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Original Research Article

The role of pharmacist in handling drug-related problems in breast cancer patients at Dr. Cipto Mangunkusumo Hospital

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ABSTRACT

Background: DRP (Drug-Related Problems) affects the outcome of chemotherapy treatment to cancer patients. Matters related to DRP can be prevented by a pharmacist by providing drug information to doctors or other health professionals. The objective of this study was to determine the description of DRP, type of DRP, recommendations given by pharmacists on DRPs, acceptance of the results of recommendations and analysis of factors that affect DRPs.
Methods: The research method was carried out through a cross sectional study in which observational data collection was conducted concurrently. The study population was all breast cancer patients from the Division of Surgical Oncology in the period January - April 2018 as many as 228 people. The collected data consisted of dosage suitability, suitability of carrier fluid volume, patient adherence to the schedule for breast cancer patients, recommendations given by pharmacists and the results of acceptance of pharmacist recommendations.
Results: Based on research findings, the incidence of DRP was 76.3%. Most problems were regarding carrier fluid volume (64.5%) and dose mismatch (30%). There was also a DRP combination of carrier fluid volume and dose of 19%. The pharmacist's recommendation was to change the dose by 15.52%, change the carrier fluid volume by 60.92%, and change the dose and volume of the carrier fluid by 23.56%. The recommended dosage received by doctors was 13 patients (7.47%), changing the volume of carrier fluid received by doctors by 106 patients (60.92%).
Conclusions: Pharmacists can prevent DRPs through providing drug information to doctors or other health professionals so that increased communication between health professionals is required.

Keywords: Breast cancer, Carrier fluid volume, Dose, Drug-related Problems

INTRODUCTION

Drug-Related Problems (DRPs) are undesirable conditions which are related to drug therapy and things that interfere with the expected treatment by the patient.[1,2] A pharmacist should be able to prevent DRPs through providing drug information to doctors or other health professionals.[3] Providing drug information has an important role in improving the patient life quality and providing quality services for patients.[4]

Pharmaceutical care is a form of service and direct responsibility of the pharmacist profession in pharmaceutical work to improve the patient life quality. In an effort to prevent drug-related problems, a pharmacist plays an important role based on

pharmaceutical service standards in hospitals listed in the Ministry of Health No. 72 of 2016.[5]

The real role of clinical pharmacy in preventing actual or potential DRPs is by screening prescription/ administrative, pharmaceutical, and clinical aspects. The role of this clinical pharmacy is listed in hospital accreditation standards.[6] To conduct screening quickly and precisely, it is necessary to map problems by identifying drug-related problems (DRPs) on outpatient prescriptions. In this study, identification of DRPs was carried out in adult patients with breast cancer since breast cancer is the most common disease in the world.[7]

Breast cancer is the most common cancer in women in developed and developing countries. Based on data from Globocan, the International Agency for Research on Cancer (IARC), in 2012, there were 14,067,894 new cancer cases and 8,201,575 cancer deaths worldwide in the following order: breast cancer 43.3%, prostate cancer 30.7% and lung cancer 23.1%. Although breast cancer is considered a disease of developed countries, nearly 50% of breast cancer cases and 58% of deaths occur in developing countries.[8]

The risk of developing DRPs will increase with the influence of several factors including age, sex, history of curative chemotherapy, the presence or absence of comorbidities and the number of drugs used. This study shows that pharmacists play a role in the implementation of palliative therapy, especially in patients with advanced solid cancer which is to minimize the risk of DRPs. Thus, the patient life quality can be improved.[9]

Based on research conducted by Megawati, a breast cancer patient at Dr. Cipto Mangunkusumo Hospital is number 2 in Dr. Cipto Mangunkusumo Hospital, 50-70% of breast cancer patients are patients with advanced stage. At an advanced stage, the patient is generally given neoadjuvant chemotherapy and palliative chemotherapy and 30% of early-stage patients undergo adjuvant chemotherapy. One of the successes of giving chemotherapy is the right dose, giving the right volume of carrier fluid and patient compliance with the chemotherapy schedule.[10]

Drug-related problems affect the outcome of chemotherapy treatment to cancer patients. The role of pharmacists is still not maximal in overcoming drug-related problems in patients receiving chemotherapy. The objective of this research is to find out the description of drug-related problems (DRP) and the role of pharmacists in Dr. Cipto Mangunkusumo Hospital in providing recommendations.

