

ORIGINAL ARTICLE

Drug utilization pattern and rational drug use at orthopedics and traumatology outpatient clinics: A cross-sectional study

İhsan Özdamar, MD¹, Emine Nur Özdamar, MD²

¹Department of Orthopedics and Traumatology, Sancaktepe Şehit Prof. Ilhan Varank Training and Research Hospital, Istanbul, Turkey ²Department of Medical Pharmacology, Yeditepe University Faculty of Medicine, Istanbul, Turkey

In parallel with the developments in medicine in the last century, the increasing number and use of drugs with the intent of the diagnosis and remediation of diseases necessitate the physicians to act rationally during the use of drugs. Rational drug use is described by the World Health Organization (WHO) as the body of rules that necessitate patients to use the drugs in conformity with their clinical necessities, at doses sufficient to fulfill their personal needs, within adequate time and least expenditure to them and the society.^[1] The steps of rational drug use are making the correct diagnosis of the patient, defining the problem carefully, establishing the treatment goals, selecting the most effective and safe therapy among the treatment options, appropriate prescribing, and monitoring and evaluation of the treatment results.^[2]

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Correspondence: İhsan Özdamar, MD. Sancaktepe Şehit Profesör Dr. İlhan Varank Eğitim ve Araştırma Hastanesi, Ortopedi ve Travmatoloji Kliniği, 34785 Sancaktepe, İstanbul, Türkiye.

E-mail: ozdmrihsan@gmail.com

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ABSTRACT

Objectives: The aim of the present study was to assess the prescriptions of patients who were admitted to the orthopedics and traumatology outpatient clinic of a tertiary care hospital according to the WHO prescribing indicators.

Patients and methods: Between January 2020 and March 2020, a total of 1,024 patients (273 males, 751 females; mean age: 51.9 ± 13.9 years; range, 19 to 103 years) were included in the study. Only patients who were prescribed drugs and 18 years of age or older were included in the study. The WHO core prescribing indicators were utilized for the assessment of rational drug use. The WHO prescribing indicators percentages between the age categories were analyzed. The average number of drugs between the age categories was also examined.

Results: The average number of drugs per encounter was 2.9. The percentage of encounters with an antibiotic prescribed was 2.6% and with an injection prescribed was 10.7%. The percentage of drugs prescribed from essential drugs list was 33.8%. There were no prescriptions consisting generic name of drugs (0%). Polypharmacy was significantly higher in the ≥ 65 age group compared to the 18-44 age group (p=0.001).

Conclusion: The percentage of encounters with an antibiotic and injection prescribed were optimal according to WHO standards, while the average number of drugs per encounter was higher than the WHO ideal ranges. Unfortunately, the parameters such as the percentage of prescribing with generic name and from essential drug list was far more behind the optimal range.

Keywords: Drug utilization; polypharmacy; orthopedics; World Health Organization.

Irrational drug use refers to the use of drugs that are not appropriate for rational use according to the definition above. Redundant use of drugs per patient (polypharmacy), improper use of antibiotics, preferring injections when oral intake would be more appropriate, administering drugs that do not comply with clinical guidelines, and non-compliance with drug therapy by patients are widespread instances of irrational drug use.^[3] According to the WHO, more than half of the medications are prescribed incompliantly.^[1] Irrational drug use is still an important health problem all over the world, particularly in the least developed countries. As a consequence of unnecessary and improper drug administration, many health problems that may even result in death may occur.^[4] In particular, drug-drug interactions, development of resistance to medications, enhancement in the incidence of adverse drug reactions, and decrease in treatment compliance are the main problems that may arise due to irrational drug use.^[4-6]

The WHO improved core drug use indicators (prescribing indicators, patient care indicators and health facility indicators) which provides a good quantitative assessment of rational drug use.^[7,8] The WHO prescribing indicators ensure beneficial data in evaluating the rational drug use particularly in the least developed countries.^[9]

The clinical trials in orthopedics and traumatology have been mainly focused on surgical procedures. In this respect, it is important to evaluate the rational drug use in orthopedics and traumatology clinics. In the present study, we, therefore, aimed to assess the prescriptions of patients who applied to the orthopedics and traumatology outpatient clinic of a tertiary care hospital according to the WHO prescribing indicators.

