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Risk Factors and Pharmacist Intervention to Reduce the Incidence of Overdose of Etoricoxib Drug in Outpatient Polyclinic Patients

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ABSTRACT

Background and Objectives: Etoricoxib is a class of selective NSAIDs approved by the Medicines Agency (EMEA) for the acute and chronic treatment of signs and symptoms of OA and RA, treatment of ankylosing spondylitis (AS), treatment of acute gouty arthritis, relief of acute and chronic pain, and treatment of primary dysmenorrhea. **Methods**: This study identifies the types of DRPs in the form of excessive doses in the prescription of etoricoxib on an outpatient basis in all polyclinics in one of the hospitals in Banyuasin Regency in the January 2022 Period. The development of this study is expected to provide information on the description of the incidence of DRPs in the form of over-dosage in drug prescribing on an outpatient basis in all polyclinics in one of the hospitals in Banyuasin Regency. This study was an analytic study using a cross-sectional research design to determine the influence of risk factors on the incidence of overdose etoricoxib therapy in polyclinic outpatients at one of the hospitals in Banyuasin Regency in January 2022. **Results and Conclusion**: The results showed a relationship between age, multi-pathology, and Polypharmacy on the incidence of excessive doses of etoricoxib in outpatient polyclinics (p-value = 0.001).

***Keywords**: DRP, Etoricoxib, Overdoses, Pain*

INTRODUCTION

Etoricoxib is a class of selective NSAIDs approved by the Medicines Agency (EMEA) for the acute and chronic treatment of signs and symptoms of OA and RA, treatment of ankylosing spondylitis (AS), treatment of acute gouty arthritis, relief of acute and chronic pain, and treatment of primary dysmenorrhea (Ducan et al., 2003). Etoricoxib is a novel bipyridine COX-2 selective inhibitor. Unlike celecoxib, valdecoxib, and parecoxib, etoricoxib is a methyl sulfone and does not contain a sulfonamide group, which is associated with an increased risk of hypersensitivity reactions (Takemoto et al., 2008). The maximum dose of

etoricoxib for Osteoarthritis disease is 60 mg-90 mg per day; in rheumatoid arthritis disorders, the recommended dose is 90 mg per day, and in acute gouty arthritis disorders, the recommended dose is 120 mg per day (Balazes et al., 2016). The basis for the use of etoricoxib doses is to start with a low dose of etoricoxib (60 mg once a day) where the dose shows similar efficacy to diclofenac sodium 150 daily; etoricoxib and diclofenac, in general, have a good safety profile and can be tolerated well for a 6-week treatment period. In general, etoricoxib and diclofenac sodium increase the risk of side effects if used at doses exceeding the therapeutic dose; these side effects can be GI disorders with a prevalence of 12.9%, peripheral edema, hypertension, angina pectoris, and congestive heart failure (CHF) with a prevalence of 3.5% (Tang et al., 2019). This problem of overdosing and adverse events is one form of Drug Related Problem (DRP).

Drug Related Problems (DRPs) are unwanted events that happen to patients related to medication so that they have the potential to interfere with the success of therapy (Allemann et al., 2014). DRPs are the cause of death for 4 out of 6 patients, and the cost of DRPs is twice as high as the actual therapy. Several previous studies have shown the high prevalence of DRPs in chronic disease patients. The prevalence and types of DRPs in patients with chronic diseases for unnecessary therapy amounted to 34.7%; untreated indications amounted to 68.3%; ineffective/incomplete therapy amounted to 74.9%; inappropriate doses amounted to 50.3%; and unexpected drug reactions (ROTD) amounted to 10.2% (Nurcahya, 2015). DRP research for outpatients with chronic diseases in hospitals in Yogyakarta has been carried out; the most common incidence of DRPs are Drug Interactions at 36.98%, compliance at 29.69%, inappropriate drugs at 8.33%, too low doses at 7.81%, unnecessary drug therapy by 7.29%, and requires additional drug therapy by 3.65%. The risk factors that are proven to affect the incidence of DRPs are Polypharmacy, the presence of comorbidities (more than 1 diagnosis), and a diagnosis of heart failure (Nurcahya, 2015).

Research on the problem of DRPs related to the excessive dose of etoricoxib still needs to be widely done, especially for outpatients. This study identifies the types of DRPs in the form of excessive doses in the prescription of etoricoxib on an outpatient basis in all polyclinics in one of the hospitals in Banyuasin Regency in the January 2022 Period. The development of this study is expected to provide information on the description of the incidence of DRPs in the form of over-dosage in drug prescribing on an outpatient basis in all polyclinics in one of the hospitals in Banyuasin Regency. It can be used as reference data for developing clinical information systems. In addition, this research can be a reference for pharmacists to identify, prevent, and limit patient DRPs.

