PREVALENCE AND THE PATTERNS OF USE OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) AND PARACETAMOL AMONG THE GENERAL POPULATION

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Manuscript received: December 2018

Abstract

Different studies published in the last 15 years reported an increased incidence of adverse drug events, particularly on cardiovascular (CV) and cerebrovascular systems, during the consumption of non-steroidal anti-inflammatory (NSAIDs) drugs. The purposes of this study were: to identify the prevalence of the NSAIDs and paracetamol use, to analyse the use patterns of these drugs and to assess the risk to develop adverse CV effects in relation to different factors in order to improve the patients' safety. The data contained by the self-administered questionnaires, fully completed by 735 patients, were analysed. The relationships between the use of NSAIDs and paracetamol by the CV/non-CV patients and different variables were comparatively analysed using the Windows 17.0 version of Statistical Package for the Social Sciences (SPSS). The main medical reasons motivating the NSAIDs use were: joint pain (41.22%), low back pain (35.10%) and headache (8.98%). Compared to non-CV patients, those with a CV disease (60.41% of the respondents using NSAIDs) have used more frequently: diclofenac (OR: 2.674; 95% CI: 1.822 - 3.924), ketoprofen (OR: 1.711; 95% CI: 0.970 - 3.018) and indomethacin (OR: 3.814; 95% CI: 1.577 - 9.222). 64.86% of the CV patients acquired NSAIDs by self-medication. High prevalence of NSAIDs current use was observed in the case of the CV patients, presenting an increased risk to develop significant side-effects in a chronic, irrational or abusive, consumption of these molecules.

Rezumat

Studiile publicate în ultimii 15 ani au raportat o incidență crescută a efectelor adverse, în special la nivelul sistemului CV și cerebrovascular în timpul consumului de medicamente antiinflamatoare nesteroidiene (AINS-urile). Obiectivele acestui studiu au fost: identificarea prevalenței consumului de AINS și paracetamol, analiza modelelor de utilizare a acestor medicamente și evaluarea riscului de dezvoltare a efectelor adverse CV în relație cu diferiți factori, pentru îmbunătățirea siguranței pacienților. Au fost analizate datele conținute în chestionarele aplicate, completate integral de 735 de pacienți. Relațiile dintre utilizarea AINS și paracetamol de către pacienții CV/non-CV și diferite variabile au fost analizate comparativ folosind Pachetul de programe statistice aplicabile științelor sociale versiunea 17.0 (SPSS). Principalele motive medicale care justifică utilizarea AINS-urilor au fost: durerile articulare (41,22%), durerile lombare (35,10%) și cefalee (8,98%). Comparativ cu pacienții non-CV, cei CV (60,41% dintre respondenți utilizatori de AINS) au utilizat mai frecvent: diclofenac (OR: 2,674; 95% CI: 1,822 - 3,924), ketoprofen (OR: 1,711; 95% CI: 0,970 - 3,018) și indometacin (OR: 3,814; 95% CI: 1,577 - 9,222). 64,86% dintre pacienții CV au achiziționat AINS-ul ca automedicație. S-a observat o prevalență ridicată a consumului curent de AINS în rândul pacienților CV, prezentând un risc crescut de a dezvolta efecte adverse semnificative în condițiile unui consum cronic, irațional sau abuziv, al acestor molecule.

Keywords: NSAIDs use, prevalence, patterns, chronic disease, cardiovascular risk

Introduction

NSAIDs are a class of drugs with the following specific characteristics: a large share for use in medical practice (to treat pain and inflammation); a wide range of adverse drug events (ADEs), particularly on gastrointestinal (GI), cardiovascular (CV) and cerebrovascular systems [27], kidney, skin and liver; an increased risk of serious

interactions with other drugs when simultaneously administered [28]. Several recommendations have been developed to limit the increase these ADEs, such as to avoid prescribing these medicines in patients with known risk factors for ADEs development, such as old age, various associated co-morbidities or concomitant use with other medications [4].

