POST-CHEMOTHERAPY TREATMENT IN NATIONAL HEALTH INSURANCE BREAST CANCER PATIENTS AT YOGYAKARTA CITY HOSPITAL

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ABSTRACT

Breast cancer accounts for approximately 16.6% of 396,914 cases of cancer and is one of the most fatal and common diseases among women. Treatment of breast cancer mostly has side effects, but the incidence of drug side effects does not always appear because the target drug does not selectively act on the target action. The aim of this study was to find a picture of post-chemotherapy treatment in breast cancer chemotherapy patients participating in the National Health Insurance at RSUD Yogyakarta. Observational method: Retrospective collection of data obtained from patients' medical records. The subjects included patients with breast cancer at RSUD Yogyakarta who met the inclusion criteria for the primary diagnosis of breast cancer and received chemotherapy medication during the period of 2020. The univariate analysis showed the distribution of frequency and percentage of respondent characteristics, including age, gender, number of patients, single and combination chemotherapy drugs, generic and commercial drugs, and single or combination post-chemotherapy medications. The results were obtained from 72 patients who underwent 4 periods of chemotherapy. The most frequently used chemotherapy regimens for each period were the period 1 combination of Brexel, Epirubicin, Carboplatin. Period 2 combination of the Brexel and Zometa regimes. Periode 3 combination brexel, epirubicine, and carboplatin. The most widely used combination of post-chemotherapy drugs in periods 1-4 was the combination of Ranitidine and Ondansetron.

Keywords: Ca Mamae, Chemotherapy, Regimen, Drugs

INTRODUCTION

According to data from the Global Cancer Observatory (2020) released by the World Health Organization (WHO), breast cancer is the most prevalent type of cancer in Indonesia. There are 65,858 recorded cases of breast cancer, accounting for approximately 16.6% of the 396,914 cases of cancer (Sung *et al.*, 2021). Breast cancer is a major health problem among women worldwide. This condition is characterized by uncontrolled or excessive growth of breast tissue cells (Aisyah *et al.*, 2018).

Riset Kesehatan Dasar (2015) reported that the prevalence of breast cancer in women is approximately 40 out of every 100,000 women diagnosed with breast cancer. Although breast cancer is more common in women, men are also at risk of developing breast cancer, compared to about 1 in 1,000 cases of breast cancer in men. The exact cause of breast cancer is unknown, and there are several risk factors that can increase a woman's risk of developing breast cancer (Arifin, 2019).

Therapy is one of the recommended treatments for breast cancer and involves the administration of anti-cancer drugs, either orally or by intravenous injection. (Masriadi, 2016). Chemotherapy can inhibit the growth of cancer cells, but approximately 70% to 80% of those receiving it experience the side effects of vomiting and nausea, so they are given additional antiemetic therapy (Fauzi *et al.*, 2021). Some types of medication have been used showing different side

effects in preventing nausea and vomiting (Navari & Apro, 2016). Single use of 5-HT3 receptor antagonists is useful in preventing the occurrence of vomiting in approximately 50% to 70% of cancer patients (Navari, 2015).

The selection of a chemotherapy regimen for patients with breast cancer is crucial. Appropriate selection is imperative because improper chemotherapy regimens can lead to side effects and unexpected drug interactions. Therefore, a careful analysis of chemotherapy regimes is required to improve the accuracy of the selection of breast cancer chemotherapeutic regimes (Arifin, 2019).

The aim of this study was to determine and provide an overview of the use of chemotherapy regimens at each period and post-chemotherapy treatment in breast cancer patients participating in the National Health Insurance (JKN) program in RSUD Yogyakarta. Most previous studies focused on chemotherapy regimens, antiemetic therapy, and acupressure therapy, while this study tried to look at it from a different perspective and focused more on chemotherapy regimen treatment per period and post-chemotherapy treatment in patients participating in the national health insurance. The side effects of chemotherapy vary depending on the chemotherapeutic regimen used. Chemotherapy side effects of nausea and vomiting are the most common and difficult to overcome. Women with breast cancer often experience nausea and vomiting after chemotherapy because chemotherapeutic agents for breast cancer combine a variety of emetogenic agents, such as cyclophosphamide, doxorubicin, epirubicin, paclitaxel, docetaxel, fluorouracil, and methotrexate (Rachmawaty & Sinrang, 2017).

