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Observation of the Reconstitution Process and Factors Influencing the Final Condition of Chemotherapy Patients in Private Hospitals

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ABSTRACT

Handling of cytostatic preparations is the aseptic handling of cancer drugs in ready-to-use packaging according to patient needs by trained pharmacists with control of environmental safety, officers, and drug preparations from toxic effects and contamination, using personal protective equipment. Resistant to handling cytostatics preparations, including preparation, mixing, handling of spills, and cytostatics waste management. This study aimed to determine the suitability of the handling of cytostatic preparations and the description of the use of chemotherapy drugs in cancer patients. This research was conducted by descriptive analytic observation, data on the handling of cytostatics preparations was obtained by observing directly in the chemotherapy drug mixing room, and data on the use of chemotherapy drugs were obtained retrospectively by looking at medical records and service sheets of mixing cytostatics preparations The population and sample of cytostatic preparation handling are all cytostatic preparation reconstitution processes that can be directly observed during the research period, while the sample for evaluating the use of chemotherapy drugs is the medical records of patients undergoing chemotherapy in 2018. The results obtained in handling cytostatic preparations in the preparation, mixing, and labeling stages are 100% to the guidelines, while the labeling stage is 86% appropriate. Evaluation of the type of use of chemotherapy drugs is known that the taxane drug class is the most widely used by 91.7%. The proper assessment of chemotherapy drugs in breast cancer patients is 92%, lung cancer is 100%, and uterine cancer is 0%. Evaluation of the correct dose of chemotherapy drugs obtained results of 0%. The conclusion of the chi-square statistical test analysis of the chemical cycle affects the patient's condition.

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INTRODUCTION

Cytostatics are chemical substances that influence the growth and proliferation of cells. Generally binds to genetic structures in the most minor parts of cells and plays a role in protein synthesis. Staff with inadequate personal protective equipment are at greater risk of experiencing mutations than those who are not exposed to carcinogens (Connor et al., 2007)

The Ministry of Health Indonesia's standard guidelines for mixing injectable drugs and handling cytostatic preparations state that mixing cytostatic drugs is divided into four stages, namely preparation, mixing, method of administration, handling spills and work accidents, and managing cytostatic waste (Ministry of Health RI, 2014). Based on research conducted by Simbolon (2020), the suitability of cytostatic handling to the hospital's Standard Operating Procedures (SOP) shows that the initial stage, process resistance, and final stage are 97%, 90%, and 95%, respectively. Cytostatic preparations themselves are medicines used in cancer treatment using chemotherapy methods.

Chemotherapy is a type of cancer treatment using chemicals. This drug is usually used to destroy dangerous cancer cells in the body. It works by inhibiting or interfering with DNA synthesis in the cell cycle. Chemotherapy treatment is comprehensive, in contrast to surgery or radiation, which is more local. The therapy given for chemotherapy consists of administering a single preparation or a combination of several drugs with chemotherapy cycles between 6 and 8 times until the desired effect is achieved (Wells et al., 2017).

Research conducted by Husna (2017) found that the use of chemotherapy drugs outside of official Food and Drug Administration (FDA)

and The National Agency of Drug and Food Control (BPOM) indications was (35.9%), 12.3% of which were supported by weak scientific evidence. In other research conducted by Sukandar et al. (2014), based on dose calculations by Body Surface Area (BSA), Fluorouracil Adriamycin Cyclophosphamide (FAC) chemotherapy regimen 92 patients received the correct dose, Cyclophosphamide Methotrexate Fluorouracil (CMF) chemotherapy regimen 67% of patients received less dose, 33% of patients received more dose, while the combination of the drug Taxon Adriamycin (AT) the drug dose is in the lower range (100%) while the combination Fluorouracil Epirubicin Cyclophosphamide (FEC), drug dosage is in the range of more (100%).

The results of research conducted by Amelia et al. showed that breast cancer patients who were treated using first-line drugs (94.44%) did not get the appropriate dose (Amelia et al., 2022). The research was conducted on dose calculations based on the decrease in glomerular filtration rate (GFR) values calculated using the Schwartz formula, and antibiotic and non-antibiotic chemotherapy drugs require a dose adjustment of 1.9% and 1.0% (Donowati et al., 2013). Inappropriate doses of chemotherapy drugs can result in reduced drug effectiveness, worsening kidney function, and increased drug toxicity in patients, so it is necessary to conduct research on the handling of cytostatic preparations and evaluate the use of chemotherapy drugs in cancer patients.