Many years the clinicians' attention had been centered on reducing the incidence and clinical consequences of GI bleeding, but more recently the European Medicines Agency (EMA) has also started considering the first CV side-effects relating to NSAIDs use, namely their prothrombotic potential effect [8]. This effect was initially observed to rofecoxib, a NSAID selective cyclooxygenase-2 inhibitor (COX-2 inhibitor) and led to its withdrawal from the market in 2004. Several further studies have suggested an increase in CV risk in case of some non-selective NSAIDs, also, such as diclofenac and ibuprofen [23]. Moreover, in case of diclofenac, the EMA's Pharmacovigilance Risk Assessment Committee even issued a warning in 2013 with regard to its CV effects after its systemic administration, regardless of its pharmaceutical dosage form (capsules, tablets or injectable) [9]. Other NSAID molecules present different degrees of CV risk also. Naproxen and low doses of ibuprofen show a CV safety profile, while the few available data for etoricoxib place it on a superior position to naproxen or ibuprofen. Although indomethacin's main adverse effects are on the GI and central nervous system, the CV risk profile is similar to that of diclofenac [18]. The potential CV risk of non-selective NSAIDs and selective COX-2 inhibitors is dependent on both the pharmacological properties, the size of the daily dose used, the selected pharmaceutical formulation, and the duration of therapy, as well as the use patterns of these drugs, namely by prescription-only or "over-the-counter" (OTC); furthermore, the presence of some patient comorbidities increases the abovementioned CV risk. Suppression by NSAIDs of the production of physiological constituents obtained *via* the COX-1 constitutive isoenzyme, but also of those released as a result of COX-2 inducible isoenzyme activation from the cells where it is expressed, is the main mechanism involved in the genesis of their ADEs such as: sodium and water retention, arterial hypertension, promoting platelet aggregation [28], worsening of heart failure. Considering all abovementioned and the fact that in many countries, NSAIDs are available as OTC (without a prescription) and as prescription-only (Rx) doctor preparations, there are concerns about the increasing use of these drugs among the population with associated CV pathology. Chronic and irrational use of OTC NSAIDs by the patients with associated comorbidities constitutes a danger to their own health, the quality of their lives and, last but not least, to public health.

Paracetamol is one of the most known and popular OTC molecules worldwide for its remarkable analgesic and antipyretic effects, which recommends it as the first-line pharmacotherapy to

combat fever and various forms of pain, of mild and moderate intensity, of different origins, symptoms that can coexist or not in the same patient [13].

In many countries, including Romania, the sales of NSAIDs and paracetamol as OTC drugs, are not recorded in patients' health databases and are not reimbursed by health insurance systems. Therefore, currently very few published studies refer to their use by patients in the real life, their use patterns, quantities in which these drugs were purchased, and the risk factors associated with this consumption. All these factors may have a negative impact on their overall risk profile, and their CV profile in particular [14, 17]. Considering the latest information, according to which the CV mortality is increased during the use of NSAIDs and among people without a history of CV disease, it is necessary to identify and improve the NSAID use patterns in the general population, especially among high-risk patient categories [11].

The main objectives of our study were to evaluate the current prevalence of self-reported use of paracetamol and various types of NSAIDs in the general population, the share of CV patients among them and the use patterns of these drugs. The study also had the following secondary objectives: 1) to highlight the medical reasons that have determined these patients to resort to this medication; 2) to identify the most frequently used molecules for the treatment of osteoarticular and other painful manifestations; 3) to assess the patients' knowledge about the potential risk of adverse events of NSAIDs chronic use.

Materials and Methods

Materials

Study design and oversight

The present research is a prospective, observational descriptive cross-sectional study which was performed between March 2018 and May 2018 and included 735 NSAIDs and paracetamol consumers. The study was conducted as a personal interview-based survey among patients who attended three community pharmacies in Timișoara during this period, buying any medicine containing an NSAID/paracetamol and who were invited to participate in our voluntary and anonymous survey.

The patients of study

Survey

In the present study, the patients' inclusion was based on the following criteria: 1) women or men aged over 18 years; 2) their demonstrated intention to acquire an NSAID/paracetamol for themselves, with or without prescription; 3) established diagnosis of osteoarthritis in medical records, but also other painful symptoms for which the patients

report the use of NSAID/paracetamol molecules; 4) informed verbal consent. The patients were excluded from the study if they bought the medicine for someone else or had previously participated in another survey of this type; other exclusion criteria were: language barriers (inability to communicate in Romanian language), evident cognitive impairment or refusal to participate in the study.