RESEARCH METHODS

Methods of observational research retrospective collection of data obtained from patient medical records. The subjects used were breast cancer patients of Yogyakarta RSUD who met the inclusion criteria for the primary diagnosis of breast cancer and were receiving chemotherapy medication during the period of 2020. The population in this study is the total number of cancer patients undergoing chemotherapy by 2020 of 72 patients. The exclusion criteria of the Yogyakarta Municipal General Hospital included patients who had died and incomplete medical records. The sampling was conducted using *total sampling* techniques. Univariate analysis showed the distribution of frequency and percentage of respondent characteristics, including age, gender, number of patients, single and combined chemotherapy drugs, generic and commercial drugs, and single and combined post-chemotherapy medications. The research was approved by the Health Research Ethics Sub-Committee of the Municipal General Hospital of Yogyakarta under letter number 33/KEP/RSUD/XI/2021 by RSUD Kota Yogyakarta. The flow of the research methods is shown in Figure 1.
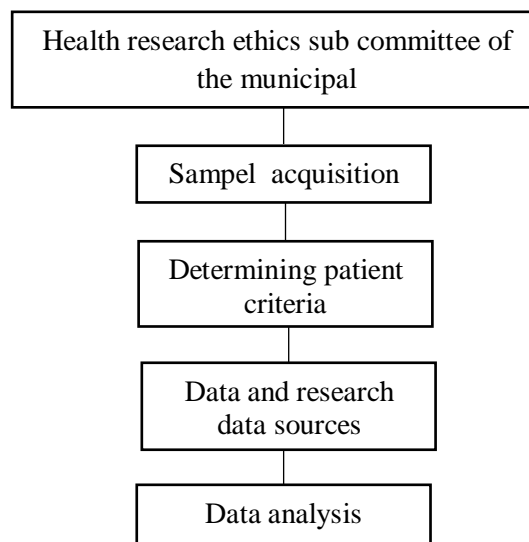

Figure 1. Research Flow

RESULTS AND DISCUSSION
A. Patient Characteristics
      Characteristics of patients undergoing breast cancer chemotherapy at Yogyakarta Municipal General Hospital based on age characteristic data are shown in **Table I**, and gender characteristics can be found in **Table II**.

Table I. Age Characteristic Data

Age	Number of patients	
	N	%
26-35 years (Early adult)	1	1%
36-45 years (Final maturity)	7	10%
46-55 years (Early old age)	22	31%
56-65 years (Final old age)	23	32%
>65 years (Elderly)	19	26%
Total	72	100%

      Based on **Table I**, the characteristics of patients undergoing breast cancer chemotherapy at Yogyakarta Municipal General Hospital are the age of the patient. It was found that the highest incidence of breast cancer was in the late age group, 56-65 years of age, with a total of 23 (32%) patients. According to Kementerian Kesehatan RI (2009), the age range of 17-25 years is the end of adolescence, the age range of 26-35 years is early adulthood, the ages range of 36-45 years is final maturity, age 46-55 is early old age, age 56-65 is final old age, and age 65 is elderly. Previous research has also found that women in the 40-60-year-old age range have a higher risk of breast cancer (Arianto *et al*., 2017). Adult women have a greater risk of developing breast cancer than women who have entered old age; this is related to hormonal factors, namely the hormone estrogen. In adulthood, exposure of breast gland cells to estrogen increases, triggering the growth of breast gland cells (Yuliastutik *et al*., n.d.). According to Menga *et al*. (2021), patients who undergo chemotherapy at an advanced age show a high risk of fatigue because they experience a more severe decline in functional status. Fatigue in chemotherapy patients is a symptom that can be influenced by many factors, such as age, race, psychological pressure, anemia, Body Mass Index (BMI), comorbidities, and initial level of fatigue before chemotherapy.