METHOD

This research is an observational descriptive study. Data evaluating the handling of cytostatic preparations was observed directly in the chemotherapy drug mixing room with evaluation of chemotherapy drugs retrospective data collection. The research obtained ethical approval No. 0383/KEPK/Adm2/V/2022 issued by the health research ethics committee of the Poltekkes Kemenkes Palembang. The study was carried out in February-July 2022 at the Palembang Muhammadiyah Hospital.

The population and sample of cytostatic preparation handling are all cytostatic preparation reconstitution processes that can be directly observed during the research period, while the sample for evaluating the use of chemotherapy drugs is the medical records of patients undergoing chemotherapy in 2018. The sampling technique is non-probability sampling using purposive sampling based on inclusion and exclusion criteria in patients diagnosed with cancer, undergoing chemotherapy, and complete medical record data. as required. The inclusion criteria are the reconstitution process of cytostatic preparations that can be observed directly, and the exclusion criteria are incomplete medical record data.

Instruments used in this research include an observation sheet prepared by researchers based on patient demographic data (patient name, medical record number, age, gender, chemotherapy cycle) and a data collection sheet on chemotherapy drug use (drug name, dose, weight, height, serum creatinine value, chemotherapy cycle, patient's final condition). The checklist sheet for handling cytostatic drugs is prepared based on guidelines for mixing injectable drugs and handling cytostatic preparations (Ministry of Health RI, 2014).

Data collection was carried out to evaluate the handling of cytostatic preparations by directly observing all stages of the reconstitution process. Data collection for evaluating the use of chemotherapy drugs was taken from the patient's medical records. The results of the reconstitution of cytostatic preparations are grouped into preparation, mixing, labeling, and labeling stages. The percentage of conformity to the preparation, mixing, labeling, and labeling stages is calculated using the following formula:

$$\% \text{ Conformance} = \frac{\text{suitable statement}}{\text{total statement}} \times 100\%$$

Evaluation data on the use of chemotherapy drugs are grouped as follows:

a. Demographic data is grouped based on patient characteristics
b. Data on the suitability of chemotherapy drug types is seen based on the Indonesian Ministry of Health's cancer management guidelines.
c. Chemotherapy drug doses are calculated based on a formula Body Surface Area (BSA). BSA is a calculation of the area of the human body. BSA can be calculated using the Mosreller 1987 formula by connecting the patient's weight and height (Mosteller, 1982; Fauzi et al., 2019).

$$BSA = \sqrt{\frac{Ht\ (cm) \times Wt\ (Kg)}{3600}}$$

Notes: Ht = height (cm); Wt = weight (kg)

The formula used in calculating the Area Under Curve (AUC) is the Calvert Formula. Calculated dose in the target area under the concentration-time curve (AUC) (Mazumdar

et al., 2000). The glomerular filtration rate (GFR) is calculated using the Cockroft-Gault formula.

Dose = AUC x (GFR + 25)

d. Evaluation of the relationship between chemotherapy cycles and the patient's final condition was analyzed using chi-square with a p-value<0.05.

RESULTS

Table 1. Data on reconstitution of cytostatic preparations

Assessment category	Assessment score	%
Preparation	10	100
Mixing	16	100
Etiquette	6	86
Labeling	3	100

Based on the research results on the reconstitution of cytostatic preparations observed directly in the chemotherapy compounding room, the preparation, mixing, and labeling results met the requirements (100%). In comparison, the labeling stage only met the requirements at 86%.

Table 2. Data on characteristics of chemotherapy patients at the hospital

Characteristics	Demographics	n	%
Age	26-35	2	2
	35-45	16	19
	46-55	37	44
	56-65	30	35
Gender	Man	20	24
	Woman	65	76
Diagnosis	Ca Breast	52	61
	Lung Ca	28	33
	Ca Rahim	5	6
Last cycle	1	13	15
	2	18	21
	3	7	8
	4	16	19
	5	6	7
	6	25	29
Final Condition of the Patient	Die	3	4
	Finished	36	42
	Stop	46	55

Data source: Medical records

Based on the results of research data on the characteristics of chemotherapy patients, it was found that the majority were between 46-55 years old at 44%, the gender was mostly female at 65%, the last cycle of chemotherapy was at most at the sixth cycle at 29%, the final condition of chemotherapy patients was at most 55%. Data on the characteristics of chemotherapy patients based on their diagnosis can be seen in each table below.

