NON-OPIOID ANALGESICS CONSUMPTION AT THE SURGERY DEPARTMENTS OF A SECONDARY CARE HOSPITAL IN GENERAL HOSPITAL IN KRALJEVO, SERBIA

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POTROŠNJA NEOPIOIDNIH ANALGETIKA NA HIRURŠKIM ODELJENJIMA BOLNICE SEKUNDARNOG NIVOA ZDRAVSTVENE ZAŠTITE U KRALJEVU, SRBIJA

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ABSTRACT

The aim of this study was to determine the amount of non-opioid analgesics consumed at the surgical departments of a secondary care hospital in Serbia, a developing country undergoing a socioeconomic transition that thus lacks sufficient funds to finance and invest in the healthcare system.

At the departments of gynaecology, urology, otolaryngology, general surgery and orthopaedics with traumatology at the General Hospital, Kraljevo from 2010 to 2012, six different non-opioid analgesics were used: diclofenac, ketorolac, ibuprofen, metamizole sodium, paracetamol (for per os and parenteral use), and meloxicam (for parenteral use only). Drugs in the M01 Anatomical Therapeutic Chemical classification group were consumed statistically significantly more than drugs in the N02 group (U=0.000; p<0.001). With regard to the average consumption amounts of all monitored drugs, diclofenac was consumed the most, followed by ketorolac. Meloxicam was the least used drug. There were significant differences in the average annual consumption of ibuprofen between surgical departments, but this was not the case for the other non-opioid analgesics. The differences in the average consumption between the individual drugs were significant for each year of observation.

Due to the incongruity of the results of previous studies related to non-steroidal anti-inflammatory drug consumption at different surgery wards, additional research in different geographical areas of our country is necessary to enhance the quality of prescription patterns on a national level and adjust them based on the latest scientific data and European trends.

Keywords: *drug use non-steroidal anti-infl ammatory drugs DDD methodology surgery departments.*

SAŽETAK

Cilj ovog istraživanja je ispitati potrošnju neopioidnih analgetika na hirurškim odeljenjima bolnice sekundarnog nivoa zdravstvene zaštite u Srbiji, zemlji u razvoju i socioekonomskoj tranziciji, koja kao takva, nema dovoljno sredstava za finansiranje i ulaganje u zdravstveni sistem.

Na odeljenjima ginekologije, urologije, otorinolaringologije, opšte hirurgije i ortopedije sa traumatologijom u Opšoj bolnici u Kraljevu, u periodu od 2010. do 2012.godine korišćeno je šest različitih neopioidnih analgetika: diklofenak, ketorolak, ibuprofen, metamizol-natrijum, paracetamol (za oralnu i parenteralnu upotrebu) i meloksikam (za parenteralnu upotrebu). Lekovi koji pripadaju grupi M01 prema anatomsko-terapijsko-hemijskoj klacifikaciji su statistički značajno više korišćeni nego lekovi koji pripadaju NO2 grupi (U=0.000; p<0.001). Diklofenak je bio na prvom i ketorolak na drugom mestu po prosečnoj potrošnji među svim analiziranim lekovima. Meloksikam je najmanje korišćen lek. Postojala je statistički značajna razlika u prosečnoj godišnjoj potrošnji ibuprofena po odeljenju, dok za druge neopioidne analgetike ova razlika nije utvrđena. Razlika u prosečnoj potrošnji između pojedinačnih lekova bila je značajna za svaku godinu ispitivanja.

Zbog nepodudarnosti rezultata različitih studija o potrošnji nesteroidnih antiinflamatornih lekova na različitim hirurškim odeljenjima neophodna su dodatna slična istraživanja u različitim geografskim oblastima naše zemlje, u cilju poboljšanja kvaliteta propisivanja ovih lekova na nacionalnom nivou kao i u cilju prilagođavanja propisivanja sa najnovijim naučnim preporukama i evropskim trendovima.

Ključne reči: *potrošnja lekova, nesteroidni antiinfl amatorni Lekovi, DDD metodologija, hirurška odeljenja*

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ABBREVIATIONS

ADE – Adverse drug events;
ATC – Anatomical Therapeutic Chemical;
COX – cyclooxygenase;
COX-2 - cyclooxygenase-2;
DDD – defined daily dose;
GI - gastrointestinal;
MI - myocardial infarction;
NSAIDs - non-steroidal anti-inflammatory drugs;
SPSS – Service Provisioning System Software;
WHO – World Health Organization.

