

OVER THE COUNTER DRUGS – COMMON GOOD? PART 1. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

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S u m m a r y. The use of Over The Counter Drugs (OTCs) in Poland is constantly increasing. Poland ranks third regarding the sale of OTC drugs in Europe. The most common OTC medications are pain relievers, anti-inflammatory drugs and cold and cough remedies. People are unaware of the dangers associated with OTC drugs misuse. Taking OTC medications without consulting a doctor first puts people at higher risk for adverse effects which include drug-drug and drug-food interactions, side effects and overdose.

K e y w o r d s: Over The Counter Drugs, self-medication, interactions, safety

INTRODUCTION

Prescription drugs are administered to patients, according to their current indications of use, all over the world, including Poland. Additionally, patients can use Over The Counter medications to self-treat most common conditions. Over the past years self-care and self-medication among patients has been increasing. Growing trends towards self-medication can be associated with easy public access to OTC drugs available both in pharmacies as well as in supermarkets or even

petrol stations. While self-care has a rather positive effect on public health, self-medication can be quite harmful. Self-care refers to all the actions which contribute to the maintenance of personal health, such as leading a healthy lifestyle, caring about personal hygiene or maintaining mental and physical well-being. Self-medication is defined as using OTC medications to treat self-diagnosed common health problems [2, 6, 7, 8, 10, 11]. Emphasising this issue to make people aware of the dangers resulting from self-medication is a very important task that all the health care providers, especially pharmacologists, should consider.

OTC drugs and safety of their use

A drug can be used without prescription in Poland when the Minister of Health assigns it to such a category, based on the opinion issued by the chairman of the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products. Generally, OTC medications should be safer and have less or no side effects compared to prescription drugs. Unfortunately, more and

more OTC drugs do not meet these criteria, as the profit from their sale is so huge that producers would rather cover the costs of any patients' claims than withdraw a product from the market. Even though drug safety in Poland is evaluated according to the EU rules, one should not forget that many drugs that initially seemed to be safe had to be withdrawn from the market a few years after registration [10].

Countless articles describing the issue of self-medication published so far have failed to change both patients' and health care professionals' approach towards the use of OTC drugs. The trust in OTCs is increasing – patients are taking them more and more often without consulting a doctor first, even in more serious conditions. According to the statement 158/2016 issued by the Centre for Public Opinion Research in Poland, approximately 30% of patients use OTC as a first line of treatment [3].

Although self-medication has its advantages (lowering the costs of health care expenses or increasing the awareness of patient's own health), one should not forget about potential dangers of such practices. Many patients are unaware of the risks resulting from the misuse of OTC drugs. Some of those medications can lead to addiction, gastric irritation or even poisoning. That is why consulting a health care professional is so important – patients are not able to consider all the factors that influence their health and wellbeing on their own. The greatest threat of self-medication is associated with an extremely easy access to OTC drugs in Poland. Taking multiple medications concurrently can lead to potentially life threatening drug interactions. Using drugs that are named differently but contain the same active substance enhances their toxicity and chances of poisoning. OTC drugs are considered by many as completely safe and harmless, which makes patients less alert when it comes to side effects or interactions. Although patients themselves take responsibility for self-medication, health care providers should take action to make people aware of the dangers of such therapy [2, 6, 7, 10].

OTC drugs are continuously becoming more and more common in Poland. As a result, Poland ranks third regarding the sale of OTC drugs in Europe [13].

It should be pointed out that there is a group of patients who follow doctors' (18%) and pharmacists' (60%) advice when choosing OTC medication, which creates an opportunity to control self-medication phenomenon to some extent. On the other hand, disturbing is the fact that OTC advertising also plays a significant role in that respect (20%). Moreover, it turns out that women in general are more prone to drug advertising than men [9].

Nonsteroidal anti-inflammatory drugs as OTC medications

Among the most commonly used OTC drugs are pain relievers, including nonsteroidal anti-inflammatory drugs (NSAIDs) aside pain relievers that do not have an anti-inflammatory effect, such as acetaminophen and metamizole. NSAIDs have anti-pain, anti-inflammatory, anti-pyretic and anti-aggregatory effect. NSAIDs block the formation of prostaglandins by inhibiting the enzyme called cyclooxygenase (COX). There are two isoforms of cyclooxygenase – constitutive cyclooxygenase COX-1, and induced cyclooxygenase COX-2.

