รูปแบบและความสมเหตุผลการสั่งใช้ยากลุ่ม NSAIDs ในผู้ป่วยนอกที่เป็นโรคข้อเสื่อมของโรงพยาบาลทั่วไปแห่งหนึ่ง
Pattern and Rationality of NSAIDs Prescribing in Out-patients with Osteoarthritis of a Tertiary-care Hospital

นิพนธ์ต้นฉบับ | Original Article

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วารสารไทยเภสัชศาสตร์และวิทยาการสุขภาพ 2566;18(4):396-404.

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Thai Pharmaceutical and Health Science Journal 2023;18(4):396-404.

บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษารูปแบบและความสมเหตุผลของการสั่งใช้ยาแก้อักเสบที่ไม่ใช่สเตียรอยด์ (non-steroidal anti-inflammatory drugs; NSAIDs) ในผู้ป่วยนอกที่เป็นโรคข้อเสื่อมของโรงพยาบาลทั่วไปแห่งหนึ่ง **วิธีการศึกษา:** ศึกษาข้อมูลใบสั่งยาย้อนหลังตั้งแต่วันที่ 1 ตุลาคม พ.ศ. 2561 ถึง 30 กันยายน พ.ศ. 2562 ประเมินรูปแบบการสั่งใช้ NSAIDs ตามตัวบ่งชี้ที่ปรับปรุงจากตัวบ่งชี้การใช้ยาขององค์การอนามัยโลก และประเมินความสมเหตุผลในการสั่งใช้ NSAIDs ตามแนวทางการดำเนินงานโครงการโรงพยาบาลส่งเสริมการใช้ยาอย่างสมเหตุผล วิเคราะห์ผลด้วยสถิติเชิงพรรณนา **ผลการศึกษา:** จากใบสั่งยาของผู้ป่วยโรคข้อเสื่อม 2,466 ใบ พบการสั่งใช้ NSAIDs ร้อยละ 64.88 จำนวนรายการยาต่อใบสั่งยาเฉลี่ย 5.06 รายการ การสั่งใช้ NSAIDs ใช้ชื่อสามัญทางยาร้อยละ100 มีการสั่งใช้ NSAIDs ชนิดฉีดร้อยละ 10.97 NSAIDs ที่สั่งใช้เป็นยาในบัญชียาหลักแห่งชาติร้อยละ 75.58 มีการสั่งใช้ NSAIDs ร่วมกับยาป้องกันแผลในทางเดินอาหารร้อยละ 66.14 และ NSAIDs ที่สั่งใช้มากที่สุด คือ naproxen 250 mg tablet ส่วนความสมเหตุผลการสั่งใช้ยา พบการสั่งใช้ NSAIDs ยาวกว่า 2 สัปดาห์ต่อใบสั่งยาร้อยละ 47.69 สั่งใช้ selective Cox-2 inhibitors ในผู้ที่ไม่มีข้อบ่งใช้ร้อยละ 38.99 สั่งใช้ NSAIDs ในผู้ป่วยที่มีระดับ eGFR น้อยกว่า 30 มล./นาที/1.73 ม.^{2} ร้อยละ 38.37 สั่งใช้ NSAIDs ในผู้ป่วยที่ได้รับยา RAS blockade และระดับ eGFR น้อยกว่า 60 มล./นาที/1.73 ม.^{2} ร้อยละ 6.09 สั่งใช้ NSAIDs ในผู้ป่วยเสี่ยงเลือดออกทางเดินอาหารระดับปานกลางร้อยละ 21.86 และระดับสูง 1 ราย **สรุป:** มีการสั่งใช้ NSAIDs ในผู้ป่วยโรคข้อเสื่อมค่อนข้างมากโดยเป็นยาในบัญชียาหลักแห่งชาติน้อยกว่าที่กำหนดสำหรับโรงพยาบาลทั่วไป และสั่งใช้ยาด้วยชื่อสามัญทางยา สั่งยาที่ไม่เหมาะสมในเกือบทุกด้าน ควรจัดทำแนวทางส่งเสริมและกำกับการใช้ NSAIDs เพื่อการใช้ยาอย่างคุ้มค่าและปลอดภัย

คำสำคัญ: รูปแบบการสั่งใช้ยา, การใช้ยาสมเหตุผล, ยาต้านการอักเสบที่ไม่ใช่สเตียรอยด์, NSAIDs, โรคข้อเสื่อม

Editorial note
Manuscript received in original form: November 2, 2022;
Revision notified: December 20, 2022;
Revision completed: May 7, 2023;
Accepted in final form: May 27, 2023;
Published online: December 31, 2023.

