

Potential Drugs Incompatibilities in Intensive Care Unit of type C Hospitals in Semarang Period January – June 2022

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Abstract. Injectable medication errors primarily occur during preparation and administration. Currently, Indonesia's Ministry of Health has a regulator for the pharmacist's role in iv admixture. But Indonesia still lacks pharmacists, so they have not routinely monitored intravenous drug incompatibility. The objective of the study is to know the potential incompatibility of intravenous admixtures. Data from the patients in the intensive care unit of two type C hospitals in Semarang who stayed from January to June 2022 were retrospectively collected. We analysed the iv drugs that had been given simultaneously. The results of the study show that patients aged >65 years are the most (32 %) and cardiovascular disease (29,82%) is the most diagnosed. From 114 patients who meet our criteria, we find 1719 iv drug simultaneously given, 7,5% are incompatible. Midazolam, dobutamine, furosemide, heparin, were the most commonly involved in potential incompatibility in our study.

Key words: Incompatibilities, Intravenous, Intensive Care Unit.

I. INTRODUCTIONS

Intensive Care Unit (ICU) is part of a hospital for intensive inpatient services who come in critical condition. The intensive care unit is equipped with a series of technologies that support treatment in patients who are at risk of experiencing organ system failure, especially lungs, cardiovascular systems, and kidneys (1). These room handles patients with diseases, trauma, or life-threatening complications. Most drugs given to ICU patients are generally through parenteral routes(. This parenteral drug administration is often done because it can provide a rapid pharmacological effect and facilitates therapy in patients who cannot use drugs orally(2). Another reason for parenteral drug administration is that it is often not well absorbed through oral routes(3). Parenteral preparations have two types, the single form or the form of being reconstituted with other parenteral preparations in a container before being given by injection or infusion. Among these, drug incompatibility is appraised to be a fatal condition(4)

Pharmacists should be able to identify potential incompatibilities by gathering information on the physical and chemical compatibility of various i.v.drugs. Numerous studies have confirmed that this is an important and growing problem(5). About half of all ward-based intravenous drug preparations and administrations are defective. These incompatibilities cause approximately 20% of all medication errors and nearly 89% of all medication errors(2) .

Drug incompatibilities can define as an unwanted interactions that occur during intravenous drug reconstitution and administration process, also when two or more drug solutions are mixed together (3)

The incompatibilities of intravenous drugs have been evaluated in a number of research. Mainly in intensive care unit, during which parenteral drug administration is often complicated by the fact that the number of concurrently administered drugs transcend the number of available infusion lines, intravenous drug incompatibilities speak for a significant problem(4).

An investigation related to intravenous drug incompatibility for patients on ICU rooms is still limited in Indonesia. This study aimed to know the potential incompatibility problems of intravenous drugs

II. METHODS

This research has received licence from the Health Research Ethics Committee of STIFAR Yayasan Pharmasi Semarang, No *Ethical Clearance* 389/YP-NA/KEPK/STIFAR/EC/VII/2022

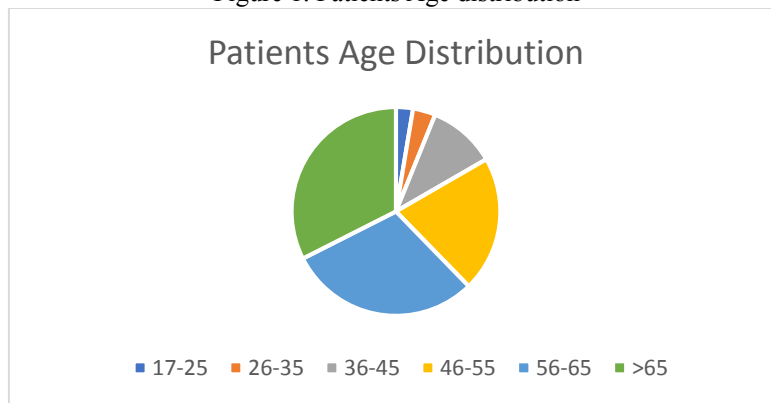
Data from the patients in the intensive care unit of two type C hospitals in Semarang were retrospectively collected. We analysed the iv drugs that had been given simultaneously (seen from the same time of

administration), concerning the potential compatibility of those intravenous drugs. We don't compare the two hospitals but combine the data because each hospital only has 3 beds so the number of patients is small. The inclusion criteria were patients hospitalized in ICU for at least 24 hours, and received minimal two iv drugs which were given simultaneously. The Patient enters ICU until the patient leaves ICU, starts from the beginning of January to the end of June 2022.