METHODS

The study was conducted using a cross sectional study and observation data collection was carried out concurrently for breast cancer patients in the Integrated Outpatient Unit of Dr. Cipto Mangunkusumo Hospital and the role of pharmacists in providing recommendations to doctors or nurses. Data sources include data from the patient's medical record and forms of mixing cytostatic drugs. The study population was all breast cancer patients who were undergoing chemotherapy in the action room of the Integrated Outpatient Unit during the January-April 2018 period.

The total sample of the study were all breast cancer patients from surgical poly who underwent chemotherapy for 4 months with the following inclusion criteria: adult women (18 years) with a diagnosis of breast cancer, breast cancer patients from poly Oncology Surgery, undergoing chemotherapy in the 4th floor of the action room of Outpatient Poly during January 2018-April 2018, obtaining chemotherapy drugs intravenously infusion. Exclusion criteria consisted of: breast cancer patients from the department of disease in hematology because of the small number of patients and to focus more on one department, patients who were enrolled in the inclusion criteria but resigned, patients who discontinued chemotherapy treatment for some reason, patients underwent chemotherapy in other place due to distant reasons during the study period.

RESULTS

The Health Research Ethics Committee of the Faculty of Medicine, University of Indonesia Number: 905/UN2.F1/Ethics/2017, has provided information passing the ethical review for this study.

Patient characteristics/ patient sociodemographic

This research was conducted by verifying the mixing forms of drugs that entered into cytostatic satellites. Then, the DRP event is identified and recommendations are given to the doctor and the results are collected.

This research involved 228 subjects. Table 1 shows that the age of breast cancer patients in surgical poly is mostly above 36-45 years as many as 72 people (31.6%). All of them were women with the most staging groups, far advanced stage (44.3%). The majority of patient education is a Senior High School graduate. Regiments are evenly distributed across all lines, but most are in the first line (39%). The incidence of DRPs was 76.3%.

The 76.3% DRPs incidence is quite high. This was also experienced by Darmais Hospital where the characteristics of the majority of breast cancer patients were 51-60 years old (35%), had a family history (61.2%); giving birth 3 to 4 times (42.7%), and high fat consumption (76.7%). Factors of exposure associated with breast cancer are smoking (76%); estrogen (43%); industrial materials (41%); and radiation (21%). Occupational factors do not play an important role but environmental factors have a high role in the occurrence of breast cancer in Indonesia.[11]

Table 1: Characteristics of breast cancer patients in surgery poly.

Characteristics		Total	
		N	%
Age	26-35 years	16	7.0%
	36-45 years	72	31.6%
	46-55 years	71	31.1%
	56-65 years	61	26.8%
	> 65 years	8	3.5%
Sex	Female	228	100.0%
	Male	0	0
Education	Elementary School	10	4.4%
	Junior High School	11	4.8%
	Senior High School	184	80.7%
	Bachelor's Degree	5	2.2%
	Associate degree	18	7.9%
Stadium	Early stage	15	6.6%
	Local advanced stage	23	10.1%
	Next advanced stage	101	44.3%
	Tx Nx M0	89	39.0%
Chemo-therapy Regimen	First line (CAF, AC-T, CEF, CMF)	89	39.0%
	Second line (TC, TCH)	69	30.3%
	Third line (Gemcitabine, Navelbine)	70	30.7%
Drug related problems	Yes	174	76.3%
	No	54	23.7%

Table 2: Types of DRP that occur in the integrated outpatient unit of Dr. Cipto Mangunkusumo Hospital in breast cancer patients in surgical poly.

