

Continuous glucose monitoring (CGM) systems are currently the fastest growing technology in the field of diabetology. Due to the increasing accuracy and sophistication of glucose monitoring systems and their widespread availability at the same time, new indicators of proper glycemic control have appeared in the literature. Of particular note is the time in range (TIR) index, which is closely related to the incidence of complications in the form of microangiopathy and macroangiopathy. In 2019, Batellino et al. published an international consensus on glycemic targets for patients using CGM systems, which has been accepted by many international societies, including the Polish Diabetes Association (PTD). "Clinical Recommendations for the Management of People with Diabetes 2023 of the PTD" include parameters from CGM systems in addition to the HbA1c index for glycemic control targets, with particular emphasis on the TIR index (70-180mg/dl, 3.9-10 mmol/l), whose target value should be $>70\%$.

This doctoral dissertation is a series of related publications, which aimed to isolate the factors affecting the prolongation of time spent in target glycemia by children and adolescents with type 1 diabetes.

The purpose of the case-control study: "Factors affecting the prolongation of glycemic time in range among children with type 1 diabetes using continuous glucose monitoring systems: A case control study." was to identify factors that affect the prolongation of glycemic time in range estimated by the CGM systems among children with type 1 diabetes. Data from 110 children (1-17 years old) with type 1 diabetes over one year, treated with continuous subcutaneous insulin infusion by an insulin pump, using CGM for at least 3 months, with data recording time over 70% were analyzed. Parents or legal caregivers were also asked to complete a questionnaire concerning daily habits, a type of using insulin, devices, and their settings in diabetes therapy. Participants were divided into two groups: those achieving therapeutic goals ($\text{TIR} > 70\%$) and those not meeting these criteria ($\text{TIR} \leq 70\%$). The group with $\text{TIR} \leq 70\%$ was characterized by repeated episodes of hyperglycemia and a high glycemic coefficient of variation (CV). Patients with $\text{TIR} > 70\%$ were significantly more likely to use the predictive low-glucose suspend system (PLGS), maintain appropriate time intervals between insulin administration and a meal consumption, use the insulin pump's function "bolus calculator", and were more likely to generate electronic reports from the insulin pump and/or CGM system software. In both groups, we recorded an acceptable rate of hypoglycemia (3%), regardless of achieved TIR values. In the above study, we presented that the main problem of patients not reaching the therapeutic goal of $\text{TIR} > 70\%$ is repeated episodes of hyperglycemia and high glycemic variability. Factors that can result in prolonged TIR include: use of advanced features

of CGM systems, maintenance of an appropriate time interval from insulin delivery to meal consumption, use of the "bolus calculator" function, and high patient involvement in the therapeutic process (regular self-generation of reports and their analysis).

Taking into consideration that the main problem of type 1 diabetes patients who do not achieve the expected metabolic control is repeated episodes of hyperglycemia, the next study was an attempt to find a solution to a very common clinical problem, which is postprandial hyperglycemia. It is commonly observed, especially with regard to high glycemic index (GI) meals. There is still no optimal way to adjust insulin to high GI meals. In recent years, the concept of a super bolus (SB), in which the dose of meal insulin is increased with subsequent decreased or suspended basal insulin, was mentioned in the literature. There is no clear definition of how SB should be created, and there are no clinical trials using this type of bolus. The available data refer to studies conducted in an in-silico model. The study, "Super Bolus-A Remedy for a High Glycemic Index Meal in Children with Type 1 Diabetes on Insulin Pump Therapy?-A Randomized, Double-Blind, Controlled Trial," and its detailed, published protocol, aimed to demonstrate whether SB is a more effective method of preventing postprandial hyperglycemia than a standard bolus (*normal bolus*, NB). Super bolus was defined as an increased by 50% dose of prandial insulin calculated on the basis of an individual's insulin-to-carbohydrate ratio (ICR) with subsequent suspended basal insulin for 2 hours. NB was defined as the dose of prandial insulin calculated based on the ICR.

Seventy-two children, aged 10-17 years, with type 1 diabetes for more than a year and treated with CSII for more than 3 months were enrolled. All patients were hospitalized during the study, ICRs were estimated accordingly. The intervention was the consumption of a high GI breakfast (cereal with milk) for the two separate days. In random order, participants received SB or NB for the breakfast. The primary endpoint was the glucose level measured with a glucometer at the 90th minute of the observation period (the observation period was 180minutes). Throughout the study, patients were connected to the same CGM and had SMBG measured every 30 minutes.

In this study, we demonstrated that SB is an effective strategy for preventing postprandial hyperglycemia. After SB administration, there were statistically significant lower glycemic values during the entire follow-up period (including the primary endpoint). In addition, patients stayed significantly longer in the glycemic time in range after SB, compared to NB. However, SB resulted in more hypoglycemic episodes. Almost 90% of these were hypoglycemia alert values in the range of 54-69 mg/dl, 3.0-3.8 mmol/L, which occurred at the end of the observation period. After NB, there was a significantly higher percentage of

hyperglycemic episodes and more than double the time spent in hyperglycemia. Taking this into account, we concluded that SB is an effective strategy for the prevention of postprandial hyperglycemia, but the time of suspending basal insulin should be extended, f.ex. up to 3 hours.