III. RESULT AND DISCUSSION

There are 114 patients who meet our criteria. The number of male and female is almost the same, 58 (51%) and 56 (49%) consecutively. Most of the patients (106 persons, 93%) stay in ICU less than 1 week. The rest stay equal to and more than 7 days. The longest is 13 days length of stay in ICU. The characteristics of prolonged ICU stay also depend on the length of hospital stay before ICU admission (4). The Patients' age distribution can be seen in figure 1.

Figure 1. Patients Age distribution



We divided the patients' age according to the Indonesia' Ministry of Health. The most are elderly patients, more than 65 years old (32%). Age was reported as a prodigy factor in critical ill patients, the study assessed disease severity, hospitalization diagnosis, but comorbidities were a more important risk factor than age(5) Accurate diagnose is very important for critically ill patients in ICU. The first diagnose can be seen on table 1

Table 1. Distribution of the patients' diagnoses

No	Diagnostic	Total patients	%
1	Cardiovascular disorder	34	29,82
2	Respiratory failure of various causes	22	19,31
3	Stroke	12	10,53
4	Septicemia and septic shock	8	7,02
5	Post major surgery	7	6,14
6	Kidney disorder	6	5,26
7	Respiratory disorder	6	5,26
8	Gastrointestinal disorder	5	4,38
9	Diabetes milletus	3	2,63
10	Loss of consciousness	2	1,75
11	Tuberculose millier	2	1,75
12	Combustio	2	1,75
13	Incomplete pregnancy	1	0,88
14	Hypertensive heart disease	1	0,88
15	Hypertensive encephalopathy	1	0,88
16	chronic obstructive pulmonary disease	1	0,88
17	Guillain barre syndrome	1	0,88

Total

114

100

The most commonly found disease is as many cardiovascular disorders, namely in 34 patients (29,82%). Cardiovascular disease is a term for various diseases that affect the heart and blood vessels, including coronary arteries heart disease (congestive heart disease), cerebrovascular disease, hypertension, and peripheral vascular disease(6). Cardiovascular disease major cause of mortality and morbidity in people. Since the 1980s, mortality due to cardiovascular disorders associated with age starts to decline, but in women fewer than men (7) However, these incompatibilities with the IV admixtures happen not only with drugs, sometimes with a diluent and a drug. When two or more drugs are added into the diluents, it can result in crystallization, clouding, and precipitation. The diluent in our research was Ringer Lactate, Normal saline (NaCl 0,9%) and NaCl 3%. Ringer Lactate was diluent which has many incompatibilities with some drugs, especially with Ceftriaxone(8).

Some incompatibilities were found between drugs and iv fluid that were given simultaneously. It can be seen in table 2.

Table 2. Incompatibilities drugs and iv fluid (n=45 from n=129 total incompatibilities)

Incompatible iv fluid + drug	Frequency	%
<i>Ringer Lactate + Ceftriaxone</i>	29	22,48
<i>Ringer Lactate + meropenem</i>	6	4,65
<i>Ringer lactate + Nicardipine</i>	2	1,55
<i>Ringer lactate + Phenytoin</i>	1	0,77
<i>Ringer lactate + Nicardipine</i>	1	0,77
<i>NaCl 0,9% + Phenytoin</i>	4	3,1
<i>NaCl 0,9% + Meropenem</i>	2	1,55
<i>Total</i>		35,64

The most was Ceftriaxone and calcium in Ringer lactate, happens 29 times (22,48%). In a study analysis reveals a relative paucity of evidence to keep up a serum precipitation events between Ceftriaxone and calcium salt in adults. Causal relationship appears to be relevant in infants receiving Ceftriaxone, but no findings were observed in the adult population(8) (9)

Patients in the ICU need a lot of drugs, because of their conditions. On table 2, we can see the number of drugs prescribed for the ICU' patients.

