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Non-steroidal anti-inflammatory drugs and paracetamol in self-therapy of various disorders in students of different fields of study

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Abstract: Over-the-counter non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol are most commonly the first-line pharmacotherapy in combating different pain and inflammatory disorders and fever. Unfortunately, those drugs might have serious side effects, especially when they are used in an inappropriate way. The aim of the study was to explore various aspects of NSAIDs and paracetamol use in the self-therapy of miscellaneous disorders in young adults. The questionnaire-based survey comprised 250 consecutive students aged 22.1 ± 1.9 years (189 women) of diverse fields of study. The drugs were applied in clinical conditions in which they should be avoided including asthma attack (1.2%), vomiting (2.4%), malaise and depression (3.6%), in autumn and winter as a preventive measure against infections (14.0%), heartburn (2.0%) and during food poisoning (16.0%). As many as 6.0% of the students claimed that studied medications are ultimately free of adverse reactions. Men more frequently than women used NSAIDs and paracetamol during alcohol consumption (49.2% vs 30.7%, p = 0.009, respectively) but less often were aware that there are maximum doses of medications which should not be exceeded (57.4% vs 76.7%, p = 0.003, respectively). The students of medical-related degree courses (n = 82) compared with individuals of other subjects (n = 168) declared they more often have the custom of always reading medications' leaflets (46.3% vs 31.0%, p = 0.017, respectively). Side effects of medicines were reported

by 65 participants — 26.0%. In conclusion, students' knowledge about NSAIDs and paracetamol is low. Participants do not search for information on drug related endangerments, the medication group choice for the given disorder is often inappropriate and the drugs are applied in conditions in which they are contraindicated.

Key words: non-steroidal anti-inflammatory drugs, paracetamol, questionnaire, adverse effects, alcohol, package leaflet.

Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) form a group of medications with analgesic, antipyretic, anti-inflammatory actions and in most cases with platelet aggregation inhibitory properties [1, 2]. Paracetamol exerts only remarkable analgesic and antipyretic effects [3]. The most frequent indications for NSAIDs comprise acute and chronic inflammatory processes, whereas NSAIDs and paracetamol are most commonly the first-line pharmacotherapy in combating pain disorders of different origin and fever [4]. The list of contraindications to NSAIDs application is relatively short and includes active peptic ulcer disease, pregnancy and breast-feeding, severe liver and kidney insufficiency, allergy to NSAIDs and hemorrhagic diathesis. Paracetamol must not be utilized in hypersensitivity to any component of drug formulations, severe hepatic or renal failure, glucose-6-phosphate dehydrogenase or methemoglobin reductase deficiencies [5, 6].

NSAIDs and paracetamol are distributed via the over-the-counter sale (OTC) and are extremely popular [7]. Considering the number of drugs' packages per person in Europe, Polish citizens are only surpassed by Frenchmen, while the Polish market alone of just paracetamol, ibuprofen and acetylsalicylic acid formulations exceeds 300 million US dollars yearly [8, 9]. Unfortunately, NSAIDs and paracetamol might have serious side effects involving not only gastrointestinal tract, kidneys, nervous system or hematological complications, but almost every organ, especially when they are used in an irrational way, with no respect to safety rules [10–13].

Although adverse reactions related to NSAIDs use are mainly associated with older people, they also concern adolescents and young adults [14]. The awareness of NSAIDs endangerments in this part of population might reduce not only present but also future drugs complications. Nevertheless, available data on young people and students knowledge about NSAIDs and paracetamol are scarce and distressing [15, 16].

The aim of the study was to explore various aspects of NSAIDs and paracetamol application in the self-therapy of different disorders in Polish students of different fields of study including disorders treated with the drugs, medications safety and efficacy, the medicines' group choice, treatment restrictions, preparations dosing and adverse reactions.

Material and methods

A specially designed questionnaire with closed-ended questions was dispensed to the students who consented to take part in the survey. It contained the table of most common trade names of OTC NSAIDs (section A) and paracetamol formulations (section B) on the Polish

market (Table 1) [6]. The combined drugs with an NSAID and paracetamol were placed in the section A and complex formulations containing paracetamol and other substances, but none of the NSAIDs, in the section B. The questionnaire was divided into sections devoted to the causes of the drugs administration, the medications' efficacy appraisal, their safety assessment, the awareness of maximum doses existence, the comparison of NSAIDs and paracetamol preparations application, combinations of various formulations, the issue of drinking alcohol at the time of the drugs utilization, habits of reading medicines package leaflets, information on medications obtained from pharmacists and physicians, and finally the matters of side effects.

Table 1. The most popular formulations names of over-the counter (OTC) non-steroidal anti-inflammatory drugs (NSAIDs — Section A) and paracetamol (Section B) on the Polish market [6].

