ISSN 2745-455X (Online)
Indonesian Journal of Pharmacology and Therapy

Antiemetic prophylaxis utilization in cancer patients in a hospital in Yogyakarta

Imaniar Noor Faridah[1], Dyah Aryani Perwitasari[1]*, Siswandi[2], Lamhot B Simanjuntak[2], Gugun Suhendra[2], Dewi Wulandari[2], Haafizah Dania[1], Muhammad Arif Rizky[1], Safira Nur Islami[1], Salma Auliya Fatimah[3]

[1]Faculty of Pharmacy/Center for Bigdata, Bioinformatics, and Precision Medicine, Faculty of Pharmacy, Universitas Ahmad Dahlan, Yogyakarta, [2]RSPAU dr Suhardi Hardjolukito, Yogyakarta, [3]Faculty of Health Science, Universitas Darussalam, Gontor, Ponorogo, East Java

https://doi.org/10.22146/ijpther.14243

Submitted: 24-06-2024
Accepted : 31-10-2024

Keywords:
emetogenic;
premedication;
cytostatic;
nausea;
vomiting

ABSTRACT

Chemotherapy is a type cancer treatment that uses anticancer drugs to inhibit cell division and kill cancer cells. Chemotherapy can cause side effect due to normal cells damages. The study aimed to investigate the use of antiemetic prophylaxis as premedication to prevent or reduce side effects on cancer patients undergoing chemotherapy. It was a observational study with retrospective design using medical records data of cancer patients who underwent chemotherapy in a hospital in Yogyakarta during May – September 2022. The results showed the cancer patients were dominated by women (85.71%) with ages 46-65 yr (63.27%) and stage III cancer (87.76%). There were 18 types of anticancer drugs and the most widely used drugs were doxorubicin 60 mg for the moderate emetogenic category and vinorelbine 37.5 mg for the low emetogenic category. The most widely used premedication regimen was a combination granisetron 3 mg, ondansetron 8 mg, and dexamethasone 10 mg regimen (72.45%). This combination was most often used for the cancer patients with the moderate emetogenic category (39 patients or 49.4%). However, not all the cancer patients undergoing chemotherapy with the low and moderate emetogenic anticancer drugs were administered the premedication. In conclusion, doxorubicin and vinorelbine are the most widely used for cancer patients undergoing chemotherapy in the hospital. In addition, a combination of granisetron, ondansetron, and dexamethasone is widely used as premedication.

ABSTRAK

Kemoterapi adalah jenis pengobatan kanker yang menggunakan antikanker untuk menghambat pembelahan sel dan membunuh sel kanker. Kemoterapi dapat menimbulkan efek samping akibat kerusakan sel-sel normal. Penelitian ini bertujuan untuk mengetahui penggunaan profilaksis antiemetik sebagai premedikasi untuk mencegah atau mengurangi efek samping pada pasien kanker yang menjalani kemoterapi. Penelitian ini merupakan penelitian observasional dengan rancangan retrospektif dengan menggunakan data rekam medis pasien kanker yang menjalani kemoterapi di salah satu rumah sakit di Daerah Istimewa Yogyakarta pada bulan Mei – September 2022. Hasil penelitian menunjukkan pasien kanker didominasi oleh perempuan (85,71%) dengan usia 46-65 tahun (63,27%) dan kanker stadium III (87,76%). Terdapat 18 jenis obat antikanker dan obat yang paling banyak digunakan adalah doxorubicin 60 mg untuk kategori emetogenik sedang dan vinorelbine 37,5 mg untuk kategori emetogenik rendah. Regimen premedikasi yang paling banyak digunakan adalah kombinasi rejimen granisetron 3 mg, ondansetron 8 mg, dan deksametason 10 mg (72,45%). Kombinasi ini paling banyak digunakan pada pasien kanker dengan kategori emetogenik sedang (39 pasien atau 49,4%). Namun, tidak semua pasien kanker yang menjalani kemoterapi dengan antikanker emetogenik rendah dan sedang diberikan premedikasi. Kesimpulannya, doksorubicin dan vinorelbin paling banyak digunakan pada pasien kanker yang menjalani kemoterapi di rumah sakit. Selain itu, kombinasi granisetron, ondansetron, dan deksametason banyak digunakan sebagai premedikasi.