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PATIENTS AND METHODS

This cross-sectional, retrospective study was conducted at the orthopedics and traumatology outpatient clinic of Sancaktepe Sehit Profesör Ilhan Varank Training and Research Hospital between January 1st, 2020 and March 1st, 2020. Of a total of 3,689 patients who were admitted to our clinic 2,665 who were not prescribed any drugs or aged below 18 years of age were excluded. Finally, a total of 1,024 patients (273 males, 751 females; mean age: 51.9±13.9 years; range, 19 to 103 years) were included in the study. Only patients who were prescribed drugs and 18 years of age or older were included in the study. The orthopedics and traumatology outpatient clinic prescriptions which covered at least one or more drugs were analyzed. The variables assessed included demographic characteristics of the patients (age, sex), International Classification of Disease (ICD-10) codes, clinical diagnoses, number of drugs prescribed, the Anatomical Therapeutical Chemical (ATC) codes and name of drugs, pharmaceutical dosage forms, routes of drug delivery, presence of antibiotics and injections in the prescription, whether drugs were prescribed by generic name or not, and whether drugs were prescribed from essential drugs list or not. Assessment of the repetitive prescriptions of the same patients and data duplications were hampered by recording the first prescription of the patient in the database. The WHO core prescribing indicators were utilized for the assessment of

TABLE I			
The calculation and optimal levels of prescribing indicators according to WHO's manual ^[7]			
The WHO core prescribing indicators	Calculation	WHO optimal levels	
Average number of drugs per encounter	Divide the total number of drugs prescribed by the number of participants surveyed	1.6-1.8	
Percentage of drugs prescribed by generic name	Divide the number of drugs prescribed by generic name by total number of drugs prescribed and multiply by 100	100%	
Percentage of encounters with an antibiotic prescribed	Divide the number of participants who were prescribed an antibiotic by the total number of participants surveyed and multiply by 100	≤30%	
Percentage of encounters with an injection prescribed	Divide the number of participants who were prescribed an injection by the total number of participants surveyed and multiply 100	≤20%	
Percentage of drugs prescribed from essential drugs list	Divide the number of drugs prescribed which were listed in essential drugs list by the total number of drugs prescribed and multiply by 100.	100%	
WHO: World Health Organization.			

rational drug use. The calculation and optimal levels of prescribing indicators according to WHO manual are depicted in Table I.^[7]

A written informed consent was obtained from each patient. The study protocol was approved by the Marmara University Faculty of Medicine Ethics Committee (IRB No: 09.2020.843, Date: 24/07/2020). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical analysis

The sample size calculation was based on a previous study of Yazıcıoğlu and Erdoğan.^[10] The study power was calculated as 98.3%.

Statistical analysis was performed using the IBM SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean \pm standard deviation (SD), median (min-max) or number and frequency, where applicable. The chi-square test was used to compare the percentages of the WHO prescribing indicators between age categories. The Kruskal-Wallis test and post-hoc pairwise comparisons were used to compare the average number of drugs between age categories. A *p* value of <0.05 was considered statistically significant.

RESULTS

Almost half of the patients (47.7%) were in the 45-64 years age category (Table II). According to the clinical diagnosis, 'pain in joint' (ICD-10 code: M25.5; 42.3%) was the most frequent diagnosis. Top 10 clinical diagnoses detected at orthopedics and traumatology outpatient clinic are depicted in Figure 1.

TABLE II Demographic characteristics of the patients (n=1,024)			
Variables	n	%	Mean±SD
Age (year)			51.9±13.9
Drug prescription			
Yes	1,024	27.8	
No	2,665	72.2	
Total	3,689	100.0	
Sex			
Female	751	73.3	
Male	273	26.7	
Total	1,024	100.0	
Age Groups			
18-44	334	32.6	
45-64	488	47.7	
≥65	202	19.7	
Total	1,024	100.0	
SD: Standard deviation.			