INTRODUCTION

The modern era is generally characterized by the increased use of medications for the treatment of various conditions and, on the other hand, by the limited financial resources of health systems. Because such widespread drug use is often associated with a higher incidence of adverse events (ADE) and high treatment costs, it is essential to monitor and analyse the consumption of medicines in order to rationalize their future use. Ensuring the appropriateness of drug use is particularly important in developing countries due to their poor financial investments in health care. (1, 2)

Non-opioid analgesics, including nonsteroidal anti-inflammatory drugs (NSAIDs) and paracetamol, are currently among the most commonly used medications in clinical practice due to their reliable effectiveness, relative ease of use, and acceptable price in most circumstances. (2) However, it is also well known that inappropriate use of these drugs generates increased risks of serious gastrointestinal and cardiovascular adverse effects as well as renal and/or hepatic impairment. (3). However, despite this fact, the majority of non-opioid analgesics are widely available, even without medical prescriptions. Furthermore, NSAIDs account for the largest portion of medicines intended for self-treatment in the home pharmacies of individuals in the community. (4)

Studies of NSAID utilization in our country and other countries in Europe have shown increasing utilization of this group of drugs. (4,5,6,7,8) In the United States of America, NSAID consumption is also high, with 34% of people older than 65 years consuming at least one dose per day and 70% consuming at least one dose per week. (9) A study in North America showed that each dollar spent on NSAIDs resulted in 0.66-1.25 cents being spent on treating gastrointestinal (GI) tract side effects. (10) NSAID utilization in hospitals depends mostly on the availability of appropriate pharmaceutical forms of these drugs for parenteral use and their pharmacological characteristics and cost. In surgery wards, the use of NSAIDs has increased in relation to the use of more toxic opioid analgesics, despite the fact that NSAIDs have less pronounced analgesic effects. (2) A study that analysed the costs associated with NSAID drugs in patients with arthritis showed that 31% of such costs are directed towards the treatment of ADE in the GI tract. (11)

The aim of this study was to determine the amount of non-opioid analgesics consumed at the surgical departments of a secondary care hospital in Serbia, a developing country undergoing socioeconomic transition that thus lacks sufficient funds to finance and invest in the healthcare system.

MATERIALS AND METHODS

This was a descriptive drug utilization study dealing with the extent of non-opioid analgesics used at the surgical units of the General Hospital in Kraljevo, Serbia, a state-owned institution with 580 beds that provides secondary health care services to approximately 250,000 inhabitants of the Raska district. The administrative centre of this hospital is in Kraljevo. In a retrospective manner, the consumption of NSAIDs and paracetamol at the Departments of: general surgery, gynaecology, urology, otolaryngology and orthopaedics with traumatology, during the 3-year period of January 1st, 2010 to December 31st 2012 was evaluated using the anatomical therapeutic chemical classification and defined daily dose (ATC/DDD) methodology adopted by the World Health Organization (WHO) Collaborating Centre for Drug Statistics Methodology (Last updated: 2013-12-19).

The data on the utilization of drugs belonging to the ATC groups M01 and N02 (i.e., NSAIDs and paracetamol, respectively) at the abovementioned surgical departments over the observed period were obtained from the annual reports of the Hospital Pharmacy, which is the department responsible for the supply and dispensing of all medicines to inpatients at the General Hospital in Kraljevo.

The Hospital's Administrative Service provided the data on the total number of patients treated at the surgical departments who were followed for non-opioid analgesic consumption. It also provided the average patient length of stay at each departments for each calendar year of observation separately. Based on these data, the total number of days patients spent at each department per year was calculated and then divided by 100 to standardize the drug consumption per 100 bad days. We did not have data regarding the sex or age of the patients to whom the therapy was administered or data about the indication for which the non-opioid analgesics were prescribed or their dosage; our data only described the total consumption of these drugs during the observation period.

Drug consumption was expressed as number of DDDs per 100 bed days, and the differences in DDDs for different drug formulations according to the routes of administration were considered. The defined daily doses for each drug formulation were obtained from the last updated version of the list of DDDs, which is available on the WHO website. (12) The number of consumed DDDs per 100 bed days per year for a particular drug was calculated separately for each surgical department.

