Original Research

Determinants of self-medication with NSAIDs in a Portuguese community pharmacy

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ABSTRACT[*]

Background: Non-steroid anti-inflammatory drugs (NSAIDs) are a widely used therapeutic group in the world, and particularly in the Portuguese population.

Objective: To compare NSAID's use by prescription and self-medication acquisition and to determine the pattern of indication of NSAIDs, their usage profile and possible implications for patients' safety.

Methods: A cross-sectional design was used where individuals presenting at a community pharmacy requesting NSAIDs during the study period (one month) were invited to answer a face-to-face interview where socio-demographic characteristics, the indication pattern and previous experience of side effects were assessed. A follow-up interview was performed one week later to assess the incidence of adverse effects. The study was ethically approved.

Results: A sample of 130 NSAIDs users was recruited, comprising mostly women (n=87; 66.9%), actively employed (n=77; 59.2%) and presenting a mean age of 49.5 years old (SD=20.49). An equal proportion of individuals acquired NSAIDs by self-medication and with medical prescription (n=65; 50%). Over 4/5 of patients (n=57; 87.7%) acquiring NSAIDs without a prescription were self-medicated by their own initiative, and only 10.8% (n=7) had been advised by the pharmacist. The most commonly acquired active substances were ibuprofen and diclofenac. Self-medicated users more frequently resorted to topical NSAIDs following short term treatments. The major underlying condition motivating NSAIDs sought were musculoskeletal disorders (45.0%), regardless of the regimen. An important proportion of prevalent users of NSAIDs reported previous experience of adverse effects (11.3%). One week after initiating NSAID therapy, a small proportion of patients reported incidence of adverse effects.

Conclusion: Self-medication with NSAIDs is sought for numerous medical conditions. Reported adverse effects (prevalent and incident) confirm the need for a more rational use of NSAIDs and ongoing pharmacovigilance.

Keywords: Anti-Inflammatory Agents, Non-Steroidal; Drug-Related Side Effects and Adverse Reactions; Pharmacies; Cross-Sectional Studies; Portugal

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INTRODUCTION

Non-steroid anti-inflammatory drugs (NSAIDs) are a widely used therapeutic group in the world and particularly in the Portuguese population. This holds true for both prescription regimes and self-medication.[1] Culturally, there is a notion of safety or low risk regarding these drugs, leading to a widespread use of these medications for common clinical situations such as fever, headaches, dysmenorrhoea, acute pains and/or chronic musculoskeletal conditions.[2,3]

The Portuguese law defines NSAIDs as prescription-only medicines (POM) or over-the-counter drugs (OTC), depending on the active ingredients and/or the dosages. Portugal is primarily state financed, having a National Health Service, where prescription-only NSAIDs are co-paid in 37%.[4] Since 2005, OTC drugs are available not only in pharmacies but also in specialized outlets[5] and since then, NSAID acquisitions have increased dramatically, becoming, in 2013, the 6th most acquired therapeutic group in Portugal.[6] This is alarming, since the literature refers that in countries where over-the-counter NSAIDs can be acquired outside of pharmacies, the increase in NSAID consumption and the decrease in professional counseling (by physicians and pharmacists) may pose a serious risk for a substantial increase in adverse effect occurrences.[7] Important prescription measures have been recently implemented, as this overconsumption raises health and financial concerns. Portugal is currently in an economic crisis and the population's financial deprivation has been suggested to diminish physicians' appointments[8], which in turn may lead to higher self-medication rates.

