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Research Article

A retrospective study on drug interaction for pediatric in-patients at Central Public Hospital Haji Adam Malik, Medan for the period of January-June 2012

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ABSTRACT

Background: Drug interaction is one of the factors causing a drug-related problem. Pharmacoepidemiology of drug interaction for pediatric patients at Central Public Hospital Haji Adam Malik, Medan has not come to light. The objective of this study was to find out the correlation between the amount of drug, the age and sex of patients, the number of patients diagnosed with drug interaction, the drug involved, the frequency, the mechanisms of drug interaction, and its severity levels for pediatric in-patients at Central Public Hospital Haji Adam Malik, Medan.

Methods: The data for this study were collected by conducting a retrospective analysis to 232 medical records, which were kept from January to June 2012. The data collected for this study included demography, the amount of drug, and patient diagnoses. The drug interaction was confirmed in the website http://www.drugs.com and Tatro Drug Facts interaction. To determine the correlation between dependent and independent variables, Spearman's bivariate correlation (for amount of drug, age of patient, and diagnoses) and Mann-Whitney's Comparative Test (for sex) were used.

Results: The frequency of drug-drug interaction was 75.43%. Based on drug interaction mechanism, the interaction was divided into pharmacokinetics interaction (24.76%), pharmacodynamics interaction (3.45%), and unknown interaction (71.78%). The drugs commonly involved in drug interactions were dexamethasone, vitamin E, captopril, spironolactone, phenytoin, and furosemide. The severity levels were major (8.83%), moderate (66.41%), and minor (24.76%).

Conclusion: The statistical data analysis results showed that there was a significant correlation between the amount of drugs and the number of diagnoses, while age and sex did not show any significant correlation.

Keywords: Drug interactions, Pediatric, In-patient, Central Public Hospital Haji Adam Malik

INTRODUCTION

A drug interaction occurs when the effect of a certain drug is altered when it is taken with another drug, herbal medicine, food, drink, or other chemical agents in the environment system.[1]

Taking a particular drug (A) can alter the action of another drug (B) and it can occur in two common mechanisms, i.e. pharmacokinetics interaction and pharmacodynamics interaction. Another category is pharmaceutics, a vitro interaction, which can make one of the two drugs losses its effect.[2]

A drug interaction is one of the factors constituting to drug-related problems (DRP). There are three other DRP, which can be caused by a drug interaction, among which are excessively low dose or high doses, and harmful drug effects. DRP is itself one of the problems, which significantly influence the success in patient therapy.[3]

The data obtained from the Central Bureau of Statistics regarding North Sumatera citizens in 2011 shows that there were 4,358,043 young people at the age of under fifteen, 8,248,526 citizens in productive age at the age of between 15 and 64, and 511,758 elderly at the age of 65 or older.[4] Based on this data, citizens in young age (pediatric) ranked second

only to citizens in productive age as the biggest population in North Sumatera.

Pediatric population has distinct physiology, and cannot be treated as a miniature of the adult population. In international level, this population is grouped into preterm newborn infants, term newborn infants (0-28 days), infants and toddlers (23 days-23 months), children (2-11 years), and adolescents (12-18 years), but this classification is subject to area.[5]

Variation in drug pharmacokinetics between drugs for adults, infants and children is an important factor in using and fixing doses so that the drugs are taken effectively. Review on the role of cytochrome-450 enzyme, which metabolizes most drugs for pediatric patients should be conducted to anticipate the change in drug clearance caused by drug-disease interactions or drug-drug interactions.[6]

A comparative study on medical records of pediatric patients for the period of May-August 2009 conducted by a hospital in Pakistan shows that 950 out of 1420 prescriptions, about 66.90%, caused drug interactions to the patients.[1]

Not all drug interactions are significantly worthwhile although they theoretically are. Some drug interactions are dangerous for certain patients. However, a pharmacist should always be alert in order to prevent the risks of morbidity or even mortality in the treatment of patients.[7]

Based on the discussion above, the writer was interested to conduct a retrospective research on drug interactions in the pediatric unit at Central Public Hospital Haji Adam Malik, Medan to find out the description of the drug interactions which occurred in this hospital.

METHODS

The population of this research was all medical records of pediatric in-patient funded by National Health Insurance Program (Jamkesmas) at Central Public Hospital Haji Adam Malik, Medan for the period of January-June 2012. The total number of those medical records was 581. The sample was selected by using a simple random sampling technique. The number of samples was determined by using formula suggested by Krejcie and Morgan.[8] The number of samples given by the formula was 232 medical records.

Inclusion criteria

1. Medical records of in-patient at Central Public Hospital Haji Adam Malik, Medan for the period of January-June 2012
2. The patients of between 0 and 18 years of age
3. The patients who were given two or more drugs
4. Gender is not specified.

