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OVER THE COUNTER DRUGS – COMMON GOOD? PART 2. MOST COMMONLY USED OTC DRUGS

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S u m m a r y. Self-medication, a phenomenon observed all over the world, is closely related to easy public access to Over-The-Counter drugs (OTCs) available on the market. First of all, taking OTCs without consulting a health care professional may cause a number of dangerous adverse effects associated with taking too many medications simultaneously, including dietary supplements. The paper discusses OTC drug-drug and drug-food interactions.

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

INTRODUCTION

Our previous article concerning OTC drugs [10] as well as other authors' articles [3, 16, 18] indicate that patients have easy access to OTCs and are unaware of the dangers resulting from their misuse. Growing tendency towards self-medication results from the convenience and efficacy of such therapy. Many a time it is the patient who decides which drug to buy, being guided by popular and omnipresent advertisements or other peoples' recommendations. Even though, both the format and the content of leaflets of OTCs is legally regulated so that they all contain indications for use, dosing, potential side effects, and a list of active and inactive substances, many patients do not read them or do not understand the information included. Thus people endanger themselves to many potential adverse effects, especially if they suffer from a coexisting disease [7].

Most commonly used OTC drugs are pain killers and anti-inflammatory drugs (as mentioned in the first part of this article), but also colds, flu and anti-allergic medications as well as drugs used to alleviate gastrointestinal problems [17, 18, 21].

OTC drugs used to treat colds and flu

Drugs that are most commonly used for treating cold and flu symptoms belong to a group of non-steroidal anti-inflammatory drugs (NSAIDs), e.g. acetylsalicylic acid, ibuprofen, alfa -1 adrenic agonist that constrict nasal mucosa vessels, e.g. pseudoephedrine, phenylephrine, and first or second generation antihistamines, e.g. pheniramine maleate, chlorpheniramine maleate, dexbrompheniramine maleate, triprolidine hydrochloride, cetirizine [12]. Some authors include anti-tussive drugs, e.g. dextromethorphan in the list.

A great number of drugs, which appear under various names, are available on the market.

They contain the same active substance in therapeutic dose. That creates a chance of overdosing a drug if one does not know their composition or the amount of active substance allowed to be taken daily. For example, a therapeutic dose of substance exhibiting similar activity is contained in a tablet or capsule of various medications which have different brand names:
Aspirin complex: acetylsalicylic acid (500mg) and pseudoephedrine (30mg); *Acatar Zatoki*: ibuprofen (200mg) and pseudoephedrine (30mg); *Modafen*: ibuprofen (200mg) and pseudoephedrine (30mg); *Infex Zatoki*: ibuprofen (200mg) and pseudoephedrine (30mg); *Metafen Zatoki*: ibuprofen (200mg) and pseudoephedrine (30mg); *Modafen Extra Grip*: ibuprofen (200mg) and pseudoephedrine (30mg); *Acatar Acti-Tabs*: pseudoephedrine (60mg) and triprolidine (2,5mg); *Claritine Active*: loratadine (5mg) and pseudoephedrine (120mg); *Gripex Max:* paracetamol (500mg) + pseudoephedrine (30mg) + dextromethorphan (15mg); *Cirrus Duo*: pseudoephedrine (120mg) + cetirizine (5mg); *Gripex Noc*: paracetamol (500mg) + pseudoephedrine (30mg) + dextromethorphan (15mg) + chlorpheniramine (2mg); *Gripex Hot Zatoki*: paracetamol (650mg) + pseudoephedrine (60mg) + dextromethorphan (20mg) + chlorpheniramine (4mg).The list of similar products is very long.

Special attention should be paid to pseudoephedrine which is found in many OTC drugs. Single active ingredient drugs containing pseudoephedrine are for example Sudafed or Abselan (60mg pseudoephedrine in one tablet). Some of the most dangerous side effects of pseudoephedrine are associated with increased blood pressure, tachycardia and central nervous system stimulation, especially in elderly patients (it can cause insomnia or hallucinations, too). It can also cause urinary retention in patients suffering from prostatic hyperplasia. Pseudoephedrine may enhance the efficacy of other sympathomimetic drugs [1].