NSAIDs can be classified based on their mechanism of action: I generation (classic) that either inhibit mostly COX-1 (acetylsalicylic acid, ketoprofen) or both COX-1 and COX-2 (ibuprofen, naproxen, diclofenac); II generation inhibit mostly COX-2 (meloxicam, nimesulid); III generation inhibit selectively COX-2 (celecoxib). COX-1 regulates many physiological processes in platelets, gastric mucosa, kidneys or endothelium. It catalyses the formation of prostaglandins E2 and I2 and thromboxane A2 from arachidonic acid. COX-1 activity guarantees cytoprotection of the gastrointestinal tract, good blood circulation flow through kidneys, and regulates platelet function [1, 5, 6, 12].

COX-2 is an enzyme facultatively expressed in inflammation. COX-2 induces increased vascular permeability leading to oedema and contributes to systemic responses to inflammation, such as pain and hypersensitivity [5, 6, 12].

Due to their mechanism of action, NSAIDs can interfere with the function of those organs in which prostaglandins play

regulatory role, especially gastrointestinal tract and kidneys. Adverse effects on gastrointestinal tract include, among others, gastric ulceration. NSAIDs inhibit the formation of prostaglandins. Gastric natural protective barrier is destroyed and submucosal blood flow is impaired, which contributes to ulcer formation in the stomach and duodenum. What is more, NSAIDs can cause both upper and lower gastrointestinal bleeding, nausea, and diarrhoea. NSAIDs can also damage kidneys. NSAIDs inhibit mostly COX-1, thus they block the formation of PEG2 and PGI2, which reduces renal perfusion and can lead to acute kidney injury. NSAIDs block the formation of both prostacyclin as well as other prostanoids that work as vasodilators. That increases the risk of thrombotic and embolic complications due to the lack of prostacyclin which would inhibit the activation of platelets and would balance out the effects of thromboxane. Moreover, hypertensive effect of NSAIDs inhibiting mostly COX-2 was observed in patients suffering from high blood pressure. It manifests itself by elevation of diastolic blood pressure by 3.5-6 mmHg, which significantly increases the risk of myocardial infarction and stroke. NSAIDs can increase blood pressure by blocking the formation of vasodilators and this effect is observed mostly in elderly patients and people suffering from hypertension. NSAIDs may reduce the benefit of drugs used to treat hypertension, especially those that work by affecting prostaglandin formation. The greatest risk is associated with using ACE-inhibitors, ARBs, beta-blockers and diuretics. The lowest risk involves using CCBs. NSAIDs have an anti-aggregatory effect on platelets. Although this effect is often used in the prevention and therapy of cardiovascular diseases (low doses 75mg of acetylsalicylic acid), it should be noted that taking those drugs chronically and in higher doses increases the risk of bleeding and bleeding time. NSAIDs may raise the efficacy of antiplatelet drugs. In combination with NSAIDs and steroids, bisphosphonates taken orally, SSRIs or spironolactone increase ulcerogenic potential of the aforementioned drugs. NSAIDs are highly bound to plasma proteins (almost 100%), which has to be noted when a patient is taking other drugs concurrently as those drugs can be replaced by NSAIDs. This is particularly important while

taking NSAIDs with antiepileptic drugs, sulfonylureas or methotrexate. As a result, free fraction of those drugs increases which leads to a greater risk of side effects. All NSAIDs used in the 1st trimester of pregnancy increase the risk of miscarriage as they can interfere with implantation. NSAIDs can also have a negative effect on pregnancy when taken during the 3rd trimester: they prolong the pregnancy and labour, decrease the amount of amniotic fluid and can cause preterm closure of the foetal ductus arteriosus [1, 5, 6, 12].

