STUDY ON THE USE OF NON-STEROID ANTIINFLAMMATORY DRUGS (NSAIDS) IN RHEUMATOID ARTHRITIS AT RSU KUMALA SIWI

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Abstract. Rheumatoid arthritis is an autoimmune disease that is characterized by joint inflammation and can occur chronically. This disease is a disease of declining immunity characterized by infection of the muscle membranes, especially in the joint tissues, often involving other organs of the body. Most sufferers show symptoms of chronic disease if not treated will worsen the condition and even lead to death. Objective: to find out how to use anti-inflammatory (NSAIDs) are sodium diclofenac, potassium diclofenac mefenamic acid, meloxicam, and ibuprofen drugs in rheumatoid arthritis output patients in the Kumala Siwi Kudus Hospital. Descriptive using a retrospective method and quantity. The types of NSAIDs given to patients at the Kumala Siwi Mijen Kudus General Hospital were ibuprofen (7.2%), Diclofenac Potassium (10.4%), Mefenamic Acid (10.4%), Meloxicam (17.6%) and Sodium Diclofenac (54.40%), there was an incidence of minor interactions based on the severity of major interactions (1.90%), moderate interactions (20.9%), and minor interactions (27.6%). While based on the level of pharmacodynamics interaction mechanism (62%), and pharmacokinetic interaction (3.77%). There is a relationship between the number of drugs with severity with a significance value of 0.20 and there is a relationship between the number of drugs and interactions based on mechanisms with a significance value of 0.018. The type of NSAID with the most sodium was diclofenac by 54.40%, and there were drug interactions based on severity and the largest mechanism of minor interactions were 29 cases (45%) and pharmacodynamics as many as 33 (62%). From these conclusions, there is a relationship between the number of drugs and drug interactions based on the severity and mechanism of the drug

Keywords: [Drug Use Study, NSAIDs, Rheumatoid Arthritis.]

INTRODUCTION

Rheumatoid Arthritis(RA) is a systemic chronic inflammatory autoimmune disease that attacks various tissues, especially the joints. This is caused by the proliferation of non-suppurative synovitis which develops and can destroy the articular cartilage and other underlying bones, resulting in inflammation of the joint. Apart from causing arthritis, rheumatoid arthritis can also attack other parts of the body, such as blood vessels, skin, eyes, and lungs (Mcinnes & Schett, 2012).

Rheumatoid arthritis sufferers worldwide have reached 335 million people and it is estimated that the number will continue to increase until 2025 with indications that more than 25% will experience paralysis. This disease appears old. WHO reports that 20% of the world's population is affected by rheumatoid arthritis, of which 5-10% are aged over 60 years (Ritonga, 2018).

In 2008, rheumatoid arthritis was the top 10 disease in West Sumatra, the number of sufferers was 7.5% of the 4,555,810 population. Based on data from health centers in fifty city districts in 2015 for the 10 most cases suffered by the community, the total number of rheumatoid arthritis sufferers who visited the health centers was 11,166 sufferers or 3.02% of the total population (Elsi, 2018).

Pharmacological therapy given to relieve pain includes non-opioid analgesics, opioid analgesics, NSAIDs, and DMARDs. The correct selection and use of therapy for rheumatoid arthritis determines the success of treatment and avoids the risk of serious side effects. Apart from that, it is possible that the use of other drugs can increase the chance of drug-related problems occurring which are often called DRP (Drug Related Problems) (Febriana, 2007). Long-term use of NSAIDs can cause damage to the kidneys and liver, especially in patients who have a history of gastrointestinal disorders and in elderly patients. DMARDs that are not appropriate for certain patient conditions can be toxic to the liver and kidneys (Husna, 2017).

METHODS

The type of research used is descriptive analysis, namely a form of research data analysis to test the generalization of research results based on one sample. This descriptive analysis was carried out through descriptive hypothesis testing (Nasution, 2017).