NSAID use patterns have been documented for various populations. In Italy, NSAID usage is common and more prevalent in the elderly and in females.[9] NSAID adverse effects have been extensively surveyed, particularly in the last decade, and in high risk patients, including the elderly.[10] The numerous factors inherent to the elderly, such as comorbidities and polypharmacy, as well as physiological changes that modify pharmacokinetics and pharmacodynamics, make the aged highly susceptible to develop drug related problems.[11] Literature supports the higher incidence of NSAID adverse effects in the elderly.[12] A Spanish study conducted in the elderly determined that NSAIDs are among the three groups with the highest percentage of potentially inappropriate medication, especially in patients with moderate and high blood pressure, heart failure and chronic kidney disease.[13] The most prevalent NSAID adverse effects are

gastrointestinal or cardiovascular in nature[10,11,13-17], with a prevalence of gastrointestinal adverse effects as high as 20%.[18] Gastrointestinal NSAID adverse effects pose a particular challenge since they may occur with short term high dosage therapies (abdominal pain, diarrhoea), as well as long term low dosage therapies (intestinal or gastric ulcers and/or perforations).[19] Although NSAIDs have been long used, the recent changes in the pharmacovigilance system suggest that ongoing evaluation of the usage profile of all drugs is extremely important, as real world tends to shift the indications initially approved, leading to unknown safety and effectiveness profiles.[4] Small scale studies are therefore emerging, which modestly contribute to an in-depth knowledge of the pattern of use.[20]

This study aims to contribute to enlighten the reality of NSAIDs acquisition and consumption pattern in Portugal and its relation with adverse effects and patient safety, namely to ascertain if self-medication is or not a risk factor for the occurrence of adverse reactions to these drugs. Adverse effects and self-medication have not been studied thoroughly in Portugal, thus studies in this field are of great importance.

This study aimed to compare NSAIDs acquired by prescription and self-medication regarding its indication, route of administration, treatment duration, reported adverse effects and socio-demographic profile of individuals. The study also aimed to ascertain how previous experience of side effects to NSAIDs influenced the acquisition pattern.

METHODS

An observational descriptive cross-sectional study was undertaken, with information being collected for each individual at one moment in time.[21] The information collected in this moment referred to present and past exposure. There was a subsample being re-evaluated after one week of exposure, constituting an exposure cohort. Recruitment of individuals was pursued over a one month period (August 2013) in one community pharmacy.

Population and sample

Sample size was estimated using Epi Info, version 7, considering the population served by each community pharmacy in Portugal, defined by law to be 3500 inhabitants[22], a prevalence of NSAIDs use in the general population of 19.4%[23] and a confidence interval of 95% (CI=95%). The estimation was for 384 participants. However, we have assumed that pharmacy users may visit the pharmacy every three months. Since the study could only last one month, we should be able to recruit 128 individuals.

Sampling was non-random, as one single pharmacy was chosen by feasibility issues (convenience sample), where the pre-registration student was in charge of patient recruitment between 10 am and 10 pm. All individuals entering the pharmacy during the study period were invited to participate in the study, constituting an exhaustive sample.

One single inclusion criterion was considered, demonstrating intention to acquire an NSAID for himself/herself or for a minor under his/hers responsibility, with or without prescription. Exclusion criteria considered were inability to communicate in Portuguese and/or English, especially by language barriers; evident cognitive impairment or refusal to participate in the study.

Data collection

A structured questionnaire was developed to be administered face-to-face to patients, and filled in by the main researcher, which was divided into 8 sections:

1. Socio-demographic characterization (e.g. age, gender, civil status, educational level and professional situation);
2. Therapeutic classification: active substance, dosage, pharmaceutical form, package dimension, frequency of use, duration of therapy and route of administration;
3. Reason for purchasing the drug: indication (complaint leading to the need of drug);
4. Person who identified the need for such therapy (prescription-based or self-medication);
5. Previous exposure to NSAIDs;
6. Legal classification of the NSAID purchased: non-prescription medicine or prescription only;
7. Concurrent medications taken;
8. History of previous adverse effects to NSAIDs.

Patients were grouped in either the Prescription group or the Self-Medication group. All situations where the patient did not have a prescription at the moment of purchase were considered 'self-medication'. Patients whose symptoms guided the pharmacist to advice using an NSAID, and those acquiring an NSAID solely on the basis of their will, were also considered self-medicating patients.

Patients were classified as first-time users if they had never been exposed to an NSAID or prevalent users if there was previous exposure.

One week after the NSAID acquisition, patients were asked by telephone to answer a second questionnaire to evaluate possible adverse effects arising from NSAID exposure.

