Potential Incompatibility, Instability And Interactions Of Prescriptive Drug Containing Corticosteroids At dr. Loekmono Hadi Kudus Hospital

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Abstract. Drug incompatibility can cause physical reactions, resulting in visible changes, alterations in color, consistency, or gas production. Chemical reactions are caused by molecular changes in one or more components of the solution. Corticosteroids are one of the most frequently prescribed drugs, but they carry the risk of serious side effects if not used rationally. The compounding process often results in incompatibility, instability, and drug interactions. This can reduce the effectiveness of therapy, and medication errors can occur. Compound prescriptions containing corticosteroids need to be evaluated to ensure the safety and stability of the preparation. Drug incompatibility, instability, and drug interactions can cause decreased drug activity or inactivity, the formation of new active ingredients that are toxic or non-toxic, increased toxicity, and organoleptic changes. This study is a type of quantitative data collection prospectively, which focuses on forward-looking observation starting by identifying variables from patient prescription sheets in April-May 2025 at Dr. Loekmono Hadi Kudus Hospital. The total sample in this study was 107 prescription sheets that met the inclusion criteria. The results of the study showed that the classification of patients based on the diagnosis of the most common disease was ISPA 45 (42.1%). The age criteria for recipients of pulveres prescriptions in the 0-5 year age group was the group with the largest number of patients, namely 83 people (77.6%). There was no potential for incompatibility, 0%. There was a potential for instability on the prescription sheet of 99 (92.5%). There was a potential for corticosteroid drug interactions of 2 (1.9%), indicating the presence of drug interactions. The severity of corticosteroid drug interactions that occurred was a moderate interaction of 1 (0.9%) and a major interaction of 1 (0.9%). The conclusion is that on the prescription sheet there was no potential for incompatibility 0%, there was a potential for instability of 99 (92.5%), and there were moderate, minor interactions, there were potential for corticosteroid drug interactions of 2 (1.9%), and the severity of corticosteroid drug interactions was moderate interaction of 1 (0.9%) and major interaction of 1 (0.9%).

Key words: [Incompatibility, Instability, Drug Interactions]

INTRODUCTION

Drugs are substances or combinations of substances, including biological products, used to influence or study physiological systems or pathological conditions, to diagnose, prevent, cure, restore, improve health, and for contraception in humans (Maemonah *et al*., 2022). The criteria considered in monitoring prescriptions by WHO include the number of drugs contained in one prescription and efforts to suppress or reduce bacterial resistance to antibiotics, and reduce cases of disease transmission (Destiani *et al*., 2016). Irrational prescribing is one of the problems that must receive special attention, especially in the use of antibiotics, corticosteroids, and multivitamins, which are most commonly prescribed to patients (Kisrini *et al*., 2018). Incorrect use of corticosteroids can cause unwanted side effects such as hypertension, hyperglycemia, and Cushing's syndrome. Evaluation in prescribing corticosteroid drugs must be carried out so that patients receive appropriate and rational therapy (Lisni *et al*., 2018). The problem of inappropriate drug use arises due to medication errors that are often prescribed, especially during the drug administration phase. One form of medication error is the occurrence of incompatibility and instability, such as physical and chemical reactions that result in rapid and reversible changes (eg, particulate formation, color change, or gas release) (Bates *et al*., 2023). Incompatibility is an event in which drugs cannot be mixed physically or chemically, resulting in loss of potency, increased toxicity, or other side effects. This refers to an unwanted reaction between drugs, solutions, containers, or other drugs (Sasangka *et al*., 2021). Instability is an unstable state in the physical and chemical characteristics of a drug. Drugs that are physically and chemically damaged can be seen from their shape, color, taste, and odor (Noviani *et al*., 2021). Evaluation of drug therapy also includes monitoring for drug interactions that can affect effectiveness or increase the risk of side effects. Identification of drug interactions needs to be done to minimize reactions to medication errors and side effects (Rahmawaty *et al*., 2024).

METHODS

This study is a descriptive observational study and prospective data collection. Data was taken from outpatient polyclinic patient prescription sheets in April-May 2025 at dr. Loekmono Hadi Kudus Hospital. The sampling technique for this study was accidental sampling with a sample size of 107 medical records. Samples were taken that met the inclusion criteria, including prescription sheets for pediatric and adolescent patients aged 0 months to 16 years, prescription sheets containing corticosteroids in pulverized compound prescriptions, prescription sheets containing more than two types of drugs, and complete.