This research uses retrospective research data in the form of observations of events that have occurred to look for factors related to the cause. In other words, disease or health status is then identified as existing or occurring in the past.

RESULTS AND DISCUSSION

This research was conducted on outpatients affected by rheumatoid arthritis in the period July – December 2020, the number of patients was 105 who met the inclusion criteria.

Table 1. Characteristics of Rheumatoid Arthritis Patients at RSU Kumala Siwi Kudus for the Period July – December 2020

Characteristics	Total (N=105)	Percentage (%)
Age		
21 – 30	4	3.81
31 – 40	27	20.95
41 – 50	22	25.71
51 – 60	43	40.95
>60	9	8.57
Gender		
Man	33	31.42
Woman	72	68.57
Number of Drugs (Scale)		
2-4	85	80.95
5-8	20	19.04
Patient's Illness		
Without Concomitant Diseases	50	47.61
a. Thyroid Gland	2	1.91
b. Nerve	4	3.81
c. Breathing	8	7.61
d. Diabetes	18	17.14
e. Hypertension and Heart	23	21.91

Source: Processed Primary Data, (2021)

The research results obtained were based on age characteristics, the highest number of patients aged 51-60 years experienced rheumatoid arthritis with a percentage value of 40.95%. The aging process is often considered to be the main cause of increased weakness around the joints, and decreased joint flexibility, which triggers rheumatoid arthritis. Generally, in older people over 50 years of age, therefore, in old age, the formation of chondroitin sulfate, which is the basic substance of cartilage, decreases and bone fibrosis can occur. In another study, it was also stated that the average age of respondents suffering from rheumatoid arthritis was 51-60 years, believed to be 99 people (26.8%) out of 114 patients (Lande, 2020).

Patient characteristics based on gender in this study were most common in women compared to men, where in the 105 samples there were 72 female patients (68.57%) affected by rheumatoid arthritis compared to 33 male patients (31.42%). This research is in line with research (Elsi, 2018) on gender characteristics as many as 72 people (68.57%) of female patients were more likely to suffer from rheumatoid arthritis. One of the reasons for the increase in rheumatoid arthritis in women is menstruation.

At least two studies have observed that women with irregular menstruation or early menopause have an increased risk of developing rheumatoid arthritis. Drug use patterns related to scales 2-4 are

(80.95%) and 5-8, namely (19.04%) obtained by patients, are adjusted to the need to reduce the administration of polypharmacy (administration of more than 5 types of medication). Existing research studies show that polypharmacy has increased over the years. Polypharmacy patients often do not fulfill their prescribed medications. Non-compliance increases linearly the number of drugs used by patients to 80% with 1 drug compared to 20% with 6 or more drugs given, so doctors need to provide direction to patients, especially geriatric patients (Martini, & Zulkarnaini, 2019).

The results of this study are based on hypertension comorbidities which are quite high in around 23 patients (21.90%) compared to other comorbidities such as diabetes (17.14%), asthma (7.61%), nerves (3.80%), and glands (1.90%). The results of another study (Heristi, 2017) showed that rheumatoid arthritis was associated with hypertension in 16 people (42.1%) with a total sample of 38 people. Rheumatoid arthritis is an inflammatory disease that affects blood vessels and joints. There is an increased inflammatory load on the vascular system. Plaque that forms in blood vessels forms at an earlier age and contributes to heart disease and high blood pressure. The results of this study are similar to other studies which state that hypertension

