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DRUG-RELATED PROBLEMS IN PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA CANCER

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ABSTRACT

Acute lymphoblastic leukemia that occurs in children is about 75% - 80%. The main treatment of acute lymphoblastic leukemia in children involves the use of chemotherapy with complex regimens and higher doses. Complex drug therapy causes a high risk of drug-related problems (DRPs). The purpose of this study was to determine the percentage of DRPs, identify the types of DRPs, and evaluate the correlation between age, gender, comorbidities, and the number of drugs with the incidence of DRPs in pediatric patients with acute lymphoblastic leukemia in Dr. Kariadi Hospital and Dr. Moewardi Hospital in the period July - October 2019. This study is an evaluative descriptive study with prospective data collection. The inclusion criteria in this study were patients diagnosed with acute lymphoblastic leukemia, patients aged 0-<18 years, and patients undergoing inpatient treatment or one-day care. Data were then analyzed using SPSS, namely Chi-Square. The use of chemotherapy regimens in this study was based on the hospital's acute lymphoblastic leukemia treatment protocol—identification of DRPs based on PCNE V8.02 2017. DRPs found in pediatric patients with acute lymphoblastic leukemia are the safety of therapy category adverse drug reactions (P2.1)

36.36% (36 patients). Adverse drug reactions are undesirable or dangerous responses to drugs that can occur at normal doses. This happens because the mechanism of action of chemotherapy drugs is not selective, so they can attack normal, active cells such as bone marrow cells, digestive tract and hair follicles. The results of the Chi-Square analysis showed no association between the risk factors of age, gender, comorbidities, and the number of drugs with the incidence of DRPs (P>0.05).

Keywords: Drug-related problems, pediatrics, acute lymphoblastic leukemia, chemotherapy.

ABSTRAK

Pengobatan utama leukemia limfoblastik akut pada anak-anak melibatkan penggunaan kemoterapi dengan regimen yang kompleks dan dosis yang lebih tinggi. Terapi obat yang kompleks menyebabkan tingginya risiko kejadian drug related problems (DRPs). Tujuan dari penelitian ini adalah untuk mengetahui persentase DRPs, mengidentifikasi jenis DRPs serta mengevaluasi hubungan faktor umur, jenis kelamin, komorbid dan jumlah obat dengan kejadian DRPs pada pasien pediatri kanker leukemia limfoblastik akut di RSUP Dr. Kariadi dan RSUD Dr. Moewardi periode Juli - Oktober 2019. Penelitian ini merupakan penelitian deskriptif evaluatif dengan pengambilan data secara prospektif. Kriteria inklusi pada penelitian ini pasien dengan diagnosa leukemia limfoblastik akut, pasien berusia 0-<18 tahun dan pasien menjalani pengobatan rawat inap maupun one day care. Data selanjutnya dianalisis menggunakan SPSS yaitu Chi-Square. Identifikasi DRPs berdasarkan PCNE V8.02 2017. DRPs yang ditemukan pada pasien pediatri leukemia limfoblastik akut adalah keamanan terapi kategori adverse drug reactions (P2.1) 36,36% (36 pasien). Adverse drug reactions merupakan respon terhadap obat yang tidak diinginkan atau berbahaya dapat terjadi pada dosis nomal. Hal ini terjadi mekanisme kerja obat kemoterapi tidak bersifat selektif maka dapat menyerang sel-sel normal yang bersifat aktif seperti sel sumsum tulang, saluran pencernaan dan folikel rambut. Hasil dari analisis Chi-Square menunjukkan tidak ada hubungan antara faktor risiko umur, jenis kelamin, komorbid dan jumlah obat dengan kejadian DRPs (P>0,05).

