Studies of anticancer drug interactions aiming to improve therapeutic safety of parenteral nutrition in cancer patients

A large number of patients with cancer suffer from malnutrition. Consequently, their prognosis is poor, a risk of complications increases manifold, therapy tolerance is compromised, and recovery protracted. There are situations when malnutrition negates recovery prospects because therapy has to be postponed due to the patient's condition. Therefore, proper nutrition is key to successful treatment. It is estimated that in 2018 alone 3.9 million cases of cancer were diagnosed and 1.9 million patients died of cancer in Europe. Neoplasms are the second most common cause of death in Poland. It should be remembered that the oncologic patient must face not only the challenge of the disease but also the hardships of anticancer therapy. Its first symptoms may be malnutrition or weight loss. Therefore, it is essential to quickly diagnose and introduce treatment and nutritional intervention, preventing further destruction of the body and improving the recovery chances. The problem of malnutrition most often affects patients with gastrointestinal cancers. Depending on the state of the patient's health and resulting nutritional needs, it is necessary to apply either orally (regular or therapeutic diet) enteral or parenteral nutrition.

Parenteral nutrition provides the patient nutritional admixture consisting of various ingredients of high chemical reactivity (water, glucose, amino acids, lipids, trace elements, electrolytes, vitamins) contained in one bag. It is important to note that PN admixtures exist in the form of an oil-in-water emulsion, which explains their thermodynamic sensitivity. The physicochemical compatibility of PN admixtures is a vital feature from the clinical point of view. Particularly in the patients who require their parallel administration. The safety of this treatment intervention is a challenging task for medical professionals in patients with limited venous access because drug and PN admixture must be administered via one catheter. In the absence of relevant literature data, the possibility exists of interaction between the mixed components manifested as drug precipitation, emulsion destabilization, color change, and/or inactivation of the drug. These may seriously endanger the patient's health or even life.

Unfortunately, there is not enough answer to which drugs can be given together with parenteral nutrition. The compatibility of supportive drugs has not been thoroughly studied. Available data are incomplete, and results are often contradictory. To meet the expectations of clinicians and hospital pharmacists in the field of pharmacotherapy of patients fed parenterally, this research project aims to determine the potential interactions between selected chemotherapy-supporting drugs and PN admixtures. Additionally, allow assessing the possibility of their administration during simultaneous infusion, thus improving infusion therapy safety in cancer patients.

According to the Polish Society of Clinical Oncology recommendations, the treatment of gastrointestinal cancer is based mainly on the following drugs: irinotecan, 5-fluorouracil, oxaliplatin, docetaxel cisplatin, epirubicin, gemcitabine. In addition, in clinical practice, very often, oncological patients undergoing chemotherapy also receive other drugs that are designed to alleviate the negative effects of oncological treatment. To supportive drugs group may be counted: ondansetron, granisetron, dolasetron, palonosetron, metoclopramide, prednisone, dexamethasone, methylprednisolone, fosaprepitant, calcium folinate, mesna, ibandronate, pamidronate, and zoledronate.

These studies will be conducted in simulated clinical conditions at room temperature (25±1ºC) with access to light. The properties of PN admixtures without and with the tested drugs will be determined by measuring the pH, osmolality, turbidity, zeta potential, and lipid emulsion particle size in three endpoints to capture potential interactions that may occur during simultaneous infusion. The content of the drug will also be examined to determine its stability in the presence of the ingredients of the parenteral nutrition admixture. Finally, it is assumed to determine the mathematical relationship between the studied physicochemical parameters and drug concentration, lipid emulsion composition, and storage time.

The methods presented above will allow proper determination of the compatibility of supportive drugs with PN admixtures, understand the source of this phenomena, and thus discover *terra incognita* in this area of knowledge. And in the future, the results will help to create therapeutic recommendations.