Data analysis

Data was analysed using SPSS (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp) and included tests to answer research questions posed. We used parametric tests, once normality distribution was verified (Kolmogorov-Sminorf Test), namely the Student's t-test and the Chi-square or Fisher, as appropriate, considering a significance level of 0.05. The research questions were:

1. Do socio-demographic characteristics influence self-medication with NSAIDs?

Table 1. Comparison of the socio-demographic profiles for prescription and self-medication regimens.

Variable	Category	Total		Prescription		Self-medication		p-value
		n	(%)	n	(%)	n	(%)	
Gender	Male	43	(33.1)	23	(35.4)	20	(30.8)	0.576[a]
	Female	87	(66.9)	42	(64.6)	45	(69.2)	
Civil state	Married	72	(55.4)	34	(52.3)	38	(58.5)	0.480[a]
	Unmarried	58	(44.6)	31	(47.7)	27	(41.5)	
Academic status	Illiterate	6	(4.6)	2	(3.1)	4	(6.2)	0.816[b]
	High school or lower	89	(68.5)	45	(69.2)	44	(67.7)	
	University degree	35	(26.9)	18	(27.7)	17	(26.2)	
Professional situation	Active	77	(59.2)	38	(58.5)	39	(60.0)	0.858[a]
	Not active	53	(40.8)	27	(41.5)	26	(40.0)	

n - number of individuals in the group, (%) - percentage, p - statistical significance, [a] Chi-square test, [b] Fisher's exact test.

2. Are the pharmacotherapeutic groups of NSAIDs determinants of self-medication?
3. Does the legal classification of medicines determine practice?
4. Does the route of administration and treatment duration influence self-medication?
5. Is previous exposure to NSAID a determinant of self-medication?
6. Are the presenting conditions determinants of self-medication with NSAIDs?
7. What are the most common drugs taken simultaneously with NSAIDs that have potential interactions?
8. Does previous experience of adverse effects with NSAIDs influence self-medication?
9. The incidence of adverse effects with NSAIDs is higher in those previously experiencing adverse effects?

Outcome measures

The main outcomes considered were previous exposure to adverse effects and incidence of adverse effects.

Ethical approval

The study protocol was approved by the Ethics committee of the Institute of Health Sciences Egas Moniz. Non-participants were not characterized as this committee rejected the possibility to use refusal forms.

RESULTS

Socio-demographic characterization of the population

The initial sample was constituted by 159 individuals, where 29 have been excluded because they were using low dose acetylsalysilic acid formulations (dosage equal or below 300 mg), for which the indication is not anti-inflammatory but antiplatelet forming.

From the final sample of 130 individuals, the majority were female (n=87; 66.9%). The mean age of study recruits was of 49.46 years old (SD=20.49), ranging from 3 to 87 years old. Most participants were married (n=72; 55.4%), employed (n=77; 59.2%) and with high school education or lower (n=89; 68.5%).

Characterization and comparison of the socio-demographic profiles for prescription and self-medication regimens

Table 1 summarizes the differences in socio-demographic profiles between patients who acquired NSAIDs with a prescription and those that self-medicated, with the same number of individuals in each group (n=65). No characteristics were found to be associated with the option to acquire under medical supervision or under self-medication ($p>0.05$ for all variables).

Distribution of NSAIDs acquired by chemical group

Propionic acid derivatives were the most requested NSAID (n=63; 48.5%), followed by acetic acid derivatives (n=29; 22.3%), and sulfonanilides derivatives (n=17; 13.1%), as depicted in table 2.

More than half of prescriptions were for propionic acid derivatives (n=41; 63.1%), which were also predominant for self-medications (n=22; 33.8%). However, the prescription group evidenced a higher rate of acetic acid derivatives (n=10; 15.4%) and COX-2 selective inhibitors (n=8; 12.3%), suggesting that the pharmacotherapeutic group is a determinant of self-medication ($p<0.005$).