Table 3. Characteristics of chemotherapy patients diagnosed with cancer

Characteristics of chemotherapy patients	Demographics	n	%
Patients with Ca mama			
Age	26-35	1	2
	35-45	9	17
	46-55	23	44
	56-65	19	37
Gender	Man	4	8
	Woman	48	92
Chemotherapy cycle	1	7	13
	2	12	23
	3	3	6
	4	12	23
	5	3	6
	6	15	29
Final condition	Die	0	0
	Finished	15	29
	Stop	37	71
Patients with a ca lung			
Age	26-35	1	4
	35-45	5	18
	46-55	13	46
	56-65	9	32
Gender	Man	16	57
	Woman	12	43
Last cycle	1	6	21
	2	6	21
	3	4	14
	4	4	14
	5	1	4
	6	7	25
Final condition	Die	3	11
	Finished	18	64
	Stop	7	25
Patients with a cervical			
Age	35-45	2	40
	46-55	1	20
	56-65	2	40
Gender	Man	0	0
	Woman	5	100
Chemotherapy cycle	1	0	0
	2	0	0
	3	0	0
	4	0	0
	5	2	40
	6	3	60
Final condition	Die	0	0
	Finished	3	60
	Stop	2	40

Data source: Medical records

Based on the results of research on the characteristics of chemotherapy patients, there

were three types of cancer, namely breast cancer, lung cancer, and uterine cancer, with the highest age being 46-55 years, numbering 37 patients (44%), while the majority of patients diagnosed with breast cancer were 46-55 years old. Years, there were 19 patients (44%), the highest age of patients diagnosed with lung cancer was 46-55 years, there were 13 patients (46%), the highest number of patients diagnosed with uterine cancer was 56-65 years, there were two patients (40%).

Table 4. Data on chemotherapy drug use

Medicine name	Therapy class	n	%
Paclitaxel, Paclimedac, doxetacel, belotaxel, brexel	Taxon	78	91.7
Chemobatin, doxorubicin, bleocin	Platinum analogue	35	41.1
Doxotin, doxorubicin, bleocin	Cytotoxic antibiotics	39	45.8
Cyclovid, cyclophosphamide	Alkylator	13	15.2
Dacarbazine	Antineoplastic	1	1.1
Vincristine	Vinca etaposit alkaloid	4	4.7

Data source: medical records

Based on the results of research on the types of chemotherapy drugs used in cancer patients, it is known that the most widely used drugs are taxane class drugs, 91.7% of 78 patients.

Table 5. Data on the suitability of the use of chemotherapy drugs

Type cancer	Drug Suitability			
	In accordance		No	
	n	%	n	%
Ca mama	48	92	4	7.7
Ca lung	28	100	0	0
Cervical Ca	0	0	5	100

Table 6. Suitability of chemotherapy drug doses

Category	n	%
In accordance	0	0
It is not by	85	100

Based on the research results, the dose is calculated based on body surface area (BSA), area under the curve (AUC), and body weight. From the results of the dose calculation, the 100% result does not follow the guidelines for the management of breast cancer, lung cancer, and uterine cancer of the Ministry of Health RI.

Table 7. Relationship between cancer type, age, gender, and chemotherapy cycle on the patient's final condition

Category	Final condition of the patient			p-value
	D	F	S	
Types of cancer				
Ca mama	0	15	37	0.072
Ca lung	3	7	18	
Cervical Ca	0	3	2	
Chemotherapy cycle				
1	1	0	12	0.001
2	1	0	17	
3	1	0	6	
4	0	0	16	
5	0	0	6	
6	0	25	0	
Age (years)				
26-35	0	0	3	0.354
35-45	2	5	11	
46-55	0	13	23	
56-65	1	7	20	
Gender				
Woman	1	19	49	0.084
Man	2	6	9	

Notes: D (died), F (finished), S(Stopped)

Based on the research results, the patient's final condition was divided into complete, death, and stopping chemotherapy for unknown reasons. As many as 36 patients (42%) finished, three died, four patients (4%) discontinued, and 46 patients discontinued (55%). The results of the Chi-Square test with a p-value of 0.001 show that there is a relationship between the last cycle of chemotherapy and the patient's final condition.

DISCUSSION

Based on the results of research on the reconstitution of cytostatic preparations, which were observed directly in the chemotherapy compounding room, it was found that the results at the preparation, mixing, and labeling stages met the requirements (100%). In comparison, the labeling stage only met the criteria at 86%. The officers did not include drug storage temperature at the labeling stage. After all, the drug is given directly to the patient without going through a storage process, while the storage room temperature can affect the stability of drug preparations (Husna, 2020). The results of other research on the suitability of the reconstitution process at the labeling stage meet the 95% requirement (Simbolon, 2020).