Table 2. Profile of Drug Use Types of NSAIDs and Non-NSAIDs

Medicine name	Total (N=105)	Percentage (%)
NSAIDs		
Ibuprofen	9	7.2
Diclofenac Potassium	13	10.4
Mefenamic acid	13	10.4
Meloxicam	22	17.6
Diclofenac Sodium	68	54.40
Non NSAID		
Thyrozol	2	1.90
Gabapentin	5	4.75
Phenytoin	1	0.95
Methyl Prednisolone	1	0.95
Salbutamol	6	5.71
Protaz	5	4.75
Acarbose	4	3.80
Metformin	5	4.75
Glimepiride	13	12.39
Candesartan	1	0.95
Captopril	1	0.95
Spironolactone	1	0.95
Propranolol	2	1.90
Nitrocaf	3	2.85
Lisinopril	4	3.80
Digoxin	4	3.80
Bisoprolol	4	3.80
Furosemide	5	4.76
Amlodipine	9	8.57

Source: Processed Primary Data, (2021)

The drug use profile is that the NSAID classes used are Diclofenac Sodium, Diclofenac Potassium, Meloxicam, Ibuprofen, and Mefenamic Acid. Based on the research results obtained in this study, Diclofenac Sodium is more often prescribed to treat rheumatoid arthritis at the Kumala Siwi Mijen Kudus Hospital with a value of 54.40%. Diclofenac is one of the NSAIDs used to relieve pain and inflammation of musculoskeletal and joint diseases, such as rheumatoid arthritis, osteoarthritis, and pain.

The largest group of non-NSAID drugs in this study was amlodipine (8.57%), this was because the comorbidities experienced by the patients in this study were mostly hypertension. Amlodipine is effective for the treatment of hypertension. Amlodipine is an antihypertensive drug mostly in tablet dosage form and when amlodipine is given orally it causes concentrations in blood plasma. Amlodipine provides pharmacological effects as an antihypertensive agent with a calcium channel blocker mechanism.

Table 3. Drug Interactions Based on Level of Redness

Drug interactions	Amount (N=53)	Percentage (%)
Total Severity Level		
Major Interaction Events	2	3.77
Moderate Interaction Events	22	41
Minor Interaction Events	29	45

Source: Processed Primary Data, (2021)

Table 4. Drug Interactions Based on Mechanism of Action

Drug interactions	Amount (N=53)	Percentage (%)
Total Mechanism Level		
Pharmacokinetic Interaction Events	2	3.77
Events of F pharmacodynamic Interactions	33	62
Unknown Interaction (Mechanism)	18	33

Source: Processed Primary Data, (2021)

The major interaction is (3.77%). Major interactions, namely interactions that have major effects that can endanger lives or cause permanent damage. For example, major severity occurred in 28 prescribers who received the drugs Ketoconazole and Alprazolam when used simultaneously causing drowsiness and breathing. Major interactions have severe effects that can be potentially life-threatening or can cause permanent damage.

Moderate interaction is (41%). Moderate interactions, namely interactions that have the potential to worsen the patient's condition so that a change in therapy may be needed. For example, moderate severity occurs in prescription 26. There is an interaction between Glimepiride and Meloxicam. When used together, it can increase the risk of hypoglycemia or low blood sugar. Moderate interactions are interactions that can be prevented by giving a time delay to the drugs, especially for drugs that interact pharmacokinetically so that drugs that are not taken simultaneously only use one drug in special circumstances. Moderate effects can cause changes in the patient's clinical status so monitoring is necessary.

Minor interactions are (54%). Minor interactions, namely interactions that can cause changes in clinical status that have an effect but are not so disturbing that they do not require additional therapy. For example, minor severity occurs in prescription 24. Mefenamic acid and glimepiride, when used simultaneously, can increase the effects of glimepiride. In minor interactions, the effects have little effect on the patient so additional intervention is rarely carried out in this type of interaction. However, to anticipate undesirable things happening, pharmacists can monitor symptoms and laboratory values related to use.