Table 1: Number of patients treated and the average patient length of stay at each surgical department for each calendar year of the observation period

Departments	Gynaecology			Urology			Otolaryngology			Surgery			Orthopaedics		
Year	2010	2011	2012	2010	2011	2012	2010	2011	2012	2010	2011	2012	2010	2011	2012
Number of patients	1751	1834	1684	1565	1484	1451	716	775	719	4300	4516	4508	653	761	818
Average patient length of stay in days	4.98	4.48	4.58	6.70	4.83	4.36	8.24	7.29	6.84	6.76	6.09	6.19	12.65	12.89	11.39

All collected data on the utilization of non-opioid analgesics are summarized as the means and standard deviations. Considering the small sample size (n<30), a nonparametric *Kruskal-Wallis* test was used to analyse the significance of differences in average annual consumption of a particular drug between surgical departments as well as differences between individual drugs in average consumption for each department and for each year of observation. Differences were considered significant when there was a probability level of the null hypothesis being true of lower than 5% (p<0.05). All statistical analyses were performed using *SPSS* software, version 18.

RESULTS

For each surgical department, the total number of patients treated that were followed for non-opioid analgesic consumption and the average patient length of stay for each calendar year of observation is shown in Table 1. The longest average length of hospital stay was in the department of orthopaedics, and the department of general surgery had the greatest number of hospitalized patients (Table 1).

In the departments of gynaecology, urology, otolaryngology, general surgery and orthopaedics with traumatology at the General Hospital, Kraljevo from 2010 to 2012, six different non-opioid analgesics were used: diclofenac, ketorolac, ibuprofen, metamizole sodium, paracetamol (for per os and parenteral use), and meloxicam (for parenteral use only).

The consumed drugs belonged to two groups based on ATC classification: M01 (diclofenac, ketorolac, ibuprofen, and meloxicam) and N02 (paracetamol and metamizole sodium). The drugs in the M01 ATC classification group

Table 2. Consumption of non-opioid analgesics at surgical departments of the General Hospital in Kraljevo over the observed three-year period

Year	Department	Utilization of non-opioid analgesics (DDD/100 bad days)							statistical test# p value
		Diclofenac	Ketorolac	Ibuprofen	Paracetamol	Metamizole Sodium	Meloxicam	Mean ± SD	
2010	Gynaecology	20.21	2.64	2.87	0.30	1.43	0	**4.57±7.75**	χ^2=24.773 **p<0.001***
	Urology	38.9	1.72	3.81	1.66	1.82	0.05	**7.99±15.19**	
	Otolaryngology	20.08	3.05	5.9	0.26	0.42	0	**4.95±7.75**	
	Surgery	44.42	14.06	0.07	0.13	0.52	0	**9.87±17.81**	
	Orthopaedics	88.53	2.60	1.21	1.62	0	0.12	**15.68±35.70**	
	Mean ± SD	**42.43±27.99**	**4.81±5.19**	**4.16±2.32**	**0.79±0.77**	**0.84±0.76**	**0.03±0.05**	Mean ± SD	
2011	Gynaecology	23.13	3.04	1.22	0.10	0.51	0	**4.67±9.11**	χ^2=21.866 **p=0.001***
	Urology	42.11	2.50	1.95	2.27	2.43	0	**8.54±16.47**	
	Otolaryngology	19.05	1.33	4.51	0.30	0	0	**4.20±7.47**	
	Surgery	48.51	11.63	0.11	0.15	0.82	0	**10.20±19.31**	
	Orthopaedics	86.50	1.04	0.2	1.63	0	0	**14.89±35.08**	
	Mean ± SD	**43.86±26.87**	**3.91±4.39**	**1.60±1.80**	**0.89±1.00**	**0.75±1.00**	**0**	Mean ± SD	
2012	Gynaecology	26.28	2.20	0	0	0.65	0	**4.85±10.53**	χ^2=22.273 **p<0.001***
	Urology	44.93	0.95	0	0	2.90	0	**8.13±18.06**	
	Otolaryngology	28.01	0.18	1.39	0.31	0.17	0	**5.01±11.28**	
	Surgery	48.90	10.32	0	0	0.85	0	**10.01±19.48**	
	Orthopaedics	87.86	1.72	0.11	0.02	0	0	**14.95±35.72**	
	Mean ± SD	**47.20±24.83**	**3.07±4.12**	**0.30±0.61**	**0.07±0.14**	**0.91±1.16**	**0**		
statistical test§ p value		χ^2=0.740 p=0.691	χ^2=2.650 p=0.266	χ^2=7.906 **p=0.019***	χ^2=5.464 p=0.065	χ^2=0.249 p=0.883	χ^2=4.286 p=0.117		

The difference in individual consumption of NSAIDs in each year of the study period (2010, 2011, 2012);
§ The difference in annual utilization of NSAIDs
NSAIDs – non-steroidal anti-inflammatory drugs; DDD- defined daily dose.

had statistically significantly higher consumption than the drugs in the N02 group (U=0.000; p<0.001).

