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# Potential Intravenous Drug Incompatibilities in PICU (Pediatric Intensive Care Unit) Patients at Dr. Moewardi Surakarta Hospital in 2024

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**ABSTRACT:** Drug incompatibility is a physical or chemical reaction between drug products that occurs outside the body and is characterized by precipitation, discoloration, gas formation, and reduced drug effectiveness. Intravenous drug incompatibilities that occur in pediatric patients are at high risk of causing medication errors. Pediatric patients who are more at risk of drug incompatibility are patients admitted to the Pediatric Intensive Care Unit (PICU) because they receive more drugs intravenously. This study aimed to identify potential intravenous drug incompatibilities among pediatric patients admitted to the PICU at Dr. Moewardi Surakarta Hospital in 2024. This study is a descriptive, observational, non-experimental study with retrospective data collection at Dr. Moewardi Surakarta Hospital. The data collected were medical records of PICU patients who met the inclusion criteria: pediatric patients aged ≥28 days to 18 years, admitted to the PICU for at least 24 hours, and who received at least 2 intravenous drugs. The potential incompatibility of intravenous drugs in PICU patients was then reviewed based on the 2021 edition of the Handbook of Injectable Drugs. The results showed that, among 81 patients with a total of 1,518 intravenous drug mixtures, 616 (40.6%) were known to be compatible, 61 (4.0%) were incompatible, and 841 (55.4%) had no information.

**Keywords:** Incompatibility; intravenous; drug; PICU

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## INTRODUCTION

Drug incompatibility is one of the problems in pharmaceutical practice that often occurs, especially in drug compounding. Drug incompatibility is an undesirable physicochemical reaction that occurs when two or more drugs are mixed. The resulting reaction can affect the safety and efficacy of therapy (Pangestika, 2022). Drug incompatibility can occur therapeutically, chemically, and physically. Chemical incompatibility occurs when chemicals degrade or change, reducing effectiveness and potentially causing toxicity. Physical incompatibility is characterized by observable changes, such as turbidity, precipitation, and discolouration (Rahmawati et al., 2018). Drug incompatibility can result from differences in polarity, acid-base reactions, ionic equilibria, and drug solubility. The impact caused by drug incompatibility is a decrease in drug effectiveness and serious side effects such as allergic reactions and toxicity (Agustin & Fitrianingsih, 2020). In addition to these impacts, patients will also face higher medical costs due to therapy failure.

Drug incompatibility can occur when various preparations are mixed, whether used orally or intravenously. In practice, it is not uncommon for intravenous drugs to be mixed, especially drugs given to emergency patients or patients with unstable conditions (Artini & Wardani, 2021). Intravenous drugs are the main choice for use because they are administered through blood vessels and do not experience an absorption phase, so the effectiveness of the drug becomes faster than drugs by other routes. The risk of intravenous drug incompatibility is very dangerous for patients because it can cause embolism, which, if left untreated, will lead to inflammation and even organ failure. This problem is caused by incorrect drug mixing and a lack of understanding of the reactions that occur during drug mixing. This certainly underscores the important role of clinical pharmacists in identifying and educating healthcare workers to prevent serious problems caused by errors in intravenous drug mixing.

Research conducted by Leal et al. (2016) found that there are 85% incidence of incompatibility in children with drugs that are at risk of causing incompatibility, including diazepam, phenytoin, and metronidazole. Another study reported that the most commonly prescribed drug combination that experienced incompatibility was ampicillin-gentamicin, with a percentage of cases as high as 31.71% (Mahendra et al., 2023). Intravenous drug incompatibility cases can occur in patients of various ages, especially pediatric patients, due to limited blood vessel size. Patients with smaller blood vessels are at high risk of blockage, which can lead to endothelial damage and inflammation (Hani et al., 2019). In addition to small blood vessels, liver and kidney function in pediatric patients is not optimal. This can affect drug metabolism and excretion. The result is that the accumulation of drugs in the body increases and causes toxicity (Herdwiani et al., 2021). Coupled with the patient's unstable condition, being admitted to the Pediatric Intensive Care Unit (PICU) will increase the potential for getting more drugs intravenously.