Legal classification of purchased NSAIDs

Most NSAIDs acquired were prescription-only NSAIDs (n=106; 81.5%), representing more than three quarters of all NSAIDs purchased. Most of these were acquired with a prescription (n=61; 57.5%), but a still considerable proportion did so without presenting a prescription (n=45; 42.5%). For over-the-counter NSAIDs, most of them were acquired under self-medication, (n=20; 83.3%), with only 4 of them being prescribed (16.7%). The vast majority of prescribed NSAIDs (93.8%) were legally classified as prescription-only, whereas 45% of purchased NSAIDs without prescription were also prescription-only. These findings suggest that although regulations in place are not strictly followed, there is a tendency to obey the law ($p<0.001$) (Table 2).

Route of administration and treatment duration

Most NSAIDs purchased during the study period were to be administered orally, both in the prescription and in the self-medication group (n=58;

Table 2. Distribution of NSAIDs chemical groups in prescription and self-medicated patients.

Chemical group	Drugs	Legal classification in Portugal	Acquisition regimen	
			Self-medication	Prescription
Salicylates	Acetylsalicylic acid 500mg	OTC	7	0
COX2 selective inhibitors	Celecoxib 200 mg	POM	0	2
	Etoricoxib 60mg, 90mg	POM	1	6
Propionic acid derivatives	Ibuprofen 200mg	OTC	2	0
	Ibuprofen 200mg/ml	OTC	5	3
	Ibuprofen 400mg, 600mg	POM	11	25
	Naproxen 250mg, 500mg	POM	0	8
	Cetoprofen 100mg	POM	0	1
	Cetoprofen 100mg/2ml	POM	0	1
	Picetoprofen 18mg/g, 20 mg/g	POM	4	1
	Dexcetoprofen 400mg	POM	0	2
Acetic acid derivatives	Diclofenac 50mg, 100 mg	POM	8	5
	Diclofenac 75mg/3ml	POM	0	1
	Diclofenac 10mg/g, 23.2mg/g, 0.074%	OTC	11	4
Oxicam derivatives	Meloxicam 15mg	POM	0	2
Sulfonanilides derivatives	Nimesulide 100mg	POM	14	3
Anthranilic acid derivatives	Etofenamate 100mg/ml	POM	2	0

POM = Prescription only medicines; OTC= Over-the-counter

89.2% and n=48; 73.8%, respectively), followed by topical NSAIDs (n=5; 7.7% and n=17; 26.2%). Intramuscular NSAIDs were exclusively acquired with prescription. These findings are somehow consistent with the results formerly presented as all intra-muscular NSAIDs are prescription-only medicines, whereas most topical ones as classified as OTC medicines (Table 3).

The duration of treatment was classified considering short-term treatment to be less than 1 week, medium-term between 1 and 4 weeks and long term any treatment lasting over 1 month, suggesting chronic use. Short-term was the most commonly found treatment in both regimens, being slightly more frequent in self-medicated patients (n=53; 81.5% vs n=39; 60.0%). Most medium-term treatments were acquired with prescription and long-time treatments showed approximately the same proportion in both groups (Table 3). Data suggests that both the route of administration and treatment duration are associated with NSAID self-medication (p<0.001).

Previous exposure to NSAIDs

Most patients were classified as prevalent users (n=109; 83.7%), among which only 56.0% were included in the self-medication group (n=61). Twenty one patients were incident users (16.2%), the majority of whom were purchasing a prescribed medicine (n=17; 81.0%). Data indicates that these variables are associated, suggesting self-medication may occur when previous experience has been obtained following medical indication (p=0.002).

Among prevalent users, most of them were acquiring the NSAID according to their own will and judgment (n=56; 91.8%), while most incident patients were acquiring the NSAID due to advise from the pharmacist (n=3; 75%). The majority of self-medicating patients (93.8%) was a prevalent user, which suggests that previous exposure to an NSAID leads to a higher probability of self-medication (p=0.005).