Pharmacodynamic interactions are (62%). Pharmacodynamic interactions are interactions that have similar or opposite pharmacological effects or side effects. This interaction can be caused by competition for the same receptor, or occur between drugs that act on the same physiological system. This interaction can usually be predicted based on the pharmacological properties of the interacting drugs. In general, interactions that occur with one drug will also occur with similar drugs. This interaction occurs with different intensities in most patients who receive drugs that interact with each other. For example, pharmacodynamic severity occurs when prescribing 25 bisoprolol and Ibuprofen can reduce the effect of bisoprolol by pharmacodynamic antagonism, using periodic monitoring of therapy for 1 week. Pharmacodynamic interactions are often caused by the drugs having similar or opposite pharmacological effects. Usually, drugs work on the same physiological system.

Pharmacokinetic interaction is (3.77%). Pharmacokinetic Interactions Pharmacokinetic interactions are interactions with drugs during the process of absorption, distribution, metabolism, and elimination (ADME). For example, the severity of pharmacokinetics occurs when prescribing 31 Diclofenac sodium and furosemide. Diclofenac, when used simultaneously, can increase the effect of furosemide and can reduce serum potassium so that the therapeutic effect felt by the patient does not reach the therapeutic target. The pharmacokinetic interactions that this interaction system works on

change the drug through the ADME system (absorption, distribution, metabolism, and excretion). These interactions increase or decrease the amount of drug available (in the body).

The size of the problem of drug interactions, especially those that can result in side effects, can increase significantly in patients who take drugs which is incorrect. To prevent or reduce the occurrence of undesirable drug interactions that may be fatal, the following things can be considered, try to give as little amount of medication as possible to each patient, including administering OTC (The Counter) drugs and herbal medicines, when administering attention should be paid to medication, especially in elderly patients, patients with serious illnesses, or patients with kidney dysfunction, and must be careful when using drugs with a narrow therapeutic index (Gitawati, 2008).

Relationship between the number of drugs and drug interactions

Drug interactions in terms of severity are divided into 3, namely minor interactions that can cause changes in clinical status, major interactions that have major effects that can endanger lives, and moderate interactions that have the potential to worsen the condition. Based on this research, which can be seen in Table 4.1.5, the results of the Spearman rank test were obtained with a significance value of $0.041 \leq 0.05$ with a closeness of 0.20, which means there is a very weak relationship between the number of non-steroidal anti-inflammatory drugs in rheumatoid arthritis patients and interactions based on level. severity. The results of the Spearman rank test with a significance value of $0.048 \leq 0.05$ with a closeness value of 0.213, which means there is a weak relationship between the number of non-steroidal anti-inflammatory drugs in rheumatoid arthritis patients and drug interactions seen based on the mechanism. This is due to the increasing number of drugs received by Patients can cause drug interactions through mechanisms, namely they can cause absorption disorders (can decrease or increase). An example of a pharmacokinetic interaction was seen in patient number 31 and a pharmacodynamic interaction was seen in patient number 1.

In Appendix 3, it can be seen that in patient number 31 who received 5 drugs, there was a pharmacokinetic drug interaction, namely between diclofenac and furosemide, diclofenac caused absorption problems in furosemide. This causes the effect of furosemide to decrease and in patient number 1 receiving more than 5 drugs, there is a pharmacodynamic drug interaction, namely between captropril and ibuprofen which can cause a significant reduction in kidney function. The mechanism of this interaction may be related to the ability of NSAIDs to reduce the synthesis of renal dilation phase prostaglandins (Medscape.com, 2021).

CONCLUSION

1. The types of NSAIDs given to rheumatoid arthritis patients at the Kumala Siwi Mijen Kudus General Hospital from July to December 2020 were ibuprofen, diclofenac potassium, mefenamic acid, meloxicam, and diclofenac sodium.
2. There are drug interaction incidents based on severity, namely minor interactions, moderate interactions, major interactions, and drug interaction incidents based on the mechanism of action, namely pharmacodynamic interactions and pharmacokinetic interactions.
3. There is a relationship between the number of drugs and the incidence of drug interactions based on the severity and mechanism of the drug in rheumatoid arthritis patients at the Kumala Siwi Mijen Kudus General Hospital.

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