ABSTRACT
Hyperglycemia is frequently occurring in critically ill patients and the incidence is particularly high in patients receiving nutrition support. One of the forms of such nutrition is enteral nutrition, which is used particularly often. There are patients with type 1 diabetes, type 2 diabetes and other forms of diabetes as well as patients who have not previously been diagnosed with diabetes in this group of patients. The basis of pharmacotherapy in this case is an insulin therapy. The principles of such a therapy in patients with previously diagnosed diabetes are regulated by PTD guidelines. According to literature data, hyperglycemic patients with no previously diagnosed diabetes require special attention. The pathomechanism of these disorders is very complex and these patients require special care in determining the insulin therapy program. So far, there are no unambiguous guidelines in this area. (Clin Diabetol 2018; 7, 5: 230–233)

Key words: enteral nutrition, hyperglycemia, diabetes, non-diabetic hyperglycemia, glycemic control, insulin therapy

Introduction
Nutrition is an important component of treatment. In patients who are in a severe condition, oral nutrition is usually impossible. An option that should be preferred in hospitalized patients who can not benefit from oral nutrition is enteral nutrition (EN, enteral nutrition).

Enteral nutrition is indicated in the prevention or treatment of malnutrition when oral food intake is impossible or insufficient. The necessary condition for its use is a properly functioning gastrointestinal tract. The indications and the way of carrying out such nutrition have been discussed in the literature [1, 2].

A special group requiring the determination of artificial nutrition are patients with cancer [3, 4]. In oncological patients, the basic energy demand is often increased. Increasing the amount of food taken by the patient, reduces the loss of body weight and tissues and improves the functional parameters of the body [5, 6]. In this group of patients, the need to implement nutritional therapy is associated not only with surgical procedures, but also with the use of chemoradiotherapy [7].

Advances in expanding therapeutic options mean that even if cancer can not be cured, in many cases it can be transformed into chronic disease. In such cases, there is a need to protect the patients against malnutrition. In this way, enteral nutrition is often used, and in special cases of parenteral nutrition (TPN, total parenteral nutrition). A comprehensive discussion of this issue has been presented by an international group of specialists [8].

Mechanisms of glucose homeostasis in patients receiving enteral nutrition
A serious problem with the use of artificial nutrition is the occurrence of hyperglycaemia. This is a serious complication because it is associated with an increased risk of complications.

An extensive discussion of this issue was presented by Gosmanov and Umpierrez [9]. The authors pointed out that the pathogenesis of this phenomenon is complex. The role plays elevated blood glucose level, resulting from increased hepatic glucose production and reduced peripheral tissue utilization during stress, increased levels of stress hormones and cytokines as
well as insulin resistance associated with the regulation of intracellular signaling by the insulin receptor. Not without significance for the occurrence of hyperglycaemia in patients receiving enteral nutrition is continuous intestinal exposure to the secretion and action of incretin hormones or reduced expression of glucose transporters in the intestines [10].

Many authors emphasize the importance of differentiation between stress-induced hyperglycaemia (SH), newly diagnosed hyperglycaemia (NDK) and hyperglycaemia in people with established diabetes (DM) [11].

Interesting research on this issue was presented by Valizadeh Hasanloei et al. [12]. These authors found that hyperglycaemia associated with stress or trauma in patients without previously diagnosed diabetes is particularly risky. In patients hospitalized in the intensive care unit receiving enteral nutrition, the incidence of hyperglycaemia in those without previously diagnosed diabetes was 14.5%.

**Alleviation of disorders**

Hyperglycaemia may be the result of the disease itself, the treatment used, it is also a frequent side effect of artificial nutrition.

At the outset, it is necessary to determine the type of glycemic disorder and determine whether the patient has diabetes or has previously had diabetes. Therapy depends on whether they are patients with type 1 diabetes, type 2 diabetes or other types of diabetes, or whether they are patients without previously diagnosed diabetes.

The glucose level > 140 mg/dL (7.8 mmol/L) is usually considered as the hyperglycaemia in hospitalized patients. Insulin treatment is usually implemented at a glucose level of ≥ 180 mg/dL (10.0 mmol/L). After the start of insulin therapy, glycemic maintenance within the range of 140–180 mg/dl (7.8–10.0 mmol/l) is recommended [13]. The lower limit is assumed to be 70 mg/dL (3.9 mmol/L). Such values are also accepted for artificially fed patients [14].