Increasing age affects the incidence of cancer. Another study concludes a relationship between age and cancer incidence (Ningrum & Rahayu, 2021). This statement aligns with research conducted by Agnessia et al. (2015). Estrogen hormone secretion in women can

increase with age, which is a risk factor for breast cancer.

In the gender category, women were the most significant number of patients. Men and women are different hormonally; estrogen is a female hormone produced by the ovaries, which is active when women begin to experience menstruation. The hormone estrogen is a risk factor for cancer in women (Nurhayati, 2018). In breast cancer, estrogen comes from the aromatization of androgens or hydrolysis of conjugated estrogens because it turns out that in breast cancer, many aromatase and hydrolytic enzymes are found (Gunawan, 2011).

Based on the research results, it is known that most chemotherapy cycles are in the sixth cycle. In theory, chemotherapy treatment has a treatment cycle consisting of several cycles. According to Yeo et al. (2020), patients who undergo chemotherapy the longest will have a better quality of life. This is because the more frequently a patient undergoes chemotherapy, it means that the patient has adapted to the physical disorders experienced as a result of the effects of the chemotherapy they are undergoing. Chemotherapy is usually carried out in stages; the cycle stages to get the desired effect with acceptable side effects are 6-8 cycles (Maria et al., 2017).

The results of the Chi-Square test showed that there was no relationship between chemotherapy and the nutritional status of breast cancer patients ($p=1.000$). However, there was a relationship between energy intake and the nutritional status of breast cancer patients ($p<0.05$) (Hidayat et al., 2020).

Based on research on the evaluation of the use of chemotherapy drugs, the results of the taxane group consisted of Paclitaxel, Paclimedac, Doxetacel, Belotaxel, Brexel were the most widely used drugs, totaling 78 drugs (45%). Doxetacel is a semisynthetic taxane; this drug is approved for second-line therapy in breast and non-small cell lung cancer (Katzung et al., 2012). The cytotoxic antibiotic group is doxorubicin, the second most common class of drugs used in this study (23%). The cytotoxic class of antibiotics works by binding to DNA and inhibiting the formation of RNA and DNA (Katzung et al., 2012). Based on research by Donowati et al. (2013), the chemotherapy class of antibiotics used is bleomycin, daunorubicin, epirubicin, dactinomycin, and doxorubicin.

From the results of research on breast cancer patients treated using vincristine, the cancer management guidelines Ministry of Health RI (2018) do not recommend the use of vincristine. Still, based on points, vincristine is recommended for the treatment of acute leukemia, lymphoma, and several solid tumors such as breast cancer and lung cancer. Vincristine treats tumor sufferers in dogs, which can be transmitted through the mating process (TMP). The research showed that one of the dogs that underwent six chemotherapy sessions experienced a high increase in ALT activity values. Giving vincristine to dogs suffering from TMP had a significant effect on increasing the activity of Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) (Shukla et al., 2024).

From the results of the dose calculation, none of the guidelines for the management of breast cancer, lung cancer, and uterine cancer of the Indonesian Ministry of Health follow the guidelines for the management of breast cancer, lung cancer, and uterine cancer. Several factors must be considered when determining the dose of chemotherapy drugs, including the patient's condition and the body's ability to receive the drug. Immunohistochemical examination is used to assess patient therapy and prognosis, so it is essential for cancer patients because patients have different characteristics. (Ministry of Health RI, 2018). According to Wiguna and Manuaba (2012), of the 1014 breast cancer patients at Sanglah General Hospital Denpasar, 147 (14.49%) patients underwent immunohistochemical examination as supporting data to obtain appropriate treatment at Sanglah Hospital Denpasar, 147 (14.49%) patients underwent immunohistochemical examination.

CONCLUSION

Pharmaceutical technical staff at the hospital carried out direct observations of the reconstitution process of cytostatic preparations, and only 86% of the labeling stages were by the provisions, which could impact the safety of cytostatic preparations in hospitals.

Based on the evaluation of chemotherapy drugs, it is known that most of the medicines in the taxane class are the most widely used. Evaluation was carried out on the factors that influence the patient's final condition. The chemotherapy cycle shows that there is an influence on the patient's final condition.

Suggestions that need to be made include further evaluating the final condition of patients undergoing chemotherapy regarding their quality of life.

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