SECTION A			
Advil	Calcipiryna	Meloxilek	Pyralgin
Aleve	Cefalgin	Metafen	Ring N
Alka-Prim	Cholinex	Miraspryn	Sachol
Alka-Seltzer	Dexak	Modafen	Salpirin
Anapiryna	Dolores	Moilec	Saridon
Anapran	Dexprofen	Nalgesin	Scorbolamid
Ascalcin	Erka	Naproxen	Septolux
Ascodan	Etopiryna	Naxii	Seractil
Aspicam Bio	Excedrin	Neopyrin ASA	Strepsils
Aspirin	Ibalgin	Nurofen	Tabletki przeciw grypie
Aspirin Complex	Ibum	Opokan	Tantum Verde
Asprocol	Ibumax	Panpiryna	Upsarin
Bestpirin	Ibuprofen	Paranalgin	Vostar
Bolinet	Ibuprom	Polopiryna	Voltaren
SECTION B			
Acenol	Codipar	Gripblocker	Pabitan
Analget	Coldrex	Gripex	Panadol
Antidol	Dafalgan	Gripotaxin	Paracetamol
Apap	Efferalgan	Grippokaps	Solpadeine
Benuron	Etoran	Grippostad	Tabcin
Calpol	Febrisan	Grypolek	Tazamol
Cerugrip	Fervex	Grypostop	Theraflu
Choligrip	Flucontrol	Novo-Gesic	Vicks

The study group constituted 253 consecutive individuals but 3 of them (1.2%) declared they do not use OTC NSAIDs and paracetamol entirely. In effect, the analysis included 250 students, who at least once a year use the surveyed drugs, aged 19–27 years (average

age: 22.1 ± 1.9 years; 61 men, 189 women). The study fields of the participants covered medicine, dentistry, economy, administration, environment protection, German, Polish or Arabic philology, law, fashion design, advertising, biotechnology, chemistry, physiotherapy, finances and banking, pedagogy, pharmacy, emergency medicine, history, nursery, management and marketing, physics, geography, medical rehabilitation, science of commodities, power engineering, electronics and telecommunication.

The statistical analysis was performed with the Statistica 10.0 PL version (Statsoft, Tulsa, USA). The Kolmogorov-Smirnov test was applied to examine a normal distribution. The mean values of certain parameters were compared with the use of the Student-t test or the Mann Whitney U test for the quantitative variables and chi-square test for qualitative variables. The statistical significance was considered when $P < 0.05$. The data are presented as mean values ± standard deviation (SD) or as a percentage share of the patients in the analyzed groups.

This study was performed in compliance with the Declaration of Helsinki.

Results

Beside inflammatory disorders and fever NSAIDs and paracetamol were applied in clinical conditions in which those drugs should be avoided: asthma attack (in 1.2% of the study participants), vomiting (2.4%), malaise and depression (3.6%), in autumn and winter as a preventive measure against infections (14.0%), in heartburn (2.0%) and during food poisoning (16.0%, Table 2).

As many as 84.4% of the students assessed the medications as efficient, whereas 13.2% claimed they have a poor curative effect and 3.6% of the survey participants perceived the drugs as devoid of therapeutic action.

When the safety of the studied preparations was rated, 52.0% of the individuals appraised them as safe with occasional adverse effects and allergic reactions when administered with respect to safety measures of the producer. Almost two thirds (65.2%) of the respondents were aware that the risk of side effects increases with time of drug therapy and soaring medicines doses. Twenty nine per cent knew that in rare cases NSAIDs and paracetamol might be harmful, even though they are applied in right amounts. In the eyes of 6.0% of the students the drugs are ultimately free of adverse reactions.

In the part of the study devoted to drugs doses limitations, 72.0% of the respondents were aware that although the medications are sold OTC, there is a maximum dose which should not be exceeded when combining different preparations within one group of the medicines. Fourteen per cent alleged that there is a maximum dose of each preparation but when needed one can use other related preparation. Over a half (53.2%) of the study group do not combine various NSAIDs or different paracetamol preparations, 24.0% utilize many NSAIDs and/or paracetamol drugs at the same time with the respect to the total maximum dose, whereas 23.2% might overdose medications of the same group, not paying attention to the combined doses limits. Almost one in five (18.0%) denied the existence of dose constraints in OTC preparations and 0.8% perceived them as absolutely harmless what makes their use unrestricted.

Table 2. The causes of the use of non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol.