However, most disturbing is the fact that pseudoephedrine is often used by adolescents to intoxicate themselves and stimulate the central nervous system. Similar effects are observed when using methamphetamine. In high doses, pseudoephedrine works like amphetamine, causing agitation and inducing euphoria [1, 6, 7]. Even though pseudoephedrine improves concentration and short term memory, it interferes with long term memory and learning abilities [7]. In high doses it reduces appetite. That is why it is sometimes used by young people, especially girls, as a way to lose weight [8, 9]. Unfortunately, overdose may result in poisoning which is manifested as hallucinations, increased aggression, anxiety and convulsions.

Addiction and tolerance may develop when taking pseudoephedrine for a longer period of time. Those are among adverse effects that all pharmaceutical companies alert patients to. For example, Bayer Pharmaceutical Company says in its leaflet: “pseudoephedrine belongs to a group of drugs that are being abused, increasing the dose may lead to poisoning; taking it for a long period of time may be the cause of tolerance development, which increases the risk of overdose; sudden withdrawal may cause depression. It can be used for not longer than 10 days, as when taken longer its efficacy decreases.” Nonetheless, patients often do not understand the information included in the leaflet, ignore all the warnings, which may lead to life threatening complications.

Moreover, all of the drugs containing sympathomimetics should be avoided or used with caution in patients with diabetes type 1, hypertension, angina pectoris or hyperthyroidism. Special care should be taken when using sympathomimetics (xylometazoline, oxymetazoline, naphazoline) topically as nose drops. This route of administering vasoconstrictors makes them reach high concentrations locally, which may lead to rhinitis medicamentosa if they are used for a longer period of time [5, 15].

Anti-histamine drugs (pheniramine maleate, chlorpheniramine maleate, dexbrompheniramine maleate, triprolidine hydrochloride, cetirizine) may produce sedation effect and cause drowsiness, especially when taken with other sedatives and hypnotics, alcohol, or drugs that lead to the central nervous system depression, e.g. dextromethorphan or pseudoephedrine.

Antitussive drugs

Dextromethorphan is a morphine derivative exhibiting central antitussive effects. Single active ingredient drugs containing dextromethorphan are for example Tussidex (30mg dextromethorphan in one capsule) or Acodin (15mg dextromethorphan in one tablet).

Dextromethorphan is metabolised by cytochrome P450 2D6 isoenzyme and interacts with many drugs that have a suppressive effect on that isoenzyme (antidepressants, some antipsychotic drugs, cimetidine, lansoprazole, terbinafine, valproic acid). Those can cause nausea, dizziness or impaired breathing [12].

Most common side effects of dextromethorphan include disorders of the digestive system, drowsiness, agitation, irritability, anxiety, even psychosis if overdosed. Dextromethorphan has addictive potential and belongs to a group of drugs that are often abused, especially by adolescents [14, 20, 22]. Many pharmaceutical companies emphasize that, e.g. US Pharmacia Ltd. mentions: "development of addiction when abused", Pfizer Company: "dextromethorphan can be addictive, especially when used in high doses for a long period of time".

Dextromethorphan is contraindicated in patients with asthma, respiratory failure or in case of excessive bronchial secretions. Dextromethorphan may enhance the effects of sedatives, hypnotics and antipsychotics on the central nervous system [7].

Codeine has antitussive effects in addition to soothing and analgesic activity. Codeine works being converted into an active metabolite – morphine (about 10%), which is also responsible for side effects such as nausea, vomiting, constipation and sedation. Codeine abuse is associated with the risk of physical and psychological dependence. Withdrawal of the drug too suddenly may cause withdrawal symptoms. Patients can develop tolerance to pain-relieving and antitussive effects of codeine if it is abused and taken in high doses for too long. Codeine overdose symptoms include nausea, vomiting, inhibition of the respiratory centre and coma [1, 7, 24]. Codeine, similarly to drugs used to treat cold and flu listed above, can be found in many combined drugs alongside with NSAIDs, acetaminophen (Antidol, Eferalgan), acetylsalicylic acid (Ascodan), or herbs such as thyme (Neoazarine) and caffeine (Solpadeine).