Abstract

Objective: To determine patterns and rationales of non-steroidal anti-inflammatory drugs (NSAIDs) prescribing in out-patients with osteoarthritis in a tertiary-care hospital. **Method:** This retrospective study examined prescriptions from October 1, 2018, to September 30, 2019. The pattern and rationale of NSAIDs prescribing were assessed based on modified World Health Organization's prescribing indicators and the guidelines of the hospital rational drug use, respectively. Descriptive statistics were used. **Results:** NSAIDs were prescribed in 64.88% of the 2,466 prescriptions of patients diagnosed with osteoarthritis. The average number of drug items per prescription was 5.06. NSAIDs were 100% prescribed by generic names. NSAIDs injections were prescribed in 10.97% of prescriptions. 75.58% of prescribed NSAIDs were on the national drug list. Prescriptions of NSAIDs with anti-ulcer drugs were 66.14%. The most common NSAIDs prescribed was naproxen 250 mg tablet. For rationality, NSAIDs were prescribed for longer than two weeks in 47.69% of prescriptions. Prescribing selective Cox-II inhibitors without indication were found in 38.99% of prescriptions. NSAIDs were prescribed to patients with an eGFR less than 30. mL/min/1.73 m² and patients who were receiving RAS blockade and had eGFR levels less than 60 mL/min/1.73 m² for 38.37% and 6.09%, respectively. NSAIDs were prescribed to 21.86% and one patient with moderate and high gastrointestinal bleeding risk, respectively. **Conclusions:** NSAIDs were prescribed with a relatively high proportion of prescription of osteoarthritis patients and certain Proportions of NSAIDs prescribed were lower than the national drug list mandate for tertiary hospitals. All were prescribed with generic names. Inappropriate prescribing were found in most aspects. Safe and economic NSAIDs rational use should be promoted.

Keywords: prescription patterns, rational drug use, non-steroidal anti-inflammatory drugs, NSAIDs, osteoarthritis

Journal website: http://ejournals.swu.ac.th/index.php/pharm/index

Introduction

Rational drug use has been promoted in Thailand and worldwide.[1] Based on the 2014 report, 163,000 Baht was for medications which was 39.82% of 409,313 Baht of total healthcare expenditure.[2] Non-steroidal anti-inflammatory drugs (NSAIDs) for moderate pain and inflammation have been widely used. With a 73 million prescriptions annually worldwide[3], 30 million individuals have been using NSAIDs.[4] In Thailand, NSAIDs have been ranked as drugs with a high volume and expense especially certain drugs not in the National Essential Drug List (NEDL). Despite their acceptable therapeutic benefit, adverse effects of NSAIDs, from mild to severe forms, are of great concern, especially those in the

gastrointestinal (GI) system. NSAIDs' adverse effects have been increasing with age. Even though selective-COX2 inhibitors which are new NSAIDs drugs with less GI adverse effects have been developed, these new NSAIDs pose cardiovascular adverse effects.[5]

Osteoarthritis is a chronic disease most prevalent in the elderly.[6] Drugs for inflammation and pain, especially NSAIDs, have been mainly used for osteoarthritis.[7,8] The Ministry of Public Health has established the Rational Drug Use as a new service plan policy. In the RDU, two indicators of NSAIDs include redundant use of NSAIDs of 5% or less of osteoarthritis patients, and use of NSAIDs in 10% or less of patients with chronic kidney disease (CKD) stage 3 or higher. Based on a national report of the fiscal year of 2019, redundant NSAIDs prescriptions were 38,134 out of the 5,647,070 prescriptions (0.68%) and 16,388 office visits with NSAIDs prescriptions out of 711,968 visits of stage 3 - 5 CKD patients (2.30%).[9] These results, even though were within the RDU criteria limits, there are other issues not stated as indicators in RDU deserving examination. For example, the use of selective COX2 inhibitor NSAIDs and the use of NSAIDs with GI protective agents in high-risk patients. Studies on NSAIDs prescribing patterns and rationales in various contexts are of great need since they could determine problems in prescribing NSAIDs. Findings could be useful in guiding RDU policy.

With a long use of NSAIDs in osteoarthritis, rationales of prescribing NSAIDs have been more critical. However, studies on the rationales of prescribing NSAIDs have been lacking. Most studies were on selective COX-2 inhibitor NSAIDs since they are costly with a high volume of prescriptions. These selective COX-2 inhibitor NSAIDs cause a high economic burden and consequently special attention. Based on a report on selective COX-2 inhibitor NSAIDs of out-patients of Khonkaen Hospital in 2010, most patients were female, had civil servant payment scheme, and were in their 15 – 59 years of age.[10] In addition, celecoxib was prescribed than etoricoxib. Most prescriptions covered a supply of 1 – 3 months and for pain relief. Most patients were screened for blood pressure, but few patients were screened for kidney functions, i.e., blood urea nitrogen (BUN) level and serum creatinine (SCr) level. Most found adverse effects were dyspepsia and about 40% of the patients were prescribed with GI protective agents.[10] A retrospective study in a hospital revealed that adverse effects of selective Cox-2 inhibitor NSIADs and traditional NSAIDs were not different from Cox-2 inhibitor NSAIDs.[11] In general, patterns and rationales of NSAIDs have not been adequately reported.

In our present study to determine patterns and rationales in prescribing NSAIDs, core drug use indicators of the World Health Organization (WHO)[12] which is for antibiotics prescriptions and the Thailand's Rational Drug Use manual for hospitals[13] were modified as indicators of NSAIDs use. We conducted the study in a 300-bed public general hospital. As a tertiary-care hospital with specialty physicians, an adequate number of osteoarthritis patients allowed for statistical power and a good representation for tertiary care nationwide.

Methods

In this retrospective descriptive research, data from medical records of patients of a 360-bed public general hospital were extracted for examination. Study population was out-patient prescriptions with at least one medication and diagnosis of osteoarthritis (ICD-10 code of M17x). Study sample was those in study population with office visit from October 1, 2018, to September 30, 2019. To be eligible, the prescriptions had to have at least one medication and with diagnosis of osteoarthritis (ICD-10 code of M17x). Prescriptions with incomplete data, i.e., drug name and regimen, were excluded.