Disorder	NSAIDs	paracetamol
Common cold	76.0%*	89.2%*
Sore throat	70.0%	75.2%
Tooth pain	64.8%	71.6%
Diarrhea	8.8%	9.6%
Posttraumatic pain (e.g. ankle twist, sprain, contusion etc.)	64.4%	59.6%
Stomach ache in food intoxication	16.0%	14.4%
Headache	90.0%	91.8%
Hangover	20.0%	21.6%
Heartburn	2.0%	1.2%
Asthma	1.2%	0.8%
Hay fever	0.8%	1.6%
Allergic rash	2.0%	1.6%
Herpes	3.6%	4.0%
Earache	56.4%*	70.8%*
Muscle pain	24.4%*	16.8%*
Sciatica, lumbago, neuralgia etc.	18.8%	14.4%
Fever	86.0%*	92.0%*
Mood disturbance, depression	3.6%	3.2%
Vomiting	2.4%	0.8%
Autumn and winter time to prevent diseases	14.0%	12.0%
Constipation	2.4%	0.8%
Stressful situations (eg. exam at a university)	1.6%	2.4%
Painful menstruation (concerns only female respondents)	40.4%	46.8%
Renal colic, hepatic colic	0.4%	0.4%
Irritable bowel syndrome	2.4%	1.2%
Blood pressure surge	1.6%	0%

*$p < 0.05$ for the comparison between NSAIDs and paracetamol

More that one third of the responders (35.2%) have a habit of taking NSAIDs and paracetamol on the occasion of alcohol consumption.

Answering the question about the practice of reading drugs package leaflets, only 36.0% of the students admit that they always look for preparations safety information and 4.0% complement their knowledge when they utilize a new medication. Another 39.2% do it irregularly, 18.0% seldom and 3.2% never.

Considering the issue of a pharmacist informing buyers on NSAIDs and paracetamol contraindications, overdose and side effects, when the purchase is done at a pharmacy,

barely 4.0% of the survey participant have been always informed, 11.2% often, but 38.0% rarely and 46.8% never. The situation when a physician administers NSAIDs or paracetamol is not much better; hardly 8.0% always receive the necessary notices, 20.0% often, 43.0% rarely and 29.0% never.

In the comparison between NSAIDs and paracetamol utilization, 52.0% of the questioned use formulations of these two groups interchangeably, only 15.0% are aware of paracetamol lacking anti-inflammatory properties and 33.0% are convinced that paracetamol is better in combating inflammation.

In the analysis of genders' habits men more frequently than women used NSAIDs and paracetamol during alcohol consumption (49.2% vs 30.7%, p = 0.009, respectively) but less often were aware that there are maximum doses of medicines which should not be exceeded (57.4% vs 76.7%, p = 0.003, respectively). Medical, pharmacy, emergency medicine, medical rehabilitation and nursery students altogether (n = 82) compared with students of other fields of study (n = 168) were younger (20.9 ± 1.6 years vs 22.7 ± 2.2 years, p = 0.026) and declared they more often have the custom of always reading medication leaflets (46.3% vs 31.0%, p = 0.017, respectively).

Side effects of NSAIDs and paracetamol were reported by 65 participants — 26.0% (Table 3).

Table 3. Side effects of non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol.

Side effects	NSAIDs	Paracetamol
Nausea, vomiting, constipation, diarrhea	16.0%*	9.6%*
Heartburn and dyspeptic symptoms	6.8%*	1.2%*
Allergic rash, hay fever	2.4%	1.2%
Dizziness	7.0%	5.2%
Tinnitus, hearing disturbances	4.4%*	0.4%*
Blurred vision	3.2%	0.4%
Dyspnea, breathing problems	1.6%	0%
Symptoms leading to hospitalization	0%	0%

*p <0.05 for the comparison between NSAIDs and paracetamol

Discussion

The huge popularity of NSAIDs and paracetamol can be attributed to their effectiveness, but it is also evidence of the power and impact of advertising sponsored by pharmaceutical companies [9, 17]. The dark and hardly publicized by medicines manufacturers side of NSAIDs and paracetamol are hospitalizations associated with the occurrence of complications related to the drugs, reaching 100 thousand cases in USA each year [18]. OTC NSAIDs were found to be the most common cause of peptic ulcer disease and a source of gastrointestinal bleeding within elderly patients [19]. They are the second most common cause of drug-induced hypersensitivity reactions and are responsible for 21–25% of reported adverse drug events [20]. NSAID hypersensitivity is particularly manifested clinically by bronchial

asthma, rhinosinusitis or urticaria and variety of late cutaneous and organ-specific reactions. Severe reactions include anaphylaxis, Stevens Johnson syndrome and toxic epidermal necrolysis and are associated with significant mortality [21]. Moreover, negative impact of selective cyclo-oxygenase-2 inhibitors — coxibs and other NSAIDs, associated with impaired balance between thromboxane and prostacycline, perturbed prostaglandins synthesis and lipid oxidation process, lead to thromboembolic complications, arterial hypertension, atherosclerosis causing increased rates of myocardial infarction, ischemic stroke, peripheral vessels thrombosis and pulmonary embolism [22–24]. NSAIDs decrease sodium excretion by kidneys what soars blood pressure. They can also cause analgesic nephropathy [25]. OTC relative safety in terms of severe complications was confirmed in our survey in which none of the participants has ever needed urgent medical care.