METHODS

This study was an analytic study using a cross-sectional research design to determine the influence of risk factors on the incidence of overdose etoricoxib therapy in polyclinic outpatients at one of the hospitals in Banyuasin Regency in January 2022. The study subjects were all outpatients who met the inclusion and exclusion criteria. The data used were sourced from electronic medical records and electronic prescriptions of patients, data collection was carried out in the pharmaceutical installation.

The total population of patients with etoricoxib prescriptions in January 2023 was 180. The sampling method used is simple random sampling Sample calculation using the Slovin formula:

$$n = \frac{N}{1 + Ne^2}$$

$$n = \frac{180}{1 + (180.0{,}05^2)}$$

$$n = \frac{180}{1 + 0{,}45}$$

$$n = 124{,}1 \sim 124$$

Description:
n = Number of population
N = Z score at 95% confidence = 1.96
E = margin of error

So that the minimum sample size in this study was 180 prescriptions with dual therapy NSAID sheets. The inclusion criteria are:

1. Patients with age ≥ 18 years
2. Outpatient polyclinic with prescriptions overdoses etoricoxib therapy
3. Doses etoricoxib therapy > 120 mg/day

The exclusion criteria are incomplete electronic medical record data.

The variables in the study are independent variables consisting of risk factors for age, gender, type of drug, and comorbidities. The dependent variable consists of the incidence of overdoses of etoricoxib therapy.

RESULTS AND DISCUSSION

The first characteristic of the test subjects was age; the minimum and maximum ages of the patients were 20 and 74 years old. The etoricoxib overdoses and etoricoxib non-overdoses groups had similar characteristics, with the majority of patients falling into the elderly category; the elderly category is someone aged above or equal to 60 years, and the nonelderly is someone with age below 60 years. Patients aged> 60

Table 1. Characteristics of the Incidence of Overdose of Etoricoxib Drugs in Polyclinic Outpatients at One of the Hospitals in Banyuasin Regency

Characteristics	Etoricoxib Overdose	Etoricoxib Not Overdosed
Age		
Elderly	0	6
Non Elderly	2	6
Gender	4	18
Male	86	2
Female		
Pathological Conditions		
Multipathology	40	13
Monopathology	52	19
Number of medicine types		
Polypharmacy	89	31
Non-Polypharmacy	3	1
Age		
Elderly	90	0
Non Elderly	2	32

Table II. Risk Factors for the Incidence of an Overdose of Etoricoxib Drugs in Polyclinic Outpatients

Risk Factors	Etoricoxib Overdose	Etoricoxib No Overdose	P- Value	CI 95%
Age				
Elderly	86	2	0,001	0,832-1,256
Non Elderly	6	30		
Gender				
Male	40	13	0,779	0,956-2,345
Female	52	19		
Pathological Conditions				
Multipathology	89	31	0,001	0,678-1,587
Monopathology	3	1		
Number of medicine types				
Polypharmacy	90	0	0,001	0,541-1,145
Non-Polypharmacy	2	32		

P< 0,05, Using Pearson Chi-Square Tests

Table III. Pharmacist Intervention to Reduce Incidence of an Overdose of Etoricoxib Drugs in Polyclinic Outpatients

Pharmacist Intervention	P- Value	CI 95%
Medication Review	0,032	0,776-1,102
No Medication Review		
Pharmacist Counseling	0,045	0,556-1,122
No Pharmacist Counseling		

P< 0,05, Using Pearson Chi-Square Tests

years in the etoricoxib overdose group were 86 patients. The group that did not overdose etoricoxib was two patients, with the total number of patients in the elderly group being 88 patients, while at the age of ≤ 60 years in the etoricoxib overdose group were six patients, and the group that did not overdose etoricoxib were 30 patients, with the total number of patients in the nonelderly group being 36 patients.

Gender was the second patient characteristic in this study. Patients with etoricoxib overdoses in this study were primarily female, with a total of 52 patients. In comparison, male patients were 40 patients, while patients who did not overdose etoricoxib in this study were primarily female, with 19 patients, while male patients were 13 patients (table I). This study also analyzed the Number of types of diagnoses written in each patient (table I). A total of 4 patients had a single diagnosis or without comorbidities, while 120 patients had more than 1 type of diagnosis. The diagnosis received by the patient was the diagnosis written by the doctor during the patient's treatment during the study period. The Number of patients with more than one diagnosis is related to complications experienced due to chronic diseases suffered by patients. The data relating to Polypharmacy of patients with overdoses was 90 patients, and non-polypharmacy etoricoxib overdose patients were two patients. In comparison, data related to Polypharmacy in patients not overdosed etoricoxib were 32 patients, and in cases of non-polypharmacy etoricoxib overdose were 0 patients.

