Sciences of Pharmacy

ETFLIN

Original Article

Profile of Intravenous Preparation Mixing in Patients at the Regional General Hospital's Intensive Care Unit Abdoel Wahab Sjahranie Samarinda

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Received: 16 September 2022
Revised: 14 October 2022
Accepted: 15 October 2022
Published: 15 October 22

Editor: Abd. Kakhar Umar

Reviewer:
Irma Rahayu Latarissa
James H. Zonthantluanga

Citation
Riningsih DA, Simbolon OM, Butar-butar MET. Profile of Intravenous Preparation Mixing in Patients at the Regional General Hospital's Intensive Care Unit Abdoel Wahab Sjahranie Samarinda. *Sciences of Pharmacy*. 2022; 1(2):18-24.

Abstract: Compatibility is one of the quality characteristics of intravenous (IV) preparations that influences the effectiveness of patient therapy in the Intensive Care Unit (ICU). The purpose of this study was to determine the compatibility profile of IV medication formulations given to ICU patients. This prospective observational research was undertaken on patients in the ICU of a private hospital in Samarinda. The data on intravenous combination of drugs were compared in this study utilizing the ASHP Injectable Drug Information literature 21st edition, Injectable drug guide, and Manual Book. Injectable Drug Mixing was published in 2009 as a resource for determining the compatibility of intravenous formulations. Using certain criteria, combinations of intravenous medicines and their solvents are classed as compatible (C), incompatible (I), and unknown (U). The ICU had 25 patients, 15 of whom were male and 10 of them were female. There is no mixing of drug compounds containing incompatible solvents. All drugs were carried out with 100% compatible solvents. The limited information related to the compatibility and stability of these intravenous preparations encourages continuous monitoring of the patient's condition and drug levels.

Keywords: Intravenous preparation compatibility; Intensive Care Unit; Intravenous admixture; Compatibility study

1. Introduction

One of the mixing of sterile preparations carried out in the hospital is IV preparations. IV preparations are sterile preparations that are injected directly into blood vessels. The preparation is in the form of a solution, while suspension or emulsion are not allowed as it will clog the veins. The volume of intravenous injections generally ranges from 1-10 ml. Intravenous injection should be pyrogen-free and contain a non-irritating liquid which can mix with water. Intravenous injection solutions must be clear, free of deposits or solid particles, as they can clog capillaries and cause death.

Compatibility is a condition of mixing multiple medicinal materials with solvents wherein no signs of chemical interactions are observed. However, during the process of mixing and administering intravenous preparations, a potential problem called incompatibility can occur. Incompatibility is an undesirable reaction that can change the chemical, physical, or therapeutic stability of a drug preparation or so-called unmixed condition (1). Therefore, the mixing of intravenous preparations needs careful evaluation to prevent physical and chemical incompatibility. The process of mixing intravenous preparations is often carried out in patients in the Intensive Care Unit (ICU) because ICU patients has

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a higher risk to experience medication errors (ME) when compared to other inpatients. The conditions of patients treated in the ICU are generally not stable and they generally receive therapy through the intravenous route (2). Drug administration via the intravenous route provides a faster therapeutic effect with an optimum dose adjusted according to the patient's condition.

The limited information related to the compatibility and stability of intravenous preparations encourages continuous monitoring of the patient's condition and drug levels. Based on these reasons, we are interested in conducting a research in the ICU of the Abdoel Wahab Sjahranie Samarinda Regional General Hospital and we aim to identify the profile of the mixing of intravenous preparations.

2. Methodology

2.1 Types of research

This type of research is a descriptive observational with a cross-sectional research design by taking population data or intravenous dosage samples only once at the same time. Data collection is carried out on a perspective basis.

2.2 Research Population

The study population was mixed intravenous preparations in the intensive care unit (ICU) room of the Abdoel Wahab Sjahranie Samarinda Regional General Hospital.