*corresponding author: diahperwitasari2003@yahoo.com

INTRODUCTION

Cancer is a disease in which some of the body's cells grow uncontrollably and spread other parts of the body.[1] Cancer can also be called as neoplasm or malignant tumour.[2] World Health Organization (WHO) reported that cancer is one of the non-communicable diseases that is the main cause of death in the world's population. Indonesia Basic Health Research 2018 (Riskesdas, 2018) demonstrated an increase in the incidence of cancer in Indonesia to 1.79 per 1000 population in 2018 from 1.4 per 1000 population in 2013.[3] The Global Center Observatory (2020) estimated that cancer patients in Indonesia have reached 396,914 people, consisting of 183,368 male cancer patients and 213,546 female cancer patients.

Yogyakarta is a region in Indonesia with the highest cancer incidence with a case rate of 4.86 cases per 1000 population and the highest incidence are cervical cancer and breast cancer. In 2019, a preliminary study conducted by Sutopo at the Yogyakarta Health Office, the Yogyakarta city became the region with the highest number of breast cancer cases of 1,710 cases, followed by Bantul regency with 266 cases, Kulon Progo regency with 26 cases and Gunung Kidul district with 22 cases.[4]

Cancer can be treated using multiple modalities including surgery, chemotherapy and radiation. Chemotherapy is considered the most effective and widely used modality in the treatment of cancer as used alone or in combination with surgery or radiotherapy. Generally, chemotherapy regimens are given gradually over 6-8 cycles which include a combination of several types of anticancer.[6] Chemotherapy can increase the effectiveness of cancer treatment. However, chemotherapy commonly causes side effects depending on physical conditions of each patient. Another factors associated with side effects of chemotherapy include chemotherapy agents used, age, gender, or any imbalances of fluid and electrolytes.[7] The side effects of chemotherapy are due to effect of cytotoxic drugs or anticancer on normal cells of the body's.[8] Some common side effects of chemotherapy include nausea and vomiting, diarrhea, constipation, hair loss, and so on depending on the physical condition of each individual undergoing chemotherapy.[9]

Premedication before chemotherapy is commonly administered to prevent or reduce side effects of the chemptherapy.[10,11] The clinical outcome of the premedication depends on type of drug, dosage, and duration of treatment. Antiemetic such as 5-HT_3 antagonist and corticosteroids are often recommended for the premedication. However, cancer patients who received chemotherapy with moderate emetogenic still experienced nausea and vomiting even premedication with antiemetic administered. This study aimed to evaluate the effect of premedication using antiemetics in cancer patients underwent chemotherapy at a hospital in Yogyakarta.

MATERIAL AND METHODS

Subjects and design

It was a observational study with retrospective design using medical records data of cancer patients who underwent chemotherapy in a hospital in Yogyakarta during May – September 2022.

Protocol

Cancer patients who underwent chemotherapy were gathered and selected to involve in this study. The inclusion criteria were cancer patients aged ≥18 years and undergoing chemotherapy in the May-September 2022 period. The criteria exclusion were incomplete medical record data. Data of cancer patients who met the inclusion

and exclusion criteria were recorded and tabulated. The data include gender, age, cancer type, cancer staging were collected. Furthermore, the data of anticancer drugs used, and dose, as well as emetogenic severity, premedication used were also recorded and tabulated.

This study received ethical approval from the Health Research Ethics Committee of Universitas Jenderal Achmad Yani, Yogyakarta (Skep/41/KEPK/IV/2022).

Data analysis

Data were tabulated and presented as frequency and descriptively analysis.

RESULTS

A total of 98 cancer patients who underwent chemotherapy in the hospital from May to September 2022 and selected in the study, only 77 patients received premedication using antiemetics before the chemotherapy. The characteristics of patients include gender, age, stage of cancer, and type of cancer suffered are presented in TABLE 1. Most of the patients were female (85.71%), with the age average was 46-65 y.o. and in the stage III of cancer (87.76%).

The anticancer drugs used for cancer patients underwent chemotherapy in a hospital in Yogyakarta are presented in TABLE 2. Paclitaxel, doxorubicin and vinorelbine were the most anticancer drugs used in the hospital.

