Detection of Drug Interaction in GICU (General Intensive Care Unit) at One Hospital in Bandung

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Abstract

ICU defined as an intensive monitoring place and life support activities as well as definite therapy in life-threatens disease patients. In this Unit, patients generally receive treatment from various doctors that a patient can receive a variety of drugs from different doctors (polypharmacy). This unit also has higher frequency of drug demand than the other units in the hospital so the potential or actual drug interactions can occur. This study begins with a retrospective pilot study in ICU, concurrent studies in GICU (General Intensive Care Unit), data analysis and conclusions. Detection of drug interactions concurrently on 185 patients obtained 78 drug interactions that consists of 46 (58.97%) pharmacodynamic interactions and 27 (34.61%) pharmacokinetic interactions.

Keywords: General Intensive Care Unit, concurrent study, drug interaction

Abstrak

ICU didefinisikan sebagai suatu tempat pemantauan intensif dan pendukung kehidupan termasuk pengobatan pada pasien dengan penyakit yang mengancam jiwa. Pada unit ini, pasien secara umum menerima pengobatan dari banyak dokter dimana pasien dapat menerima berbagai macam obat dari dokter yang berbeda-beda (polifarmasi). Unit ini juga memiliki frekuensi permintaan obat yang lebih besar dibandingkan dengan unit lain di rumah sakit, sehingga dapat menimbulkan potensi interaksi atau interaksi yang nyata. Penelitian ini dimulai dengan sebuah penelitian awal berupa studi retrospektif di ICU, studi konkuren kemudian dilakukan di GICU (*General Intensive Care Unit*), dilakukan analisis data dan pengambilan kesimpulan. Dari pencarian interaksi obat secara konkuren yang dilakukan pada 185 pasien, didapatkan 78 interaksi obat yang terdiri dari 46 (58,97%) interaksi farmakodinamik dan 27 (34,61%) interaksi farmakodinamik.

Introduction

Intensive Care Unit is one of the hospital are as that provide maximum services, vital support functions and certainly therapeutic for patients with acute failure and volatile and vital multi-system failure (lung, heart, kidney, and nervous system). In addition, the ICU is also defined as intensive monitoring place and life support activities as well as definite therapy in patients with a life-threat endisease/condition that in this unit, patients generally receive treatment from various doctors that a patient can receive a variety of drugs from different doctors (polypharmacy). This unit also has higher frequency of drug demand than the other units in the hospital.

Pharmacist shave a responsibility to identify, prevent and provide solutions drug related problems, although it is not always easily achieved. Patient complience factors take responsibility for healing the patient. Therefore pharmacists should also be able to provide coun seling, information and education to patients. Some studies showed that one of the hospitals in Germany detected 9.2% due to drug-drug interactions (Gerdemann, 2011), in Indonesia at one gained 8.89% pharmacokinetic interaction Case (Budiastuti, 2007), at RSAL dr. Ramelan found that drug interactions occurred in 19 patients (15.83%) (Rahajeng, 2007).

Detection of drug interactions important to systematically and if followed will help treat the wiser treatment for people (Aslam, *et al.*, 2003).

Therefore, this study aims to detect drug interactions in the GICU at the hospital. Expected results of this study would give important information for policy makers in the hospital so that the morbidity and mortality due to drug use can be reduced. In the end, the role of the pharmacist as a partner physicians in clinical decision-making in improving therapeutic efficacy of patients in the GICU over again intensified to prevent clinically significant drug interactions.

Experimental

Cross sectional Study

a. Design studies using cross-sectional due to prevalence profile. Data on each would fill in the form includes patient demographic data (sex, age of onset, LOS (length of stay), the status of entry and exit), primary diagnosis and

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comorbid diagnosis, drug name, drug dosage, route of administration and time drug delivery. In addition conducted drug interaction study using various relevant literature.

b. This data is obtained through:
   a. Patient Monitoring condition
   b. Patient monitoring
   c. Book status of patients
   d. Interviews with families of patients
   e. Communicate with physician and the patient about the condition of patients with treatment-related issues by following the relevant doctor visit.

Data Analysis

The data obtained and analyzed by an analytical approach to obtain information about the profile of drug interactions incidence that occur in actual and potential treatment of patients in GICU.

Result and Discussion

A. General Characterictic Of GICU Patients

All of the GICU patients (116 patients) used as subjects for this study which period of November 3rd, 2009 - January 5th, 2010. The characteristics shown in Table 1 below.

Tabel 1. Demography Data Of GICU Period November 3rd, 2009 – January 5th, 2010

Demography Data	Classification	GICU ∑	GICU %
Sex	Female	69	59.48
	Male	47	40.52
Age	Adult (14-64 thn)	106	91.38
	geriatric (≥ 65 thn)	10	8.62
Length Of Stay (*LOS*)	1-7 days	77	66.38
	8-14 days	21	18.10
	15-28 days	7	6.03
	In ward	11	9.48
Entry status	*Composmentis*	65	56.03
	Somnolent	14	12.07
	Medicine interfering	31	26.72
	Sopporus	6	5.17
Exit status	Move	69	59.48
	Die	31	26.72
	In Ward	12	10.34
	Forced home	4	3.45
TOTAL		**116**	

Notice = ∑ : Number of patients

B. Detection of Drug Interaction at GICU

Pharmacodynamic interactions occur in 105 patient swhich detailed in Table 2, whereas pharmaco-kinetic interactions occurred in 81 patients are detailed in Table 3 below.