2.3 Research Sample

Sample used was all populations in the intensive care unit (ICU) room of the Abdoel Wahab Sjahranie Samarinda Regional General Hospital.

2.4 Patient Sample Criteria

Patient sample criteria were split into the inclusion criteria and the exclusion criteria. Inclusion criteria consisted all observed intravenous preparation mixing processes are classified into the 4 most widely used drugs for ICU patients of Abdul Wahab Sjahranie Samarinda Hospital. Exclusion criteria consisted the process of mixing intravenous preparations which are classified into the 4 most widely used drugs for ICU patients at Abdul Wahab Sjahranie Samarinda Hospital but not all of them were observed.

2.5 Data Analysis Technique

Data were analyzed with the measures carried out that were included in the data collection, classification of data processing, making conclusions by comparing written provisions in the literature. The results of the mixed profile analysis are expressed in the form of a percentage value (%) calculated with the formula Percentage=(Number of compatible intravenous mixture preparations)/(Total Mixing) x100 %. Data collection was carried out by looking at the patient's medical record (RM). The data taken were the patient's name, gender (Male and Female), age, diagnosis, medication given. The results of the analysis of intravenous drug mixtures are classified into compatible (K), incompatible (I), unknown (U). The references used to classify these intravenous drugs are ASHP Injectable Drug Information edition 21, and injectable drug guide.

3. Results and Discussion

Based on the results of observations of patient characteristics during this study period, there were 25 patients who met the inclusion criteria from July - August 2022. The majority of patients in the ICU of the Abdoel Wahab Sjahranie Regional General Hospital in Samarinda City are men (n=15) and the most diagnosed disease was typhoid (n=10).

3.1 Patient Demographic Data

The patients in the ICU of the Abdoel Wahab Sjahranie Regional General Hospital, Samarinda City, were 15 patients and the most diagnoses obtained by typoid disease as many as 10 patients can be seen in Table 1.

Table 1. Patient Demographic Data

Demographic Data	Amount & Percentage (n=25) patient
Gender	
Male	15 (57%)
Female	10 (43%)
Diagnosis	
Typoid	10 (58%)
Phenumonia	7 (30%)
Sepsis	5 (8%)
Meningitis	4 (4%)

This study used 200 mixings conducted in the ICU room of the Abdoel Wahab Sjahranie Regional General Hospital with 26 patients. Patient characteristics and patient diagnoses are presented in Table 1 Gender is divided into 2 categories. The results of the analysis of the mixing profile are expressed in the form of a percentage value, that is, a 100% result is obtained.

Research by fauzi I, (2020) stated that data analysis was seen from the P Value using the chi square method with results of more than 0.05, namely 0.776, meaning that there was no significant relationship between the patient's sex and patient therapy (3). This can be interpreted to mean that gender has no correlation or no relationship with the incidence of therapy in the patient, or in other words the sex of the patient does not determine how big the incidence in the patient's therapy. Based on the results of the study obtained the results of the most frequent diagnosis was typoid disease and the second most common diagnosis was phenumonia ollowed by other diseases.

3.2 List of Drug That Are Mixed

Based on the results of the observation of the percentage of the drug list carried out by mixing intravenous preparations in the ICU room of the Abdoel Wahab Sjahranie Regional General Hospital, it can be seen in Table 2.

Table 2. Table of the list of drugs for which mixing was carried out.

No.	Drug Name	Dosage Form of The Drug	Dosage Strength	Amount	Percentage (100%)
1	Ceftriaxone	Vial	1 g	80	40
2	Omeprezole	Vial	40 mg	70	35
3	Tramadol	Ampoule	100 mg	30	15
4	Meropenem	Vial	1 g	20	10
			Total	200	100

According to the Ministry of Health (2009), the process of preparation and mixing of parenteral preparations must be carried out by pharmacists or pharmaceutical personnel who have been trained under the responsibility and supervision of hospital pharmacy installation pharmacists (4). However, at RSUD Abdoel Wahab Sjahranie, we observed that the process of preparation and mixing of drugs was carried out by nurses in the ICU room who were competent and attended dispensing training for sterile preparations. This is due to the absence of pharmacists or pharmaceutical technical personnel.