Table II. Gender Characteristic

Gender	Number of patients	
	N	%
Woman	71	99%
Men	1	1%
Total	72	100%

      Based on **Table II**, it was found that the majority of breast cancer patients were women, with the percentage of women being 99% and men being 1% of the total of 72 patients. It can be caused by hormonal changes associated with the reproductive cycle and a decrease in estrogen levels (Momenimovahed & Salehiniya, 2019). Estrogen production by local fatty tissues can affect the growth of cancer cells. The risk of breast cancer in women around menopause increases due to a decrease in estrogen levels and increased production of estrogen by fatty tissues around the breast. Hormonal changes during pregnancy and lactation also affect breast cancer risk (Nurhayati, 2018). According to Sipayung *et al*. (2022), delaying having children until the age of thirty can increase the risk of breast cancer. The age at which one gives birth to their first child is ≥ 30 years. This is because breast tissue is extremely sensitive to hormonal imbalances that occur between menarche and the first pregnancy, indicating that this is the time when breast cancer first develops. Previous research states that women who have never given birth or have never been pregnant have a

higher risk of developing breast cancer than women who are multiparous or have more than three children. During pregnancy, the breasts rest and the hormone estrogen is borrowed by the uterus; however, during breastfeeding, the breasts are filled with other hormones that inhibit estrogen production, thereby reducing the risk of breast cancer in women who have children (Katharina, 2014).

B. Chemotherapy Per Period Patients

The results of the number of patients per period during 2020 examined in patients undergoing breast cancer chemotherapy at the Yogyakarta Municipal General Hospital are shown in Figure 2.
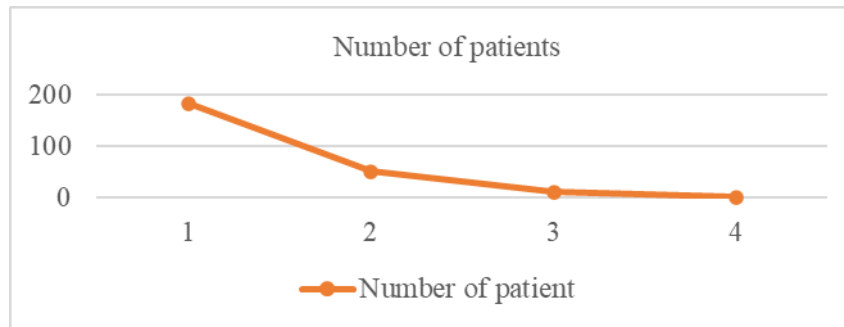

Figure 2. Data Number of Patients Per Period

Based on Figure 2, the number of patients undergoing chemotherapy in RSUD city of Yogyakarta was the highest in period 1, with a total of 184 patients; in the second period, the number of patients decreased to 52 patients, in the third period to 11 patients, and in the fourth period, there was only one patient. In the first period, 184 patients had the highest number of patients among the four periods. The decrease in the number of patients from period to period occurred because some patients chose to move to another hospital based on their medical records. Factors such as geographical reasons, patient preferences, and other medical reasons can cause patient transfers between hospitals.

C. Chemotherapy Drug Data

The results of chemotherapy drug data for the period 2020 that were studied in breast cancer chemotherapeutic patients at Yogyakarta Municipal Public Hospital are shown in Figure 3.
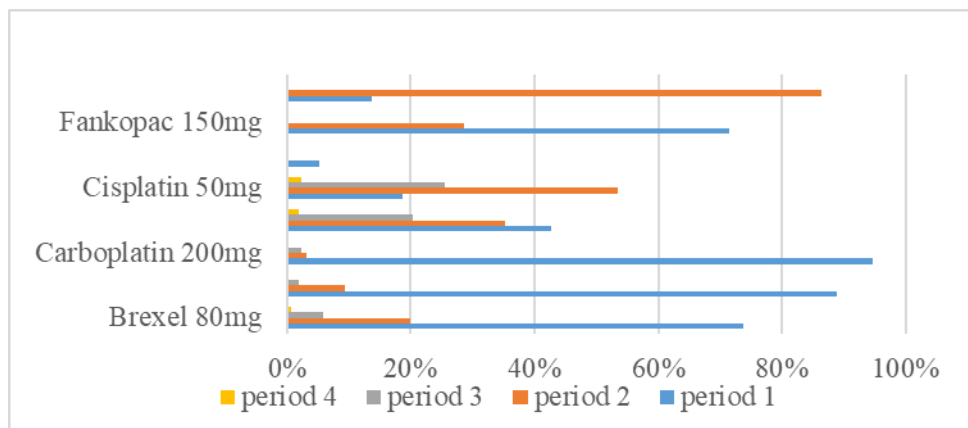

Figure 3. Chemotherapy Drug Data

As shown in Figure 3, in period 1, carboplatin (95 %) was the most widely used chemotherapeutic drug. In period 2, the drug with the highest percentage of use was zometa (86%). In period 3, cisplatin was used in as much as 26% of cases, and in period 4, drug use was divided between cisplatin and doxorubicin by 2 percent, respectively.