Types of DRPs	n	%
Carrier fluid volume	96	55.17%
Appropriate dose	27	15.52%
Carrier fluid volume and dose	41	23.56%
Patient compliance and carrier fluid volume	9	5.17%
Patient compliance, carrier fluid dose and volume	1	0.57%
Dose Issue		
Appropriate dose	160	70.2%
Lower dose	49	21.5%
Higher dose	19	8.3%
Carrier fluid volume		
In accordance with protocol	81	35.5%
Not in accordance with protocol	147	64.5%
Patient compliance with chemotherapy schedules		
Compliant	212	93.0%
Not compliant	16	7.0%

Types of DRPs

Types of DRP that occur in the Integrated Outpatient Unit in breast cancer patients in surgical poly can be seen in Table 2. Drug-Related Problems, experienced by 76.3% of subjects with the most problems, were regarding the carrier fluid volume of 64.5% and dose mismatch of 30%. Some subjects also experienced DRP in combination of the two main problems above for example a combination of carrier fluid volume problems and dose problems that occurred in 23.56% of subjects.

Pharmacist recommendations

Recommendations given by Pharmacists regarding DRP can be seen in Table 3.

Table 3: Recommendations given by pharmacists regarding DRP in the Integrated Outpatient Unit of Dr. Cipto Mangunkusumo Hospital.

Recommendations	n	%
Change the dose	27	15.52%
Change the carrier fluid volume	106	60.92%
Change the carrier fluid volume and dose	41	23.56%

The most recommended recommendations from pharmacists are to change the dose to 15.52%, to change the carrier fluid volume to 60.92%, and to change the dose and volume of the carrier fluid to 23.56%.

Pharmacist recommendation results

Results of acceptance of recommendations from doctors toward pharmacist recommendations can be seen in Table 4.

Table 4: Results of acceptance of recommendations from doctors toward pharmacist recommendations.

Results of Recommendations	n	%
Changing the dose is accepted	13	7.47%
Changing the dose is not accepted	14	8.05%
Changing the carrier fluid volume is accepted	106	60.92%
Changing the dose is not accepted, changing the carrier fluid volume is accepted	41	23.56%

From the recommendations for changing the dosage, doctors accepted 13 patients (7.47%) while 55 patients (31.61%) were not accepted. Then, the doctor accepted to change the carrier fluid volume by 106 patients (60.92%).

The reason doctors do not want to change the dose is because the patient's condition is weak and the side effects that will arise are more burdensome to the patient. Meanwhile, doctors want to accept pharmacist recommendations for carrier fluid volume because it complies with the anti-cancer drug protocol.

Results of analysis of the factors that influence DRPs

Analysis of dose and regimen factor

Analysis of dose and regimen can be seen in Table 5. Chi square analysis results obtained a value of p=0.874. A value of p>0.05 means that there is no relationship between the type of regimen and the dose appropriateness, or it is not significant because p=0.874. Supposedly, the more complications, the more inappropriate, but it turns out that in each line there are different dosage mismatches. Writing doses in each line needs to be considered because many doses of writing are not appropriate.

Table 5: Analysis of dose and regimen.

Regimen	Dose				
	Appropriate		Not appropriate		p
	n	%	n	%	
First line	62	69.7%	27	30.3%	0.874
Second line	50	72.5%	19	27.5%	
Third line	48	68.6%	22	31.4%	

Analysis of dose problem and regimen factor

Analysis of dose problem and regimen factor can be seen in Table 6.

Table 6: Analysis of dose problem and regimen factor.

Regimen	Dose Problems				
	Lower dose		Higher dose		p
	n	%	n	%	
First line	24	88.9%	3	11.1%	0.006
Second line	17	89.5%	2	10.5%	
Third line	12	54.5%	10	45.5%	

Analysis of dose mismatches to the regimens obtained insignificant results, but if we look at the results of the analysis of the problem of doses to the regimen, it obtained a value of p=0.006 and a value of p<0.05 means that there were significant differences in each line in the dosing of chemotherapy drugs, as follows:

- It turns out that the mismatch dose results in lower doses and higher doses.
- In the first-line regimen there are many doses lower than the protocol and the higher the line so that the lower the dose decreases.
- At higher doses, the lining looks higher (in the third line). There is an increase in the administration of higher doses so that the dosing on each line needs to be considered.