Procedures

The research was carried out using self-administered questionnaire given to each NSAIDs/paracetamol user by the pharmacist. The questionnaire method was applied for all the people who buying any medicine containing an NSAID/paracetamol. The questionnaires were anonymous, and the obtained data were used exclusively for statistical processing. The questionnaire contained five sections intended to evaluate the following issues: (1) socio-demographic characteristics of the patient (age, sex, marital status and educational level); (2) the molecule used (type and reason for use); (3) person who identified the need for such therapy (prescription-based or self-medication); (4) relevant co-morbidities and concurrent medications taken (one's medical history, including concomitant chronic use of prescription medicines); (5) patients' perception of possible risks caused by the NSAIDs use with a visual analogue scale and knowledge about potential adverse events (previous exposure to NSAIDs/paracetamol and previous experience of side-events were assessed - what adverse events the patient had experienced).

According to the International Standard Classification of Educational Degrees (ISCED 2011), the patients' education level was evaluated, and it was classified in low, medium and high [26]. Regarding the marital status variable, we mention that people were divided into two states: married (including those who co-habit with their partner) and unmarried (who are single, separated, divorced or widowed). All situations in which the patient did not have a medical prescription (MP), at the time of purchase, were considered self-medication (SM). All patients who requested pharmacist counselling for their symptoms and have its acquisition of an NSAID according to the will and decisions were considered all as self-medication also. The pattern of use of NSAIDs and paracetamol was analysed in general population and on subgroups. Subgroup analysis was performed for CV and non-cardiovascular (non-CV) patients.

Ethical considerations

Participants provided written informed consent prior to interview and as the patient's contact information was not collected, all information was stored in an irreversibly anonymized fashion. We

used questionnaire identification numbers instead of other patient identifier parameters for all the collected information through the self-administered questionnaires. Therefore, our research group considered that no approval from an ethics committee was required.

Statistical analyses

The Windows 17.0 version of Statistic Package for the Social Sciences (SPSS) was used to examine the data and the relationships between different variables and the use of NSAIDs and paracetamol by the CV versus non-CV patients. The two types of analysed variables, namely qualitative and continuous variables, were expressed as frequencies (percentage) or as mean and standard deviation (SD) respectively. Group differences were considered statistically significant for p-values less than 0.05. Descriptive statistics were used to analyse all the variables; data were presented as odds ratio (OR) with 95% confidence intervals (CI).

Results and Discussion

Of the total of 800 questionnaires which were initially distributed in the three community pharmacies, 758 (94.75%) were collected/returned, and of these 23 questionnaires (3.03%) were removed because they were blank or not fully completed (incomplete on demographic, clinical, or medication data). The respective 23 patients were considered non-participants at our study. So, 735 interviews were completed, and the participation rate was of 91.87%.

Concerning the use of NSAIDs and paracetamol among the general population

The pain as a symptom, with acute or chronic onset, with various osteoarticular and extra-osteoarticular localisations, was the main reason, self-reported by 681 (92.65%) patients participating in our study, for acquiring an NSAIDs/paracetamol molecule. The prevalence and multivariable associations for reported NSAIDs and paracetamol use in various socio-demographic categories are reported in Table I. Concerning the use of these molecules among the general population, our study highlighted that the respondent users of NSAIDs and paracetamol were women (n = 381; 51.84%) and they represent the majority in the age group of 45 - 64 years (n = 381; 51.84%); the mean age of study recruits was of 49.46 years old (SD = 20.49).

It is already known that women use more NSAIDs than men, which is most probably related to an increased prevalence of chronic non-malignant pain in women compared to men, observed in current practice [10] and confirmed by the results of the present study, where female gender was the majority.