Thus, drug incompatibility must be addressed to minimize the serious impact that can occur in pediatric patients. Research related to cases of intravenous drug incompatibility in PICU patients is still minimal in Indonesia. There are more studies on incompatibility issues in ICU patients, both prospective and retrospective, than in PICU patients. This is why this study is urgently needed to identify intravenous drug incompatibility in PICU patients.

## METHODS

This is a non-experimental, descriptive-observational study using the cross-sectional method. The data collection period spanned from February to March 2025, and the collected data comprised retrospective patient data from January to December 2024. This study aims to identify intravenous drug mixture incompatibilities descriptively by analyzing drug administration data from medical records rather than through clinical confirmation obtained from direct observation of the intravenous drug-mixing process. The inclusion criteria for this study were as follows: patients receiving care at the Pediatric Intensive Care Unit (PICU) who received a minimum of two intravenous medications, in addition to complete medical records that included patient age, gender, length of hospitalization, number of intravenous drugs used, diagnosis, and intravenous drug data.

The exclusion criteria in this study were as follows: unreadable or incomplete medical records, and patients who were discharged at the request of their families. The primary variable in this study was the potential for intravenous drug incompatibility, which was determined by observing the medical records for intravenous drug combinations administered concurrently and considered as a single mixture.

The potential for incompatibility was then analyzed using the 2021 ASHP Handbook Injectable Drug Information. The assessment of intravenous drug incompatibility in this study covers all infusion routes administered to patients. The study has met the research requirements, as evidenced by ethical approval and approval from Dr. Moewardi Hospital Surakarta. The data collected were the medical records of pediatric patients treated at the PICU (Pediatric Intensive Care Unit) of Dr. Moewardi Hospital Surakarta, with number 212/I/HREC/2025.

## RESULT AND DISCUSSION

This study aims to determine the potential for intravenous drug incompatibility in PICU (Pediatric Intensive Care Unit) patients at RSUD Dr. Moewardi Surakarta in 2024 and requires a total sample of 81 patients that are stated in accordance with the inclusion criteria.

### Patients Profile

Analysis of demographic data on patient age characteristics based on table 1 states that the most pediatric patients admitted to the PICU are patients with an age range of 12-18 years as many as 37 patients (45.7%) and are patients in puberty where physical, psychological, and social growth and development are filled with pressure so that it can increase morbidity (Wulandari, 2014). However, according to Dewi & Fatimatuzzuhroh (2019), the number of PICU patients was successively dominated by those aged <1 year (27.9%) and 1-5 years (25.6%). So, age is not the main factor affecting the number of PICU patients. The patient profiles are shown in Table 1.

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**Table 1.** Profile of PICU Patients at Dr. Moewardi Hospital in 2024

| Profile Patients | | N | % |
|---|---|---|---|
| Age | 28 hari—12 months (Infancy) | 20 | 24.7 |
| | 13 bulan — 2 years (Toddler) | 3 | 3.7 |
| | 2—5 years (Early childhood) | 11 | 13.6 |
| | 6—11 years (Middle childhood) | 10 | 12.3 |
| | 12—18 years (Early adolescence) | 37 | 45.7 |
| Gender | Male | 48 | 59.3 |
| | Female | 33 | 40.7 |
| Length of hospitalization | 1—7 days | 33 | 40.7 |
| | >7 days | 48 | 59.3 |
| Number of drugs used | 1—5 drugs | 16 | 19.8 |
| | >5 drugs | 65 | 80.2 |

Analysis of demographic data on patient gender characteristics based on Table 1 states that male patients are the most treated patients and are the patients most diagnosed with infectious diseases. The results of this study are in line with other studies, which state that there is a relationship between the number of male patients admitted to the PICU and high rates of infection. This is proven through a study conducted by Angele et al., 2014, namely the immune response is influenced by gender where the disease condition is more severe in men because TNF, IL-6, IL-10 which are pro-inflammatory mediators increase, while in women there are more anti-inflammatory mediators so that it can be proven that there is an influence of gender differences on the increase in morbidity due to infection. However, it cannot be proven that male patients admitted to the PICU are generally more than female patients because gender does not affect the morbidity rate of patients admitted to the PICU, but the patient's condition itself (Almossawi et al., 2021).