Definition of indicators of rational use of NSAIDS were based on the WHO core drug use indicators and those of the Thailand Rational Drug Use manual for hospitals. NSAIDs were defined as those prescribed for osteoarthritis and available at the study hospital during the study period including traditional NSAIDs (i.e., diclofenac, ibuprofen, indomethacin, naproxen, and mefenamic acid) and selective Cox-2 inhibitors (i.e., celecoxib, etoricoxib, meloxicam, and parecoxib). NSAIDs prescribed for diseases other than osteoarthritis such as aspirin with the dose of less than 325 mg for cardiovascular diseases were excluded.

Indicators modified from the those of WHO core drug use indicators included (1) number of medications per prescription, (2) percentage of prescriptions with osteoarthritis diagnosis and NSAIDs over all prescriptions with osteoarthritis diagnosis, (3) percentage of prescriptions with osteoarthritis diagnosis and injectable NSAIDs over all prescriptions with osteoarthritis diagnosis, (4) percentage of prescriptions with osteoarthritis diagnosis and generic name NSAIDs over all

prescriptions with osteoarthritis diagnosis, and (5) percentage of prescriptions with osteoarthritis diagnosis and NEDL-listed NSAIDs over all prescriptions with osteoarthritis diagnosis. The researcher added relevant indicators of the percentage of prescriptions with more than one oral NSAIDs and the percentage of prescriptions with NSAID and proton-pump inhibitor for GI protection.

Based on the Thailand RDU manual for hospitals included (1) percentage of oral NSAIDs prescriptions with a supply of not more than 2 weeks over all prescriptions with NSAIDs, (2) percentage of oral selective Cox 2 inhibitor NSAIDs prescriptions for patients with a risk of GI bleeding as indicated by either a) being diagnosed with GI ulcer, b) age of 65 years or older, or c) having a history of medications with GI ulcer risk such as aspirin, antithrombotic drugs, and oral corticosteroids, (3) percentage of stage 3 – 5 CKD patients (i.e., eGFR < 30 mL/min/1.73^2) or patients receiving renin-angiotensin (RAS) blockade drugs prescribed with NSAIDs and having eGFR < 60 mL/min/1.73^2 who were prescribed with NSAIDs, (4) percentage of patients with a moderate-to-high risk of GI bleeding (i.e., at least one of American College of Gastroenterology (ACG) risk who were prescribed NSAIDs, (5) percentage of prescriptions with redundant NSAIDs excluding injectable NSAIDs or oral NSAIDs for immediate pain relief or aspirin for antithrombic effect to prevent cardiovascular events, (6) percentage of indomethacin prescriptions in patients aged 65 years, and (7) percentage of patients prescribed with selective cox-2 inhibitor NSAIDs and patients with ischemic heart disease (ICD-10: I10-I25), cerebrovascular disease (ICD-10: I50), peripheral vascular disease (ICD-10: I60-I69) and heart failure (ICD-10: I70-I79) who were prescribed with selective Cox-2 inhibitor or diclofenac.

Ethical consideration

The study was approved by the Ethic Committee for Human Study of Silpakorn University (approval number: REC 64.1224-210-8800). Individual patients could not be identified.

Data collection instrument

Electronic medical record data were retrieved using GUI Tools. Retrieved data were managed and analyzed using Microsoft Excel 365 (2018).

Data collection procedure

The researcher contacted the information technology center for electronic medical record data retrieval. The dataset was based on the HosXP version 3.63.4.25 which contained data modules of OPITEMPCE, Service, Person, Doctor, Drugitems, DrugUsage, and LAB. SQL was used to retrieve fields necessary for the study including hospital number (HN), office visit number, date of office visit, ex, age, underlying diseases, ICD-10 codes, eGFR, physician identifications, physician's specialty, drug code, administration method, number prescribed, data of prescription, and special administration. Data of patient sample receiving out-patient care from October 1, 2018, to September 30, 2019, with at least one medication prescribed were extracted to Excel-1 database of all prescriptions within the study period. This Excel-1 database was further extracted for patients with osteoarthritis diagnosis (ICD-10 code of M17x) to firm the Excel-2 database of prescriptions for osteoarthritis during the study period. Data were checked for completeness and correctness, and modified HN, physician identification, and office visit number so that patient could not be identified.

Excel-2 database was further extracted for prescriptions of NSAIDs to from Excel-3 database of prescriptions of NSAIDs of osteoarthritis patients during the study period. This Excel-3 database was extracted conditionally from each RDU indicator. Specifically, oral NSAIDs prescriptions with a supply of not more than 2 weeks, oral selective Cox 2 inhibitor NSAIDs prescriptions, prescriptions of NSAIDs with RAS blockade drugs, prescriptions of patients with CKD receiving NSAIDs, prescriptions of patients with GI bleeding receiving NSAIDs, prescriptions of patients with a moderate-to-high risk of GI bleeding receiving NSAIDs, and prescriptions of patients with ischemic heart disease (ICD-10: I10-I25), cerebrovascular disease (ICD-10: I50), peripheral vascular disease (ICD-10: I60-I69) and heart failure (ICD-10: I70-I79) receiving selective Cox-2 inhibitor or diclofenac. Data based on each of the conditions were saved separately for convenience in data analysis.