The number of nursing personnel working in the ICU room was 34. For the compounding process in the ICU room, only 1 nurse was involved. Based on Table 2, there are four top rankings of drugs that are often compounded before being properly administered namely ceftriaxone (40%), omeprazole (35%), meropenem (15%), and tramadol (10%). Based on the results of observations, the most frequently used drug was ceftriaxone.

3.3 Visual Observation Results

The results of visual observations (physical quality test of mixing intravenous preparations) is given in Table 3.

Table 3. Visual Observation of Intravenous Preparations.

No.	Drug Name	Parameters observed	Information according to literature	Observations	Amount	Percentage (%)
1	Ceftriaxone 1 g	Solution Color	Light yellow	Light yellow	80	40
		Lucidity	The solution must be clear and particle-free	Clear, particle-free solution		
2	Omeprazole 40 mg	Solution Color	Colorless	Colorless	70	35
		Lucidity	The solution must be clear and particle-free	Clear, particle-free solution		
3	Tramadol 100 mg	Solution Color	Colorless	Colorless	30	15
		Lucidity	The solution must be clear and particle-free	Clear, particle-free solution		
4	Meropenem 1 g	Solution Color	Colorless	Colorless	20	10
		Lucidity	The solution must be clear and particle-free	Clear, particle-free solution		
				Total	200	100

Visual observations can be made with the help of dark backgrounds. Observations were made to see physical discrepancies including deposition, the presence of particles, fog, as well as changes in color, smell and gases. The results of visual observations showed that the drugs Ceftriaxone, Meropenem, Omeprazole, and Tramadol showed clear, clean, bright results with no precipitate and no discoloration. From the results it can be concluded that the mixing of the four drugs with water for injection and NaCl 0.9% was compatible.

3.4 Drug Preparation Procedure

The drug preparation procedure is given in Table 4. The mixing technique carried out by at the hospital was not in accordance with the literature because based on the observation results, the vial was shaken while the needle stayed inside the vial. However, due to limited facilities and infrastructure, there was no LAF in the mixing room. During the mixing process, the needle can be left in the vial with the aim of preventing contamination of the syringe. Then to dissolve the powder, a J-Motion movement was sufficient until the entire powder in the vial was dissolved (Ministry of Health, 2009). This movement aims to prevent the presence of powder attached to the rubber vial which causes the drug to not dissolve completely. Rubbing should be done at a position of 90° because in this position the contact between the substance and the solvent is greater and can be dissolved properly. Based on the observation results, there are several solvents used in mixing based on the solvent of each type of drug to be dissolved.

Table 4. Types of Intravenous Dosage Solvents.

No.	Drug Name	Dosage form of the drug	Strength of medicinal preparations	Types of Solvents according to the literature	Observations
1	Ceftriaxone	Vial	1 g	*Water for injection*	*Water for injection*
2	Omeprazole	Vial	40 mg	*Water for injection*	*Water for injection*
3	Tramadol	Ampoule	100 mg	NaCl 0.9 %	NaCl 0.9 %
4	Meropenem	Vial	1 g	NaCl 0.9 %	NaCl 0.9 %

In the Injectable Drug Guide literature (2012) and the Injectable Drug Guidelines and Cytostatics, (2009) ceftriaxone and omeprazole are compatible with 0.9% NaCl but based on the results of research Ceftriaxone is compatible dissolved with water for injection, omeprazole is compatible dissolved with water for injection, tramadol is compatible dissolved with NaCl 0.9%, and compatible meropenem is dissolved with NaCl 0.9% it can be concluded that the solvent is in accordance with the ASHP Injectable Drug literature Infromation 21st edition (5).

