ASPECTS OF DRUG-DRUG INTERACTIONS BETWEEN COMPOUNDED DOSAGE FORMS AND DRUGS OF OTHER PHARMACOLOGICAL GROUPS

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Abstract. With the development of the pharmaceutical market and the increasing number of medicines, one of the most important problems is polypragmatic treatment by physicians**.** Usage of medications during self-treatment with various chemicals or that are marketed under a different brand name (thus appearing to be different but actually containing the same ingredients) may lead to different side effects.

To date, the Food and Drug Administration has noted the following main types of dosage-form interactions as: drug-food-beverage interactions (the absorption of tetracycline antibiotics is reduced by 20-80% through drinking milk), drug-condition interactions (if person have high blood pressure, they could experience an unwanted reaction if take a nasal decongestant, grapefruit juice is a potent inhibitor of the cytochrome P450 enzyme) and drug-drug interactions. Especially relevant is the last of them. Drug interactions are quantitative or qualitative changes in the effects caused by drugs when two or more drugs are used simultaneously or sequentially. Such processes can reduce a drug's effectiveness, induce unforeseen side effects, or boost a drug's activity [1].

Research objective. To track down current available compounded dosage forms in the assortment of pharmacies in Kharkiv and study the feasibility of using such medicines in combination with other medicines on the basis of a case example.

Materials and Methods. Theoretical processing, as well as analysis of foreign and domestic sources of information about the possible drug interactions was conducted. Looking for a relevant reference sample a range of produced medicines by pharmacy chains "Leda", "Istok-plus" and "MedAcademy" in the city Kharkiv was analysed.

Results. Drug-drug interactions can involve prescription or nonprescription (over-the-counter) drugs. Mechanistically classifying drug–drug interactions provides important insights on how to predict, detect, and avoid them. When medicines are combined the following types of drug interactions can occur: pharmaceutical, pharmacokinetic and pharmacodynamic interactions as well as absorption distribution (protein binding, tissue binding) metabolism (hepatic, nonhepatic) excretion (renal, nonrenal) modification of these combinations [2].

Pharmaceutical interactions are based on the physical, physico-chemical and chemical reactions of drugs that are in the same dosage form or that occur when several drugs are used together. Pharmaceutical interactions usually occur outside the body when drugs are manufactured, in clinical practice when drugs are mixed in the same syringe or infusion system. Negative examples of such careless mixing are, for the most part, combinations of different vitamins. The use of ascorbic acid and thiamine in the same syringe causes the combined degradation of both substances. Pharmaceutical interaction may lead to the formation of insoluble complexes, changes in colour, odour

and pharmaceutical properties of the medicinal substances. This type of interaction usually occurs in irrational drug formulations. For example, cardiac glycosides partially disintegrate in alkaline environment, resulting in loss of their activity [3].

During pharmacokinetic interactions, one drug of the combination usually alters the absorption, distribution, binding to proteins, metabolism or elimination of the other drug. Accordingly, the amount and duration of effect of the first drug on the receptor is altered. Pharmacokinetic interactions alter the severity and duration of an effect but not its type. Often, it can be predicted based on the characteristics of individual medicines or detected by monitoring their concentrations or clinical symptomatology [4]. Barbiturates like phenobarbital, for example, increase the activity of liver enzymes, causing the anticoagulant warfarin to be inactivated more quickly and hence less effective when taken at the same time. Drugs like erythromycin and ciprofloxacin, on the other hand, can enhance the action of warfarin by lowering the activity of the enzyme system, increasing the risk of bleeding.

Pharmacodynamic interaction occurs when drugs are used together to produce changes in their pharmacological effects by affecting specific receptors, cells, organs or systems. The result of this interaction is a reduction or disappearance of the effect, a perversion of the effect of the drugs or an increase in the effect up to the development of toxic effects. For example, the association of a monoamine oxidase inhibitor with fluoxetine leads to serotonin syndrome, which is a result of direct drug-mediator interactions.

Back to the range of compounded drugs, more attention should be paid to preparations containing metal ions, such as zinc and magnesium. These dosage forms have proven to be quite widespread among manufacturer pharmacies' catalogues. The company "Istok-plus" producing magnesium available in powder form for oral use. One sachet contains magnesium sulphate 25 g. The drug has found its use as a laxative. Its effect is caused by a change in osmotic pressure, delayed absorption of water in the intestine, rarefaction and increase in the volume of intestinal contents, irritation of the enteroreceptors, which facilitates the act of defecation. Also has diuretic and choleretic properties and can be used as an antidote for barium poisoning. However, it should be noted that the drug reduces the effect of oral anticoagulants, cardiac glycosides and phenothiazines. Decreases absorption of ciprofloxacin, tetracyclines, weakens the effect of streptomycin and tobramycin by reducing their bioavailability. This phenomenon is caused by antibiotics forming intramolecular complexes with magnesium.

Such cases are not unique, and decreased efficacy of antibiotic therapy is common in cases of simultaneous use with drugs containing metal ions such as magnesium, aluminium, bivalent and trivalent iron, calcium and zinc.

The zinc formulation from the “Leda” pharmacy is an oral capsule. In the case of standalone administration, this preparation is used in the treatment of patients suffering from infectious diseases, reduced immunity, disorders of lipid and carbohydrate metabolism and increased vascular permeability and decreased elasticity of the vascular wall. But if the patient simultaneously combines this drug with antibiotics, an inhibition of their therapeutic activity will be observed. Zinc citrate can cause a decrease in the absorption of Ciprofloxacin resulting in a reduced serum

concentration and potentially a decrease in efficacy. Also, it can decrease the absorption of other drugs such as tetracycline antibiotics (including doxycycline, minocycline), bisphosphonates (e.g., alendronate), and quinolone antibiotics (e.g., ciprofloxacin, levofloxacin).

Another metal ion preparation produced by the pharmacy, the dosage form is a magnesium and vitamin B6 complex in capsule form. Composition 1 capsule: magnesium lactate 470 mg and pyridoxine hydrochloride 5 mg. It intended to replenish magnesium deficiency in the body. Magnesium is involved in many metabolic processes, in particular in reactions related to muscle contraction and transmission of nerve impulses. Vitamin B6 improves the absorption of magnesium in the digestive tract and promotes its penetration and retention in cells.

Conclusions. The main objective of the doctor and the patient is to minimize drug interactions during treatment. Thus, Clinicians should be familiar with all of their patients' current medications, including those given by other doctors as well as over-the-counter, herbal, and nutritional supplements. It's a good idea to ask patient about their diet and alcohol intake. In turn, the patient should separate doses of medications as far as possible from doses of other drugs, ask family practitioner about how long should wait between doses and for help finding a dosing schedule that will work with all medications. In the same way, the pharmaceutical manufacturers must also be responsible and provide detailed information on possible drug-drug interactions exactly in the package insert of the medicine.

References

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