A total of 3,004 drugs were prescribed to 1,024 patients. Most of the patients (79.8%) were prescribed two to four drugs, while the prescriptions containing >5 drugs constituted a small percent (7.5%) (Table III). According to the route of drug delivery, oral (92.0%) and topical (79.3%) route of administrations were the most common ways. According to the pharmaceutical dosage forms, tablets (80.0%) and gels (76.4%) were the most frequent ones (Table III).

Of a total of 3,004 drugs were prescribed, "Musculoskeletal system drugs" (ATC-1 code: M; 69.3%) were the most commonly prescribed ATC-1 group. According to the ATC-2 group evaluation, "Anti-inflammatory and antirheumatic products" (ATC-1 code: M01; 38.5%) were the most frequently prescribed group. According to the drug names, pantoprazole (ATC-5 code: A02BC02; 11.4%), diclofenac (M01AB05; 7.1%) and dexketoprofen+thiocolchicoside (M02AA27+M03BX05; 7.0%) were the most commonly prescribed drugs, respectively. ATC-1 groups, top

TABLE III			
Drug use characteristics of the patients (n=1,024)			
Variables	n	%	
Number of drugs			
1	130	12.7	
2-4	817	79.8	
≥5	77	7.5	
Routes of drug delivery			
Oral	942	92.0	
Topical	812	79.3	
Intraarticular	70	6.8	
Intramuscular	24	2.3	
Subcutaneous	14	1.4	
Intravenous	1	0.1	
Pharmaceutical dosage forms			
Tablet	819	80.0	
Topical gel	782	76.4	
Capsule	308	30.1	
Sugar-coated pill	135	13.2	
Effervescent tablet	109	10.6	
Ampoule	95	9.3	
Vial	35	3.4	
Topical cream	25	2.4	
Oral drop	16	1.6	
Pre-filled syringe	14	1.4	
Sachet	9	0.9	
Topical spray	8	0.8	
Pomade	4	0.4	
Liquid	2	0.2	

10 ATC-2 groups, and top 10 drugs prescribed are shown in Table IV.

According to the prescriptions based on the WHO core prescribing indicators, the average number of drugs per encounter was 2.9. The percentage of encounters with an antibiotic prescribed was 2.6% and with an injection prescribed was 10.7%. The percentage of drugs prescribed from essential drugs list was 33.8%. There was no prescription consisting generic name of drugs (0%) (Table V).

Polypharmacy was significantly higher in the \geq 65 age group than the 18-44 age group (p=0.001). The percentage of drugs prescribed from essential drugs list was significantly lower in the 18-44 age group (28.4%), compared to the other age categories (p=0.038). On the other hand, there were no significant association of prescribing antibiotics (p=0.776) and injections (p=0.123) with the age groups. Comparison of the WHO core prescribing indicators according to the age categories is depicted in Table VI.

TABLE IV		
ATC-1 distributions and top 10 ATC-2 distributions of drugs and top 10 dru	gs prescribe	ed at the
orthopedics and traumatology outpatient clinic (n=3,004	+)	24
Variables	n	%
ATC-1 codes		
Musculoskeletal system (M)	2,083	69.3
Alimentary tract and metabolism (A)	626	20.8
Nervous system (N)	137	4.6
Systemic hormonal preparations, excluding sex hormones and insulins	74	2.5
General anti infectives for systemic use (J)	27	0.9
Respiratory system (R)	23	0.8
Blood and blood forming organs (B)	15	0.5
Dermatological (D)	10	0.3
Cardiovascular system (C)	9	0.3
ATC-2 codes		
Anti-inflammatory and antirheumatic products (M01)	1,156	38.5
Topical products for joint and muscular pain (M02)	665	22.1
Drugs for acid related disorders (A02)	515	17.1
Muscle relaxants (M03)	259	8.6
Analgesics (N02)	111	3.7
Corticosteroids for systemic use (H02)	73	2.4
Vitamins (A11)	60	2.0
Mineral supplements (A12)	47	1.6
Antibacterials for systemic use (J01)	27	0.9
Cough and cold preparations (R05)	18	0.6
Others	73	2.4
Drug names (ATC-5 Codes)		
Pantoprazole (A02BC02)	343	11.4
Diclofenac (M01AB05)	212	7.1
Dexketoprofen + thiocolchicoside (M02AA27 + M03BX05)	211	7.0
Escin + diethylamine salicylate (M02AC55)	207	6.9
Piroxicam (M01AC01)	191	6.4
Ibuprofen (M01AE01)	160	5.3
Diclofenac + thiocolchicoside (M01AB05 + M03BX05)	133	4.4
Phenyramidol (M03BX30)	102	3.4
Acemetacin (M01AB11)	95	3.2
Naproxen (M01AE02)	94	3.1
ATC: Anatomical therapeutical chemical.		