TABLE 3 presents the pattern of anticancer drugs used in the hospital, including the name, dosage and frequency of administration.

TABLE 4 presents the use of antinausea-vomiting premedication, based on the emetogenic category. Combination of granisetron, ondansetron, and dexamethasone was the most premedication used in this study. The combination was administered to the cancer patients with mostly moderate emetogenic severity.

TABLE 1. Characteristics of subjects (n=98) underwent chemotherapy at a hospital in Yogyakarta during May-September 2022

Characteristics	Ca.[a] LNH[b]	Ca. Recti	Ca. Ovari	SCC[c]	Ca. Nasofaring	Ca. Colli	Ca. Mammae	MBC[d]	[n (%)]
Gender									
• Male	8	2	0	2	1	1	0	0	14 (14.29)
• Female	6	0	4	0	0	0	60	14	84 (85.71)
Age (y.o.)									
• 26-45	2	2	0	0	1	0	12	3	20 (20.41)
• 46-65	10	0	3	1	0	1	40	8	63 (64.27)
• >65	2	0	1	1	0	0	8	3	15 (15.31)
Cancer staging									
• I	0	0	0	0	1	0	2	0	3 (3.06)
• II	0	0	0	0	0	0	3	2	5 (5.10)
• III	13	2	4	2	0	1	52	12	86 (87.76)
• IV	1	0	0	0	0	0	3	0	4 (4.08)
Total	14	2	4	2	1	1	60	14	
%	14.29	2.04	4.08	2.04	1.02	1.02	61.22	14.29	

[a]Ca:cancer; [b]LNH:limfoma non-Hodgkin; [c]SCC:squamous cell carcinoma; [d]MBC: metastasis breast cancer.

TABLE 2. Anticancer used in a hospital in Yogyakarta during May-September 2022

Drug class/Name	Frequency [n (%)]
Antimicrotubule agents	
• Brexel® (docetaxel)	15 (10.7)
• Fonkopac® (paclitaxel)	26 (18.6)
• Paclitaxel	1 (0.7)
• Reditux® (rituximab)	5 (3.6)
• Rituxical®(rituximab)	3 (2.1)
• Vincristine	6 (4.3)
• Vinorelbine	23 (16.4)
Alkylating agents	
• Carboplatin	4 (2.9)
• Cisplatin	5 (3.6)
• Cisteen® (cisplatin)	2 (1.4)
• Cyclophosphamide	6 (4.3)
• Eloxatin® (oxaliplatin)	1 (0.7)
• Oxaliplatin	2 (1.4)
Topoisomerase active agents	
• Doxorubicin	24 (17.1)
• Epirubicin	13 (9.3)
• Naprodox®(doxorubicin)	2 (1.4)
Antimetabolit agents	
• 5FU (5-fluororacil)	2 (1.4)
• Fonkogem®(gemcitabine)	1 (0.7)
Total	14 (100)

TABLE 3. Anticancer used in a hospital in Yogyakarta based on the emetogenic level during May-September 2022

Emetogenic severity	Dosage (mg)	Frequency [n (%)]
High	Cisplatin	
	• 50	1 (0.7)
	• 80	1 (0.7)
	• 90	1 (0.7)
	• 100	1 (0.7)
	• 500	1 (0.7)
	Cisteen® (cisplatin)	
	• 50	2 (1.4)
	Sub total	7 (5.0)

TABLE 3. Cont.

Emetogenic severity	Dosage (mg)	Frequency [n (%)]
Moderate	Carboplatin	
	• 300	1 (0.7)
	• 450	1 (0.7)
	• 500	2 (1.4)
	Cyclophosphamide	
	• 500	3 (2.1)
	• 700	1 (0.7)
	• 750	2 (1.4
	Doxorubicin	
	• 60	19 (13.6)
	• 50	3 (2.1)
	• 75	2 (1.4)
	Eloxatin® (oxaliplatin)	
	• 150	1 (0.7)
	Epirubicin	
	• 100	7 (5.0)
	• 90	5 (3.6)
	• 80	1 (0.7)
	Naprodox® (doxorubicin)	
	• 50	2 (1.4)
	Oxaliplatin	
	• 150	2 (1.4)
	Sub total	52 (37.1)
Low	5-Fluorouracil	
	• 500	2 (1.4)
	Brexel® (docetaxel)	
	• 120	2 (1.4)
	• 100	13 (9.3)
	Fonkogem®(gemcitabin)	
	• 1200	1 (0.7)
	Fonkopac® (paclitaxel)	
	• 75	2 (1.4)
	• 100	1 (0.7)
	• 150	4 (2.9)
	• 180	16 (11.4)
	• 250	1 (0.7)
	• 260	1 (0.7)
	Paclitaxel	
	• 250	1 (0.7)
	Sub total	44 (31.4)
	Reditux® (rituximab)	

TABLE 3. Cont...