Kata Kunci : Drug related problems, pediatri, leukemia limfoblastik akut, kemoterapi

INTRODUCTION

According to data from the Union for International Cancer Control (UICC), every year there are about 176,000 children diagnosed with cancer. 25% of acute lymphoblastic leukemia occur in children before the age of 15 years and 19% who are less than 20 years old (Hunger *et al.*, 2014). In Indonesia, there are about 11,000 cases of childhood cancer each year, and there are about 650 cases of childhood cancer in Jakarta. One-third of childhood cancers are generally leukemia (Kementerian Kesehatan, 2014). In 2012, in Indonesia, cancer accounted for 10% of deaths in children (Novrianda *et al*., 2016). Leukemia is divided into several types, namely acute myeloblastic leukemia (LMA), acute lymphoblastic leukemia (LLA), chronic myeloblastic leukemia (LMK), and chronic lymphoblastic leukemia (LLK) (Simanjorang *et al*., 2013). The most common leukemia in children is acute lymphoblastic leukemia, about 75% - 80% (Novrianda *et al*., 2016). The main treatment of LLA in children involves chemotherapy with more complex regimens over a long period (treatment duration of 2 - 3 years) (Brown *et al*., 2017). Drug regimens given in pediatrics tend to be more numerous, including methotrexate, pegaspargase, vincristine, and steroids (prednisone and dexamethasone) overall, given at higher doses (Brown *et al*., 2017).

Complex medication therapy leads to a high risk of drug-related problems (DRPs) (Fog *et al*., 2017). Drug-related problems are drug-related problems that actually or potentially interfere with the achievement of therapeutic goals *(Pharmaceutical Care Network Europe*, 2017). The classification of drug-related problems according to PCNE version 8.02 consists of 3 main problem domains: therapeutic effectiveness, therapeutic safety, and others. The causes of DRPs, according to PCNE, comprised eight main domains: drug selection, drug form selection, dose selection, therapy duration selection, dispensing, drug use process, patient behavior, and others.

Previous research shows the incidence of drug-related problems in pediatric patients with acute lymphoblastic leukemia cancer. Ertanti's study (2010) on the evaluation of drug-related issues in chemotherapy treatment in pediatric patients with acute lymphoblastic leukemia stated that 27% required additional drugs, 2.7% did not require additional drugs, 2.7% underdose, and 2.7% overdose. Based on research by Budiastuti et al. (2019), DRPs that occur in LLA patients include adverse drug reactions because chemotherapy drugs can damage normal cells, causing side effects (Aslam *et al*., 2014). Research by Sitaresmi et al. (2009) on side effects that are often reported by parents of pediatric patients with acute lymphoblastic leukemia include infection, leg weakness, hair loss, nausea, vomiting, oral mucositis, abdominal pain, and bleeding. Another study by Isnani (2017) on the evaluation of 6-mercaptopurine toxicity is associated with the occurrence of hepatotoxicity so that liver function tests become abnormal. Cancer patients have the potential to experience DRPs due to high toxicity and the use of complex chemotherapy regimens (Doherty, 2009). Pharmacists have an important role in detecting, preventing, and overcoming drug-related problems (Budiastuti *et al*., 2019; Hohmann *et al.*, 2012). Based on research by Ramadaniati et al. (2016) on clinical pharmacy interventions in pediatric hematology-oncology, satellite pharmacies can improve medication safety and pharmaceutical care and minimize medication errors. Based on the above, the researchers identified drug-related problems with DRPs in pediatric patients with acute lymphoblastic leukemia cancer at Dr. Kariadi Hospital and Dr. Moewardi Regional Public Hospital.