Tabel 2. Pharmacodynamic Drug Interaction

Drug Interaction	Clinical Significance	No. Of patients	Type
Midazolam + Morphine[1]	3	25	Actual
Furosemid + Dipirhone[1]	2	8	Potencial
Ciprofloxacine + morphine[1]	1	6	Potencial
Midazolam + Fentanyl[1]	3	4	Potencial
Levofloxacin + Fluconazole[3]	1	4	Potencial
Insulin + Dexamethazo[5]	2	4	Actual
Tramadol + Ketorolac[1]	3	3	Potencial
Propofol + Midazolam[1]	3	3	Potencial
Heparin + cefoperazone[8]	2	2	Potencial
Phenytoin + Furosemid[1]	3	2	Potencial
Fenitoin + Insulin[1]	2	2	Actual
Insulin + Dobutamin[4]	2	1	Actual
Dexamethason + Aspirin[1]	2	1	Potencial
Furosemid + Amikasin[4]	2	1	Potencial
Midazolam + Diphenhyhydramine[2]	-	1	Potencial
Furosemide + Digoxin[1]	2	1	Potencial
Furosemide + Albuterol [7]	2	1	Potencial
Cyfloxamine + Morphine[1]	1	6	Potencial
Midazolam + Phentanyl[1]	3	4	Potencial
Levoflxacinn + Flukonazol[3]	1	4	Potencial
Insulin + Dex amethason[5]	2	4	Actual
Tramadol + Ketorolac[1]	3	3	Potencial
Propofol + Midazolam[1]	3	3	Potencial
Heparin + Cefoperazon[8]	2	2	Potencial

Drug Interaction	Clinical Significance	No. Of patients	Type
Phenytoin + Furosemid[1]	3	2	Potensial
Phenytoin + Insulin[1]	2	2	Aktual
Insulin + Dobutamin[4]	2	1	Aktual
Dexamethason + Aspirin[1]	2	1	Potencial
Furosemid + Amikacine[4]	2	1	Potencial
Midazolam + Diphenylhidramine[2]	-	1	Potencial
Furosemid + Digoxin[1]	2	1	Potencial
Furosemide + Albuterol [7]	2	1	Potencial
Methyldopa + Bisoprololfumarate[4]	1	1	Potencial
Midazolam + Aminophyllin[1]	3	1	Potencial
Insulin + Isoniazid[1]	3	1	Actual
Phenytoin + Clorpromazin[1]	3	1	Potencial
Gentamicin + Cephazoline[1]	2	1	Potencial
Gentamisin + Seftazidim[1]	2	1	Potencial
Gentamisin + Seftriakson[1]	2	1	Potencial
Gentamisin + Hemasel[1]	1	1	Potencial
Chlorrpromazin + Captopril[1]	3	1	Potencial
Cefazolin + Heparin [8]	2	1	Potencial
Atracuriumbesylat + Midazolam[1]	2	1	Potencial
Vecuroniumbromide + Cefepim[4]	2	1	Actual
Verkuroniumbromide + Dibekacin[9]	2	1	Potencial
Vecuroniumbromide + Diltiazem[1]	3	1	Potencial
Vecuroniumbromide + Phentanyl[1]	3	1	Potencial
Amiodaron + Ciprofloxacin[1]	1	1	Potencial
Amiodaron + Furosemide[10]	1	1	Potencial
Clopidogrel + Aspirin[1]	2	1	Potencial
Clopidogrel + Simvastatin[1]	-	1	Potencial
Clopidogrel + Atorvastatin[1]	-	1	Potencial
Teophyline + Dobutaminr[1]	3	1	Potencial
Teophyline + Midazolam[1]	3	1	Potencial
Linezolid + Dobutamine[1]	1	1	Potencial
Linezolid + Phenyl propanolamine [1]	1	1	Potencial
Linezolid + NoradreNaline [1]	1	1	Potencial
Linezolid + Diphenhidramine[12]	2	1	Potencial
Tramadol + Ondansetron[1]	3	1	Actual
Tramadol + $MgSO_4$[1]	-	1	Potencial
Nifedipin + Diltiazem[1]	2	1	Actual