Presenting conditions for purchasing NSAIDs

The most common presenting condition was musculoskeletal disorders (n=58; 45.0%), with an homogenous distribution between cases of prescription and self-medication. Prescription patients presented an important representation of toothache situations (n=11; 17.2%). All kidney disease patients acquired the NSAID presenting a prescription. There was a high representation of acute pain and/or inflammatory states in self-medication (n=17; 26.2%), followed by flu-like diseases, feverish diseases and upper airways/ear infections (n=16; 24.6%), as well as acquisitions to have a “stock” of the NSAID at home (n=2; 3.1%). Data suggests that the presenting condition influences self-medication (p=0.010) (Figure 1).

Polypharmacy and potential interactions

Most patients acquiring NSAIDs were simultaneously taking other therapeutic classes (n=75; 57.7%), in even proportion between prescription and self-medicating patients (p>0.05). The most commonly found pharmacotherapeutic groups taken simultaneously were antihypertensive

Table 3. Route of administration and treatment duration in prescription and self-medication regimens

Variable	Categories	Total		Prescription		Self-medication		p-value
		n	(%)	n	(%)	n	(%)	
Route of administration	Oral	106	(81.5)	58	(89.2)	48	(73.8)	0.005[a]
	Topical	22	(17.0)	5	(7.7)	17	(26.2)	
	Intramuscular	2	(1.5)	2	(3.1)	0	(0.0)	
Treatment duration	Short term	92	(71.3)	39	(60.0)	53	(81.5)	0.005[a]
	Medium term	21	(16.3)	17	(26.2)	4	(6.2)	
	Long term	16	(12.4)	9	(13.8)	8	(12.3)	

n - number of individuals in the group, (%) - percentage, *p* - statistical significance, [a] Fisher's exact test.

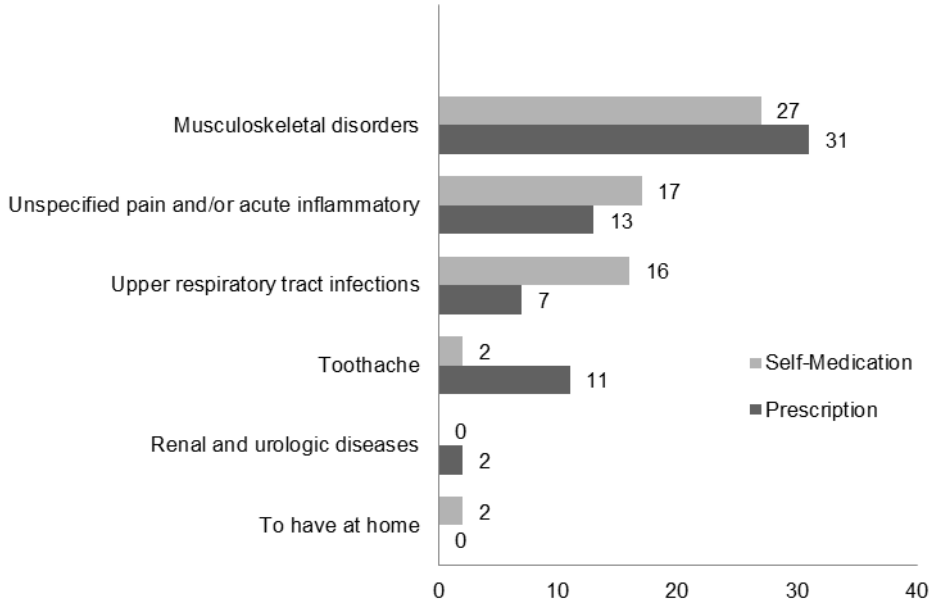

Figure 1. Reasons for NSAID purchase in prescribed and self-medication regimens.

drugs (n=38), followed by lipid-lowering drugs (n=17), oral anti-diabetic drugs (n=12), anxiolytic drugs (n=15) anti-acid/anti-ulcer drugs (n=11), oral contraceptives (n=8) and antidepressant drugs (n=7). Worth noting that many of these therapeutic groups have drug-drug interactions with NSAIDs described in the literature.