Cancer patients who are treated with chemotherapy will not benefit from more doses of chemotherapy but instead will endanger the patient him/herself.[12]

In this study, researchers did not monitor the progress of the use of chemotherapy drugs until the protocol used was completed due to limited research time.

Analysis of Compliance and Regimen Factor

Analysis of factors of compliance to chemotherapy schedules and regimens can be seen in Table 7. In the Chi Square test analysis of compliance to chemotherapy and regimen, it has a value of p=0.753 then the value of p>0.05 which means:

- The level of compliance of patients to the chemotherapy schedule in the first line decreased the

level of adherence to the second line and has increased again in the third line even though the increase is less than 5%.

- Non-compliance of patients in the second line is greater (8.7%) than in the first and third lines but the difference is not statistically significant.
- On the higher lines, the level of patient non-compliance with the chemotherapy schedule should be even higher.

Table 7: Analysis of factors of compliance to chemotherapy schedules and regimens.

Regimen	Compliance to chemotherapy schedules				
	Compliant		Not compliant		p
	n	%	n	%	
First line	84	94.4%	5	5.6%	0.753
Second line	63	91.3%	6	8.7%	
Third line	65	92.9%	5	7.1%	

Based on the results of the study by Entris Sutrisno, patient compliance was 72% compared to non-compliance to the chemotherapy schedule by 28% with various factors causing it.[13]

Analysis of carrier liquid factors in the treatment regimen

Factors associated with carrier fluid volume in the treatment regimen can be seen in Table 8.

Table 8: Factors associated with carrier fluid volume in the treatment regimen.

Regimen	Carrier fluid volume				
	In accordance with the protocol		Not in accordance with the protocol		p
	n	%	n	%	
First line	11	12.4%	78	87.6%	0.000
Second line	25	36.2%	44	63.8%	
Third line	45	64.3%	25	35.7%	

Analysis on the regimen with carrier fluid was 87.6% which was not in accordance with the protocol in the first line, in the second line (63.8%), in the third line (35.7%) with a value of p=0,000, then the value of p<0.05 means:

Analysis of patient compliance with chemotherapy schedules and patient cycles

Analysis of compliance with chemotherapy schedules and chemotherapy cycle factor can be seen in Table 9.

Table 9: Analysis of compliance with chemotherapy schedules and chemotherapy cycle factor.

Compliance data	Patient chemotherapy cycle										
	2nd cycle		3rd cycle		4th cycle		5th cycle		6th cycle		p
	n	%	n	%	n	%	n	%	n	%	
1 week delay	2	5.6%	7	19.4%	7	19.4%	8	22.2%	12	33.3%	0.709
2 weeks delay	0	0.0%	2	33.3%	0	0.0%	2	33.3%	2	33.3%	
3 weeks delay	0	0.0%	0	0.0%	1	25.0%	0	0.0%	3	75.0%	
4 weeks delay	1	25.0%	1	25.0%	0	0.0%	0	0.0%	2	50.0%	
5 weeks delay	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	100%	
7 weeks delay	0	0.0%	1	100%	0	0.0%	0	0.0%	0	0.0%	

The p value in the chi-square analysis shows the number 0.709 which indicates that the patient's non-compliance with the chemotherapy cycle can occur in each cycle. However, a delay of 1 week on the chemotherapy schedule can still be tolerated. However, if delays occur in the 2nd week until the 6th week, it needs to be aware of.

DISCUSSION

Dose problems have a regimen of p=0.006, then a p-value <0.05. It was found that many dose problems were found in the first-line regimen namely lower doses of the following protocol: 1) the doctor did not want to accept the dose recommendations because the doctor saw the patient's condition which looked weak so it was feared that the side effects of using chemotherapy drugs would make the patient even weaker, 2) the doctor did not inform the pharmacy about the cause of the dose reduction; for instance, SGOT SGPT laboratory results increase 5 times so the dose must be lowered, 3) if the administration of the drug is lower than the usual dose, the therapeutic effect cannot reach the maximum effect. When the dose of the drug is higher than the usual dose, this can result in: 1) increased side effects such as nausea and vomiting can reduce patient life quality, 2) strengthen the work of the kidneys thereby reducing kidney function, 3) causes death due to drug poisoning.

