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Submission date: 19-Aug-2019 12:24AM (UTC+0800)
Submission ID: 1161078884
File name: Jurnal-dr.Finny2.pdf (152.17K)
Word count: 2037
Character count: 11914

International Journal of Pharmacy Teaching & Practices 2013, Vol.4, Issue 2, supplement II, 662-665.

Identification of Adverse Drug Interactions in Pediatric Patients of Lower Respiratory Tract Infection Diseases at Children's Ward of Dr. M. Djamil Hospital, Padang-Indonesia

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Please cite this paper as: Rahmi Yosmar[1], Helmi Arifin[1], Deswinar Darwin[1], Finny Fitry Yani[2]. Identification of Adverse Drug Interactions in Pediatric Patients of Lower Respiratory Tract Infection Diseases at Children's Ward of Dr. M. Djamil Hospital, Padang-Indonesia. IJPTP, 2013, 4(2), supplement II, 662- 665.

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Abstract

To identify the incidence of adverse drug interactions in the treatment of acute Lower Respiratory Tract Infection (LRTI) in pediatric patients as it has high mortality and morbidity especially in infants and children. This study was conducted prospectively in pediatric patients diagnosed with acute LRTI with or without co-morbidities in the Children's Ward of Dr. M. Djamil Hospital, Padang-Indonesia within April-June 2010 by census. Data were analyzed by descriptive analysis method. Twenty three pediatric patients were found diagnosed with acute LRTI with comorbidities. Adverse drug interactions occurred in 9 out of 23 patients (39.13%). The type of the most common adverse drug interaction was pharmacodynamic interaction which was the concomitant use of amoxicillin and chloramphenicol (21.73%) which might reduce the efficacy of amoxicillin. Another common type of adverse drug interaction was pharmacokinetic interaction in the concomitant use of chloramphenicol and paracetamol (17.39%) which could extend the plasma half-life of chloramphenicol. Adverse drug interactions occurred in 9 patients out of 23 patients (39.13%). The most common adverse drug interaction was the concomitant use of amoxicillin and chloramphenicol (21.73%) and pharmacokinetic interaction in the concomitant use of chloramphenicol and paracetamol for (17.39%).

Keywords: *adverse drug interactions, acute lower respiratory tract infection diseases, bronchiolitis, pneumonia, pediatrics.*

Introduction

Acute respiratory tract infection is an infection disease that attacks one or more sections of the respiratory tract, started from nose (upper tract) to alveoli (lower tract) and also adnecsa tissue like sinus, middle ear cavity, and pleura for 14 days [(1)]. Upper Respiratory Tract Infections (URTI) include rhinitis, sinusitis, pharingitis, laringitis, epiglottitis, tonsilitis and otitis media. Whereas Lower Respiratory Tract Infections (LRTI) include infections of bronchiolus and alveoli like bronchiolitis and pneumonia. When the URTI is incompletely treated, it can develop to LRTI. The URTI rarely cause death eventhough the incident is higher than LRTI [(2,3)].

Pneumonia and bronchiolitis are acute LRTIs that cause high mortality rate in pediatrics significantly contributing to cause high Infant Mortality Rate (IMR). Around 4 million children are dying from pneumonia and bronchiolitis in developing countries. Acute respiratory tract infections cause four million mortalities out of fifteen million mortalities in children under 5 years old every year. Over all mortalities causes of acute respiratory tract infection diseases, about 20-30% of death are caused by pneumonia in babies aged under 2 months [(7,12,13)].

The National Health Survey on 2001 showed 27,6 % mortalities in infants and 22,8 % in children under five years old were caused by respiratory diseases especially pneumonia [(9)]. Bronchiolitis is the most common acute respiratory tract infection in infants aged 2 – 24 months, and most frequently on 2 – 8 months of age. About 95 % of cases occurred in infant under 2 years old and 75 % in infants under 1 year old [(14)].

The drug therapy is intended to increase or to maintain the quality of life of patients. This can be achieved by treating the patient to reduce or abolish the symptoms, to stop or delay the diseases and also to prevent the diseases as well as the symptoms. However many potential problems can happen in medication such as the risk of adverse drug interaction. Thus, we need to study about the therapy of acute LRTI diseases at children's ward of government hospital DR. M. Djamil Padang-Indonesia on the risk of adverse drug interaction.

Material and Methods

This study was conducted prospectively and the sample collected by census to entire patients whether with or without comorbid diseases at the Children's Ward of DR. M. Djamil Hospital, Padang-Indonesia within April-June 2010 by census. The data were analyzed using descriptive method.

Data source included medical record of acute LRTI patients, nursing records, drug instruction cards in pharmacy, direct monitoring to the patients and also interviewing the patients or their families at the children's ward. These sources were studied to find the incidence of adverse drug interactions.

Table 1. Incidence of adverse drug interaction in pediatric patients of lower respiratory tract infection diseases with comorbid conditions

No.	Drug Interactions	Number of Patients	Percentage (%)
1.	Drug interactions occur	9	39.13
2.	Drug interactions don't occur	14	60.86

Results and Finding

There were 23 cases of acute infections of lower respiratory tract that consisted of bronchiolitis and pneumonia occurring in the children's Dr. M. Djamil Hospital, Padang within April-June 2010. The entire cases were accompanied with comorbid diseases. Adverse drug interactions occurred in 9 out of 23 patients (39.13%). The most common adverse drug interaction was the concomitant use of amoxicillin and chloramphenicol (21.73%) and the concomitant use of chloramphenicol and paracetamol (17.39%).