Six patients (4.6%) were taking two NSAIDs simultaneously: naproxen and celecoxib; ibuprofen and eterocoxib; picetoprofen and diclofenac; picetoprofen and flubiprofen; eterocoxib and diclofenac; and dual diclofenac, suggesting irrational drug use.

Characterization of previous side effects

There was a prevalence of 13.1% patients reporting previous adverse effects to NSAIDs (n=17), where 2 patients reported previous side effects to more than one NSAID. Table 4 displays the number of patients in the sample taking the medicine at the time of study (N) and those previously experiencing adverse effects with that same medicine (n), not necessarily the same patient.

Table 4. Absolute and relative frequencies of drug that previously caused adverse effects and description of side effects.

NSAID	N	n
Ibuprofen	46	7
Diclofenac	32	3
Nimesulide	18	1
Naproxen	9	1
Etoricoxib	8	3
Acetylsalicylic acid	7	1
Piroxicam	0	1
Total	**130**	**17**
Side effects	**n**	**(%)**
Dyspepsia	9	52.9
Hypersensitivity	3	17.6
High blood pressure	2	11.8
Constipation	1	5.9
Nausea and vomiting	1	5.9
Dyspnea	1	5.9
Total	**17**	**100.0**

The frequency of side effects shows that more than half of all effects were under the form of dyspepsia (table 4). Each adverse effect was distributed by the NSAID that self-reportedly provoked it. Increased blood pressure cases were associated with etoricoxib. Constipation was associated with naproxen, nausea and vomiting with ibuprofen, dyspnea with piroxicam, hypersensitivity with ibuprofen, diclofenac and acetilsalylic acid. Abdominal pain was associated with diclofenac (n=2), nimesulide (n=1), etorocoxib (n=1) and ibuprofen (n=5).

The proportion of patients experiencing previous side-effects was evenly distributed between prescription and self-medication, suggesting these two phenomena to be independent ($p>0.05$).

One week after NSAIDs acquisition, from the initial 159 patients, only 31 answered the second questionnaire, invalidating bivariate analysis. From these 31 patients, only 3 reported adverse effects (9.7%). The drugs involved were ibuprofen and nimesulide purchased as self-medication (n=2) which caused stomach pain in both patients, and prescribed etoricoxib (n=1) which was associated with high blood pressure. All 3 patients had already previously reported adverse effects to NSAIDs and the patient taking etoricoxib had previously suffered from high blood pressure with the same drug. This data suggests patients with previous experience of adverse effects may be at higher risk of developing new and repeated adverse effects.

DISCUSSION

Previous studies confirm our findings that NSAIDs are mostly sought by young active married females.[9,24,25]

NSAIDs were evenly acquired upon presentation of a medical prescription and by self-medication (50%), consistent with a previous Italian study[9], but double from the reported in the Portuguese urban population.[26] However, it should be noticed that the latter study did not focus on NSAIDs specifically but rather on the overall self-medication pattern. Additionally, one may consider that the present financial crisis Portugal is facing could impact on self-medication as Mendes *et al*. have pointed that individuals who seek the Portuguese National Health Service (PNHS), as opposed to private health services, display a higher tendency for self-medication.[26] The increase in moderating fees recently witnessed in Portugal, may have conditioned access to PHNS and indirectly led to an increase in self-medication. Moderating fees have been introduced in the PNHS in 1986, imbedded in the 2nd revision of the Constitution. These represent direct partial payments and are referred to as "mainly free health service". These are payments the citizens make when they use the services and values differ according to the type of service; they exist for citizens to refrain from abusing the service.