Exclusion criteria

1. Medical records of in-patient at Central Public Hospital Haji Adam Malik, Medan for the period of other than January-June 2012
2. The patients who were given one drug so that drug-drug interaction could not be identified
3. Incomplete medical records (any information required for this research was absent).

Procedures

The data were collected by gathering medical records of pediatric in-patient at Central Public Hospital Haji Adam Malik, Medan for the period of January-June 2012. The kinds of data collected were demography, amount and types of drug, and number of patient diagnoses. The drugs written in the medical records were checked for the potential drug interaction in website http://www.drugs.com and Tatro Drug Interaction Facts (2009). The drug interactions were sorted into five occurrences for each category of major, moderate, and minor.

Analysis

The data analysis was conducted only for one period data. For the characteristics of the research subject, a descriptive analysis was applied. Spearman's bivariate correlation analysis was used to determine the correlation between the independent variables of the amount of drugs, the age of patients, and the number of diagnoses and the dependent variable, that is, the number of potential drug interaction occurrences. In addition, Mann-Whitney of comparative test was used to find out the correlation between sex and potential drug interaction occurrences.

RESULTS

General characteristics of research subjects

According to the sample, that is, 232 medical records of in-patient at Central Public Hospital Haji Adam Malik, the general, most common characteristics of the subjects were that the percentage of patients at the age of between 2 and 11 years was 55.6%, the percentage of patients taking 6 drugs was 18.5%, the percentage of male patients was 50.9%, and the maximum number of diagnoses was 2 with the percentage of 18.9%. The detail on these characteristics is presented in Table 1.

Potentials of drug interaction occurrences

Based on the research results on 232 medical records, the total number of potential drug interaction occurrences was 521. This potential occurrence was grouped based on the severity levels as shown in Table 2.

Table 2 shows that the potential occurrences for unknown interactions were the highest, followed by pharmacokinetics, then pharmacodynamics.

Table 1: Characteristics of research subjects.

The characteristic of subjects	Percentage (%)
The amount of drugs	
Two drugs	12.93
Three drugs	11.2
Four drugs	14.7
Five drugs	17.7
Six drugs	18.5
Seven drugs	10.3
Eight drugs	5.2
Nine drugs	3.4
Ten drugs	1.3
Eleven drugs	3
Twelve drugs	0.9
Thirteen drugs	0.9
Age	
0-28 days	7.3
>28 days-23 month	10.8
2-11 years	55.6
12-17 years	26.3
Sex	
Male	50.9
Female	49.1
The number of diagnoses	
One diagnoses	24.6
Two diagnoses	28.9
Three diagnoses	22.8
Four diagnoses	12.9
Five diagnoses	8.2
Six diagnoses	1.3
Seven diagnoses	1.3

Table 2: Grouping potentials of drug interaction occurences based on the severity levels.

Grouping	The total number (%)
Based the mechanisms	
Pharmacokinetics	129 (24.76)
Pharmacodynamics	18 (3.45)
Unknown	374 (71.78)
Total	521 (100)
Based the severity levels	
Major	46 (8.83)
Moderate	346 (66.41)
Minor	129 (24.76)
Total	521 (100)

Based on the results of medical record analysis, the drugs written in the medical record were grouped into three categories-based on their severity levels, i.e. minor, moderate, and major. The five most common occurrences in each category is presented in Table 3.

The factors related to potential drug interaction occurrences

Based on the statistical analyses, the factors-related to potential drug interaction occurrences are presented in Table 4.

DISCUSSION

The objectives of this study was to find out the correlation between the amount of drug, the age and sex of patients, the number of patients diagnosed with drug interaction, the drug involved, the frequency, the mechanisms of drug interaction, and its severity levels for pediatric in-patients at Central Public Hospital Haji Adam Malik, Medan.

In this study, the unknown interactions are interaction mechanisms, which have not come to light. Pharmacokinetics interaction is the interaction, which can influence the process of absorption, distribution, metabolism, and excretion.[9] Pharmacodynamics interaction occurs when the effect of a particular drug is altered by another drug. Drug interaction in pediatric patients should be controlled because some crucial organs in their bodies have not been matured as they are in an adult body. Therefore, a drug interaction

Table 3: The five most common occurrences in each category.

The category	The total number
Minor	
Dexamethason ↔ vitamin E	43
Ceftriaxone ↔ phenytoin	11
Ranitidine ↔ parasetamol	10
Digoxin ↔ spironolactone	7
Furosemide ↔ phenytoin	5
Moderate	
Furosemide ↔ dexamethason	60
Ceftriaxone ↔ furosemide	19
Ceftazidime ↔ gentamicin	17
Captopril ↔ furosemide	14
Furosemide ↔ prednison	12
Major	
Captopril ↔ spironolactone	14
Calcitriol ↔ calcium	4
Methotrexate ↔ co-trimoxazole	8
Rifampin ↔ phenytoi	5
Rifampin ↔ enyrazinamide	4

Table 4: Factors related to potential drug interaction occurrence.