D. Period 1 and 2 Chemotherapy Drug Regimen

The results of the chemotherapy drug regimes period 1 and period 2 during 2020, which were studied in breast cancer chemotherapeutic patients at the Yogyakarta Municipal General Hospital, are shown in Figure 4 and 5.
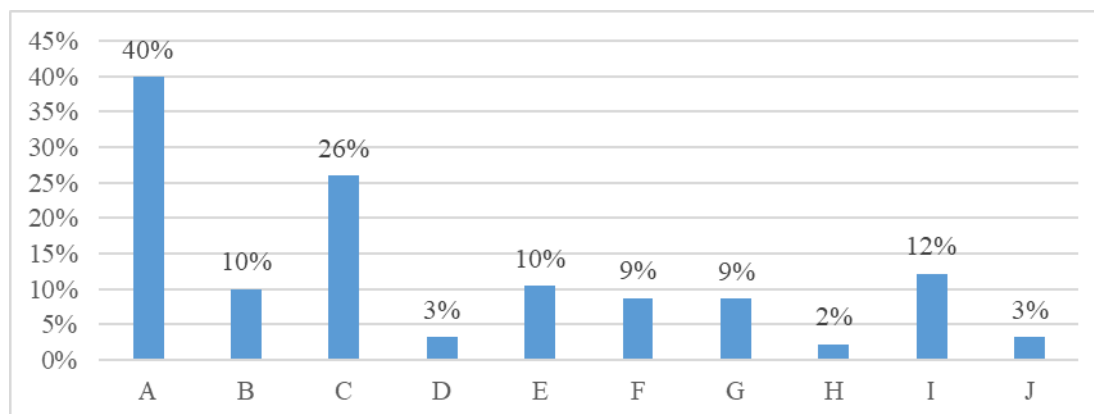

Figure 4. Period 1 Chemotherapy Regimen

Description   :

A. Brexel 80 mg, epirubicil 100 mg, carboplatin 200 mg
B. Brexel 80 mg, doxorubicin 50 mg, cisplatin 50mg
C. Fancopac 150 mg, epirubicin 100 mg, carboplatin 200 mg
D. Brexel 80 mg, zometa 4mg (da boneva)
E. Brexel 80 mg, epirubicin 100 mg

F. Doxorubicin 96 mg, cyclophosphamid 96 mg
G. Brexel 80 mg, doxorubicin 100 mg, carboplatin 200 mg
H. Doxorubicin 90 mg
I. Brexel/doxotacel 80 mg
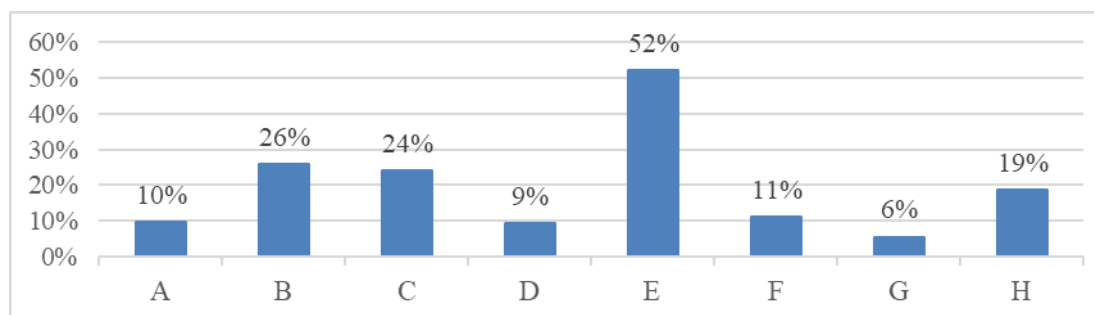J. Fancopac 150 mg, Epirubiocin 100 mg, vincristin 2mg