Table 3. Pharmacokinetic Drug Interaction

Drug Interaction	Clinical Significance	No. Of patients	Type
Metoclopramid + Paracetamol[1]	3	11	Potencial
Paracetamol + Morphine[1]	3	9	Potencial
Metochlopramid + Morphine[1]	-	8	Potencial
Midazolam + Fluconazol[1]	3	7	Potencial
Fluconazol + Omeprazol[1]	4	5	Potencial
Rifampicin + Morfin[1]	3	4	Potencial
Phentanyl +Flukonazol[1]	2	3	Potencial
Phenitoin + Paracetamol[1]	-	3	Potencial
Phenitoin + Deksametason[1]	2	3	Potencial

Drug Interaction	Clinical Significance	No. Of patients	Type
Paracetamol + Petidin[1]	3	3	Potencial
Fentanil + Paracetamol[1]	3	3	Potencial
Propofol + Noradrenalin[1]	2	2	Potencial
Fluconazol + Propranolol[1]	-	1	Potencial
Dexamethasone + Ephedrine[1]	3	1	Potencial
Sukralfat + Levofloxacin[1]	3	1	Potencial
Ranitidin + Vitamin B12[1]	4	1	Potencial
Rifampicin + Midazolam[1]	-	1	Potencial
Rifampicin + Fluconazol[1]	2	1	Potencial
Rifampicin + Dexamethasone[1]	3	1	Potencial
Rifampicin + Dipiron[1]	2	1	Potencial
Gentamicin + Digoksin[1]	2	1	Potencial
Pethidin + NHCl[1]	3	1	Potencial
Methylprednisolon + Fluconazol[11]	2	1	Potencial
Voriconazol + Omeprazol[1]	3	1	Potencial
Teophylline + Amiodaron[1]	-	1	Potencial
Zafirlukas + Aminophylline[13]	2	1	Potencial
Total		**81**	

Result and Discussion

A. Patient Characteristic

The mortality rate of men was higher than women, but women had a higher rate of morbidity than men. This was due to biological factors (menstruation and menopause) and psychosocial factors were more influential for women (Popay, 1993). While the largest age distribution in adult patients indicating that adult susceptible to chronic illness or severe infections. This was due to an unbalanced diet and unhygienic, activity factors, stress, poor sanitation, and health-damaging lifestyle such as smoking and drinking alcohol.

LOS is the duration of treatment since the patient entered GICU. Based on the results of the study indicated that the LOS most 1-7 days. This was consistent with the literature that said care in the intensive care unit required a minimum of about 1-4 days until the patient vital signs (pulse, heart rate, respiration, and blood pressure) and other physiological conditions met criteria for patients coming out of the unit intensive care to be transferred to a usual care (McLeod, 1981).

Composmentis was the higest condition when patients entered to GICU. Composmentis is a condition when the patients can answer questions correctly and could be oriented over time, place and person. While the exit status of patients at highest GICU space was a status change that occurred in 69 patients (59.48%). It was performed on patients who had been stabilized hymodynamic status and no longer need intensive care, in addition to prevent nosocomial infection in GICU.

The most primary diagnosis in GICU was Sectio Caesarea (SC) in 19 patients (16.38%). Comorbid diagnosis, include respiratory failure that occurred in 10 patients (9.80%).

Of 116 patients, 40 patients had a single diagnosis and 76 patients had a comorbid diagnosis with varying amounts for each patient. The number of comorbid diagnoses was 1 comorbid diagnose that were 43 patients (56.58%).

B. Drug Interaction

Drug interactions are one or moreeffect modification of drug which concurrently given initially or when two or more drugs interact such that the effectivities or toxicity of a drug or changed. However, be aware of food, cigarette smoke, ethanol, and environmental chemicals that can affect the drug's effects. When combined therapeutic result of unwanted changes/complications of the condition of the patient, the interaction was described as a clinically significant interaction Aslam, *et al.*, 2003).

Interactions that occur in the body can be divided into two, pharmacodynamic and pharmacokinetic interactions. The pharmacodynamic interaction which works on the same receptors, causing synergistic or antagonistic effects interactions. Pharmacokinetic interaction is the interaction between two or more drugs are given together and

affect each other in the process of ADME (absorption, distribution, metabolism, and elimination) so as to increase or decrease drug levels in the blood.

From Table 1 and 2 we conclude that 11 actual type and 67 potencial type of drug interaction. It means there were 11 drug interaction happened during the treatment in GICU and probably happened in 67 cases.

Drug interactions that occur most had clinical significance 2 (36.25%), followed by 3 clinical significance (33.75%), and clinical significance of 1 (11.25%) and the last four clinical significance (2.50%). That was because this type of interaction had the highest incidence of clinical significance then it is usually a combination of two drugs be avoided, but if given a combination of drugs is carried out by close monitoring of the patient.Clinically significant drug interactions is important which resulted increasing of toxicity and/or a reduction in drug effectiveness. It would be more attention, especially which drugs with narrow safety margin (therapeutic index is low), such as cardiac glycosides, anticoagulants and cytostatic drugs

Conclusion

Detection of drug interactions concurrently on 185 patients obtained 78 drug interactions that consists of 46 (58.97%) pharmacodynamic interactions and 27 (34.61%) pharmacokinetic interactions.

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