Emetogenic severity	Dosage (mg)	Frequency [n (%)]
Minimal	• 300	1 (0.7)
	• 400	4 (2.9)
	Rituxical® (rituximab)	
	• 350	1 (0.7)
	• 400	2 (1.4)
	Vincristine	
	• 1.5	5 (3.6)
	• 2	1 (0.7)
	Vinorelbine	
	• 37.5	23 (16.4)
	Sub total	37 (26.4)
	Total	140 (100)

TABLE 4. Administration of premedication treatment to cancer patients (n=98) in a hospital in Yogyakarta during May to September 2022

Drug and dose (mg)	Emetogenic severity	Frequency [n (%)]
Granisetron 3 mg,	High	7
Ondansetron 8 mg,	Moderate	39
Dexamethasone 10 mg.	Low	1
	Minimal	24
	Total	71 (72.4)
Granisetron 3 mg,	High	0
Ondansetron 8 mg,	Moderate	3
Dexamethasone 10 mg,	Low	0
Diphenhydramine 10 mg.	Minimal	1
	Total	4 (4.04)
Dexamethasone 10 mg,	High	0
	Moderate	1
Diphenhydramine 10 mg.	Low	0
	Minimal	1
	Total	2 (2.04)
Dexamethasone 20 mg,	High	0
Diphenhydramine 50 mg,	Moderate	1
Ranitidine 50 mg.	Low	0
	Minimal	0
	Total	1 (1.02)
Dexamethasone 10 mg,	High	0
Diphenhydramine 50 mg,	Moderate	1
Ondansetron 8 mg.	Low	0
	Minimal	0
	Total	1 (1.02)
No drugs (not premedicated)	-	19 (19.39)

DISCUSSION

This study demonstrates that premedication is not provided to the all cancer patients underwent chemotherapy with anticancer drugs. This finding in line with a study at PKU Muhammadiyah Hospital, Yogyakarta that shows among 30 female cancer patients, only 24 patients receiving premedications.[13] Breast cancer became the most common cancer suffered by female patients (60 patients or 61.22%).[14] Several risk factors such as an unhealthy lifestyle, consuming fatty foods, and excessive production of estrogen and progesterone hormones in the body can be a trigger for cancer in women.[15] Previous study showed that respondents exposured by reproductive hormones are associated with a reduced risk of NHL subtypes, particularly diffuse large-cell lymphoma (DLCL).[16] This is also in line with the research of Priliana *et al.*,[17] that reported NHL cancer patients are dominated by male patients (28 patients from 41 patients).

According to the age, the majority of cancer patient in this study were between the ages of 46 and 65 yr (64.27%). This result similar with the previous study conducted at RSU Dadi Keluarga Purwokerto, which found that 38 of 67 respondents of cancer patients aged 46-65 yr.[18] Cancer could be occurred at any age, however one of risk factors for cancer is advancing age.[19] About 80% of breast cancer patients aged >50 yr, while 57% of NHL cancer patients were diagnosed in aged >65 yr.[20,21]

The class of anticancer drugs is classified into several groups including alkylating agents, antimetabolites, antitumor antibiotics (anthracycline), topoisomerase-active agents, antimicrotubule agents, and others.[23] This study showed that 18 types of anticancer drugs are used in the chemotherapy. The most widely used in the hospital is antimicrotubule agent drug classes (7 types) with the Fonkopac® (paclitaxel) and vinorelbine is the most widely used. According to MASSC/ESMO, the use of cytostatics based on emetogenic levels is categorized into several levels, namely minimal (level 1), low (level 2), moderate (level 3), and high (level 4).[24] Minimal categories are anticancer drugs that cause the risk of nausea-vomiting events in <10% of patients; low category, namely anticancer drugs that cause the risk of nausea-vomiting events in 10-30% of patients; moderate category, namely anticancer drugs that cause the risk of nausea-vomiting events in 30-90% of patients; and the high category namely anticancer drugs that cause the risk of nausea-vomiting events in >90% of patients.