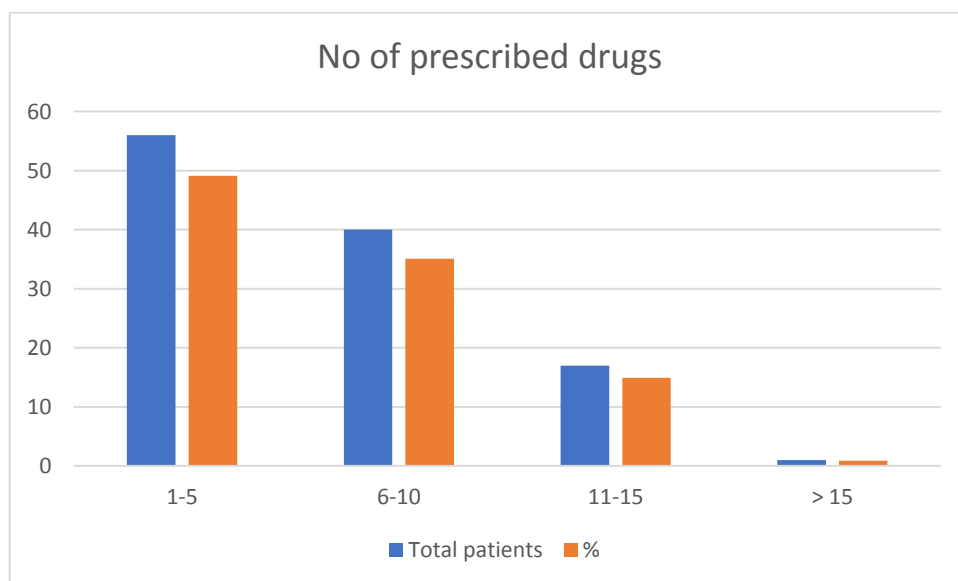


Figure 2. Number of prescribed drug

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The study of Machotka in Czech Republic (10) shows the average prescription of drugs per patient in ICU is far less, namely 6 drugs. WHO has got a standard that the total drugs in a recipe is 1,6-1,8 drugs. But different with our study, cause the patients were in a critical condition. There are 68 kinds of iv drugs prescribed for the patients. We found 1719 iv admixture that was simultaneously given to the patient and we found 129 (7,5%) incompatibility between it. Patients in ICU had a high failure rate. Medicine incompatibilities can be identified and ruled out by the pharmacist on a base multidisciplinary team, reduce patients' adverse effects (11) Particular attention should be given to midazolam, dobutamine, furosemide, heparin, as these drugs were the most commonly involved in potential incompatibility on our study. We can see in table 3

Table 3. Incompatible Drugs pair

Drug A	Drug B	No incompatibility
Midazolam	omeprazole	5
	furosemide	5
	meropenem	4
	dobutamine	3
	hydrocortisone	2
	ampicilline	1
Dobutamine	heparin	7
	furosemide	4
	meropenem	3
	sodium bicarbonat	1
Furosemide	omeprazole	6
	levofloxacin	3
	nicardipine	2
	pantoprazole	2
	amiodarone	1
	ondansetron	1
	heparin	5
Heparin	amiodarone	5
	isosorbide dinitrat	4
	levofloxacin	3

Minimizing the risk of coadministration of injectable drugs remains important as polymedicine is common practice in various patient populations such as cancer patients, post-transplant patients and intensive care patients (neonates, children, adults) (12)

We were not assessing the clinical appropriateness of the medicine in all prescription. However, so many medicines for therapy in ICU, because of it is nearly impossible to administer only one drug, especially medicines that are taken regularly dripping as an infuse.(13)

Limitation

Our research has a few limitations, such as the data was collected retrospectively and only got a few patients. Also, we can't observe to identify the real incompatibilities, especially physically incompatibilities.

IV. CONCLUSION

In this retrospective study, we highlight that potential incompatibilities that are very common in ICU (7,5 %) to simultaneously administration of incompatible drugs. Ceftriaxone and Ringer Lactate is the most incompatibility, iv liquid with drugs. Furosemide is the most common drugs' pair.

We suggested, to lower the IV incompatibilities in ICU, the pharmacist should be placed an IV incompatibility chart for the frequently used drugs.

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