Acetylsalicylic acid

Acetylsalicylic acid (Aspirin) is one of the most common drugs from NSAID group. It is very easily accessible, and is widely advertised as a safe and effective remedy for first symptoms of flu. However, it should not be taken by children under 12, especially in cases of a viral infection as it can lead to a serious complication – Reye's syndrome. It is a very rare though life-threatening disease that affects mostly children aged 4-12. Generally, it develops as a side effect of a viral infection treated with acetylsalicylic acid. It leads to acute mitochondrial destruction. As a result, children develop non-inflammatory encephalopathy and liver failure. Therefore, it is advised to use acetaminophen instead of acetylsalicylic acid in children under the age of 12 years as it also has anti-pyretic and anti-pain effect, and is a lot safer in this group of patients [1].

Acetaminophen

Acetaminophen is one of the most common anti-pain and anti-pyretic OTC drugs. When it comes to this medication, the statement by Paracelsus that only "the dose makes the poison" turns out to be particularly true. The maximum daily dose for acetaminophen is 4g. There are at least a dozen of different products containing acetaminophen available on Polish market (for example Apap, Codipar, Efferalgan, Panadol, Paracetamol). Patients are not always aware of the fact that they take drugs that are named differently, but in fact contain the same active ingredient. That is why one should always check if the next anti-pyretic or anti-pain medication does contain acetaminophen, and control how much

of that substance is taken daily, as acetaminophen taken in large doses or taken chronically is toxic. Acetaminophen is metabolized in the liver. However, high doses of acetaminophen can permanently damage the liver. NAPQI (N-acetyl-p-benzoquinone imine) is a toxic by-product produced during the metabolism of acetaminophen. If the drug is used in recommended doses, this substance can be neutralized and removed by conjugation with glutathione. Unfortunately, if the maximum daily dose is exceeded, there is not enough glutathione to bind all of the toxic substance, and this by-product causes irreversible liver failure. The only option in such cases is liver transplantation. Alcohol abusers, people infected with HCB, HBV or those trying to lose weight or malnourished are particularly prone to acetaminophen toxicity. It should be pointed out that one should not exceed the maximum single and daily dose of acetaminophen. It cannot be used frequently or chronically. Acetaminophen is recommended as a safe anti-pain drug during pregnancy and lactation, provided the liver function is not impaired. It is also recommended as a first choice anti-pyretic drug for children. Their liver enzyme systems are not fully developed yet, so the toxic by-product cannot be produced [1, 4, 5, 6].

Metamizole

Metamizole, widely used, proved to be a very effective anti-pain and anti-pyretic drug. It was first produced in Germany in 1920, and then sold on a large scale as an OCT drug until the '70s when it turned out that it could cause agranulocytosis – a very dangerous and potentially fatal blood disorder. That is why this drug was withdrawn in several countries including Australia, Norway, the USA, Denmark, Sweden, Lithuania and Ireland. In many others, e.g. Switzerland, Spain, The Czech Republic, Greece, Italy and Hungary it is only available as a prescription drug. Uncontrolled use of metamizole can impair the function of bone marrow causing agranulocytosis. As a result, the number of infection fighting white blood cells, i.e. neutrophils decreases. Metamizole is contraindicated in pregnant women and nursing mothers, as it can cause Wilms' tumour and acute leukaemia in infants [5, 6].

Interactions between NSAIDs and other drugs

Interactions can occur between different groups of drugs. One of the most common drug combinations is taking NSAIDs and proton-pump inhibitors (PPIs) concurrently. PPIs are used in the prevention and treatment of gastric ulcers. They increase pH of gastric acid which alters the absorption of many drugs, including NSAIDs. Taking NSAIDs and PPIs concurrently on one hand protects gastrointestinal mucosa, but can also decrease the absorption of NSAIDs which reduces their anti-inflammatory and anti-pain effect [1, 4, 5, 6].

CONCLUSIONS

Self-medication is a very common phenomenon. That is why it is crucial to emphasise the consequences and dangers of such practices. There is a great need to educate patients in order to increase public awareness. Additionally, proper law regulations should be established in order to reduce this alarming phenomenon. According to the WHO definition, rational use of medicines requires that patients receive medications appropriate to their clinical needs in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community. There is no such thing as a totally safe and harmless drug; all depends on the dose and the period of time it is used for. Taking any medicines should be consulted with a healthcare professional in order to avoid any potential interactions or adverse effects of pharmacotherapy.

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