Independent variables	Potential drug interaction occurrences, n (%)		Analysis	Correlation (r)
	Yes: 175 (75.43)	No: 57 (24.57)		
Jumlah obat			Bivariat Spearman (p=0.00)	0.645
Two drugs	6 (2.59)	24 (10.3)		
Three drugs	11 (4.7)	15 (6.5)		
Four drugs	28 (12.1)	6 (2.6)		
Five drugs	36 (15.5)	5 (2.2)		
Six drugs	39 (16.8)	4 (1.7)		
Seven drugs	21 (9.1)	3 (1.3)		
Eight drugs	12 (5.2)	0 (0)		
Nine drugs	8 (3.4)	0 (0)		
Ten drugs	3 (1.3)	0 (0)		
Eleven drugs	7 (3.0)	0 (0)		
Twelve drugs	2 (0.9)	0 (0)		
Thirteen drugs	2 (0.9)	0 (0)		
Age			Bivariat Spearman (p=0.418)	-
0-28 days	17 (7.3)	0 (0)		
>28 days-23 month	16 (6.9)	9 (3.9)		
2 years-11 years	94 (40.5)	35 (15.1)		
12-17 years	48 (20.7)	13 (5.6)		
Sex			Comparatif test Mann-Whitney (p=0.801)	-
Male	91 (39,2)	27 (11,6)		
Female	84 (36,2)	30 (12,9)		
The number of diagnoses			Bivariat Spearman (p=0.00)	0.262
One diagnoses	36 (15.5)	21 (9.1)		
Two diagnoses	47 (20.3)	20 (8.6)		
Three diagnoses	44 (19.0)	9 (3.9)		
Four diagnoses	24 (10.3)	6 (2.6)		
Five diagnoses	18 (7.8)	1 (0.4)		
Six diagnoses	3 (1.3)	0 (0)		
Seven diagnoses	3 (1.3)	0 (0)		

can influence the process of drug pharmacokinetics, and the changes will take place following their maturity, which will effect their response to drugs.[2]

According to the research results show that the most common drug interaction was in the moderate category, i.e., furosemide - dexamethasone interaction, which reached 60 cases. The second most common drug interaction was in the minor category, i.e., Dexamethasone - Vitamin E interaction, and 43 cases were found in this category. The least common drug interaction was in the major category, i.e., captopril-spironolactone interaction, which was found in 14 cases.

The major category was clinically very significant. The combination of these drugs should be avoided because the risk of drug-drug interactions is higher than their benefits. The drug-drug interaction in the moderate category was also quite significant so that the combination of these drugs is not recommended, except for special cases. The minor category has minor clinical effect and the risk is low. However, alternative drugs should be made as a step to prevent drug interaction risks or, if these drugs must be prescribed, the patients should be closely monitored.

The factors related to the potential drug interaction occurrences, according to Spearman. drug interaction

risks owere the amount of drugs (p=0.000) and diagnoses (p=0.000). The amount of drugs has a strong correlation with potential drug interactions (r=0.645), while the diagnoses has weak correlation (r=0.262). This conclusion is confirmed by the standard proposed by Cohen 1988, which states that r= 0.50-1.00 shows a strong correlation and r<0.50 shows weak correlation. On the other hand, the age factor did not show any significant correlation with potential drug interactions (p=0.418), which means that the correlation is not significant since p is >0.05.[10]

The Mann-Whitney comparative test results showed that sex and potential drug interaction occurrences did not show any significant difference (p>0.05), which means that sex factor has no connection with drug interaction occurrences.

CONCLUSION

Based on the statistical analysis on factors influencing drug interactions at Central Public Hospital Haji Adam Malik, it can be concluded that:

1. The amount of drugs has a strong correlation with potential drug interactions (r=0.645) while the diagnoses has weak correlation with potential drug interactions (r=0.262). However, age and sex do not have any correlation with drug interaction occurrences
2. The frequency of drug-drug interactions for in-patient funded by Jamkesmas at Central Public Hospital Haji Adam Malik was very high, i.e., 76.43%
3. The drug interaction mechanisms for in-patient funded by Jamkesmas at Central Public Hospital Haji Adam Malik were pharmacokinetics (24.76%), pharmacodynamics (3.45%), and unknown (71.78%)
4. The drugs commonly involving for in-patient funded by Jamkesmas at Central Public Hospital Haji Adam Malik were Dexamethasone, Vitamin E, Captopril, Spironolactone, Phenytoin, and Furosemide
5. The severity levels of drug interactions for in-patient funded by Jamkesmas at Central Public Hospital Haji Adam Malik were major (8.83%), moderate (66.41%), and minor (24.76%).

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