Data analysis

Descriptive statistics including frequency with percentage and mean with standard deviation was used.

Results

From October 1, 2018, to September 30, 2019, there were 54,888 out-patients with 193,427 prescriptions. There were 1,350 patients diagnosed with osteoarthritis (2.46%) with 2,466 office visits. A total of 934 osteoarthritis patients were prescribed with NSAIDs (69.19%) for the 1,600 office visits. Most patients were in their 60 – 69 years of age (35.43%). A total of 298 patients had stage 3 – 5 CKD (22.07%) and 96 of them were prescribed with NSAIDs (32.21%) (Table 1).

Table 1 Characteristics of all patients with osteoarthritis and those with NSAID prescriptions.

Characteristics	All osteoarthritis patients		All osteoarthritis patients with NSAID prescriptions	
	Number of patients (N = 1,350)	Number of office visits (N = 2,466)	Number of patients (N = 934)	Number of office visits (N = 1,600)
Sex				
Men	262	466	164	265
Women	1,088	2,000	770	1,335
Age				
0 - 19	0	0	0	0
20 - 29	7	12	4	12
30 - 39	34	46	32	43
40 - 49	114	205	109	211
50 - 59	327	643	266	525
60 - 69	454	877	331	577
70 - 79	292	485	154	177
80 - 89	109	181	35	52
90 - 99	13	17	3	3
CKD stage (eGFR as mL/min/1.73^2)				
1 (≥ 90)	393	724	336	592
2 (60 - 89)	499	923	360	616
3 (30 - 59)	216	420	80	156
4 (15 - 29)	51	113	13	22
5 (< 15)	31	45	3	6

Patterns of NSAIDs prescriptions

A total of 1,350 osteoarthritis patients had 2,466 office visits. With a mean of 5.06 medications per prescription, the highest number of medications was 22 (1 prescription) and the lowest one was 1 medication per prescription. The majority of prescriptions contained 4 medications (27.85%). These 2,466 visits resulted in 1,600 prescriptions with NSAIDs (64.88%). There were 195 injectable NSAIDs prescriptions (12.18%). All NSAIDs were prescribed with generic names. As high as 75.53% of NSAID prescriptions where those NSAIDs were not listed in the NEDL (Table 2).

Among 1,778 prescriptions with NSAIDs, there were 1,583 prescriptions of oral NSADs of which 178 prescriptions of oral and injection NSAIDs together. There were no two oral NSAIDs prescribed. Of all prescriptions of NSAIDs, proton pump inhibitors were prescribed in 66.14%. The three most prescribed NSAIDs were naproxen 250 mg tablet (38.36%), diclofenac 25 mg tablet (21.54%) and etoricoxib 90 mg tablet (11.19%) (Tablet 3).

Table 2 Patterns of NSAID prescriptions according to indicators modified from the WHO core drug use indicators.

Indicators	N	%
Number of medications per prescription	5.066	
Number of prescriptions with NSAIDs (n = 2,466)	1600	64.88
Number of prescriptions with injectable NSAIDs (n = 1,600)	195	12.18
Number of prescriptions with NSAID generic names (n = 1,778)	1778	100
Number of prescriptions with NSAIDs listed in the NEDL (n = 1,778)	1343	75.53

Table 3 Number of individual NSAIDS prescriptions (N = 1,778).

NSAIDs	N	%
Naproxen 250 mg tablet	682	38.36
Diclofenac 25 mg tablet	383	21.54
Etoricoxib 90 mg. tablet	199	11.19
Celecoxib 200 mg capsule	186	10.46
Diclofenac 25 mg/mL injection	184	10.35
Ibuprofen 400 mg tablet	64	3.60
Meloxicam 7.5 mg tablet	39	2.19
Piroxicam 10 mg. capsule	22	1.24
Parecoxib 40 mg injection	11	0.62
Indomethacin 25 mg capsule	8	0.45

Rationales for prescribing NSAIDs

Based on the Thailand Rational Drug Use manual for hospitals, there were 755 prescriptions with more than 2-week supply of oral NSAIDs (47.69%). Of these 755 prescriptions, 272 prescribed not more than 30-day supply of NSAIDs (17.18%), and 483 did so for more than 30 days (30.51%). Of the 378 selective Cox-2 inhibitors prescriptions, 241 of them were appropriate for the specific indications (63.76%).

For cases that NSAIDs should be avoided, of the 86 prescriptions of osteoarthritis patients with eGFR of less than 30 mL/min/1.73^2, 33 were with NSAID prescribed (38.37%). Among patients with eGFR of less than 60 mL/min/1.73^2 receiving RAS blockade drugs, 12 out of 197 prescriptions were with NSAIDs (6.09%). For patients with moderate risk of GI bleeding, of the total of 718 prescriptions, there were 65 prescriptions of traditional NSAIDS with no necessary PPI and 92 selective Cox-2 inhibitors with unnecessary PPI resulting a 21.87% of inappropriate prescriptions. For one patient with high risk of GI bleeding, instead of selective Cox-2 inhibitor

with PPI as recommended, the patient was prescribed with a traditional NSAID with PPI.

Regarding redundant NSAID prescriptions, none were found. For the prescription of indomethacin in the elderly, two prescriptions with at least NSAID out of 674 prescriptions (0.29%) for individuals older than 65 years of age were found. There were no prescriptions of selective Cox-2 inhibitors and diclofenac in patients with cardiovascular diseases (Table 4).

