1. Streszczenie w języku angielskim

Parenteral nutrition is a fundamental method of nutritional therapy. It enables the delivery of essential nutrients to patients for whom the use of the gastrointestinal tract is impossible or insufficient.

This method has been used for many years at the Children's Memorial Health Institute in Warsaw. Particular importance is placed on the home parenteral nutrition program, which currently includes 160 patients. Initially, parenteral nutrition was administered using a system of multiple bottles containing macro and microelements, connected sequentially or in parallel. Errors related to improper mixing of preparations, electrolyte disturbances, and metabolic complications led to the preference for the all-in-one (AIO) method in modern parenteral nutrition, which involves preparing an intravenous mixture in a single container.

For over a decade, complete parenteral mixtures have been prepared at IPCZD for home patients in two-chamber bags with a 7-day shelf life. The complexity of preparing parenteral nutrition in two-chamber packages and additional manual activities performed by parents at home before connecting nutrition to the patient, i.e., the need to activate the two-chamber bag by transferring the lipid emulsion from the lipid chamber to the fat-free fluid chamber, led me to attempt preparing pediatric home parenteral nutrition mixtures in single-chamber bags in recent months.

The subject of my doctoral dissertation is the evaluation of the physicochemical and microbiological safety of mixtures used in home parenteral nutrition in children, as this issue is highly complex and represents a significant scientific and clinical challenge. The stability of such mixtures depends on many interrelated factors, such as their composition, conditions of preparation, storage, and administration. Insufficient consideration of these elements when developing an individualized parenteral mixture formula can lead to solution destabilization, precipitation of sediments, degradation of active ingredients, or even the risk of microbiological contamination, which directly threatens patient safety. The limited number of available studies and the lack of comprehensive analyses in this field highlight a significant research gap, further increasing the importance and difficulty of this issue. Research of this kind requires not only interdisciplinary scientific collaboration involving clinicians, pharmacists, and formulation scientists but also the application of advanced research methodologies, specialized equipment, and consideration of various often unpredictable environmental and clinical conditions. Particular challenges arise from the need to simulate real-life usage scenarios, such as variable temperatures, storage times, or light exposure. This issue becomes even more complicated in pediatric settings, where specific environmental factors—such as high temperatures in incubators for neonatal patients—can affect the stability of these mixtures. Developing a comprehensive understanding of the

problem and providing practical solutions required me to adopt an advanced research approach, which underscores both the extraordinary difficulty and importance of this topic.

An important aspect of the doctoral dissertation was the evaluation of the possibility of extending the shelf life of parenteral nutrition mixtures prepared at the Institute "Children's Memorial Health Institute" in Warsaw for home patients in single-chamber bags with a 15-day shelf life through a comprehensive analysis of the stability of physicochemical and microbiological parameters. This required analysis of laboratory and theoretical physicochemical stability parameters and confirmation of microbiological stability for parenteral mixtures prepared in this scheme. The study included 186 compositions of all-in-one (AIO) parenteral nutrition mixtures used in home pediatric parenteral nutrition prepared at the IPCZD Pharmacy.

An additional aim of the analysis was to determine the impact on the stability of home pediatric parenteral mixtures of the type of packaging used, i.e., single-layer single-chamber bag versus multi-layer single-chamber bag, and the impact of the type of lipid emulsion used, i.e., Smoflipid versus Lipidem. The physicochemical stability assessment analyzed theoretical parameters such as osmolarity, critical aggregation number (CAN), and mono- and divalent ion concentrations. Laboratory tests included measurements of zeta potential, conductivity, oil droplet size (D 0.5, D 0.9, Z-average), polydispersity index, and mixture pH.

Microbiological stability was assessed according to Polish Pharmacopoeia requirements, with particular attention paid to maintaining aseptic conditions during mixture preparation and workspace cleanliness control. Studies were conducted under controlled temperature conditions 2-8°C for 15 days.

Statistics were based on variable distribution analysis, which proved not to have normal distribution characteristics in the Shapiro-Wilk test, determining the choice of non-parametric tests as the main analytical tools.

It was demonstrated that extending the shelf life of home parenteral nutrition mixtures from 7 to 15 days is possible provided specific physicochemical and microbiological stability criteria are met. Physicochemical parameters are fundamental screening tools in assessing the safety of parenteral nutrition mixtures. Particularly important is the analysis of zeta potential as an indicator of emulsion stability and oil droplet size, i.e., D 0.5, D 0.9, Z-average. These are sensitive and specific parameters for assessing the stability of home parenteral mixtures. The analysis also showed that multi-layer bags and Lipidem emulsion provide better stability of parenteral nutrition mixtures compared to single-layer bags and Smoflipid emulsion. Theoretical parameters, i.e., CAN and mono- and divalent ion concentrations, are not sufficient indicators for assessing mixture stability, as there are both stable mixtures with high CAN and unstable ones with low CAN, and a similar situation applies to ion

concentrations, where exceeding theoretical threshold values does not determine mixture instability. Additionally, in the conducted doctoral dissertation analysis, based on completed microbiological studies, microbiological stability of home parenteral nutrition mixtures was confirmed for 15 days during refrigerated storage 2-8°C and for an additional 24 hours during mixture administration at room temperature.

Demonstrating the physicochemical and microbiological safety of AIO parenteral mixtures stable for 15 days has significant practical importance in the context of modifying the prescription, preparation, and supply scheme for patients in the home parenteral nutrition program. The proposed changes will improve the comfort of pediatric patient care in home conditions by reducing the number of manual operations performed by caregivers and significantly lower logistical costs associated with mixture transport. The conducted analysis and research will also enable the creation of a database of stable parenteral mixtures, which in the future may be integrated with the 'Żywczyk' parenteral nutrition prescription program, supporting the process of selecting safe concentration ranges for individual components based on the patient's individual clinical needs.