Pain was self-reportedly the main reason for acquiring NSAIDs in this study, which is in line with previous studies.[9] Data suggests that acute, painful states are associated with self-medication. This finding may have safety implications as it was suggested that among patients seeking NSAIDs following musculoskeletal complaints, 6% incur in adverse events.[27]

Prescription-only represent the majority of purchased NSAIDs, but an important proportion of self-medicating patients acquired prescription-only medicines, which is a worrisome finding. Although prescription-only medicines can only be purchased when presenting a medical prescription, as the functioning of the health care system leads to long waiting time for medical appointments. This may create a dilemma between blindly obeying the law and deprive the patient from needed therapy or dispense the medicine ahead of prescription, where the patient assumes the compromise to present it later. However, creating exceptions may lead pharmacists to fall into situations of malpractice, when clinical judgment is not correctly applied. Even though this malpractice is not properly documented in the literature, it certainly exists in Portugal, as it does in other countries, such as Brazil and Spain, two culturally similar countries.[23,28] However, it should be noted that in such situations, it would be even more important for the pharmacist to intervene in the interest of patient safety, namely by ensuring there were no previous side-effects, that other medicines taken simultaneously do not interact, and that if the therapy is indeed to be prolonged, perhaps it would be appropriate to evaluate if the patient may be considered at high risk of gastrointestinal bleeding, needing additional gastroprotection.

Low health literacy or the idea of the ineffectiveness of certain doses not subject to medical prescription, allied to poor pharmacist's counseling are probably playing a significant role in the phenomenon of self-medication with prescription-only NSAIDs. However, it should be noted that all medicines purchased without a prescription were considered as self-medication cases. This is a methodological option that may be discussed as in some cases, patients were purchasing a medicine following the doctor's recommendation (e.g. to be taken for 1 month and the package lasted only 15 days or recommended over the phone, etc) and simply not having the physical prescription at the moment. This fact assumes higher importance when analyzing pediatric formulations. Nonetheless, the effects of this practice on patient safety should be considered, as the safety profile is the main reason determining the legal classification of medicines.

Another point that should be considered is the inclusion of children in the study population, as the therapeutic options for them available on the market are scarce. In fact, currently, only paracetamol and ibuprofen exist in pediatric formulations (both as prescription-only and as OTC), which may have skewed results presented. However, analysis was performed excluding children and proportions reported did not differ significantly. Therefore, the authors opted to include children. This option is also justified because data on safety and effectiveness profile of NSAID use in children are scarce. Although we could not study this sub-sample in depth, due to its limited size, the high exposure to ibuprofen was consistent with international data, which suggests a possible association with asthma exacerbation.[29] Given the safety implications, in future studies, we may want to address this topic using a different study design.

The vast majority of self-medicated patients adopted such behaviour by their own initiative. A small proportion of the sample was classified as incident users, and the majority of these cases occurred on prescription regimes. Still, it is worth noting that there were 4 cases of self-medicating incident users. This reinforces the notion that prior experiences are a key factor in self-medication for NSAIDs and emphasizes the role of the pharmacist, who should advice patients about the most appropriate therapy in light of their current clinical status and present comorbidities.[30,31]

The pharmacotherapeutic group was associated with self-medication, where an important proportion opted for propionic acid derivatives, probably due to the safety illusion associated with this class, which needs to be addressed in the general population by more active information campaigns.

In self-medication, there was a small number of medium termed treatments, probably because when symptoms show themselves persistent, the patient has a tendency to go visit a physician. The somewhat high number of self-medication cases for long term treatments can be justified by the small price difference resulting from a low co-payment attributed by the PNHS when presenting a prescription. On the other hand, the national

economic conjecture coupled with the increase of user fees can help to explain many situations of ongoing treatments that do not present a prescription at the time of purchase.

In addition to these factors, the poor information provided by the physician and/or pharmacist about the duration of treatment may induce the patient to assume continuity of treatment, an aspect with potential impact on patient safety that should be more closely monitored by responsible bodies for observing compliance with best standards of practice. This should be a concern since the literature suggests that over 20% of OTC NSAID users prolong treatment duration for over 7 days.[32] The Portuguese Pharmaceutical Society, through their statutes, foresees as an important role of the pharmacist, ensuring rational use of medicines. All pharmacists do this, but the degree in which they actively engage in advanced services, most of which demand an updated pharmacotherapeutic profile, is variable. There are studies suggesting that only 20% of community pharmacies are providers of pharmaceutical care.[33] This suggests there are missed opportunities for pharmacists.