RESULTS AND DISCUSSION

This research was conducted at RSUD Dr. Loekmono Hadi Kudus, and the ITEKES Cendekia Utama Kudus Pharmacy Laboratory has gone through an ethical review process approved by the Chairperson of the Health Research Ethics Committee of RSUD Dr. Loekmono Hadi Kudus, with Registration Number: 24/KEPK/RSLH/III/2025, which aims to guarantee the rights of research subjects in terms of privacy, confidentiality, and justice because it involves patient medical records as a data source.

The classification of prescription sheets containing corticosteroids based on characteristics seen from the age and gender of the patient can be seen in the following table:

Table 1. Patient Age Classification

Classification	Number	%
Age		
0-5 years	83	77.6
6-11 years	21	19.6
12-16 years	3	2.8
Total	**107**	**100**
Gender		
Male	59	55.1
Female	48	44.9
Total	**107**	**100**

Source: Processed Secondary Data, (2025)

Based on the results of this study, it shows the classification of patients based on age group, the majority of patients are in the children's age group. This study is based on the age group 0-5 years is the group with the largest number of patients, namely 83 people (77.6%). This shows that most patients are toddlers, who generally have an imperfect immune system and are susceptible to various diseases.

This condition causes physiological functions to be less than optimal, thus affecting the pharmacokinetic process of the drug. As a result, the way the child's body absorbs, distributes, metabolizes, and excretes drugs is different from adults (Virgiana, 2014). Infections in childhood are expected to have a higher frequency of infection may involve part of the innate or adaptive immune system, and it may affect an organ system (George & Govindaraj, 2023).

The occurrence of incompatibility and instability in this study is presented in the following table:

Table 2. Incompatibility and Instability

Type of Event	Number	%
Compatibility	107	100
Incompatibility	0	0
Total	**107**	**100**
Stability	8	7.5
Instability	99	92.5
Total	**107**	**100**

Source: Processed Secondary Data, (2025)

The potential for incompatibility and instability in this study was examined by observing the physical and chemical properties of the active substances in the prescription drugs in an observational manner by observing the temperature, as well as based on related study literature. Incompatibility and instability. The process involves mixing several types of drugs prescribed by a doctor by grinding the drugs in a mortar until evenly mixed.

This study found no potential or incident incompatibilities (0%) in the pulverizer recipe. This was

because the entire formula was mixed evenly (homogeneously). Mixing was carried out using a mortar and pestle, allowing for flexibility in mixing all ingredients and grinding the drug more precisely. Furthermore, none of the preparations in the recipe were in film-coated tablets, which could impact the mixing process.

Aztriana *et al*. (2021) study found that dexamethasone and methylprednisolone were not incompatible, while Sasangka *et al*. (2021) study found that corticosteroids were not incompatible. The organoleptic test conducted in this study showed no color change in the powder and no clumping of the powder.

Observations of instability events in this study on pulverized preparations were carried out for 3 days after compounding. On the first and second days, no changes were seen in the preparation. However, on the third day, signs of instability began to appear in several pulveres, marked by the appearance of powder grains that separated from the pulveres mixture. This observation was carried out at a room temperature of 25˚C, and there were several prescription sheets that experienced instability, namely 92.5%. In this observation, there were several drugs that experienced instability, such as Vitamin B Complex, Vitamin C, and Tremenza. This instability can occur during the compounding process, such as when the drug is crushed, mixed, or repackaged. In these stages, the active ingredients in the drug can be exposed to air, light, and humidity, which can affect the stability of the preparation. Drugs that are physically and chemically damaged can be seen from the shape, color, taste, and smell (Noviani *et al*., 2021).