METHODS

This study used a non-experimental research design with an evaluative descriptive design. Patient tracking and data collection were conducted prospectively using medical record data. Interviews were conducted with parents of pediatric patients with acute lymphoblastic leukemia and other health workers at Dr. Kariadi Hospital and Dr. Moewardi Regional Public Hospital. The identification of drug-related problems was then analyzed using the *Pharmaceutical Care Network Europe* 2017. The research subject is the sample needed in this study. The research samples were pediatric patients with acute lymphoblastic leukemia cancer. Sampling using a consecutive sampling technique is a sample that meets the inclusion criteria. The minimum sample size used in this study was calculated using the following equation (Naing *et al.*, 2006; Pourhoseingholi *et al*., 2013).

$$\frac{Z^2_{1-\frac{\alpha}{2}}\, x\, P\,(1-p)}{d^2}$$

explanation :

n = Number of Samples

$Z^2_{1-\alpha/2}$ = Z score at 1 - α/2 1.96 with a value of α = 0.05

p = The estimated proportion of DRPs was 37.9% or 0.37 (Ertanti, 2010)

d = *precision 10% or 0.10*

The following results are obtained using the sample formula above.:

$$n = \frac{1{,}96^2 x\ 0{,}37\ x\ (1 - 0{,}37)}{0{,}10^2}$$

n = 89,54 patients rounded up 90

Based on the above calculation, the sample required,d, is 89.54 and then rounded to 90 patients. Researchers need 90 patients as a sample to get 95% confidence with a relative precision of 10% in estimating the incidence of drug-related problems in pediatric patients with acute lymphoblastic leukemia. In this study, the number of patients used was 99 patients. The following are the inclusion and exclusion criteria for drug-related problems in pediatric patients with acute lymphoblastic leukemia cancer:

Inclusion Criteria

a. Pediatric patients with cancer diagnosis of acute lymphoblastic leukemia who underwent chemotherapy at Dr. Kariadi Hospital and Dr. Moewardi Hospital.
b. Patients aged 0 - <18 years old.
c. Patients received treatment for acute lymphoblastic leukemia either inpatient or one day care.
d. The patient's parents are willing to be respondents in the study.

Exclusion Criteria

a. Pediatric patients with a diagnosis of leukemia cancer were admitted due to the deterioration of their condition rather than for chemotherapy.
b. The patient died before chemotherapy.

Data analysis techniques performed in the study include DRP identification analysis and statistical analysis. DRPs analysis is based on the classification found in PCNE 2017. The data that has been obtained is then analyzed using the Statistical Package for Social Science (SPSS) with the following stages: Univariate analysis, which is used to obtain a description of the observed variables, namely age, gender, number of drugs, and comorbidities.

RESULTS AND DISCUSSION

1. Characteristics of Patients

Table 1 shows the characteristics of pediatric patients with acute lymphoblastic leukemia cancer at Dr. Kariadi Hospital and Dr. Moewardi Hospital with 99 patients.

Table 1
Characteristics in LLA Pediatric Patients

Characteristics	Total (N=99)	Percentage (%)
Gender		
Male	55	55,55
Female	44	44,44
Age		
1 - 9 years	66	66,66
≥10 years	33	33,33
Comorbidities		
Metabolic disorders	9	21,95
Hematologic disorders	18	43,90
Febrile neutropenia	3	7,31
UTI	1	2,43
Cholestatis	1	2,43
Cerebral leukemia	2	4,87
Sepsis	1	2,43
Bronchopneumonia	1	2,43

Pneumonia	1	2,43
Acute kidney Injury	1	2,43
Miliaria abdomen	1	2,43
Miliaria ruba	1	2,43
Rhinitis vasomotor allergy	1	2,43

Description: Urinary tract infection (UTI), metabolic disorders (hypokalemia, hyponatremia, hypophosphatemia, hyperkalium, hyperphosphatemia, hyperleukocytosis, hyperchloride and hyperuricemia) and hematological disorders (anemia and thrombocytopenia).

In this study, the number of male patients was 55 patients (55.55%), and female patients were 44 patients (44.44%). The data above shows that pediatric patients with acute lymphoblastic leukemia aged 1 - 9 years were 66 patients (66.66%) and aged ≥10 years 33 patients (33.33%). According to Hunger et al. (2014), acute lymphoblastic leukemia is more common in children before the age of 15 years. According to Voute et al. (2005), the highest rate of acute lymphoblastic leukemia in children is at the age of 2 - 7 years.