Table I

The socio-demographic patients' characteristics associated with the prevalence (n, %) of NSAIDs and paracetamol users, the odds ratios with 95% confidence intervals (OR, 95% CI) and p values

Socio-demographic variables		Number (n) and % of CV patients (444, 60.41%)	Number (n) and % of non-CV patients (291, 39.59%)	Total no. of patients (735, 100%)	OR (95% CI) p value
Gender	Female	231 (52.03%)	150 (51.55%)	381 (51.84%)	1.019 (0.758 to 1.370) p = 0.899
	Male	213 (47.97%)	141 (48.45%)	354 (48.16%)	0.981 (0.730 to 1.319) p = 0.899
Age	20 - 44	12 (2.70%)	150 (51.55%)	162 (22.04%)	0.026 (0.01 to 0.048) p < 0.0001
	45 - 64	276 (62.16%)	105 (36.08%)	381 (51.84%)	2.910 (2.142 to 3.955) p < 0.0001
	> 65	156 (35.14%)	36 (12.37%)	192 (26.12%)	3.837 (2.573 to 5.722) p < 0.0001
Marital status	Married	255 (57.43%)	138 (47.42%)	393 (53.47%)	1.496 (1.111 to 2.014) p = 0.008
	Unmarried	189 (42.57%)	153 (52.58%)	342 (46.53%)	0.669 (0.497 to 0.899) p = 0.008
Educational level	Low	87 (19.59%)	21 (7.22%)	108 (14.69%)	3.133 (1.897 to 5.177) p < 0.0001
	Medium	234 (52.70%)	90 (30.93%)	324 (44.08%)	2.489 (1.824 to 3.395) p < 0.0001
	High	123 (27.70%)	180 (61.86%)	303 (41.22%)	0.236 (0.173 to 0.324) p < 0.0001

In the present conception of the biopsychosocial model of chronic pain [29], the gender differences, regarding the choice of these NSAIDs molecules and the differentiated response to their use, can be explained by a multifactorial aetiology, consequence of the interaction of several factors, such as: genetic and biological factors (eg. age, gonadal hormones); psychosocial factors (feelings of helplessness and the tendency to catastrophise events, abuse or trauma history in childhood); pathological factors (the presence of comorbid conditions, specific to each gender); cultural and educational factors. All these factors have different consequences in the personal self-care process, in order to maintain one's overall well-being [25]. In our study, middle-aged people were the majority group of patients consuming NSAIDs, their consumption decreasing almost at half with the patients aging (> 65, n = 192; 26.12%) (Table I). This observation is important, because it is consistent with current medical guidelines and recommendations that urge prescribers to a restrictive use of these molecules in the elderly

population, considering that, according to the physiological process of aging and the musculo-osteo-articular damage, the prevalence of pain increases with age [2]. In terms of marital status, the patients who requested NSAIDs/paracetamol for personal use were married (n = 393; 53.47%) (Table I). Considering that the person's social network is a determining factor of one's well-being [15], it was found that married individuals reported better levels of psychological well-being compared to the unmarried, for both genders, but marital satisfaction seems to play an even more important role in the process of health self-assessment and self-care [5]. Our results confirmed, once again, the increased attention that people, with a wider social network and access to various sources of social support, give to a better health-care [20], for himself, and for his own family. The educational level of the patients was also taken into consideration, as a measure of their socio-economic status, and reflected in the health-related differences between them. Most of the interviewed participants had a medium educational level (n =

324, 44.08%) and at just a few percent, the second place was occupied by the group with high educational level ($n = 303$; 41.22%) (Table I). Thus, one can state that more than three-quarters of the study's patients had a high degree of educational training. To our knowledge, there are only few studies evaluating the role of other social variables, like the educational level of patients, in the use of NSAIDs. The higher the level of patient's education, the greater the chance to a higher monthly income, that can contribute to health improving through healthier behaviours (improving the physical condition by practicing a sporting activity) or through differentiated access to health care. Regarding this issue the results of the previous studies are quite contradictory: a study in Spain showed that individuals with higher-income were more likely to take OTC analgesics [3], while another study conducted on American adults revealed that subjects with lower-income had less chances to use OTC-type NSAIDs than those with higher incomes [7]. It also can be considered that, a higher income allows an intellectual greater consumption of OTC analgesics (whose costs he bears directly), while individuals with low incomes can not afford the purchase of NSAIDs as OTC drugs. Our study showed that the request for various NSAID molecules/paracetamol had as the main medical reason the joint pain ($n = 303$; 41.22%) with various localizations (Table II), independently of comorbidities. The joint pain is the principal symptom of osteoarthritis, a medical condition that is today one of the most common chronic disabilities associated with the depreciation of the individual's quality of life and a significant increase in primary health care costs. Also, osteoarthritis presents a steadily increase in the coming decades due to the increasing life expectancy of the population and the progressive diminishing of the physical activity of the individual. This type of pain is more common in females, middle-aged, which is consistent with our results. Low back pain ($n = 258$; 35.10%), another symptom having different aetiologies and identified in the interviewed patients (Table II) is also more common for middle-aged individuals and is a major cause of disability among people of working age.