Patients of PICU are pediatric patients who are intensively treated because they have chronic medical conditions and complex severity (Hasmuddin et al., 2022). The severity of the condition cannot necessarily be stabilized in a short period of time, so special care and a long period of treatment are needed. The severity of the disease affects the length of hospitalization for patients. This is evidenced by a study by Hidayah et al. (2022), which found that patients with severe disease or chronic conditions are more likely to be treated for a long period than those with mild conditions. This is also supported by the research of Abqariah et al. (2024), which found a relationship between the severity of disease complications and hospitalization length. The more severe the patient's condition, whether due to a single disease or complications, the longer treatment is needed.

Data analysis of the number of intravenous drugs used in PICU patients based on Table 1 states that 65 patients received >5 drugs. This is related to the severity of the patient's condition, so that a greater number of intravenous drugs are needed to improve the patient's recovery. According to Wahyuni et al. (2023), patients who receive >5 drugs do so because, in addition to their primary disease, they also have comorbidities, necessitating more drugs to improve patient recovery.

The analysis based on the diagnosis results in Figure 1 indicates that 36 patients (44.4%) were diagnosed with infectious diseases. According to Sovira et al. (2020), the immune system in pediatric patients is not fully developed, making them more likely to become infected. The results of the study are consistent with the research of Visser et al. (2023), which found that pediatric patients and neonates are highly vulnerable to infectious diseases. Infectious diseases that occur either as the initial diagnosis of the patient or occur during the treatment period, or nosocomial infections.

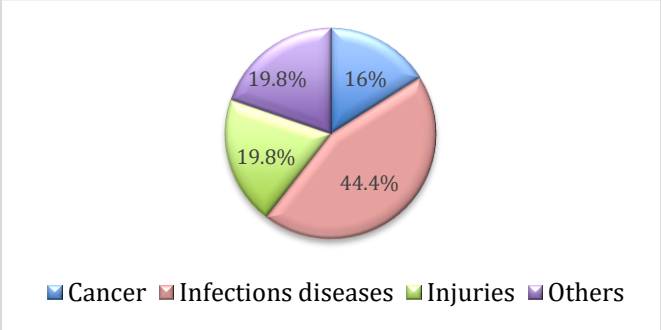


**Figure 1.** Diagnosis of PICU patients

## Intravenous Drug Compatibility

The level of potential drug incompatibility based on the number of patients in Table 2 states that of the total sample of 81 PICU patients, there were 43 patients (53.1%) who were declared to have the potential drug incompatibility.

**Table 2.** Level of Potential Drug Incompatibilities Based on the nominal of Patients

| Drug Compatibility Data | | N | % |
|---|---|---|---|
| Incompatibilities based on the nominal of patients | Potentially incompatible | 43 | 53.1 |
| | Not potentially incompatible | 38 | 46.9 |

The level of potential incompatibility in this study was higher than in patients without such potential. The results of this study prove that PICU patients have the potential to experience drug incompatibility. This is supported by research indicating that as many as 80% of pediatric patients (222 patients) may experience drug incompatibility (Leal et al., 2016). The results of Hanifah (2018), research also state that the use of IV drugs in 200 PICU patients is known to be 95% of patients getting at least 2 drugs at one time of administration and the potential for drug encounters in the infusion line, while as many as 68.7% of NICU patients get 2 drugs at a time and 28.5% only get 1 drug so that IV drug administration in PICU patients is more complicated and has the potential for incompatibility. Thus, there is a need for direct pharmaceutical intervention to address drug incompatibility issues and improve patient safety, preventing the severity of patient

conditions. Analysis of potential incompatibilities in 81 patients with a total of 1.518 drug mixtures is recorded in Table 3.