Table 2. Adverse drug interactions in pediatric patients of lower respiratory tract infection diseases with comorbid conditions

No.	Drugs involved	Effect of interactions	Type of Interaction	Pharmaceutical care plan	Incidences	%
1.	moxicillin + chloramphenicol	reduced plasma level of amoxicillin	Pharmacodynamic	one hour interval of adminsitration	5	21.73
2.	Paracetamol + chloramphenicol	extended plasma half-life of chloramphenicol	Pharmacokinetic	separated administration	4	17.39
3.	Chloramphenicol + Isoniazid	Increased effect of isoniazid due to irreversible inhibition of P-450 cytochrome	Pharmacokinetic	separated administration	1	4.34
4.	Luminal + prednisone	Increased clearance of corticosteroids (prednisone)	Pharmacokinetic	Increase the dose of prednisone	1	4.34
5.	Lasix® + Luminal	reduced effect of Lasix®	Pharmacodynamic	separated administration	1	4.34
6.	Dexamethasone + luminal	increased metabolism of corticosteroids (dexamethasone)	Pharmacokinetic	Doses of corticosteroids improved	2	8.69
7.	Salbutamol + luminal	Reduce effect of salbutamol as it can induce enzymes CYP3A4.4	Pharmacokinetic	separated administration	1	4.34
8.	Teofillin + Isoniazid	Increased plasma concentration of theophylline after a few weeks of isoniazid use. Some patients may experience toxicity of theophylline	Pharmacokinetic	separated administration; avoid prolonged use of theophylline	1	4.34
9.	Dexametason + Isoniazid	reduced plasma concentration of isoniazid	Pharmacokinetic	separated administration	1	4.34
10.	Rifampicin + dexamethasone	Reduce plasma level of dexamethasone	Pharmacokinetic	separated administration	1	4.34
11.	Aminofillin + dexamethasone	increased plasma level of aminophyllin e	Pharmacokinetic	separated administration	1	4.34
12.	Diazepam + ranitidine	Altered absorption of diazepam and reduced plasma levels up to 25%	Pharmacokinetic	at least 1 hour interval of administration	1	4.34

Discussion and Conclusion

During April to June 2010, there were 23 pediatric patients charged in the children's ward of Dr. M. Djamil Hospital for infectious diseases of lower respiratory tract accompanied by comorbid conditions. The incidence of adverse drug interactions in these patients was 39.13% (Table 1). Drug interactions are events in which the action of a drug is altered or affected by other drugs given concomitantly [8]. Drug interactions involve two drugs [4]:

- Object drug: the drug whose action of effect is influenced or changed by other drug.
- Precipitant drug: the drug that affects or alters the action or the effect of other drugs.

The current study found various drug interactions. The most common drug interaction was the concomitant use of amoxicillin and chloramphenicol that occurred in 21.73% of the entire adverse drug interactions (Table 2). This adverse interaction could reduce plasma level of amoxicillin in the plasma, thus decrease its efficacy. The interaction could cause antagonistic effect as the chloramphenicol works by inhibiting bacterial protein synthesis and could change the active growth of bacterial colonies to be static. This could cause the bactericidal effect of amoxicillin to be obstructed and bacterial killing becomes slower. This kind of interaction is a pharmacodynamic interaction. The drugs administration should be separated to avoid this adverse drug interaction. Pharmacodynamic interactions occur due to changes in the pharmacological effects of object drug influenced by precipitant drug due to its effect on the site of action or drug receptors [4,5,6]. The combination of amoxicillin and chloramphenicol can also provide a favorable interaction which causes a synergistic effect as directed against both gram-positive and negative bacteria. Another frequent drug interaction found in this study was the concomitant use of chloramphenicol paracetamol (17.39%). This interaction could extend the plasma half-life of chloramphenicol, which could cause toxic effect. The administration should also be separated in sufficient time. This kind of interaction is a pharmacokinetic interaction, which occurs when the precipitant drug influences or alters the absorption, distribution (binding protein), metabolism, and excretion of the object drugs [5,10,11].

Another type of adverse drug interaction is pharmaceutical interaction, a physicochemical interaction in which the physical and chemical reactions occur between drugs that alter or eliminate the pharmacological activity of the drugs [4].

Current study concludes that adverse drug interactions have occurred in 9 out of 23 pediatric patients (39.13%) in the children's ward of Dr. M. Djamil Hospital. The most frequent adverse drug interactions is a pharmacodynamic interaction in the concomitant use of amoxicillin and chloramphenicol (21.73%) which may reduce the effficacy of amoxicillin. Another frequent type of adverse drug interaction is pharmacokinetic interaction in the concomitant use of chloramphenicol and paracetamol (17.39%) which can extend the plasma half-life of chloramphenicol. But overall, all potential adverse drug interactions that occur can be overcome by providing a sufficient interval for each drug's administration.

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AUTHORS' CONTRIBUTIONS

Authors contributed equally to all aspects of the study.

PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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