Figure 5. Period 2 Chemotherapy Regimen

Description :

A. Brexel 80 mg, epirubicin 100 mg, carboplatin 200 mg
B. Brexel 80 mg, doxorubicin 50 mg, cisplatin 50 mg
C. Fancopac 150 mg, doxorubicin 60 mg, cisplatin 60 mg

D. Fancopac 150 mg, epirubiocin 100 mg, zolenic 4 mg
E. Brexel 80 mg, zometa 4mg
F. Brexel 80 mg, epirubicin 100 mg, cisplatin 50 mg
G. Paclitaxel 150 mg, cisplatin 50 mg H. Fancopac 150 mg, epirubicin 100 mg

Based on Figure 4 and 5, in period 1 the most widely used drug combinations were 80 mg brexel regimes, 100 mg epirubicin, and 200 mg carboplatin at a percentage of 40%. In

Period 2, the most commonly used medication combination was brexel and zometa regimes at 52 per cent. In Period 3, there was only the use of the 80 mg Brexel regimen, 100 mg epirubicine, and 100 mg carboplatin at 25%. During Period 4, only one patient was undergoing chemotherapy and used 80 mg brexel, doxorubicin 50 mg, and 50 mg cisplatin at a percentage. Previous research has shown that the most widely used medication regimen is CAF (Cyclophosphamide + Doxorubicin + 5-FU) (Haryani, 2022). According to the PNPK Kemenkes RI (2015), several chemotherapy combinations that have become the standard first-line (first line) are CMF (Cyclophospamide + Methotrexate + 5-FU, CAF (cyclophosphamide+ Doxorubicin + 5FU), CEF (cyclophosphamide + epirubicin + 5 FU). In addition to the chemotherapeutic regimens, including AC (Adriamicin + Cyclophospamid), TA (Combination of Taxane – DoxoRubicin] (paclitaxel + doxorubicin or docetaxel + docetaxel), and ACT TC (Cisplatin + DocetaXel).

E. Use of Generic Drugs and Drugs with Trademarks

The results of data on the use of generic drugs and drugs with trademark names during 2020 that were studied in patients undergoing breast cancer chemotherapy at the Yogyakarta Municipal General Hospital are shown in Figure 6.
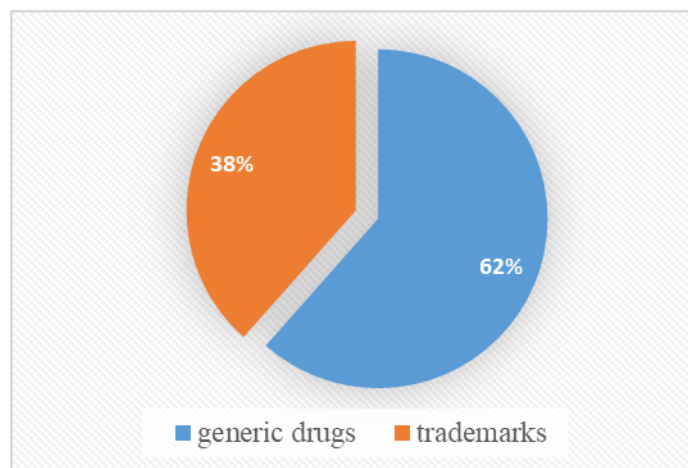

Figure 6. Use of Generic Drugs and Drugs with Trademarks

As shown in Figure 6, the percentage of patients taking generic drugs was 62%, whereas the percentage of patients using trade drugs was 38%. Generic drugs were used based on the results, including paclitaxel, epirubicin, cisplatin, doxorubicin, carboplatin, cyclophosphamide, vincristine, and docetaxel. The use of drugs with trademarks was based on the results of Brexel, Epirol, Fancopac, Zometa, and Zolenik. Several generic medicines and medicines with trademarks have the same active substance used in the treatment of breast cancer in RSUD Yogyakarta, including Brexel with docetaxel, E Pirol with epirubicine, and Fankopac with Paxilacel.