Table 4 Patterns of NSAID prescriptions according to indicators modified from the Thailand RDU manual for hospitals.

Indicators	N	%
Prescriptions with more than 2-week supply (n = 1,583)	755	47.69
15-30-day supply	272	17.18
More than 30-day supply	483	30.51
Prescriptions of selective Cox-2 inhibitors with non-recommended indications (n = 378)	241	63.76
Patients older than 65 years old	231	58.48
Patients with GI ulcer history (ICD-10 code: K25-K30)	7	1.77
Patients using drugs with GI ulcer risk	3	0.76
Prescriptions of NSAIDs in CKD patients		
Patients with eGFR < 30 mL/min/1.73^2 (n = 86)	33	38.37
Patient with eGFR < 60 mL/min/1.73^2 receiving RAS blockade drugs (n = 197)	12	6.09
Prescriptions of NSIADs in patients with GI ulcer risk		
● **Patients with moderate risk** (n = 718)		
Prescribed with traditional NSAIDs	65	9.05
Prescribed with traditional NSAIDs + PPI	477	66.43
Prescribed with selective Cox-2 inhibitors	84	11.28
Prescribed with selective Cox-2 inhibitors + PPI	92	12.81
● **Patients with high risk** (n = 1)		
Prescribed with traditional NSAIDs + PPI	1	100
Prescribed with selective Cox-2 inhibitors + PPI	0	
Prescriptions with 2 oral NSAIDs (n = 1,583)	0	0
Prescriptions of indomethacin in patients older than 65 years old (patients older than 65 years old with at least one NSAID prescribed = 674)	2	0.29
Prescriptions of selective Cox-2 inhibitors and diclofenac in patients with cardiovascular diseases§ (ICD-10 codes: I20-25, I60-69, I70-79, and I50) (n = 768)	0	0

* PPI = Proton-pump inhibitors.

§ Cardiovascular diseases: ischemic heart disease, cerebrovascular disease, peripheral arterial disease, and heat failure.

Discussions and Conclusion

In this retrospective, descriptive study on the patterns and rationales of 1-year NSAIDs prescriptions in osteoarthritis out-patients in a general hospital could suggest situations based on certain new indicators modified from the WHO core drug use indicators and indicators other than those in the Thailand RDU manual for hospitals. For WHO indicators which are solely on antibiotics prescriptions, they have been modified for our study on NSAIDs.

Our main findings based on indicators modified from the WHO core antibiotics indicators were as follows. For the number of medications per prescription, an average of 5.06 items per prescription in our study was much higher than 1.6 – 1.8 as stated our modified indicators. For proportion of osteoarthritis patients with NSAID prescriptions, even though no indicator was stated in our study, 64.88% found was higher than the original 20 – 26% stated in the original WHO indicators. A 10.97% of injectable NSAID prescriptions was overtly disappointing when compared with 0.0% modified indicator. It was acceptable for 100.0% of prescriptions of NSAIDs with generic names. A 75.53% of prescriptions of NSAIDs listed in the NLED was lower than the indicator of ≥ 80.0%. No prescription of redundant oral NSAIDs prescribed which was consistent with the indicator of 0%.

Table 5 Summary of NSAIDs prescriptions against WHO core indicators for antibiotic prescriptions.

Original WHO core indicators	Modified indicators for NSAID prescriptions in this present study	Results
Number of medications per prescription (1.6 - 1.8)	Number of medications per prescription (1.6-1.8)	5.06
Proportion of prescriptions with antibiotics (20 – 26%)	Proportion of prescriptions with NSAIDs (not specified)	64.88%
Proportion of injectable NSAID prescriptions (13.4 – 24.0%)	Proportion of injectable NSAID prescriptions (0.0%)	10.97%
Proportion of NSAID prescriptions with generic names (100.0%)	Proportion of NSAID prescriptions with generic names (100.0%)	100%
Proportion of prescriptions of NSAIDs listed in the NLED (none)	Proportion of prescriptions of NSAIDs listed in the NLED (≥ 80.0%)	75.53%
	Proportion of prescriptions of redundant oral NSAIDs (0.0%)	0%
	Proportion of NSAID prescriptions with PPI (0.0%)	66.14%

Based on the indicators modified from the Thailand Rational Drug Use manual for hospitals, irrational drug prescribing was found and resented in Table 6.

Table 6 Summary of NSAIDs prescriptions against the Thailand Rational Drug Use manual for hospitals.

Indicators	% Irrational drug use prescriptions
Prescription of selective Cox-2 inhibitors with no indications	63.76
Prescriptions of NSAIDs for more than 2-week supply	47.69
Prescriptions of NSAIDs in CKD patients	44.46
Prescriptions of NSAIDS for patients with a moderate risk of GI bleeding	21.86
Prescriptions of NSAIDS for patients with a high risk of GI bleeding	100
Prescriptions of indomethacin for patients older than 65 years old	0.29
Prescriptions of redundant oral NSAIDs	0
Prescriptions of selective Cox-2 inhibitors and diclofenac in patients with cardiovascular diseases	0

* Cardiovascular diseases: ischemic heart disease, cerebrovascular disease, peripheral arterial disease, and heat failure.

