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Insulin Pump Therapy in Children and Adolescents with Type 1 Diabetes – Personal Observations

Własne obserwacje leczenia cukrzycy typu 1 u dzieci i młodzieży za pomocą osobistej pompy insulinowej

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Abstract

Objectives. The appreciation of the metabolic control in patients with diabetes type 1 treated with a personal insulin pump.

Material and Methods. The examination included 52 children and adolescents (30.8% boys and 69.2% girls) aged 3–21 years ($\bar{x}$ 14.40 ± yrs) with a diabetes duration from 0.3 to 19 years ($\bar{x}$ 7.56 ± yrs). The duration of the treatment with the CSII (continuous subcutaneous insulin infusion) varied from 3 to 60 months ($\bar{x}$ 15.1 months). During the pump therapy all the patients received an insulin analogue Humalog (Lys B28 ProB29). First the patients and their families were thoroughly instructed, and both the adequate dose of the basal insulin as well as the requirement of carbohydrate exchangers were set; then the treatment with the CSII started. Before the treatment, blood samples had been collected in order to estimate HbA_{1c}, cholesterol-HDL, LDL. The examination HbA_{1c} was repeated every 3–4 months. The patients measured their glycemia individually using their own Glucotrend – glucometers and marked the episodes of hypoglycemia.

Results. In patients with diabetes type 1 treated with the CSII turned out to have a statistically significant decrease of the insulin requirement ($p = 0.00004$) and lower HbA_{1c} value ($p = 0.000001$). Before the treatment with the CSII, neuroglikopenia was observed in two children, whereas during the continuous subcutaneous insulin infusion (CSII) only once. Hypoglycemia was diagnosed both before (1.3 patient/week) and during the therapy with a pump (1.13 patient/week) but the difference was statistically insignificant. BMI, and the lipid metabolism were within the norm both before and during the pump therapy. In the case of two children the pump therapy was stopped because of intensive local allergic reactions within a few hours after injection.

Conclusions. 1. During the CSII therapy a significant decrease of the insulin requirement was observed. 2. A decrease of HbA_{1c} values was observed. 3. A better metabolic diabetes control, especially of the postprandial glycemia and the Somogy effect, was observed **(Adv Clin Exp Med 2004, 13, 6, 933–937)**.

Key words: personal insulin pumps, diabetes type 1, metabolic control.

Streszczenie

Wprowadzenie. Ocena wyrównania metabolicznego u chorych na cukrzycę typu 1 leczonych za pomocą osobistej pompy insulinowej (OPI).

Materiał i metody. W pracy oceniano 52 osoby (30,8% chłopców i 69,2% dziewczynek) w wieku 3–21 lat ($\bar{x}$ 14,4 lat) chorych na cukrzycę typu 1 leczonych 0,3–19 lat ($\bar{x}$ 7,5 lat). Leczenie metodą OPI stosowano 3–60 miesięcy ($\bar{x}$ 15,1 miesiąca). Wszyscy pacjenci leczeni OPI otrzymywali w pompie analog insuliny – Humalog (LysB28 ProB29). Przed rozpoczęciem leczenia OPI pacjenci i ich rodziny byli dokładnie pouczeni, jak obsługiwać urządzenie, ustalano dawkę insuliny bazalnej oraz zapotrzebowanie na wymienniki węglowodanowe. Przed rozpoczęciem leczenia pacjentom pobierano do badania krew i oznaczono HbA_{1c}, cholesterol – HDL, LDL. Badanie HbA_{1c} było powtarzane co 3 miesiące. Pacjenci oznaczali stężenie glukozy za pomocą osobistego glukometru – Glukotrend oraz odnotowywali epizody hipoglikemii.

Wyniki. U chorych na cukrzycę typu 1 leczonych OPI stwierdzono statystycznie znamienne zmniejszenie się zapotrzebowania na insulinę ($p = 0{,}00004$), statystycznie niższe wartości HbA_{1c} ($p = 0{,}000001$). Przed leczeniem OPI neuroglikopenię rozpoznano u dwójki dzieci, a w czasie leczenia OPI u jednego chłopca. Przed leczeniem OPI hi-

poglikemię stwierdzono u 1,3 pacjenta na tydzień, natomiast w czasie leczenia OPI u 1,13 pacjenta/tydzień. Różnica nie była statystycznie istotna. BMI pacjentów oraz stężenie lipidów zarówno przed, jak i w czasie leczenia OPI było prawidłowe. U dwójki dzieci przerwano leczenie OPI z powodu miejscowej reakcji alergicznej, która wystąpiła po kilku godzinach leczenia.