The high percentage of this generic drug use is consistent with all breast cancer patients in this study who are members of the National Health Assurance (JKN). According to DEPKES (2022), the existence of the national medicine list forms of JKN is very useful in ensuring that patients can obtain the right medicines of choice, nutrition, quality, safety, and remain affordable. Generic drugs generally have lower prices than drugs with patent names because they do not involve high research and development costs, such as patent drugs. This makes generic medications a more affordable choice for many JKN participants, who may have financial constraints (Proinov, 2022). According to E-Fornas Kemkes (2023), all generic chemotherapy drugs used by patients are covered by JKN/BPJS as well as patented drugs that have the same active substance as generic drugs.

F. Post-Chemotherapy Treatment

The results of the post-chemotherapy treatment data for 2020 that were studied in breast cancer chemotherapy patients at Yogyakarta Municipal General Hospital are shown in Figure 7.
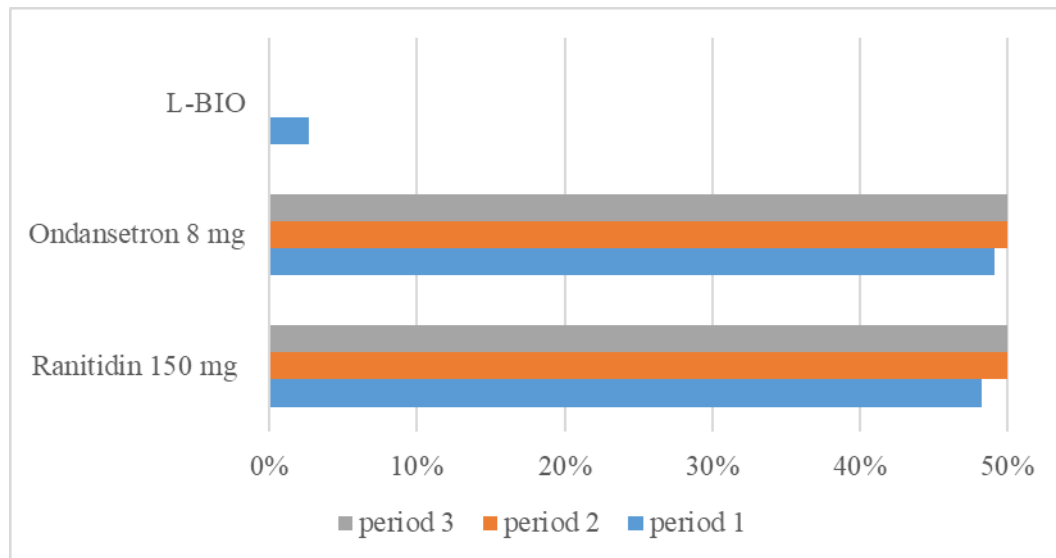

Figure 7. Post-Chemotherapy Treatment

As shown in Figure 7, the percentage of patients using post-chemotherapy drugs in periods 1, 2, and 3 was most commonly found for treatment, namely, ranitidine 150 mg and ondansetron 8 mg. In period 1, the rate of use of ranitidin was 49% and that of ondasetron was 48%. In Periods 2 and 3, the rate was 50%. However, for the use of LBIO drugs, only in period 1. In period 4, only 1 patient underwent chemotherapy and used the drugs Ranitidina and ondansetrone post-chemotherapy. Ranitidine is not a post-chemotherapy drug used in chemotherapy patients; it is an H-2 receptor antagonist that blocks the H-2 receptors of gastric parietal cells and inhibits gastric secretion. Therefore, the combination of ondansetron and ranitidine is often used to treat nausea and vomiting due to chemotherapy (Giovani *et al.*, 2020). According to the *National Comprehensive Cancer Network* (2012), H2 blocker drugs such as ranitidine can be recommended as additional therapy to prevent nausea and vomiting due to the administration of chemotherapy agents with high, moderate, low, and minimal risk of nausea and vomiting. L-Bio is a supplement that contains the probiotic Lactobacillus acidophilus to maintain the balance of good bacteria in the digestive tract. In addition, L-bio is useful for restoring normal digestive function in patients undergoing chemotherapy. Therefore, it can be concluded that the efficacy of ondansetron is the best among the others.