The medical reason was an important predictor of both consumption and type of the chosen NSAID molecule. The prevalence of the use of different NSAIDs was higher in those who reported the two forms of chronic pain, compared with those who experienced acute pain and who were mainly ibuprofen/paracetamol users. From Table II, it can be observed that diclofenac was the most commonly used and requested NSAID molecule ($n = 180$; 24.49%), followed by ibuprofen ($n = 153$;

20.82%), and etoricoxib ($n = 108$; 14.69%), while acetylsalicylic acid was seldom used. Higher frequency of diclofenac and ibuprofen use has been reported also in Serbia [21]. Contrary to the evidence that naproxen is associated with a low risk of vascular events [6] compared to other NSAIDs, its use has been low in our study. Similarly, paracetamol was very rarely acquired, under 5%, although according to the guidelines of new pharmacological strategies for mild pain suppression, this molecule is the first therapeutic option. Paracetamol was chosen by our respondents for the treatment of fever and headache, symptoms often present in the context of a common cold.

Also, this study has shown that the practice of SM with these molecules is wide spreaded among the general population, the most of the NSAIDs have been requested as SM ($n = 513$; 69.80%) to relieve the pain without any prior medical consultation, while those acquired as MP-only occupied a second place ($n = 222$; 30.20%). Our data are higher than those reported by other studies, 23.7% in Spain [3], 33% in the case of American adults [30], or 55% in the case of Australian adults [24]. It can be observed that the practice of SM with NSAIDs is spreaded worldwide. It is to be mentioned that the patients who did not have a MP, have requested the NSAID medicines based on their own previous experience, on the experience and advice of the pharmacist, but also on information held by family members, friends and even those obtained through advertising media, internet, etc. Study data suggests that acute painful states (headache and toothache) are associated with SM, but also chronic painful clinical manifestations urges the patient to resort in high proportion to the practice of SM, in order to suppress as soon as possible the physical and psychological discomfort, independently of comorbidities.

Analysing patients' perception of safe use (whether some possible risks exists or not) of these molecules, with an analogous visual scale where the value 1 represents the safest and the value of 10 is the most dangerous drug, our respondents estimated the risk of NSAIDs consumption at 3.4 ± 1.2 , thus perceiving them almost harmless, which gives the patients, psychologically, a justification for the use of these molecules unrestricted by time or dose. This low awareness of the risk of NSAIDs use among respondents can be attributed to the intervention of many factors, including low levels of patient knowledge about NSAIDs risks as well as poor communication of physicians and pharmacists with patients; these factors were identified in recent studies [22].

Table II

Prevalence (n, %) of medical reasons, of the molecules used (as type and mode of acquisition) and odds ratios with 95% confidence intervals (OR, 95% CI) and p values among study respondents