**Table 3.** Potential Incompatibility Based on the Nominal of Drug Mixtures

| Level of Potential Incompatibility | N | % |
|---|---|---|
| Compatible | 616 | 40.6 |
| Incompatible | 61 | 4.0 |
| *No Information* | 841 | 55.4 |

Analysis of the level of potential drug incompatibility based on Table 3, which is unknown or does not have drug compatibility information, as many as 841 (55.4%) mixtures. According to Syahbarni et al. (2021), the mixture lacks information because the reference does not clearly state whether it is compatible or incompatible. The highest number of mixtures declared to have no information in this study was the paracetamol-omeprazole mixture. Another study reported that cases of no information (NI) regarding intravenous drugs among patients at one hospital in Tasikmalaya reached 54.9% among 73 patients (Resta et al., 2021). Research by Bismantara et al. (2023) also reported that NI cases were quite high, with an incidence of 102 out of 284 mixtures. Compared with drug incompatibility data, the lack of information on drug mixtures suggests that research on drug mixing is still relatively limited, so further studies are needed to confirm the status of these mixtures.

**Intravenous Drug Incompatibility**

Analysis of intravenous drug incompatibility data in Table 4 shows that 61 mixtures (4.0%) were incompatible. The most potential incompatibility is the mixture of ampicillin and gentamicin. This is consistent with another study reporting that 50% of the total 702 incompatible combinations were ampicillin and gentamicin; the combination of these two drugs has been shown to result in a 50% reduction in gentamicin levels within 2 hours when stored at room temperature (ASHP, 2021). To prevent incompatibility between ampicillin and gentamicin, gentamicin can be administered 1 hour before ampicillin administration (Pacifici, 2017). Incompatibility between ampicillin-sulbactam and D5 ½ NS is the second most common incompatibility, after ampicillin-gentamicin. The presence of hydroxide ions in dextrose has been shown to catalyze the formation of sodium ions in ampicillin, thereby reducing the stability of the preparation (Matdoan et al., 2023). The duration of drug interaction also affects pH changes. Mixing ampicillin-sulbactam in D5 ½ NS can only last for 4 hours because ampicillin becomes incompatible as the mixing time increases (ASHP, 2021).

The incompatibility of the midazolam-omeprazole mixture, as reported by Swart & Moorren (1995), was evidenced by a change in color to brown and the formation of precipitate. This is caused by the difference in pH of the two mixtures. Another study also reported that omeprazole inhibited the formation of oxidized metabolites of midazolam, resulting in increased sedation effects (Bibi, 2008). Thus, mixing the two drugs should not be done to avoid therapeutic problems.

**Table 4.** Intravenous Drug Incompatibility Data

| Drug Incompatibility | N | % |
|---|---|---|
| Ampicillin + Gentamicin | 20 | 32.8 |
| Ampicillin-Sulbactam + D5 1/2 NS | 11 | 18.0 |
| Midazolam + Omeprazole | 10 | 16.4 |
| Ampicillin + Ondansetron | 7 | 11.5 |
| Ampicillin + Midazolam | 5 | 8.2 |
| Ondansetron + Methylprednisolone | 2 | 3.3 |
| Gentamicin + Furosemide | 2 | 3.3 |
| Ciprofloxacin + Methylprednisolone | 1 | 1.6 |
| Ciprofloxacin + Furosemide | 1 | 1.6 |
| Ondansetron + Acyclovir | 1 | 1.6 |
| Paracetamol + Acyclovir | 1 | 1.6 |

Ampicillin and ondansetron are incompatible because of their different pHs. Ampicillin has a pH of 8-10, while ondansetron has a pH of 3.3-4, so mixing the two preparations can cause turbidity or precipitation. This is consistent with research by Estan-Cerezo et al. (2017), which found that mixing ampicillin with ondansetron can cause incompatibility reactions due to differences in the pH of the preparations. The problem of pH differences also occurs in mixtures of ondansetron with acyclovir and ondansetron with methylprednisolone, where acyclovir and methylprednisolone have an alkaline pH so that they can form precipitation immediately after mixing with ondansetron (ASHP, 2021)

The incompatibility between ampicillin preparations and midazolam results in a visually observable reaction: a mist that forms immediately upon mixing the two drugs (ASHP, 2021). The reaction occurs due to the difference in pH: ampicillin (pH 8-10) and midazolam (pH 3), so the pH difference is cited as the cause of the incompatibility between the two drugs.