3.5 pH Measurement Results

The pH measurement results is given in Table 5.

Table 5. pH Intravenous Preparations.

No.	Drug Name	pH according to the literature	Sample pH	Percentage (%)
1	Ceftriaxone 1 gram	6,7 (6-8)	6	40
2	Omeprazole 40 mg	8,8-10	9	35
3	Tramadol 100 mg	6-7	7	15
4	Meropenem 1 gram	4,0-6,0	6	10
			Total	100

The pH measurement of the mixture was carried out because the mixture was said to be incompatible if the mixture produces a change in pH from the initial reading to the next reading or the final pH test. Such changes in the pH value that do not correspond to the literature may indicate active changes in the mixture that are chemical instable. pH measurements can be carried out with the help of a universal pH indicator tool.

According to Housman et al. (2011), many important components must be considered in mixing parenteral preparations. The pH of the drug will have an impact on the occurrence of incompetence (6). Chemical incompatibility describes how the chemical degradation of one or more drugs that were mixed together, causes a toxicity or therapeutic inactivation. Degradation is not always directly observable. A specific pH value or a narrow range of pH values is necessary to maintain the stability of the drug after mixing. It can be concluded that the pH of the samples are in accordance with the pH in the literature.

3.6 Compability and Incompability

Compatibility is one of the determining factors for the quality of intravenous preparations (IV) which has an impact on the success of therapy for ICU patients. The results of mixing obtained from Ceftriaxone, Omeprazole, Tramadol, and Meropenem suggests no changes (2). Physical incompatibility that can occur from the results of observations includes the formation of white particles that float in the liquid, become cloudy after mixing, and the presence of foam and gas after mixing.

From the observations, the results of research observations were obtained that the results of physical observations can be known from visual tests of discoloration, and turbidity where the parenteral drug preparations Cefriaxone, Omeprazole, Tramadol, and Meropenem physically, namely there is no color change and is not cloudy / clear. Incompatible that occurs can be in the form of the formation of deposits, loss of active substances, the formation of fog,

and the adsorbs of drugs on the packaging materials based on the results of research do not occur when the mixing process is carried out. The results of chemical observations can be known from the changes in pH that occurred during the observation time. The mixing of Ceftriaxone, Omeprazole, Tramadol, and Meropenem is compatible, both the solvent and also the volume used are appropriate.

In this study, IV preparation was divided into 2 types, namely, small volume parenteral preparation and large volume parenteral preparation. Parenteral preparations of small volumes are interpreted as sterile drugs packaged in containers under 100 ml because in this study there were preparations of the drugs ceftriaxone 1 g and omeprazole 40 mg dissolved in a syringe of 10 ml with solvent water for injection. With the category of parenteral preparations of small volumes are pharmaceutical products consisting of organic and inorganic chemicals in solution, suspensions, emulsions, freezing dry products or as sterile powders then Biological products made from biological sources include vaccines, toxoids, biological extracts. Meanwhile, in this study, large volume parenteral preparations are sterile liquid preparations containing drugs packaged in containers of 100 ml or more and intended for humans, such as in infus bag infusion containers in tramadol drug preparations of 100 mg/2 ml and meropenem 1 g dissolved with 0.9% NaCl in infus bag.

4. Conclusion

Based on the results of the research conducted from June-August 2022 in the ICU room of the Abdoel Wahab Sjahranie Samarinda Regional General Hospital, the mixed of intravenous preparations were in accordance with the literature with a percentage result of 100% and no incompatibility events were found in the patients of the ICU room. The stability of the mixing results was supported by pH measurements as there was no difference in the pH value measured in the pH range based on the literature. We also recommend that only pharmacists should be given responsibility for mixing IV preparations in any type of clinical settings.

Authors contribution

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Funding Information

The study receive no funding

Informed Consent Statement

Not applicable

Data Availability Statement

Data sharing is available upon request

Conflict of Interest

The authors declare no conflicts of interest

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