Paracetamol therapy is associated with rare complications what was also reflected in our study. Apart from rash and mild symptoms from the gastrointestinal tract and casuistic examples of hematological disorders, the fact of overdose leading to severe liver failure and even death of the patient is commonly known [6, 26, 27].

The problem of drug consumption by young people does not arouse such interest, but it should be emphasized that precisely at this age the attitudes of behavior for life, including medicines use, are shaped. Moreover, some of the interrogated students of medical fields might play roles in governing bodies in health policy in the future or act as health educators [28]. Furthermore, in the presented study almost all of young adults (98.8%) confirmed the active use of OTC NSAIDs and paracetamol which is coherent with the observations of Plichta et al. of students of public health who all and sundry have ever taken such drugs and more common than in older people of general populations (71–85%) [24, 29, 30].

We have investigated that students in the self-treatment of different disorders hardly ever read drugs leaflets and seldom receive any information on drug related endangerments from physicians and pharmacists. As other studies show package inserts are ignored by 25–50% of the medications users, drug leaflets do not comply with the European Union formal regulations and use difficult language with specialized terms what makes them incomprehensible to even 40% of people including those with university education [31–34]. This is also consistent with the Czech study on non-prescription ibuprofen which showed that only one third of new users of the medicine consult with a physician prior obtaining it, while generally 40% of participants do not ask for any information regarding the drugs [35].

We also encountered students who were convinced that NSAIDs and paracetamol have no side effects. Similar observations come from papers of Reguła et al. and Matoulková et al., where similarly around 16% of the subjects shared the same belief [36, 37].

Unfortunately, significant portion of young and healthy students suffer from NSAIDs and paracetamol adverse reactions — from 26.0% in our study up to 28.0% in Turkish medical students and 30.4% in young Poles [38, 39]. The scale of the problem in general population is greater as show the results of the interview-based study of Albsoul-Younes et al. in which more than a half of participants (58%) reported having side effects upon NSAIDs consumption with gastrointestinal symptoms as the most common upset [40]. Noteworthy, NSAIDs complications have a poor correlation with clinical presentation — in many cases dyspeptic symptoms are not associated with significant endoscopic lesions while even in

40% of patients with chronic NSAIDs pharmacotherapy are detected to have asymptomatic gastric or duodenal ulcers [41, 42]. As Polish survey on over 38,000 participants show, only 60% of the individuals who reported at least one potential adverse reaction were aware that it might be the effect of prolonged NSAIDs treatment [37].

Alarmingly, we also have discovered that the medication group choice for the given disorder is often inappropriate and the drugs are applied in conditions in which they are contraindicated what is in concordance with observations of the survey of Ngo *et al.* in which the majority of patients had no knowledge about indications of ibuprofen [43]. Kozłowski and colleagues investigated that only 38% of the surveyed OTC painkillers buyers know what analgesic substance they are receiving [34]. In the aforementioned study of Matoulková *et al.* two per cent of participants even believed that ibuprofen was a sleeping aid [36]. This ignorance might lead to inadvertent combinations of drugs of one group or the same compound with different trade names, what was validated in our survey.

A potentially harmful composition of NSAIDS or paracetamol and alcohol might lead to liver failure, blood coagulation disturbances and increases the risk of gastrointestinal bleeding, especially in patients with chronic diseases and is observed not only in students but in remarkable numbers of people in general population trials reaching 40% [34, 44].

Interestingly, paracetamol was more eagerly chosen by our respondents to treat inflammatory diseases than NSAIDs like in common cold, what in theory could be less efficient but as clinical trails show is not necessarily inferior [45]. The students seldom combined NSAIDs and paracetamol, using their adjunctive actions [46, 47].

Gender affects different aspects of drug consumption. In the Czech survey men used pharmacists' counseling about OTC drugs significantly more often than women and in the Polish one by Plichta and colleagues men's knowledge on such medicines was more frequently based on television commercials [28, 36]. Differences in our study concerned prevalent drug consumption at the time of medicaments utilization in male respondents and their lower awareness of maximum doses of the drugs existence.

Summing up, low level of knowledge seems to be a global issue. In other studies young age and higher level of education correlated with better awareness of various aspects of NSAIDs therapy [36]. Unfortunately, in the presented survey the comparison of medical and pharmacy students with other participants shows that medical fields of study as opposed to others do not guarantee markedly more aware and safer OTC drugs consumption practice.

In conclusion, students' knowledge about OTC NSAIDs and paracetamol is low. Participants do not search for information on drug related endangerments, the medication group choice for the given disorder is often inappropriate and the drugs are applied in conditions in which they are contraindicated.

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Conflict of interest

None declared.

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