Paracetamol incompatibility with acyclovir is one of the incompatibility reactions characterized by the formation of particulates. Based on previous research, the particulate measurements from mixing the two drugs were reported to increase at the 4th hour at room temperature (Anderson et al., 2014). This indicates that the mixture can be stabilized within 4 hours of mixing. A drug combination that also affects the mixture's stability is ciprofloxacin with methylprednisolone, which produces temporary turbidity that quickly disappears, and crystals form within 2 hours at 24°C (ASHP, 2021).

Incompatibility of gentamicin with furosemide is a case of incompatibility characterized by precipitation of furosemide. To avoid this incompatibility reaction, the two drugs are administered separately (Thompson et al., 1985). Incompatibility in the mixture of ciprofloxacin with furosemide is an incompatibility that occurs with a total of 1

occurrence. The incompatibility of mixing ciprofloxacin (pH 3.5-4.6) or acidic with furosemide (pH 8-9) or alkaline has been studied by previous researchers who stated that visually turbidity and precipitates were formed, which microscopically in the mixture formed crystals whose particle size increased to> 1μm and a decreasing pH value (Liona & Priska, 2020).

Preventing intravenous drug incompatibility will be more effective if clinical pharmacists play a direct role, including screening intravenous drug mixtures, educating other healthcare professionals, and proposing regulations requiring pharmacist visits to monitor the stability of intravenous drug mixtures in patients with special conditions, such as PICU patients. Based on the cases of intravenous drug incompatibility that occurred in this study, pharmacists must pay attention to the pH value of the drug, the storage temperature of the mixture, separate intravenous drugs through other routes, clean the injection and infusion lines, and another method that can be used is the use of filters to overcome turbidity or sedimentation (Hanifah, 2018).

## CONCLUSION

The profile of PICU patients at RSUD Dr. Moewardi Surakarta in 2024 who were mostly treated were patients aged 12—18 years as many as 37 patients (45.7%), male as many as 48 (59.3%), the number of hospitalizations >7 days as many as 48 (59.3%), the number of intravenous drugs >5 drugs as many as 65 (80.2%), and diagnosed with infectious diseases as many as 36 (44.4%). The most commonly used intravenous drugs were antibiotics, namely ampicillin, ampicillin-sulbactam, and gentamicin, as treatment for infectious diseases. The types of intravenous drugs that experienced incompatibility were 61 mixtures with the highest number being ampicillin with gentamicin as many as 20 (32.8%), ampicillin-sulbactam with D5 ½ NS as many as 11 mixtures (18.0%), midazolam with omeprazole as many as 10 mixtures (16.4%), ampicillin with ondansetron as many as 7 mixtures (11.5%), and ampicillin with midazolam as many as 5 mixtures (8.2%). The level of potential intravenous drug incompatibility in 81 patients with a total of 1,518 intravenous drug mixtures, consisting of 616 mixtures (40.6%) were compatible, 61 mixtures (4.0%) were incompatible, while as many as 841 mixtures (55.4%) had no information.

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## AUTHOR CONTRIBUTION

STD: Ideas, design, literature search, data analysis, manuscript preparation, and manuscript editing.
AWA: Data collection; data analysis.
RR: Design; Definition of intellectual content.

## ETHICS APPROVAL

This study was approved by the ethics commission of Dr. Moewardi Hospital Surakarta with number 212/I/HREC/2025.

## CONFLICT OF INTEREST

None to declare

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