Other factors (as variables)		Number (n) and % of CV patients (444, 60.41%)	Number (n) and % of non-CV patients (291, 39.59%)	Total no. of patients (735, 100%)	OR (95% CI) p value
Medical reasons (symptoms)	Joint pain	216 (48.65%)	87 (29.90%)	303 (41.22%)	2.221 (1.625 to 3.036) p < 0.0001
	Low back pain	186 (41.89%)	72 (24.74%)	258 (35.10%)	2.193 (1.582 to 3.039) p < 0.0001
	Headache	18 (4.05%)	48 (16.49%)	66 (8.98%)	0.214 (0.122 to 0.376) p < 0.0001
	Toothache	12 (2.70%)	42 (14.43%)	54 (7.35%)	0.165 (0.085 to 0.319) p < 0.0001
	Fever	12 (2.70%)	42 (14.43%)	54 (7.35%)	0.165 (0.085 to 0.319) p < 0.0001
NSAIDs drugs and paracetamol	Diclofenac	138 (31.08%)	42 (14.43%)	180 (24.49%)	2.674 (1.822 to 3.925) p < 0.0001
	Ibuprofen	51 (11.49%)	102 (35.05%)	153 (20.82%)	0.241 (0.165 to 0.351) p < 0.0001
	Ketoprofen	45 (10.14%)	18 (6.19%)	63 (8.57%)	1.711 (0.969 to 3.018) p = 0.064
	Nimesulide	42 (9.46%)	27 (9.28%)	69 (9.39%)	1.022 (0.615 to 1.697) p = 0.934
	Etoricoxib	51 (11.49%)	57 (19.59%)	108 (14.69%)	0.533 (0.353 to 0.804) p = 0.003
	Acetylsalicylic acid	3 (0.68%)	12 (4.12%)	15 (2.04%)	0.158 (0.044 to 0.566) p = 0.005
	Paracetamol	9 (2.03%)	27 (9.28%)	36 (4.90%)	0.202 (0.094 to 0.437) p < 0.0001
	Naproxen	42 (9.46%)	0 (0%)	42 (5.71%)	-
	Indomethacin	33 (7.43%)	6 (2.06%)	39 (5.31%)	3.814 (1.577 to 9.222) p = 0.003
	Meloxicam	30 (6.76%)	0 (0%)	30 (4.08%)	-
NSAIDs acquiring mode	MP	156 (35.14%)	66 (22.68%)	222 (30.20%)	1.847 (1.319 to 2.585) p = 0.0004
	SM	288 (64.86%)	225 (77.32%)	513 (69.80%)	0.542 (0.387 to 0.758) p = 0.0004

MP = medical prescription, SM = self-medication

The results of assessing the level of information of our patients regarding the potential adverse effects of chronic NSAID use have highlighted the following: for 621 (84.49%) patients the most known adverse reactions reported by them were gastrointestinal reactions like abdominal pain (320;

43.54%), peptic ulcer (418; 56.87%), dyspepsia (215; 29.25%); 45 (6.12%) patients know the potential risk of renal adverse events, without being able to specify a specific one; 9 (1.22%) patients reported being aware of the potential risk of decompensation of hypertensive disease or heart failure, and none of

the patients was aware of the possible risk of heart attack with chronic consumption of certain NSAID

molecules (Table III).

Table III

The surveyed patients' level of information about the potential adverse events in the case of chronic consumption of NSAIDs

NSAIDs adverse events known by the respondents	Yes (number and % of respondents)	No (number and % of respondents)
<i>Gastrointestinal damages</i>	621 (84.49%)	114 (15.51%)
<i>Kidney lesions</i>	45 (6.12%)	690 (93.88%)
<i>Cardiac adverse events (decompensation of HTA or heart failure)</i>	9 (1.22%)	726 (98.78%)
<i>Other cardiac adverse events (risk of heart attack, etc.)</i>	0	735 (100%)

Although the NSAIDs benefit from widespread use in the general population and 621 (84.49%) respondents of the present study know very well the drug digestive risks, it was observed that there is also a large number of surveyed patients who are consumers of these molecules, but do not know the potential renal and/or cardiac adverse events (690, 93.88% respectively 726, 98.78%) related with a long-term consumption or with the co-presence of comorbidities. This fact could be supported by their perception of this group of molecules, considered to be relatively safe and harmless (the risk of NSAID use was estimated at 3.4); therefore, some principles of pharmacotherapy permit their unrestricted use. Patient's lack of information, about possible risk of numerous adverse reactions, but especially of CV or renal toxicity of NSAIDs, has been highlighted for a long time by several previous studies [12], and can raise major safety issues in current practice given the wide availability of these molecules without medical prescription.