Table 2
Comorbidities in LLA Pediatric Patients

Comorbidities	patient number	Total (N=24)	Persentage (%)
Metabolic disorders	2, 15 dan 20	3	12,5
Hematologic disorders (anemia and plateletpenia) + febrile neutropenia + metabolic disorders	4, 10, 5, 34, 45, 41, 53, 68, 38, 25 and 101	11	45,8
Hematologic disorders+febrile neutropenia+cerebral leukemia+bronchopneumonia	6	1	4,1
Hematological disorders (anemia)+febrile neutropenia+pneumonia+cerebral leukemia	24	1	4,1
Hematologic disorders (anemia and thrombocytopenia)+metabolic disorders+acute kidney injury.	37, 65 and 66	3	12,5
Sepsis+hematological disorders (anemia and thrombocytopenia)+cholestatis+metabolic disorders	74	1	4,1
Urinary tract infection	76	1	4,1
Abdominal miliaria and miliaria ruba	83 of 40	2	8,3
Hematologic disorder (thrombocytopenia) + allergic vasomotor rhinitis.	39	1	4,1

Table 2 shows that patients who received chemotherapy had comorbidities caused by disease or side effects of chemotherapy drugs. The number of patients with comorbidities was 24 patients (24.24%) and without comorbidities 75 patients (75.75%).

Table 3 shows the drug-related problems that occurred in pediatric patients with acute lymphoblastic leukemia at Dr. Kariadi and Dr. Moewardi.

Table 3
Types of DRPs in Pediatric ALL Patients

Code V8.02	Types of DRPs	Total (Percentage %)
	Therapeutic Effectiveness	
P1.1	There is no therapeutic effect of the drug	0 (0%)
P1.2	The treatment effect is not optimal	0 (0%)
P1.3	Indications or symptoms are not treated	0 (0%)
	Therapy safety	
P2.1	Adverse drug reactions	36 (36,36%)
	Others	
P3.2	Unnecessary drug therapy	0 (0%)

Table 4 shows the results of the BMP examination of the three patients who can prove the effectiveness of the therapy

Table 4
BMP Examination Results in Pediatric ALL Patients

Patient Number	The examination result of *Bone Marrow Puncture* (BMP)
23	Cellularity of hypocellular bone marrow Bilineage dysplasia with erythroid hyperplasia. Lymphoblast 1%
38	Impression: Picture of complete remission with dysplasia due to therapy. Cellularity of hypocellular bone marrow Bilineage dysplasia with moderate erythroid hyperplasia. Lymphoblast 2% Impression: Picture of complete
72	Cellularity of hypocellular bone marrow Bilineage dysplasia with moderate erythroid hyperplasia. Lymphoblast 2% Impression: Picture of complete remission with dysplasia due to therapy.

Table 5 shows the genesis of adverse drug reactions that occurred in pediatric acute lymphoblastic leukemia cancer patients at RSUP Dr. Kariadi and Dr. Moewardi.

Table 5
Adverse Drug Reactions in Pediatric ALL Patients

Organ System	*Adverse Drug Reactions* (N= 36)	Percentage (%)
Digestive system disorders	Nausea and Vomiting (n=24)	66,66
	Oral Mucositis (n=6)	16,66
lood and lymphatic system disorders	Febril neutropenia (n=1)	2,7
Skin and subcutaneous tissue disorders	Alopecia (n=1)	2,7
Heart problems	Cardiotoxicity (n=2)	5,55
Immune system disorders	Hipersensitivity (n=2)	5,55