Regarding the average consumption of all monitored drugs, diclofenac consumed the most, followed by ketorolac. Meloxicam was the least used drug (Table 2).

The analysis of the average metamizole sodium consumption during the three-year period showed that the highest consumption of this medicine was at the urology department, and the orthopaedics department did not use metamizole sodium at all during the observation period (Table 2).

There were significant differences between the surgical departments in the average annual consumption of ibuprofen, but this was not observed for the other non-opioid analgesics. The differences in the average consumptions between the individual drugs were significant for each year of observation (Table 2).

DISCUSSION

This study showed that diclofenac, a conventional, non-selective inhibitor of cyclooxygenase (COX), was consumed the most (Table 2). Although diclofenac is listed in the category of NSAIDs with a moderate risk of causing ADE (13), according to one study, the introduction of a new analgesic generation of drugs, namely selective cyclooxygenase-2 inhibitors (COX-2), did not decrease the use of conventional NSAIDs (4, 7). However, this finding contrasts with those of other studies (6). A study of the consumption trends of NSAIDs at the departments of general and endocrine surgery at the hospitals in our country showed that diclofenac, ketorolac and ibuprofen were the most used NSAIDs; in the five-year observation period, they constituted 90% of the consumed NSAIDs (2). One of the reasons for this is the traditional prescription patterns, the low frequency of updates to pharmacotherapy guidelines and the low price of diclofenac, which is the cheapest NSAID on the market in our country. The high consumption of diclofenac is also enabled by the recommendations of family doctors and by its availability as an over-the-counter medication. (7)

Ketorolac was the second most frequently consumed non-opioid analgesic (Table 2), and its level of consumption is high considering that this drug has a powerful inhibitory effect on platelet aggregation that contraindicates its use pre-, intra- and postoperatively. (13)

Diclofenac is still the most frequently consumed medication in this group of drugs despite studies that have shown that long-term diclofenac therapy increases the risk of myocardial infarction (MI). The risk of MI remains in patients who used diclofenac for a long time but are not using it anymore. Therapeutic doses of ibuprofen do not cause an increased risk of MI, and it was the third most frequently consumed non-opioid analgesic according to the results of our research (Table 2). For both diclofenac and ibuprofen, the use of a daily dose higher than the therapeutic dose also increase the risk of MI (14).

The highest drug consumption among the investigated departments was in the department of orthopaedics. At the orthopaedics department, compared with all the departments combined, diclofenac was the most frequently consumed non-opioid analgesic (Table 2). One study of non-opioid analgesic consumption at an orthopaedics department showed that the most frequently used drug was the COX-2 selective inhibitor rofecoxib, which accounted for 30.4% of the drugs consumed; in that study, diclofenac was the second most frequently consumed drug. The same study showed a higher incidence of ADE in patients who received conventional NSAID therapy than in patients who received selective NSAIDs. (15) A study that examined the prescription of non-steroidal analgesics among general practitioners and various specialists showed that orthopaedists prescribed the highest amount of fixed doses of non-opioid analgesics (ibuprofen+paracetamol and diclofenac+paracetamol). (16)

The department of urology had the highest consumption of paracetamol in all years except 2012 (2010 – 3.46%; 2011 – 4.43%; 2012 – 0%; Table 2). A study conducted at the University Hospital in New Delhi showed that the most frequently used analgesic, paracetamol, accounted for 31.51% of total analgesic consumption, and this was greater than the percentage of total analgesic consumption accounted for by COX-2 selective inhibitors. (17)

The least used drug in the three-year observation period was meloxicam (Table 1), a COX-2 selective NSAID that causes a low incidence of ADE in the gastrointestinal tract. However, according to a recently conducted meta-analysis, COX-2 selective NSAIDs should be used with caution because of their side effects on the cardiovascular system and because they increase the risk of MI (18).

Metamizole sodium was withdrawn from the United States market in the 1970s because of the high risk of agranulocytosis (6); however, in our study, only orthopaedics with traumatology department did not use this drug during the three-year observation period (Table 2).

In the pharmaceutical market, which provides numerous choices for drugs of the same group, the quality of prescription patterns is low. In addition, prescriptions are influenced by the ability of doctors to choose a drug appropriately, the intensity of the marketing of drugs by pharmaceutical companies, and the prices of NSAIDs (19).

Due to the incongruity of the results of previous studies related to NSAID consumption in different surgery wards, additional research in different geographical areas of our country is necessary to enhance the quality of prescription patterns on a national level and adjust them based on the latest scientific data and European trends.

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