It should be pointed out that using a number of combined drugs increases the risk of adverse effects. Side effects from the CNS, such as drowsiness, confusion, impaired ability to drive and operate machinery should be alarming both to patients as well as health care professionals. What is more, patients should be warned about the consequences of alcohol consumption during treatment, not just because of its effects on the CNS, but also because of numerous interactions in the liver [4].

OTC drugs used in gastrointestinal disorders

Cimetidine (Tagamet) – H2 receptor antagonist is currently used very rarely in peptic ulcer disease due to its numerous adverse effects. Ranitidine (Zantac, Ranigast) and famotidine (Pepcid) are recommended to treat symptoms of gastric hyperacidity, e.g. heartburn. Taking ranitidine or famotidine, as well as proton pump inhibitors can mask symptoms of gastric cancer, thus leading to delayed diagnosis. Special care should be taken when the character of dyspeptic symptoms has changed or if they appeared for the first time [23]. Prothrombin time should be monitored while taking ranitidine as it can enhance the efficacy of anticoagulants (warfarin) [2]. Taking ranitidine and NSAIDs should be supervised by a health care professional, especially in elderly people with peptic ulcer disease.

Drug-food interactions

Over the last few years, much attention has been paid to how much dietary patterns can influence pharmacotherapy. It was proven that many side effects of pharmacotherapy are associated with adverse effects of food on absorption, metabolism and elimination of drugs.

Those interactions can already appear during drug absorption phase. Food can delay or accelerate drug absorption, or have no influence at all. This interaction takes place most often when drug is taken about an hour and a half before, during or up to two hours after meal. All drugs whose absorption can be impaired by food should be taken either two hours before, or at least two hours after meal [11]. Interactions during absorption also depend on quantitative and qualitative composition of diet. High-fat foods can accelerate and increase the absorption of drugs such as anti-fungal medicines, psychotropic medications and beta-blockers. Products rich in calcium (dairy products) decrease the absorption of some antibiotics for example fluoroquinolones and tetracyclines. Tannin, which can be found in tea, decreases the absorption of iron when taken orally. Products containing fibre decrease absorption of cardiac glycosides and tricyclic antidepressants [11].

Interactions can also occur during the metabolism of drugs. It depends on whether food and drug are metabolised by the same cytochrome P450 enzymes. A very well known example of such interaction is the influence of grapefruit juice on the metabolism of drugs such as calcium channel blockers, statins or cyclosporine. Grapefruit juice contains plenty of flavonoids which are metabolised in the liver by the same group of cytochrome P450 enzymes, as in drugs listed above. Drinking grapefruit juice right after taking those drugs leads to functional failure of CYP3A enzyme. The drug cannot be metabolised which increases its blood concentration. That is why one should wait at least 4 hours after taking a drug before drinking grapefruit juice [13, 25].

Drug-drug interactions

Interactions can also occur between different groups of drugs. One of the most common drug combinations is NSAIDs and proton-pump inhibitors (PPIs). 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. On one hand, concurrent administration of NSAIDs and PPIs protects gastrointestinal mucosa, but it can also decrease the absorption of NSAIDs, which reduces their anti-inflammatory and analgesic effects.

CONCLUSIONS

Self-medication is becoming a more and more common phenomenon, which unfortunately carries many dangers. It is essential to constantly keep that in mind and raise public awareness about the risks associated with such practice, which include OTC drugs' adverse effects as well as drug-food and drug-drug interactions. Pharmacists and doctors should play a major role in overcoming this alarming phenomenon, remembering Paracelsus's words that "only the dose makes the poison" [19].

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