DISCUSSIONS

In this study the number of male patients was 55 patients (55.55%) and 44 female patients (44.44%). This shows that the incidence of acute lymphoblastic leukemia is more common in men. According to research by M. Telvik Dorak (2006), the risk of leukemia in male children is 3.05 times greater than that of female children. Research by Setiawan (2011) shows that men suffer from ALL more often than women with the ratio of men to women being 1: 2. Research by Dat (2016) shows that the prevalence of pediatric acute lymphoblastic leukemia at Sanglah General Hospital is more common in boys. with ages 18 months to 10 years. Men are exposed to more carcinogens and have hormonal or metabolic differences from women (Lufritayanti et al, 2015). Based on the data above, it shows that there are 66 pediatric patients with acute lymphoblastic leukemia aged 1 - 9 years (66.66%) and 33 patients aged ≥10 years (33.33%). According to Hunger et al (2014) acute lymphoblastic leukemia occurs more often in children before the age of 15 years. According to Voute et al (2005) the highest rate of acute lymphoblastic leukemia in children is aged 2 - 7 years.

1. Characteristics of Chemotherapy Drugs in Pediatric ALL Patients

The main treatment for patients with acute lymphoblastic leukemia takes place over a long period of approximately 2 - 3 years. ALL therapy consists of several phases, namely induction, consolidation, intensification and maintenance (NCCN, 2017). The chemotherapy protocols used are the 2018 standard risk protocol, the 2018 high risk protocol, the 2006 standard risk protocol, the 2016 IGH-RISK/very-high-risk-b-cell protocol, the hyper-CVAD protocol and the 2008 R3 protocol. The

protocol lies in the amount of drug, drug dose and treatment phase. In this study, the patient (no. 46) who used the hyper-CVAD protocol was a patient who experienced ALL relapse. This patient had previously used the 2013 high risk ALL protocol and the 2018 high risk protocol. chemotherapy treatment profile in the induction phase using a combination of drugs including methotrexate, vincristine, L-asparaginase and daunorubicin. Chemotherapy agents used during the induction phase are methotrexate, vincristine, L-asparaginase/PEG-asparaginase, corticosteroids with the addition of an anthracycline regimen, usually daunorubicin or doxorubicin (Cooper & Brown, 2015).

2. Comorbidities in Pediatric ALL Patients

In this study, comorbidities were found in the form of hematological disorders, febrile neutropenia, electrolyte disorders, metabolic disorders, bronchopneumonia, cerebral leukemia, allergic vasomotor rhinitis, cholestasis, sepsis, urinary tract infections, abdominal miliaria, miliaria ruba and acute kidney injury (AKI). Comorbidities that often occur are hematological disorders and metabolic disorders. Hematological disorders that often occur in patients are anemia and thrombocytopenia. This is because in patients with acute lymphoblastic leukemia there are leukemia cells in the bone marrow, resulting in a decrease in the number of megakaryocytes, resulting in a decrease in platelet and erythrocyte production (Pertiwi et al., 2012). Hematological disorders can also be caused by the use of chemotherapy which is myelosuppressive (suppresses or suppresses the growth of blood stem cells in the bone marrow) by inducing apoptosis of young hematopoietic cells (Bartucci et al., 2011). Febrile neutropenia is a serious complication and often occurs in children with malignancy, making patients susceptible to infection (Muliyani et al., 2017). Hyperleukocytosis is an increase in the number of peripheral blood leukocytes exceeding 100.00/µL. This is due to impaired release of leukocyte cells from the bone marrow (Taylor et al., 2002). Metabolic disorders usually occur in tumor lysis syndrome which is often found in patients with acute lymphoblastic leukemia (Nugroho, 2010).

3. The genesis of DRPs in pediatric ALL patients

Identification of DRPs is carried out based on PCNE version 8.02 2017. PCNE classifies types of DRPs into 3, namely therapeutic effectiveness, therapeutic safety and other problems.