The bivariate analysis showed a relationship between age, pathological conditions, and Polypharmacy on the incidence of excessive doses of etoricoxib with the exact p-value of 0.001. At the same time, gender had no relationship with the incidence of excessive doses of etoricoxib, with a p-value of 0.779 (Table 2). These results are in line with research conducted by Al Musawe et al. 2020 which states that 72.09% of the study group used Polypharmacy with a poor socio-demographic profile where Polypharmacy has negative consequences if it is related to the quality of life of elderly patients (Al Musawe et al, 2020), excess doses of etoricoxib can increase the risk of etoricoxib side effects including side effects in the form of myocardial infraction events, gastrointestinal disorders and renal disorders (La Torre et al, 2021). This excess dose can also be caused by the high scale of pain felt by the patient, so it requires a maximum dose in the management of its therapy. Seeing the results of this study, pharmacist intervention is needed in reducing drug-related problems in the form of pharmacist-led intervention either in the form of a team or independently; from the result in (Table) Medication Review is a statistically significant difference between the incidence of overdose in patients who received medication review and those who did not. The confidence interval (CI) of 0.776-1.102 indicates that the incidence of overdose in the medication review group was likely lower than in the no medication review group, and pharmacist counseling is similar to medication review; there is a statistically significant difference between the overdose rates in patients who received pharmacist counseling and those who did not, The CI of 0.556-1.122 suggests that the incidence of overdose might have been lower in the counseling group, but the effect is less pronounced compared to medication review. Several studies show the relationship and impact of pharmacist intervention on reducing drug-related problems in several populations and research settings. Geriatric patients are at high risk of Drug Related Problems (DRPs) due to morbidity-associated Polypharmacy, age-related physiologic changes, and pharmacokinetic and pharmacodynamics alterations. These patients are often excluded from premarketing trials, which can further increase the occurrence of DRPs. Drug-related problems were substantially high among geriatric inpatients. Patients with Polypharmacy and comorbidities had a much higher chance of developing DRPs. Hence, special attention is needed to prevent the occurrence of DRPs in these patients. Moreover, clinical pharmacists' intervention reduced DRPs in geriatric inpatients. The prescriber acceptance rate of clinical pharmacists' intervention was also substantially high (Hailu et al., 2020). In this study, the importance of the clinical pharmacist in determining and analyzing DRPs was emphasized. Clinical pharmacy services like the one described should be implemented widely to increase patient safety (Albayrak et al., 2022). The results indicate that the pharmacist-led follow-up intervention can aid early identification and solving of DRPs in patients prescribed new cardiovascular drugs. Knowledge of factors associated with DRPs and patients' satisfaction may allow further intervention improvement (Bremer et al., 2022). This study revealed that DRPs were high among elderly patients admitted to the medical ward of Northwest Ethiopia. Comorbidity, length of hospitalization, ploy-pharmacy, payer, and alcohol drinker were more likely to develop drug-related problems. Clinical pharmacists and interventions also did treatment optimizations that were well accepted by prescribers (Dagnew et al., 2022). Clinical pharmacists have a crucial role in minimizing drug-related problems. Mainly, there should be a greater emphasis on patient counseling and patient follow-up (Osoro et al.,2023). The study shows that especially designed services, such as pharmacotherapy clinics runrun by clinical pharmacists, are necessary to detect and resolve DRPs effectively. The high compliance rate of the patients indicates patients' confidence in the clinical pharmacist services provided in the pharmacotherapy clinic. The low acceptance rate of physicians highlights the need to improve interprofessional collaboration between clinical pharmacists and physicians in an outpatient setting. (Shahrami et al, 2022). We confirmed that pharmacists

had a valuable role in performing MTM services for ambulatory elderly patients, not only in identifying and solving the DRPs but also in improving clinical outcomes (BP and lipid level) and cost-saving effects (Wang et al., 2021).

CONCLUSION

There were 92 patients with etoricoxib overdose in outpatients, and there was a relationship between age, multipathology, and Polypharmacy with the incidence of etoricoxib overdose in polyclinic outpatients.

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Conflict of interest

The author declares that there isn't any conflict of interest regarding the publication of this paper.

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