducted by (Ariyani et al., 2017) it was stated that as many as 23 out of 30 (76.7) research subjects experienced nausea and vomiting after chemotherapy so they had to be given nausea and vomiting medication. The problems that often occur are acute and delayed types of vomiting. Vomiting type*acute emesis* defined as nausea and vomiting that occurs within 24 hours after administering the chemotherapy regimen. The time most at risk of vomiting is from the first hour to the sixth hour after chemotherapy with various chemotherapy agents so ondansetron injections are given to treat nausea and vomiting *acute*. Meanwhile, when the patient went home, he was given the oral antiemetic drug ondansetron 4mg to prevent nausea and vomiting *postpone*. *Delayed emesis* this occurs more frequently in patients receiving Cisplatin, Carboplatin (Paraplatin), or Cyclophosphamide (Cytoxan, Neosar). In some patients,*delayed emesis* appears early in less than 24 hours*delayed emesis* usually occurs after administration of high doses of the chemotherapy agents Cisplatin (> 600 mg/m2), Carboplatin (> 300 mg/m2), Cyclophosphamide (> 600 mg/m2), or Doxorubicin (> 50 mg/m2) (Hariyanto, 2015) .

Table 1.3 Use of pre-chemotherapy antiemetic drugs in breast cancer patients at Baladhika Husada Hospital, Jember Regency.

Drug category	Medicine name	Frequency (f)	Percentage (%)
Combination	Ondansetron inj 4mg + ranitidine inj 100mg + dexamethasone inj 15mg	39	100%

Table 1.4 Use of post-chemotherapy antiemetic drugs in breast cancer patients at Baladhika Husada Hospital, Jember Regency.

Drug category	Drug name and dosage	Number of patients	Percentage (%)
In the hospital	Ondansetron 8mg injection	39	100%
Brought home	Ondansetron 4mg per oral	39	100%

According to research conducted by Utami (2013) stated that as many as 80 patients (80%) experienced nausea and vomiting in *acute emesis phase* and 90 people (90%) experienced nausea and vomiting during the phase *delayed emesis*. According to Chan, et al (2012) the relationship between the incidence of acute CINV and delayed CINV is not yet known with certainty, but good control of acute CINV can minimize the development *late* CINV just got better. Valle, et al (2006) in their research also stated that the incidence of acute nausea and vomiting cannot be a predictor of delayed emesis, but patients undergoing a chemotherapy program who experience acute nausea and vomiting are at risk of experiencing *delayed emesis* by 33%.

CONCLUSION

The use of antiemetic drugs in breast cancer patients was given pre-chemotherapy drugs using a combination of ondansetron injection 4mg, ranitidine injection 100mg, dexamethasone injection 15mg as many as 39 patients (100%). Meanwhile, to treat post-chemotherapy nausea and vomiting, a single injection of 8mg ondansetron is given and to prevent nausea and vomiting after the patient goes home given 4mg oral ondansetron.

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