Premedication aims to prevent nausea-vomiting during and/or after chemotherapy conducted. Premedication is generally given 30 min to 1 hr before chemotherapy. Premedication drugs in this study include granisentron, ondancentron, dexamethasone, diphenhydramine, and ranitidine. In this study, cancer patients who are not given premedication are patients who get treatment using zoledronic acid. Zoledronic acid is a drug that belongs to the biphosphate class and it is not included in the category of anticancer drugs that cause nausea-vomiting due to chemotherapy. This causes patients not to be given premedication before chemotherapy.

This study demonstrated that the premedication regimen is more widely used for cancer patients with moderate and low emetogenic category. The use of the regimen is different from the guidelines of the American Society of Clinical Oncology (ASCO), namely the use of anticancer drugs in cancer patients who cause moderate category emetogenic premedication to get a combination of two classes of drugs, namely 5-HT3 receptor antagonists (ondansetron, granisteron, dolasetron, tropisetron or palonosetron) and dexamethasone, and for cancer patients who get minimal category anticancer drugs do not get antiemetic premedication.[25] In addition,

there has been no research on the use of combination antiemetic premedication regimens between granisetron, ondansetron, and dexamethasone for cancer patients receiving moderate and minimal cytostatics.

This study has limitation due to the limited sample size then the profile of high emetogenic cytostatic can not be explored

CONCLUSION

In conclusion, doxorubicin and vinorelbine are the most widely used for cancer patients undergoing chemotherapy in the hospital. In addition, a combination of granisetron, ondansetron, and dexamethasone is widely used as premedication. However, not all patients are administered the premedication.

ACKNOWLEDGMENT

All authors thank to the Director of the hospital and all staffs who already manage the medical record properly in this study.

REFERENCES

1. Kim SJ, Baker CH, Kitadai Y, Nakamura T, Kuwai T, Sasaki T, *et al*. The pathogenesis of cancer metastasis: relevance to therapy. Princ Cancer Biother 2009; 17-40. https://doi.org/10.1007/978-90-481-2289-9_2
2. WHO. Cancer (who.int). (2022). accessed on 24th June 2024
3. Riskesdas. Laporan Nasional RKD2018 FINAL. Badan Penelitian dan Pengembangan Kesehatan 674 (2018).
4. The Global Center Obsevatory. GLOBOCAN: Indonesia. (2020), accessed on 24th June 2024.
5. Sutopo DYH. Pengaruh pendidikan kesehatan terhadap perilaku sadari pada remaja putri sebagai deteksi dini kanker payudara. Poltekkes Kemenkes, Yogyakarta, 2020. https://poltekkesjogja.ac.id
6. Kementerian Kesehatan RI. Panduan nasional penanganan kanker payudara. 2015.
7. National Cancer Institute. Nausea and vomiting related to cancer treatment (PDQ) - health professional version. National Cancer Institute. https://www.cancer.gov/about-cancer/treatment/side-effects/nausea/nausea-hp-pdq (2023). accessed on 24th June 2024
8. Amjad MT, Chidharla A, Kasi A. Cancer chemotherapy. StatPearls Publishing. 2023. https://www.ncbi.nlm.nih.gov/books/NBK564367/
9. Pratiwi SR, Widianti E, Solehati T. Gambaran faktor-faktor yang berhubungan dengan kecemasan pasien kanker payudara dalam menjalani kemoterapi. J Pendidik Keperawatan Indones 2017; 3(2):167. https://doi.org/10.17509/jpki.v3i2.9422
10. Gupta K, Walton R, Kataria SP. Chemotherapy-induced nausea and vomiting: pathogenesis, recommendations, and new trends. Cancer Treat Res Commun 2021; 26:100278. https://doi.org/10.1016/j.ctarc.2020.100278
11. Clemmons A, Gandhi A, Clarke A, Jimenez S, Le T, Ajebo G. Premedications for cancer therapies: a primer for the hematology/oncology provider. J Adv Pract Oncol 2021; 12(8):810-32. https://doi.org/10.6004/jadpro.2021.12.8.4
12. Escobar Y, Cajaraville G, Virizuela JA, Álvarez R, Muñoz A, Olariaga O, *et al*. Incidence of chemotherapy-induced nausea and vomiting with moderately emetogenic chemotherapy: ADVICE (Actual Data of Vomiting Incidence by Chemotherapy Evaluation) study. Support Care Cancer 2015; 23(9):2833-40. https://doi.org/10.1007/s00520-015-2809-3
13. Suprayitno E, Prasetyo DY. Karakteristik kualitas hidup pasien dalam menjalani kemoterapi. JHeS