Drug interactions that occur in prescriptions containing corticosteroids in this study are presented in the following table:

Table 3. Drug Interactions Containing Corticosteroids

No	Types of drugs prescribed	Drug interactions with corticosteroids	Number	%
1.	*Amoxcillin* + *Metronidazole* + Paracetamol+ *Dexamethasone*	Metronidazole will increase the levels or effects of dexamethasone by affecting enzyme/intestinal metabolism	1	0.9
2.	*Ketoconazole* + *Dexamethasone* + CTM	Ketoconazole will increase the levels or effects of dexamethasone via the P-(glycoprotein) efflux transporter (MDRT)	1	0.9
3.	CTM 4mg + *Dexamethasone* + *Cefadroxil*	-	1	0.9
4.	CTM 4mg + *Dexamethasone* + *Cefadroxil*	-	1	0.9
5.	*Cefixime* + *Methylprednisolone*	-	2	1.9
6.	*Cefadroxil* + *Dexamethasone*	-	1	0.9
7.	*Dexamethasone* + CTM + Vit.B complex	-	1	0.9
8.	*Dexamethasone* + CTM + Vit C	-	2	1.9
9.	*Methylprednisolone* + *Acetylcystein* + Vit C	-	4	3.7
10.	*Methylprednisolone* + Vit C	-	1	0.9
11.	Tremenza+Cetirizine+ *Methilprednisolone* + Salbutamol	-	81	75.7
12.	Tremenza+Cetirizine+ *Methilprednisolon*	-	5	4.7
13.	Tremenza+Cefixime+ *Dexamethasone* + *Ambroxol*	-	1	0.9
14.	Tremenza + *Dexamethasone*	-	1	0.9
15.	Tremenza+*Ambroxol* +*Dexamethasone*	-	1	0.9
16	Tremenza+*Ambroxol*+ *Amoxicillin*+Salbutamol+ *Methylprednisolone*	-	2	1.9
17.	CTM 4mg + *Dexamethasone* + *Cefadroxil*	-	1	0.9

No	Types of drugs prescribed	Drug interactions with corticosteroids	Number	%
18.	*Cefixime* + *Methylprednisolone*	-	2	1.9
19	*Amoxicillin* + *Dexamethasone* + CTM	-	2	1.9

Source: Processed Secondary Data, (2025)

Based on the table above, the results of drugs containing corticosteroids in the prescriptions that have been reviewed, there are only two drug combinations that show significant drug interactions with corticosteroids, especially dexamethasone prescriptions. This drug interaction occurs when dexamethasone is used together with metronidazole and ketoconazole.

Metronidazole can increase dexamethasone levels in the body because this drug affects the liver enzyme that is responsible for metabolizing dexamethasone. Ketoconazole can also increase dexamethasone levels through a different mechanism. Ketoconazole inhibits the work of the P-glycoprotein protein, a protein that functions to remove drugs from cells (Medscape, 2025).

The potential for drug interactions in this study, based on the conclusions of the Interactions of drugs containing corticosteroids that have been prescribed, can be seen in the following table:

Table 4. Potential Corticosteroid Drug Interactions

Potential Corticosteroid Drug Interactions	Number	%
Interaction Occurred	2	1.9
Not Occurred	105	98.1
Total	**107**	**100**

Source: Processed Secondary Data, (2025)

Based on the data, the use of corticosteroids based on drug interactions that occurred only occurred in only 2 prescriptions (1.9%), which showed drug interactions, while 105 prescriptions (98.1%) did not show drug interactions. This shows that most drug combinations with corticosteroids are considered safe.

The severity of drug interactions in this study can be seen in the following table:

Table 5. Severity of Drug Interactions

Severity of Drug Interactions	Number	%
Minor	0	0
Moderate	1	0.9
Mayor	1	0.9
No interaction	105	98.1
Total	**107**	**100**

Source: Processed Secondary Data, (2025)

In Table 5, it can be concluded that the drug interactions that occurred were moderate interactions of 1 (0.9%), namely, Metronidazole tablet preparations with Dexamethasone. This interaction can generally still be prevented, one of which is by providing a time gap in administering the drug (Hanutami & Dandan, 2019). The potential for major drug interactions at 1 (0.9%) occurred in corticosteroids given together with azole antifungals (itraconazole, fluconazole, ketoconazole) (Bexter, 2010).

CONCLUSION

It can be concluded that on the prescription sheet, there is no potential for incompatibility 0%, there is potential for instability as much as 99 (92.5%). and there is moderate, minor interaction, there is potential for corticosteroid drug interaction 2 (1.9%), and the severity of moderate corticosteroid drug interaction is 1 (0.9%) and major as much as 1 (0.9%)

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