TABLE V Summary of the assessment of rational drug use with the WHO core prescribing indicators at the orthopedics and traumatology outpatient clinic			
The WHO core prescribing indicators	Analysis results	WHO optimal levels	
Average number of drugs per encounter	2.9	1.6-1.8	
Percentage of drugs prescribed by generic name	0%	100%	
Percentage of encounters with an antibiotic prescribed	2.6%	≤30%	
Percentage of encounters with an injection prescribed	10.7%	≤20%	
Percentage of drugs prescribed from essential drugs list	33.8%	100%	
WHO: World Health Organization.			

			TABLE VI		
Comparison of the WHO core prescribing indicators by age categories					
	Average number of drugs per prescription		Prescriptions with an antibiotic	Prescriptions with an injection	Drugs prescribed from essential drugs list
Age groups (year)	Median	Min-Max	%	%	%
18-44	3	1-7	3	8.1	28.4
45-64	3	1-7	2.7	11.5	35.9
≥65	3	1-6	2.0	13.4	37.6
<i>p</i> value	0.0	01*	0.776	0.123	0.038**

* Kruskal Wallis test and post hoc pairwise comparisons was used to compare the average number of drugs between age categories; ** The chi-square test was used to compare the WHO prescibing indicators percentages between age categories.



DISCUSSION

Considering that drug utilization studies are scarce in developing countries,^[11] this retrospective study is valuable in revealing the current situation regarding rational drug use. To the best of our knowledge, this is the first study to evaluate the rational drug use based on WHO prescribing indicators at an orthopedics and traumatology outpatient clinic in Turkey.^[12]

In the present study, drug utilization patterns and rational drug use practices at the orthopedics and traumatology outpatient clinic of a tertiary care hospital were analyzed retrospectively based on WHO core prescribing indicators. The demographic features showed that most of the patients were female (73.3%). This is in accordance with the results of a study conducted in orthopedic outpatient department which reported female preponderance.^[13] This finding could be explained by a higher prevalence of musculoskeletal disorders reported in women than men.^[14] Almost half of the patients were between 45 and 64 years of age (47.7%) in our study. Similar to our results, two studies reported middle aged group as the most common age group at orthopedic departments.^[13,15]

According to the clinical diagnosis, musculoskeletal pains constituted the majority of the diagnoses (Figure 1). Unlike our findings, two studies reported acute trauma and fractures as the most common diagnoses at the orthopedic departments.^[15,16]

Non-steroidal anti-inflammatory drugs (NSAIDs) are frequently used drugs for the management of musculoskeletal conditions.^[17] Gastroprotective agents are commonly prescribed concomitantly with NSAIDs to reduce the adverse effects (gastrointestinal ulcers, bleeding), morbidity and mortality due to NSAIDs long-term use.^[18] In the present study, among drug classes, NSAIDs and drugs for acid-related disorders were the most frequently prescribed drug groups. Similar to our results, two studies from India and Nepal which assessed rational drug use at orthopedics and traumatology outpatient departments reported NSAIDs and anti-ulcer drugs as the most common drug classes.^[19,20]

Although polypharmacy, which is an important example of irrational drug use, is usually known as the use of two or more drugs, there is no consensus on the exact definition. According to the current literature, it is commonly described as five or more drugs daily.^[21] In addition, using 10 or more drugs is defined as hyper-polypharmacy which is a problem among elderly.^[21] In our study, a great majority of the patients were prescribed two to four drugs (79.8%), while a small percentage of patients were given five or more drugs (7.5%). The average number of drugs per encounter in the present study was 2.9, which is higher than the WHO standard values (1.6-1.8).^[7] Similar to our results, many studies from distinct countries reported higher values than WHO ideal ranges, differing from 2.36 to 5.79.^[13,15,16,22-26] Polypharmacy was significantly higher in patients aged \geq 65 years (average number of drugs per prescription: 3.1) than young adults aged between 18 and 44 years (p=0.001). This is an anticipated result due to the increased number of drugs used by increasing age related to existing comorbidities.^[27] Similarly, a study from Jordan which evaluated rational drug use at primary