In a study of NSAIDs prescribing pattern in a large military hospital in Thailand, WHO core indicators were not used.[14] They found 64.5% NSAIDs prescriptions among osteoarthritis patients which is comparable to our present study (64.88%). They found as high as 84.1% prescriptions of selective COX-

2 inhibitors (i.e., etoricoxib, celecoxib and parecoxib); while ours was only 22.27%. This discrepancy could be attributable to the unique context of military hospitals which is much different from hospitals under the supervision of the Ministry of Public Health in Thailand. In India, three studies on prescribing NSAIDs in tertiary-care hospitals with two on NSAIDs prescriptions irrespective of osteoarthritis[15,16] and one in an orthopedic clinic.[17] With prescriptions for osteoarthritis patients, the proportion of NSAIDs prescriptions in our study was higher than those studies from India (i.e., 30.83%[15] and 31.03%[16]); but close to the one from a military hospital in Thailand (64.5%)[14] and a study in orthopedic patients in India (62.20%).[17] Prescriptions of injectable NSAIDs were found to be 12.18% in this present study which is consistent with studies in India (i.e., 4.32%[17] and 7.2%[16]).

Regardless of types of medications and illnesses, our study found an average of 5.06 medications per prescription which is higher than 1.6 – 1.8 medications per prescription reported by the WHO[18] and those reported in three studies in India (i.e., 3.15[15], 2.29[16] and 2.19[17]). Higher number of medications per prescription indicates a higher risk of adverse events and drug interactions, noncompliance issues and a higher healthcare expenditure.[12]

All NSAID prescriptions were in generic names. This was because the prescriptions were entered and processed through a computerized system where all medications were written in generic names with the rule of one generic name for one medication. Prescribing drugs 100% by generic name is consistent with the WHO standard for the most economic prescriptions for individuals and society. Prescribing expensive brand-name products despite the available cheaper generic alternatives is irrational. Drug policy for hospitals indicates that there should be only one generic product for a given drug item to avoid biased prescribing. No matter what names are keyed into the computer system, only a single generic name is shown for the prescriber.

The WHO recommends prescribing 100% drugs listed in the national essential drug list (NEDL), while the RDU service plan of Thailand indicates an 80% cut-off for general hospitals. Our finding of 75.53% of NSAIDs prescribed was lower than the 80% standard which indicates noneconomical prescribing of expensive drugs not listed in the national essential drug list. However, the results could be inconclusive since the prescriptions of non-NEDL NSAIDS could include the incidence of switching from NEDL to non-NEDL NSAIDs because of the ineffectiveness of the former one. Our study did not distinguish prescriptions related to such switching because both new and old patients were studied. This is one of the limitations in our study.

Our study in a general hospital found that the most prescribed NSAIDs included naproxen 250 mg tablets, diclofenac 25 mg tablets, etoricoxib 90 mg tablets, celecoxib 200 mg capsules and ibuprofen 400 mg tablets. While celecoxib 200 mg capsules, celecoxib 400 mg capsules and etoricoxib 60 mg tablets which all are selective Cox-2 inhibitors were the most prescribed NSAIDs in a military hospital. In India, diclofenac was the most prescribed NSAIDs.[15] Our findings suggest that this general hospital followed the Thailand RDU service plan policy with the prescriptions of ibuprofen and naproxen, generic drugs listed in the NEDL, as the two most prescribed NSIADs. Based on the orthopedic and joint disease section in the Thailand RDU manual for hospitals, it is recommended that for osteoarthritis patients, NSAIDs should be prescribed only for pain and not more than 2 weeks. Our study found 17.18% of NSAIDs prescriptions were for 15 - 30 days and as high as 30.51% for more than 30 days which did not meet the RDU standard. This could be attributable to many osteoarthritis patients which did not allow for frequent office visits, i.e., the next appointment within 20 days. Specialists thus needed to prescribe at least 30-day supply of NSAIDs.

We found 66.14% of NSAIDs prescriptions with PPI to prevent GI ulcers. This finding is higher than those in India where 24.32%[15], 25%[16], and 40%[17] were found. We found that the proportion of NSAIDs prescription with no PPI when needed (33.86%) was lower than 51% in a study of osteoarthritis patients aged 65 years old.[19] However, the study was conducted in 2014 when RDU service plan policy was not enforced.[19] Finding in our study indicates the success of safety policy on the use of NSAIDs with GI ulcer protection. Prescriptions of selective Cox-2 inhibitors for patents with no indication were 36.24% which were mostly for patients younger than 65 years old with no GI ulcer history. A study in military hospital revealed 68% of this kind of prescriptions.[14] Studies in India show 0% and 29% of selective Cox-2 inhibitors prescriptions.[15,17] It is obvious that the use of selective Cox-2 inhibitors in our study was unnecessarily high. In addition, NSAID prescription discrepancy between hospitals under jurisdiction of the Ministry of Public Health and those military hospitals is obvious. Therefore, differences in policy

among offices affect prescribing patterns. RDU service plan policy affects mainly hospitals under the Ministry of Public Health.