Patient non-compliance with the regimen (p=0.753, p value >0.05), there was no significant difference on each line, the difference was less than 5%. There are several things that can cause non-compliance with treatment in breast cancer patients such as the condition and treatment in breast cancer patients can cause stress so that it not only affects the physical condition but also affects the psychological. There are several side effects that can be caused by chemotherapy, including: reduced appetite, alopecia (hair loss), weight loss, pain in the breast area. This is the cause of non-compliance of patients in having chemotherapy. Noncompliance of patients with the chemotherapy cycle schedule is caused by the patient's condition which is the side effects of chemotherapy drugs one of which affects blood levels including leukopenia, thrombocytopenia or anemia. A person's economic level will affect compliance. A person's higher economy will make them more obedient to treatment. In this case the patient has no problems with economic factors because the treatment is borne by Social Security Administration Agency (BPJS). Availability of drugs also affects patient compliance with chemotherapy schedules. However, at the time of the study the availability of drugs was available and was in accordance with the Analysis on the regimen with carrier fluid was 87.6% which was not in accordance with the protocol in the first line, in the second line (63.8%), in the third line (35.7%) with a value of p=0.000, then the value of p<0.05 means: Writing the volume of carrier fluid in the chemotherapy regimen has more incompatibility with the protocol in the first line than the second and third lines. Thus, writing the carrier fluid volume in the first line needs to be considered because more patients get first-line therapy. It is the same with the second and third lines because there are still writing errors even though the percentage is decreasing.

Writing the volume of carrier fluid with chemotherapy regimen has a value of p=0.000, then the value of p<0.05. Proposals to change the carrier fluid volume are accepted because it is in accordance with the existing protocol. Volume of carrier fluid that is not in accordance with the protocol will affect the therapeutic effect of the patient, one of which can cause extravasation where the drug enters the tissue which can damage the tissue. It can cause discomfort and harm the patient, so the writing needs to be obeyed according to the protocol. Factors causing extravasation include the concentration of cytostatic drugs, the length of time tissue is affected by drug infiltration, and the amount of infiltrated drug.

Analysis on the regimen with carrier fluid was 87.6% which was not in accordance with the protocol in the first line, in the second line (63.8%), in the third line (35.7%) with a value of p=0.000, then the value of p<0.05. Writing the volume of carrier fluid in the chemotherapy regimen has more incompatibility with the protocol in the first line than the second and third lines. Thus, writing the carrier fluid volume in the first line needs to be considered because more patients get first-line therapy. It is the same with the second and third lines because there are still writing errors even though the percentage is decreasing.

An example of starting Navelbine is 30 mg/m^2 given weekly. The recommended method of administration is intravenous injection over 6 to 10 minutes. Navelbine can cause enough irritation, local tissue necrosis or thrombophlebitis. If extravasation occurs, the injection must be stopped immediately, and the remaining portion of the dose should be inserted into another vein.[14]

CONCLUSION

DRPs in breast cancer patients in surgical poly were experienced by 76.3% of patients aged 36-45 years (31.6%), all women, next advanced stage (44%), Senior High School educated. Most regimens are in the first line (39%). The most common problems are carrier volume (64.5%) and dose mismatch (30%). Some subjects also experienced DRP combined carrier fluid volumes and doses which occurred in 19% of the subjects. Pharmacist recommendations include changing the dose 15.52%, changing the carrier fluid volume 60.92%, and changing the dose and volume of the carrier fluid 23.56%. Changing the dose that is accepted by doctors was 13 patients (7.47%) while 55 patients (31.61%) are not accepted by doctors. Changing the carrier fluid volume is accepted by doctors in 106 patients (60.92%).

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