Wnioski. 1. Podczas leczenia OPI statystycznie znamiennie zmniejszyło się zapotrzebowanie na insulinę. 2. Obserwowano obniżenie wartości HbA_{1c}. 3. Leczenie OPI wpłynęło na poprawę kontroli metabolicznej, a szczególnie glikemii poposiłkowej oraz efektu Somogy **(Adv Clin Exp Med 2004, 13, 6, 933–937)**.

Słowa kluczowe: osobista pompa insulinowa, cukrzyca typu 1, kontrola metaboliczna.

Continuous subcutaneous insulin infusion (CSII) with a personal insulin pump imitate the physiological rhythm of insulin excretion by a healthy pancreas. It has been proved that multiple daily doses of short acting insulin-Actrapid or Regular do not prevent postprandial hyperinsulinemia and that hyperglycemia occurring within a few hours after the insulin application causes the risk of the development of hypoglycemia [1–3]. This problem may be for the most part solved by the application of an insulin analogue Lys-Pro. The twice a-day application of isophan insulin only in an approximate degree imitates the physiological insulin excretion by a healthy pancreas. There is still a problem of hyperinsulinemia, which appear about 1–2 am and which is accompanied by the risk of the occurrence of hypoglycemia, whereas a deficit of insulin in the second half of the night is the cause of hyperglycemia in the morning. At present the therapy with a continuous infusion of insulin is the best way to obtain an optimal metabolic control of diabetes because it would be possible [4–8]: to adapt the basal infusion to the individual requirement for the patient, to give insulin injections before each meal (bolus), to differentiate the bolus in accordance with a meal, the time it is consumed and the glycemic index of carbohydrates, to adapt the basal infusion to the physical effort, additional disease and morning hyperglycemia, to decrease the risk of hypoglycemia, which is dangerous especially in little children.

Multicentre studies have shown that the CSII therapy enables a better control of glycemia, a decrease of ketoacidosis and hypoglycemia as well as the normalisation of LDL and VDL in comparison to the patients treated with multiple daily injections of insulin [9, 10].

The WHO and many other international scientific researches prove that the optimal glycemic compensation prevents the development of chronic diabetic complications [11–13].

The appreciation of the degree of compensation in children with type 1 diabetes treated with a personal insulin pump for six years and the frequency of acute diabetic complications.

Material and Methods

The Department of Endocrinology for Children and Adolescents in Wroclaw Medical University there have been 52 children and adolescents aged 3–21 years ($\bar{x}$ 14.40 ± yrs), 16 boys (30.8%) and 36 girls (69.2%) with a diabetes duration from 0.3 to 19 years ($\bar{x}$ 7.63 ± yrs). The duration of the treatment with the continuous subcutaneous insulin infusion (CSII) varied from 3 to 60 months ($\bar{x}$ 15.12 ± months) (Fig. 1).

All patients are presently being treated with an insulin analogue Lys B28 ProB29 in a continuous infusion with the following pumps: MiniMed 506,507c (10 patients – 20%) and Disetronic H Tron (42 patients – 80%). Before the CSII treatment 24 patients (46%) received short acting insulin HM (Actrapid, Regular with Insulatard, Neutral) and the remaining 28 patients (54%) – Humalog in 4–5 shots a day and intermediate insulin once or twice daily. The insulin pump was connected after the children with type 1 diabetes and their parents agreed on a more frequent glycemic control and a precise instruction given to at least 2 people living together with the patient. 24 hour basal infusion was set and the quantity of the bolus before the particular meals was settled according to the amount and kind of meal. Special consideration was given to the glycemic carbohydrate index of meals. The basal infusion of insulin was calculated in relation to a dose or doses of insulin received by the patient before the pump therapy; whereas the insulin requirement for carbohydrate exchangers (BE) was calculated according to the former requirement of short acting insulin or Humalog for BE in particular hours of the day. Before the connection of the pump, were blood samples collected for HbA_{1c}, HDL, LDL examination.

The calculation of the average daily requirement of insulin/kg body mass before the pump therapy was based on the data recorded during seven successive days of treatment and during the pump therapy were read from the pump memory (MiniMed pump).