Based on the RDU of Thailand, there should be less than 10% of patients with CKD stage 3 or above prescribed with NSAIDs. In this study, 38.37% pf patients with eGFR of less than 30 mL/min/1.732 which were considered CKD stage 3 were prescribed with NSAIDs. This finding is somewhat alarming and deserves further monitoring for adverse events from NSAIDs. Based on the national data from the Health Data Center (HDC), 1.73% of CKD stage 3 patients were prescribed with NSAIDs[20] which is much lower than that in our study. Such low incidence in the HDC could be attributable to identifying CKD patients based on ICD-10 diagnosis code not on eGFR as in our study. Patients in HDC with low eGFR but not diagnosed with CKD were probably not included for analysis. This discrepancy could alert the study whether ICD-10 diagnosis code or eGFR values as the indicator for CKD stage. It was found that 6.09% of patients with eGFR of less than 60 mL/min/1.73^2 receiving RAS blockade drugs were prescribed with NSAIDs. This finding alerted the inappropriate prescribing. A study in 33 community hospitals in Nakhonratchasima province found that CKD patients were also prescribed with NSAIDs at a sizable level.[21] Even though this problem is not substantial, the consequences are and need more vigilance.

Patients with a moderate risk of GI ulcer were those with at least 1 – 2 of these indicators, i.e., age of more than 65 years, a history of GL bleeding, and receiving drugs with a risk of GI bleeding such as aspirin, anticoagulant, and oral steroids. In our study, most patients with moderate GI ulcer were those older than 65 years old. If needed, patients with moderate risk of GI bleeding should be prescribed with traditional NSAIDs with PPI[22] or selective COX-2 inhibitor. In our study, 9.05% of these patients were prescribed with traditional NSAIDs without PPI which could pose a risk of GI bleeding and 12.81% received selective Cox-2 inhibitors with PPI which is unnecessary. For patients with a high risk of GI bleeding which were those with more than 2 indicators, only one was found prescribed with traditional NSAID with no PPI which posed the high risk. This patient should be prescribed with a short-course selective Cox 2 inhibitors with PPI. With many other factors influencing prescribing of NSAIDs, i.e., drug effectiveness, patient's safety, payment scheme, drug policy, drug price, and others, more studies on prescribing patterns of NSAIDs should be conducted.

A low incidence of 0.29% of indomethacin prescriptions for patients older than 65 years old was of a certain concern. In the elderly, indomethacin causes central nervous system adverse effects such as drowsiness and confusion. It is a preventable risk and should be monitored. Redundant prescriptions of NSAIDs increase GI bleeding risk with no additional therapeutic benefit. The RDU policy suggests less than 5% of the prescriptions. We found no redundant prescriptions of NSAIDs. The monitoring and prevention of inappropriate prescribing in the hospital could be done with information technology at prescribing point toward prescribers. Records of patient's medication history from various departments can be retrieved and shown to prescribers. Redundancy could be alerted to prescribers and pharmacists. This study found no prescriptions of selective Cox-2 inhibitor with diclofenac in patients with ischemic heart disease, cerebrovascular disease, peripheral arterial disease, and heart failure. With licenses of selective Cox-2 inhibitors revoked because of cardiovascular effects in some countries, policy upon the use of selective Cox-2 inhibitors among healthcare professionals has been reconsidered for patient safety.

This study has certain limitations. The NSAIDs indicators in this study were modified from the WHO core indicators for antibiotics. No standard indicators are available. There should be studies to develop and test reliability of the standard indicators for NSAID prescriptions which could be useful in research and monitoring on the prescribing NSAIDs in all levels of healthcare settings. Since data were from only one general hospital, results might not perfectly represent other general hospitals and hospitals at other levels of care. More general hospitals and hospitals at other levels should also be studied.

Findings could be useful for patient safety practice. Generic name should be used in prescribing for societal economic purpose. NSAIDs listed in the NLED should be considered for new cases if not contra-indicated. The duration of next visit for disease monitoring could be consistent with the indicators on the rational longest NSAIDs supply. All public hospitals under the jurisdiction of different authorities should be under the RDU policy for the national comprehensive monitoring of drug use. Instead of following patients with CKD based on ICD-10 diagnosis code in the HDC, the cut-off of eGFR of 60 mL/min/1.73^2 could be a better indicator of CKD

for monitoring the use of RAS blockade drugs. It could help identify and include more patients with CKD in the analysis. Conditions for prescribing NSAIDs in patients with a moderate risk of GI bleeding should be used, for example, prescribing is not allowed for patients older than 65 years, with a history of GI bleeding, or receiving drugs with a high risk of bleeding such as aspirin, anticoagulants, or oral steroids. Finally, prescribing indomethacin for patients older than 65 years should be prohibited for safety concerns.

In conclusion, NSAIDs were prescribed in 64.88% of the 2,466 prescriptions of patients diagnosed with osteoarthritis. The average number of drug items per prescription was 5.06. NSAIDs were 100% prescribed by generic names. NSAIDs injections were prescribed in 10.97% of prescriptions. 75.58% of prescribed NSAIDs were on the national drug list. Prescriptions of NSAIDs with anti-ulcer drugs were 66.14%. The most common NSAIDs prescribed was naproxen 250 mg tablet. For rationality, NSAIDs were prescribed for longer than two weeks in 47.69% of prescriptions. Prescribing selective Cox-II inhibitors without indication were found in 38.99% of prescriptions. NSAIDs were prescribed to patients with an eGFR less than 30. mL/min/1.73 m² and patients who were receiving RAS blockade and had eGFR levels less than 60 mL/min/1.73 m² for 38.37% and 6.09%, respectively. NSAIDs were prescribed to 21.86% and one patient with moderate and high gastrointestinal bleeding risk, respectively. There were prescriptions of indomethacin in patients older than 65 years old. There were no prescriptions of two oral NSAIDs or specific Cox-2 inhibitor or diclofenac in patients with ischemic heart disease, cerebrovascular disease, peripheral arterial disease, and heart failure. Safe and economic NSAIDs rational use should be promoted.