DRPs analysis related to the effectiveness of acute lymphoblastic leukemia therapy can be seen after the induction phase by examining the spinal cord (BMP). Based on the research results, there were 2 patients using the 2018 standard risk protocol where the BMP examination was carried out at the end of the 6th week and 1 patient with the 2018 high risk protocol where the BMP was carried out at the end of the 7th week. The results of the BMP examination showed that the three patients achieved complete remission with leukemic blasts (blast cells) <5% with the results of the BMP examination shown in table 4. The second category was that the treatment effect was not optimal, which could be analyzed in the three patients. The effect of non-optimal treatment is that the patient experiences incomplete remission at the end of the induction phase of treatment (5% - 20% blast cells). The percentage obtained was 0% because the patient experienced complete remission based on the results of the BMP examination. The third category is indications or untreated symptoms with a percentage of 0%. This is because patients experience complaints or clinical signs due to side effects after chemotherapy has received treatment. Other problems consist of category P3.2, namely unnecessary drug therapy. Based on the analysis carried out, the percentage obtained is 0%. The DRPs problem that occurred in this study was the safety of therapy (adverse drug reactions).

Adverse drug reactions are responses to drugs that are undesirable or dangerous and can occur at normal doses (Doherty, 2009). Based on research by Sitaresmi et al (2009), the most frequently reported side effects by parents of pediatric patients with acute lymphoblastic leukemia are

infection, leg weakness, hair loss, nausea, vomiting, oral mucositis, abdominal pain and bleeding. Chemotherapy drugs are curative in that they can eradicate all cancer cells. The mechanism of action of chemotherapy drugs is not selective, so they can attack normal, active cells such as bone marrow cells, digestive tract and hair follicles, causing side effects (Ariawati et al., 2007). Side effects of chemotherapy can occur acutely or over a long period of time. Acute side effects that occur within a few hours or up to several weeks after administration of chemotherapy include nausea, vomiting, mouth ulcers, mucositis, allergies and local ulceration. The level of organ damage due to the side effects of chemotherapy is different for each individual depending on various factors including the type of chemotherapy, dose of chemotherapy, time of administration, individual factors (race), nutritional status, condition of the organ where the drug is detoxicated and excreted (Ariawati et al., 2007) .

In this study, for the category of therapeutic effectiveness, only 3 patients from the total sample could be analyzed because treatment of pediatric patients with ALL has a special protocol in the therapy process so that researchers adjust it to the patients obtained during the research process. Based on the research results, it shows that drug related problems that occurred in this study were 100%. In table 3 is the incidence of adverse drug reactions that occurred in pediatric patients with acute lymphoblastic leukemia cancer at Dr. RSUP. Kariadi and Dr. Moewardi. The incidence of nausea and vomiting is the highest ADRs. Nausea and vomiting due to chemotherapy induction or what is called chemotherapy induced nausea and vomiting (CINV) occurs in 70% - 80% of patients receiving chemotherapy (Fitriani et al., 2016). This is caused by the activity of neurotransmitter receptors located in the chemoreceptor trigger zone (CTZ), vomiting center and gastrointestinal tract (Fitriani et al., 2016). Oral mucositis in 6 patients. Oral mucositis is an erythema and ulceration lesion on the oral mucosa that occurs in cancer patients given chemotherapy (Chaveli-lopez & Bagan-sebastian, 2016). Alopecia in 1 patient. Alopecia is a toxic disorder of the skin and subcutaneous tissue that is not life threatening but worsens the patient's quality of life (Sitaresmi et al., 2009). Cardiotoxicity in 2 patients with the SR 2006 protocol with a daunorubicin dose of 30 mg/m2 (used during the induction phase). Based on the results of a chest X-ray examination carried out in the maintenance phase (week 102), the apex of the heart shifted laterocaudally, giving the impression of cardiomegaly of the left ventricle (LV). Hypersensitivity was in 2 patients who underwent the 6th week of chemotherapy (induction phase) with the 2018 high risk protocol. The patient experienced a hypersensitivity reaction in the form of red spots appearing all over the body and coughing and shortness of breath after administering L-asparaginase (50 cc). Febrile neutropenia score 1 - 4 "Possible" in 1 patient (patient no. 46). The patient underwent long cycle chemotherapy for 4 days (8/7/2019 to 11/7/2019) with hyper-CVAD protocol. Febrile neutropenia is a symptom characterized by the occurrence of fever (≥38.80C), one measurement or measurement for 1 continuous hour or measurements at a minimum interval of 12 hours and neutropenia is defined as a total neutrophil count, absolute neutrophils count (ANC) (Hapsari et al ., 2016). Hyperglycemia in 1 patient. The patient was admitted for chemotherapy week 6 (induction phase) with the standard risk 2018 protocol. The chemotherapy drugs the patient received were IT methotrexate, IV vincristine, IV L-asparaginase and PO prednisone. Based on laboratory tests, the patient experienced hyperglycemia with a GDS (instantaneous blood glucose) of 229 mg/dL. Hyperglycemia is one of the side effects that occurs due to the combination of steroids and L-asparaginase in the induction phase (Aisyi et al., 2019).