Only 265 (36.06%) respondents reported a previous consumption of NSAIDs, and 192 (26.12%) of them had experienced one or more adverse digestive events described as: heartburn ($n = 42$; 21.88%), regurgitation ($n = 29$; 15.10%), nausea ($n = 19$; 9.89%), stomach aches ($n = 35$; 18.23%) and associations of these symptoms ($n = 67$; 34.90%). A smaller number of patients have manifested other adverse events: hydrosaline retention ($n = 63$; 8.57%), 10 (1.36%) skin reactions (such as pruritus or cutaneous erythema) and 121 (63.94 %) of all interviewed persons did not show any adverse reactions to previous use of such preparations. 349 (47.48%) interviewed people have reported an occasional history of adverse events for these molecules and 121 (16.46%) of respondents have not recalled if they have ever presented adverse events after using these molecules. Although more than one-third of the participants in this study reported the development of side-events (most frequently GI) following a history of NSAID use, it is noteworthy that these dyspeptic symptoms did not correlate with clinical presentations of patients to highlight endoscopic lesions, according to their personal statements. The importance of this

digestive problem in the general NSAID-consuming population occupies the first place according to recent studies [19], and shows a wide range of variation, up to 58% according to others reports [1].

Following the analysis of the medical history of the interviewed patients, it was observed that the patients presented also several other health-related comorbidities, especially different CV diseases. From the total of 735 NSAIDs users, 636 (86.53%) of them had associated several risk factors, such as various comorbidities, that may increase the risk of ADEs. 444 (60.41%) presented CV comorbidities (e.g. arterial hypertension, chronic heart failure, coronary artery disease), 138 (18.78%) of them presented diabetes mellitus, 84 (11.43%) asthma, 63 (8.57%) kidney disease, 63 (8.57%) peptic ulcer disease, 33 (4.49%) liver disease and 99 (13.47%) did not associated any pathology (Figure 1). There were also patients who had two or more associated comorbidities.

Figure 1.

Types of patients' comorbidities in the studied population

The NSAID molecules most frequently used by the CV patients were diclofenac (OR: 2.674; 95% CI: 1.822 - 3.924), ketoprofen (OR: 1.711; 95% CI: 0.970 - 3.018) and indomethacin (OR: 3.814; 95% CI: 1.577 - 9.222) (Table II). This irrational and inappropriate use of NSAIDs cannot be attributed to the patient's isolation from health care services, as the present study was conducted entirely in the urban environment and the majority of patients (> 80%) had a medium and high educational level.

The close association between a series of health-related comorbidities (especially CV disease) with the principal medical reasons based on which NSAIDs were requested (joint and low back pain), has also been observed and discussed in various aspects by other studies in the field [16].

Conclusions

In conclusion, in this pharmacoepidemiology study, which examined the prevalence and the use patterns of NSAIDs and paracetamol in the general population, it was found that these drugs are mainly consumed as automedication (69.80%), for joint pain treatment (41.22%) by female patients, middle-aged, married and with a medium educational level. The following issues have been identified: erroneous risks perception, a high degree of ignorance regarding these risks, and a low level of knowledge about the potential adverse events resulting from a chronic, abusive or irrational use of NSAIDs. These issues are likely the result of an individual, informational deficit, but also educational, insufficiently practiced by the primary medical and pharmaceutical care staff.

The present study revealed a high proportion of patients with increased risk of significant adverse events, the CV pathologies being a central key (60.41%). Alarming, we found that the choice of the drug molecule for the treatment of pain is often inappropriate and the NSAIDs drugs are used in chronic conditions in which they are contraindicated. Taking into account the potential consequences of NSAIDs prolonged use, the patterns of use in the general population should be monitored more closely in order to identify as early as possible all potential modifiable risk factors. Increased attention should be directed to high-risk groups of patients with various associated comorbidities (cardiovascular, renal etc.) and to those who consume multiple drugs simultaneously.

The problem identified by our study requires efforts to improve the community health education, efforts that will be reflected in reducing the burden of disease and increasing the patient's quality of life. Our study being limited to the urban environment of a certain geographical area, there is the possibility of significant regional differences in NSAIDs use patterns across the country.

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