Acknowledgement

The author would like to express a great gratitude to the Director and staff at the Department of Informatic Technology of Nakhonnayok Hospital for their assistance.

References

1. World Health Organization (WHO). Chapter 8. Rational use of medicines. (Accessed on Oct. 29, 2018, at http://apps.who.int/medicinedocs/en/d/Js6160e/10.html)
2. 2. Office of the National Economic and Social Development Council. Social and quality of life database system. 2018. (Accessed on Oct. 10, 2019, at http://social.nesdb.go.th/SocialStat/StatReport_Final.aspx?reportid=1260&template=1R1C&yeartype=M&subcatid=18) (in Thai)
3. Simon LS. Actions and toxicity of nonsteroidal anti-inflammatory drugs. Curr Opin Rheumatol 1995;7(3):159-166.
4. Singh G, Triadafilopoulos G. Epidemiology of NSAID induced gastrointestinal complications. J Rheumatol Suppl 1999;56:18-24.
5. Pirlamarla P, Bond RM. FDA labeling of NSAIDs: Review of nonsteroidal anti-inflammatory drugs in cardiovascular disease. Trends Cardio Med 2016;26:675-680.
6. Jeeravipoolvarn P. Osteoarthritis. J Dep Med Serv 2017;3:28-33. (in Thai)
7. Hochberg MC, Altman RD, April KT, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res 2012;64:465-474.
8. Thai Rheumatism Association. Guideline for the treatment of osteoarthritis of knee. 2010. (Accessed on Apr. 30, 2023, at https://thairheumatology.org/phocadownload/36/Guideline_003.pdf) (in Thai)
9. Health Data Center, Ministry of Public Health. 2019 (Accessed on Oct. 10, 2019, at https://hdcservice.moph.go.th/hdc/reports/page.php?cat_id=03b912ab9ccb4c07280a89bf05e5900e) (in Thai)
10. 10. Lertsinudom S. Utilization reviewing of COX-2 specific non-steroidal anti-inflammatory drugs at orthopedic out-patient department at Khon Kaen hospital. North-Eastern Thai J. Neurosci 2010;7(1):15-32. (in Thai)
11. Meesawad N, Boonchoong P, Kunawaradisai N. Cardiovascular adverse events of selective COX-2 Inhibitors in patients with osteoarthritis and rheumatoid arthritis. Thai Pharm Health Sci J 2010;5(3):218-27. (in Thai)
12. WHO: Promoting rational use of medicines: Core components, (Accessed on Sep. 15, 2016, at http://www.apps.who.int/medicinedocs/pdf/h3011e/h3011e.pdf)
13. Rational Drug Use Sub-Committee. Rational Drug Use Hospital Manual. Nonthaburi. The Agricultural Cooperative Federation of Thailand. 2015: pp.7.
14. Wongkumhaeng Y, Rojpibulstit M, Thanawuth Ni, Wongpoowarak WI. Non-steroidal anti-inflammatory drug prescribing pattern in osteoarthritis patients at general hospitals under the Ministry of Defense. Thai J Pharm Pract 2020;12(3):827-837. (in Thai)
15. Vaishnavi PR, Gaikwad N, Dhaneria SP. Assessment of nonsteroidal anti-inflammatory drug use pattern using World Health Organization indicators: A cross-sectional study in a tertiary care teaching hospital of Chhattisgarh. Indian J Pharmacol 2017;49(6):445-450.
16. Dey S, Sinha V, Kachhawa P. Prescribing trends in patients of the pain-clinic in a tertiary care teaching hospital, Hapur, Uttar Pradesh. Asian J Med Sci 2019;10(4):55-60.
17. Kandasamy G, Almaghaslah D, Almanasef M. A study of prescribing patterns for non-steroidal anti-inflammatory drugs in a tertiary care teaching hospital. Indian J. Pharm 2021;83(2):287-292.
18. Atif M, Azeem M, Sarwar MR, et al. WHO/INRUD prescribing indicators and prescribing trends of antibiotics in the Accident and Emergency Department of Bahawal Victoria Hospital, Pakistan. Springerplus 2016;5(1):1928. (doi: 10.1186/s40064-016-3615-1. eCollection 2016)
19. Jitthaisong N, Rattanachotphanit T, Sooksa N. Prescribing trends of NSAIDs and long-acting benzodiazepines with high risk for unsafety in elderly patients. Thai J Pharm Prac 2020;12(3):870-879. (in Thai)

20. Thai FDA. Data of service plan. 2022. (Accessed on Oct. 24, 2022, at https://hdcservice.moph.go.th/hdc/reports/page.php?cat_id=03b912ab9ccb4c07280a89bf05e5900e) (in Thai)
21. Kongchanmitkul W, Kawkratoke T. The situation of medical treatment for chronic kidney disease in hospital, Nakhon Ratchasima province. J Health Res Dev 2021;7(2):132-146. (in Thai)
22. Rational Drug Use Sub-committee. Rational drug use hospital manual. Nonthaburi. The Agricultural Cooperative Federation of Thailand, 2015: pp.69-71. (in Thai)