G. Post-Chemotherapy Combination Treatment

The results of combination treatment after chemotherapy in 2020 that were studied in breast cancer chemotherapeutic patients at Yogyakarta Municipal General Hospital are shown in Figure 8.
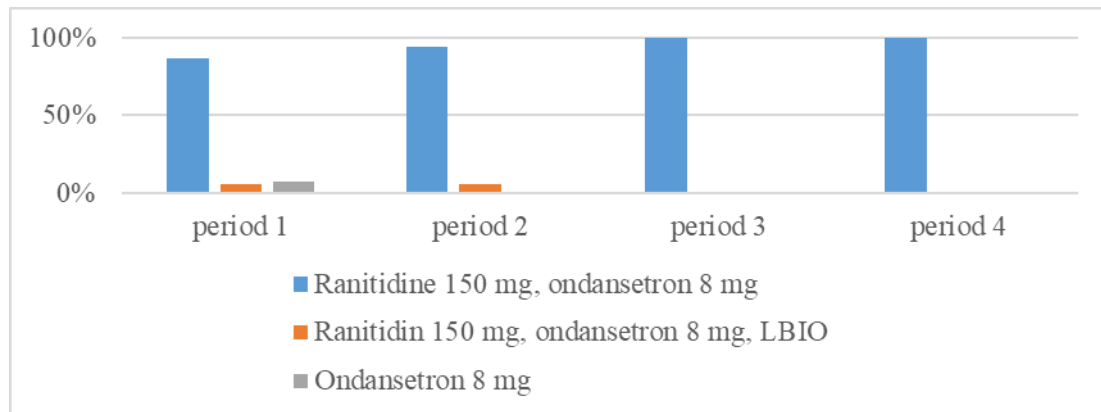
Figure 8. Post-Chemotherapy Combination Treatment

Based on the results shown in Figure 8, periods 1 to 4 of the most commonly used post-chemotherapy drug combinations were ranitidine 150 mg and ondansetron 8 mg. In period 1, the percentage of use of this combination was 87%; in period 2, 94%; and in periods 3 and 4, 100%. This is consistent with previous studies that reported that the most frequent side effects of chemotherapy were nausea and vomiting in addition to alopecia (Effendi & Anggun, 2019). According to the indications, the drugs Ranitidine and Ondansetron in chemotherapy are useful for reducing nausea and vomiting post-chemotherapy.

Ranitidine is an H-2 receptor antagonist that inhibits gastric secretion, whereas ondansetron is an effective antiemetic drug used to treat nausea and vomiting (Haryani, 2022). According to the *National Comprehensive Cancer Network* (2020), H2 blocker drugs such as ranitidine may be recommended as additional therapy for the prevention of nausea and vomiting caused by the administration of chemotherapy agents with a high, moderate, low, and minimal risk of vomiting. According to previous studies, the incidence of nausea and/or vomiting in patients receiving a combination of OD (Ondansetron and Dexametason) and OR (Onansetrone and Ranitidine) is much higher than that in patients treated with a combination of ODRs (Oundansetrons, Dexamethasons, and ranitidines) (Dzikriyani & Setiawan, 2021). Based on data from Medscape (2023), the long-term effects of ondansetron are headaches (9-27%) and malaise/fatigue (9-13%), and the long-term effects of drug administration are headaches (3%). L-Bio medication containing Lactobacillus acidophilus does not have side effects if consumed for a long period of time because L-Bio can help to maintain the normal function of the gastrointestinal tract and to restore the system in unstable conditions such as chemotherapy.

CONCLUSION

Based on the research that has been carried out, it can be concluded that patients in the Yogyakarta Regional General Hospital had a final age category (56-65) years (32 %). The most frequently used chemotherapy regimen drugs for each period were Brexel, Epirubicin, Carboplatin in period 1 by percentage (40%), period 2 regimen Brexel, Zometa by percentage (52%), and period 3 regimen of brexel drugs, epirubicin, and carboplatin (25%). The combination of post-chemotherapy drugs with the highest percentage was found in Ranitidine and Ondansetron. In period 1, the use of this combination was 87%, in period 2 it was 94%, and in periods 3 and 4 it reached 100%. This suggests that the combination of Ranitidin and Ondasetron is effective in treating nausea and vomiting after chemotherapy in patients with breast cancer.

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