4. Analysis of Risk Factors: Age, Gender, Number of Medications and Comorbidities with the Occurrence of Drug Related Problems.

In this study, a statistical test was carried out to determine the risk factors for DRPs in pediatric patients with acute lymphoblastic leukemia cancer. In table 6, bivariate analysis was carried out using the Pearson Chi-Square test. The risk factors of age and gender are not related to the

incidence of drug related problems in pediatric patients with acute lymphoblastic leukemia, indicated by a p value> 0.05. This is similar to research by Birarra et al (2017) which states that gender and age are not significantly related to the incidence of drug related problems. Research by Rashed et al (2012) shows that age and gender have no relationship with the occurrence of drug related problems. Comorbid risk factors are not related to the incidence of DRPs, indicated by a p value> 0.05. This research is different from Birara et al (2017) which shows that patients who have three or more disease conditions (comorbid) have a significant relationship with the occurrence of DRPs. Apart from that, Sisay et al (2015) stated that comorbidities are related to the incidence of drug related problems. The risk factor for the number of drugs is not related to the incidence of DRPs, indicated by a p value> 0.05. This result is different from research by Sisay et al (2015) which showed that the number of drugs was related to the incidence of DRPs with a p value <0.05 (p=0.02). Research by Birara et al (2017) shows that patients who use >5 drugs are around 4 times more likely to experience DRPs than patients who use <5 drugs.

LIMITATION OF THE STUDY

Determination of DRPs in this study has limitations, including no allergy examination with skin tests or measurement of specific immunoglobulin E (IgE) levels in the blood to determine whether the patient has allergies resulting in adverse drug reactions (ADRs). Determination of ADRs is measured from real allergy signs or symptoms experienced by the patient. This study also did not measure blood drug levels evaluate the potential/occurrence of toxic effects. Determination of potential/existing toxic effects in patients is evaluated by looking at whether the patient receives drugs that are at risk of experiencing organ toxicity based on literature studies (evidence based medicine) and laboratory examinations related to organ function. Lastly, this research cannot evaluate the effectiveness of therapy (therapy outcomes) in all patients.

CONCLUSIONS AND SUGGESTIONS

The conclusions obtained in this study include the actual percentage of drug related problems in pediatric patients with acute lymphoblastic leukemia cancer is 36.36% with 36 patients. The type of drug related problems in pediatric patients with acute lymphoblastic leukemia cancer is the safety of adverse drug reaction therapy, including nausea. vomiting, oral mucositis, febrile neutropenia, alopecia, cardiotoxicity, hypersensitivity and hyperglycemia.

There is a need to increase the role of pharmacists (clinical pharmacists) in pediatric wards to monitor drug therapy in acute lymphoblastic leukemia cancer patients, monitor the incidence of adverse drug reactions, and ensure that the drugs given to patients are in accordance with the protocol. There needs to be a role for pharmacists (clinical pharmacists) in the chemotherapy treatment room to ensure that the drugs given to patients are in accordance with the protocol

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