The route of administration was associated with self-medication. Physicians seem to prefer prescribing oral NSAIDs, whilst self-medicated patients exhibited a tendency for topical NSAIDs. Although this observation may also be related with the legal classification, it should be noted that it has been documented that topical NSAIDs display the same efficacy in certain musculoskeletal pathologies as oral NSAIDs, and yet display considerably less side effects.[34-37]

The wide spectrum of NSAID use, coupled with the evidenced established here that self-medications are mostly based on previous experiences, point toward a collective medical responsibility in prescription. Whenever a health professional advises or prescribes a medication, he/she must be aware not only of the present situation, but must also be aware of the future. Whenever a patient encounters a new medication, this event must be seen as a new opportunity for the establishment of new self-medication habits. In the future, NSAID prescription/advising should be addressed by health professionals to foster a more rational use of medicines.

Prevalent adverse reactions

The prevalence of adverse reactions from previous exposures was 11.3%, with 3 main NSAIDs involved, ibuprofen, diclofenac and etoricoxib. Gastric complications represented 52.9% of adverse reactions reported in this study, a much higher value than the 20% reported elsewhere[18,38], being dyspepsia, abdominal pain and diarrhoea those considered more common. Adverse gastrointestinal effects are classified as a very common effect in most package inserts, which means that they are likely to occur in more than 10% of subjects exposed.[1] Hypersensitivity was the second most self-reported manifestation, followed by increased blood pressure. The prevalence of hypersensitivity (including dyspnea) to NSAIDs in the population is 2.5%, which may be greater in patients with certain pathologies (chronic rash, nasal polyps and asthma).[39] The two cases of elevated blood pressure were associated with etoricoxib, an effect described in the product characteristics as common, i.e., occurring between 1-10%.[40] Although the small power of this study leads to careful interpretation of the findings, data suggests the known safety profile of NSAIDs may be shifted by real-life situations, such as off label use, polypharmacy or even patients' characteristics.

Incident adverse reactions

Less than 10% of the telephone surveyed patients reported having experienced a new adverse reaction to the drug taken at the time of study (n=3; 9.7%). This value is more in line with the literature. However, it should be noted that this subsample was very reduced to draw any valid conclusions. However, it is important to note that the 3 patients experiencing adverse effects had previously reported adverse effects with other NSAIDs, or even with the same drug, suggesting irrational use of medicines.

Limitations

This study, although reporting important information, presents some important limitations, namely the fact that it portraits a study undertaken in one single pharmacy, making extrapolations invalid. However, it should be noted that the general characteristics of the sample are in line with national data.[41] All data collected about experience of adverse effects was retrospective, favouring recall bias. Information was collected by a pre-registration pharmacist, leading to a potential social desirability bias. On the other hand, because the researcher was not familiar with regular clients, the probability of bias was minimized, including selection bias.[41] The inexperience of the main researcher also had the downside of not taking these opportunities where adverse effects have been identified to actively engage in pharmacovigilance, by notifying the competent authorities. Perhaps the most important limitation was the inability to include a larger sample in the prospective evaluation of incident adverse effects, which limited the in-depth analysis of the findings. This issue should be more carefully planned in future studies. This study did not focus on pharmacists' interventions. However, it will be interesting in the future to use our results to develop specific training for community pharmacists to more actively engage in interventions aimed at increasing NSAIDs users' safety, particularly if targeted at patients with high risk of upper gastrointestinal complications, namely the elderly.[42]

Self-medicated patients displayed good choices of active substances for their conditions, as well a general good sense for frequency of use. Still, the widespread use of NSAIDs, whether with a prescription or through self-medication, is leading to an illusion of safety of these drugs in the population. Polypharmacy and the presence of comorbidities need to be thoroughly addressed by all health professionals whenever they are prescribing or advising NSAIDs, as it was found that self-

medication is used in numerous medical conditions. This information should help shape future public health campaigns and advanced pharmaceutical interventions for a more rational use of NSAIDs.

CONFLICT OF INTEREST

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