Antibiotic overuse is an important issue worldwide due to the risk for occurrence of antibiotic resistance.^[29] The percentage of encounters with an antibiotic prescribed in the present study was 2.6%, which is within normal limits according to the WHO standard value ($\leq 30\%$).^[7] Similarly, several studies from distinct orthopedic departments reported antibiotic use within normal ranges differing from 1.09 to 8.43.^[16,19,25,26] In contrast, quite high levels of antibiotic use (60.4%) were reported in a study by Abhilash et al.^[15] which was conducted among orthopedic inpatients.

healthcare centers reported that polypharmacy was

significantly higher among elderly.^[28]

Keeping the injection prescribing to a minimum level both reduces the pharmacotherapy cost and minimize the risks of complications due to parenteral use.^[24] In contrast to other studies by Abhilash et al.^[15] (76.3%) and Srividya et al.^[30] (46.84%), we found a low injection prescribing percentage (10.7%), which is normal according to the WHO standard value ($\leq 20\%$).^[7]

The essential drug list of Turkey could be attained from the website of the Turkish Medicines and Medical Devices Agency under the head of 'SKRS3 e-prescription drug and other pharmaceutical products list' which is updated regularly.[31] The essential drug list of Turkey has been prepared based on the WHO Model List of Essential Drugs and harmonized with relevant lists for essential drugs. The rate of drugs from essential drug list in our study was 33.8% which was quite low than the expected WHO value (100%)[7] and was found to be significantly lower in young adults compared to elderly (p=0.038). Our result is consistent with those reported by Karki et al.^[16] who found that 34.3% of drugs were prescribed from essential drug list at the orthopedics department. In a recent

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study, which evaluated the rational drug use at the obesity outpatient clinic of a tertiary care hospital in Turkey, higher percentages of drugs prescribed from essential drug list were found (61.4%).^[32] This discrepancy could be attributed to the type of outpatient clinic and the difference of prescribed drugs.

Prescribing with generic name not only lowers the pharmacotherapy costs, but also provides drug treatments to be more rational.^[4] Since the drugs are prescribed with their trade name in our country, we found the percentage of generic prescribing was 0%, as expected. Similarly, a study conducted at an orthopedic outpatient department in India reported generic prescribing percentage as 0%.[26] Several studies evaluating the rational drug use at distinct orthopedic departments reported higher generic prescribing percentages than our study, although the values were far from the WHO expected percentage.^[13,15,16,19,25,30] For the rationalization of pharmacotherapy, it would be an outstanding step to launch prescribing drugs with generic names rather than trade ones in our country, as well.

Since irrational drug use is a global health problem which is both an important economic burden on society and also causes negative health consequences such as therapy failure, resistance to antibacterial drugs, adverse drugs reactions, considerable morbidity and mortality,^[33] it is crucial to emphasize the importance of rational drug use to physicians during both underand postgraduate education.

The present study has some limitations. Our study was conducted with a small sample size for a short period of time in a single tertiary care hospital and, thus, the results may not be representative for the Turkish population. Nevertheless, we believe that the present study would further shed light into the future multi-center studies with larger sample sizes in the long-term.

In conclusion, our study is the first to assess the drug use patterns and rational drug use practices based on the WHO prescribing indicators at an orthopedics and traumatology outpatient clinic in Turkey. Based on these findings, the percentage of encounters with an antibiotic and injection prescribed were found to be optimal according to WHO standards, while the average number of drugs per encounter was higher compared to the WHO ideal ranges. Unfortunately, the parameters, such as the percentage of prescribing with generic name and from essential drug list, were far more behind the optimal range. It is expected that our study would shed light 765

into both the rationalization of pharmacotherapy and the implementation of relevant regulations on rational drug use by health authorities.

Declaration of conflicting interests

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