(Journal of Health Studies) 2021; 5(2):73-83. https://doi.org/10.31101/jhes.2325
14. Yi M, Li T, Niu M, Luo S, Chu Q, Wu K. Epidemiological trends of women's cancers from 1990 to 2019 at the global, regional, and national levels: a population-based study. Biomark Res 2021; 9:55. https://doi.org/10.1186/s40364-021-00310-y
15. Ratna R, Supadmi W, Yuniarti E. Kualitas hidup pasien kanker rawat jalan yang menjalani kemoterapi di RSUD Kota Yogyakarta. Maj Farm 2021; 17:278-86. https://doi.org/10.22146/FARMASEUTIK.V17I2.62832
16. Lee JS, Bracci PM, Holly EA. Non-Hodgkin lymphoma in women: reproductive factors and exogenous hormone use. Am J Epidemiol 2008; 168(3):278-88. https://doi.org/10.1093/aje/kwn119
17. Priliana WK, Indriasari FN, Pratiwi E. Hubungan usia, jenis kelamin dan jenis kanker terhadap kualitas hidup anak dengan kanker. J Keperawatan Notokusumo 2018; 6(1):48-55.
18. Siwi A, Sumarni T, Fadly A, Hidayat A. Kualitas hidup pada pasien kanker yang menjalani kemoterapi. Prosiding Semin Nas Penelit dan Pengabdi Kd Masy 2021; 340-47.
19. White MC, Holman DM, Boehm JE, Peipins LA, Grossman M, Henley SJ. Age and cancer risk: a potentially modifiable relationship. Am J Prev Med 2014; 46(3 Suppl 1):S7-15. https://doi.org/10.1016/j.amepre.2013.10.029
20. Łukasiewicz S, Czeczelewski M, Forma A, Baj J, Sitarz R, Stanisławek A. Breast cancer-epidemiology, risk factors, classification, prognostic markers, and current treatment strategies-an updated review. Cancers (Basel) 2021; 13(17):4287. https://doi.org/10.3390/cancers13174287
21. Thandra KC, Barsouk A, Saginala K, Padala SA, Barsouk A, Rawla P. Epidemiology of non-Hodgkin's lymphoma. Med Sci (Basel) 2021; 9(1):5. https://doi.org/10.3390/medsci9010005
22. Hutajulu SH, Prabandari YS, Bintoro BS, Wiranata JA, Widiastuti M, Suryani ND, *et al*. Delays in the presentation and diagnosis of women with breast cancer in Yogyakarta, Indonesia: a retrospective observational study. PLoS One 2022; 17(1):e0262468. https://doi.org/10.1371/journal.pone.0262468
23. DiPiro JT, Yee GC, Haines LMPS, Nolin TD, Ellingrod V. Pharmacotherapy: a pathophysiologic approach, 11th Ed. Philadelphia: McGraw Hill., 2020).
24. Roila F, Molassiotis A, Herrstedt J, Aapro M, Gralla RJ, Bruera E, *et al.* 2016 MASCC and ESMO guideline update for the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting and of nausea and vomiting in advanced cancer patients. Ann Oncol 2016; 27(suppl 5):v119-33. https://doi.org/10.1093/annonc/mdw270
25. Hesketh PJ, Kris MG, Basch E, Bohlke K, Barbour SY, Clark-Snow RA, *et al*. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol 2020; 34(28):3240-3261. https://doi.org/10.1200/JCO.20.2017.74.4789