Procedures for the treatment of patients with previously diagnosed autoimmune diabetes mellitus (type 1 diabetes, type LADA diabetes), in which the basis of treatment is intensive insulin therapy, are strictly defined [15–17]. In these patients, continuous subcutaneous insulin infusion (CSII) with continuous monitoring of glucose (CGM) is most commonly used. This allows for good glycemic control and reducing the risk of hypoglycaemia [18, 19]. Insulin analogues are usually used in these patients.

In patients with type 2 diabetes who have not previously received insulin, insulin therapy usually starts with a low dose of basal insulin with the possible addition of fast-acting insulin. For enteral nutrition, 1 unit of fast-acting insulin per 10–15 g of carbohydrates is usually administered subcutaneously before each meal [20, 21].

A comprehensive discussion of this issue based on literature was presented by Corsino et al. [22]. In most patients, these authors recommend as the starting dose of insulin 0.3 to 0.5 U/kg m.c./day. The treatment of choice in these conditions is insulin therapy. It is recommended to maintain the blood glucose values in the range of 100–180 mg/dl (5.6–10.0 mmol/l).

The subject of discussion is the treatment of patients with type 2 diabetes and patients with hyperglycaemia without previously diagnosed diabetes. According to current recommendations, these patients should be treated with insulin therapy [15]. This applies to patients with type 2 diabetes treated with oral hypoglycaemic agents. This also applies to patients without previously diagnosed diabetes who have experienced glucose homeostasis disorders as a result of septic stress or trauma [23].

**Insulin therapy during enteral nutrition**

Extensive discussion of the issue of glycemic control in demanding patients of nutrition on the basis of a literature review recently presented by Vennard et al. [24]. The authors state that the best glycemic control is ensured by continuous infusion of insulin, however administering insulin subcutaneously to patients fed enterally or parenterally is a safe and effective way of treating hyperglycaemia. However, there are no definitive findings regarding insulin therapy in such patients. The authors believe that further randomized studies are needed to determine the optimal therapy for hyperglycaemia in patients requiring enteral or parenteral nutrition.

McCulloch et al. based on a review of the literature, found that in patients fed parenterally, the dose necessary for metabolic insulin balancing varies within very wide limits [25]. Recently, the American authors presented the analysis of glycemic control in enteric fed patients [26]. Fatati et al. presented results in the group of patients with type 2 diabetes mellitus and without previously diagnosed diabetes, in which the use of insulin therapy during enteral or parenteral feeding was found [27]. The Spanish authors have made recommendations on insulin dosing when switching from intravenous (IV) insulin to subcutaneous (S.C) insulin delivery [28]. The authors pointed out that at the transition from IV to S.C. the initial dose of insulin at 50% of the previous dose is suitable for enteral nutrition (TPN).
Difficulties in metabolic glycemic control in patients with previously diagnosed diabetes requiring continuous enteral nutrition therapy (CENT) were noted by Hijaze and Szalat [29]. Verçosa Viana et al. [30] also analyzed the literature regarding insulin therapy in patients with nutritional support (NS) [30]. Attempts are made to determine the composition of the food used in nutrition support in oncological patients [31]. Even though, there are no established guidelines, one can use the guidelines developed for patients in critical conditions [32–34].

Summary

The use of artificial nutrition in seriously ill patients is an important therapeutic challenge. These patients usually due to the underlying disease have various metabolic disorders, including glucose metabolism disorders. One of the most physiological forms of nutrition support is enteral nutrition. To maintain glycemic control, pharmacotherapy is required in these patients. At present, insulin therapy is the treatment of choice regardless of the underlying disorders. Rules for its use in patients with insulin-dependent diabetes are clarified. More discussion raises such a therapy in patients without previously diagnosed diabetes. According to the literature, these patients are particularly vulnerable to the adverse course of such disorders and require very careful metabolic control and individually selected therapy. At the moment, there are no explicit recommendations regarding the nutritional treatment of oncological patients and, according to many authors, this issue requires urgent elaboration.

REFERENCES