During control visits, the degree of diabetic compensation was controlled and the changes of

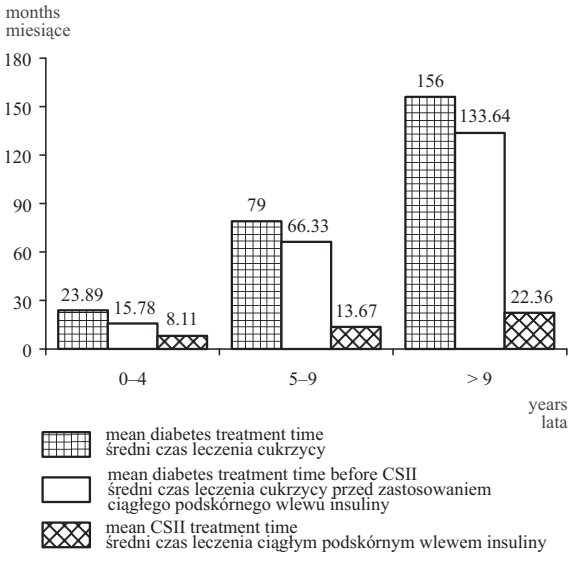

Fig. 1. Diabetes treatment in children with type 1 diabetes

Ryc. 1. Czas trwania cukrzycy typu 1 u dzieci

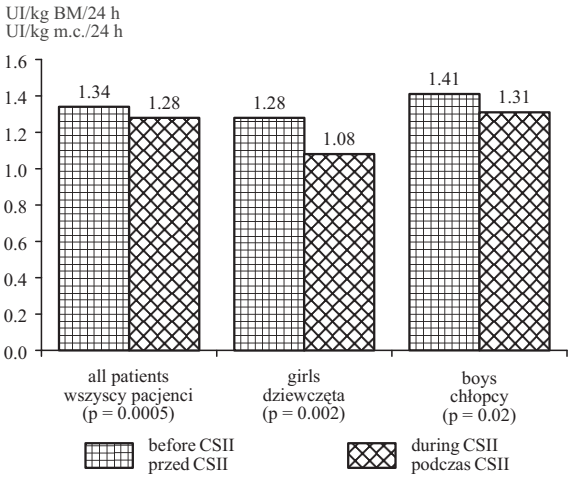

Fig. 2. Insulin doses

Ryc. 2. Dawki insuliny

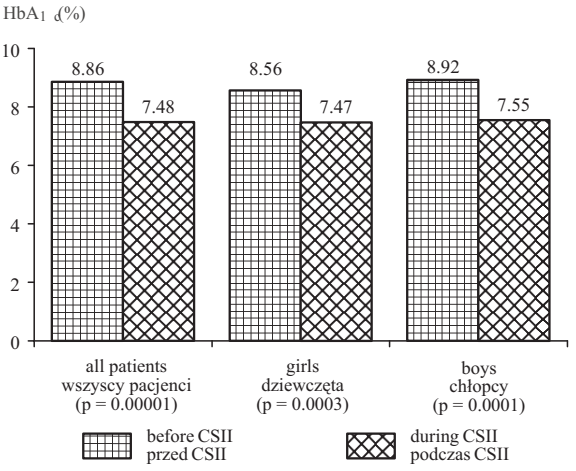

Fig. 3. Mean level of HbA_{1c}

Ryc. 3. Średni poziom HbA_{1c}

the doses of both basal insulin and the insulin in bolus were introduced in relation to the results of glycemia examination. HbA_{1c} was examined in 3–4-month intervals. Hypoglycemia episodes were appreciated in the period of 12 weeks before and in the last 12 weeks of the pump therapy.

The statistical analysis was performed with the *t*-Student test. A statistically significant difference was considered to $p < 0.05$ and the results are presented as $\bar{x}$ and $\pm$ SD.

The relation between particular parameters was defined using Pearsons' coefficient correlation.

Results

During the therapy with a personal insulin pump observed was that the value of HbA_{1c} (8.8% to 7.5%) and of the insulin requirement decreased (1.34 UI/kg bm/24 h to 1.28 UI/kg bm/24 h). In comparison to the data obtained before the pump therapy the difference was statistically significant ($p = 0.0001$ vs. $p = 0.0005$) (Fig. 2 and 3).

The levels of LDL ($\bar{x} = 3.6$ mmol/l) and HDL ($\bar{x} = 2.1$ mmol/l) were within the normal range both before and during the therapy with the pump. Mild hypoglycemia was diagnosed both clinically or with the glucometer before (1.3 patient/ /week) and during the therapy with a pump (1.13 patient/week), but the difference was statistically insignificant (48 mg/dl to 56 mg/dl).

Before the pump therapy, neuroglycopenia was observed in two children at night-time, whereas during the therapy – only in one boy, after an intensive physical effort in gardening. During the three months preceding the therapy with the personal insulin pump ketoacidosis was observed 4 times in three patients, during the pump therapy – 5 times in 3 patients. The reason for ketoacidosis in patients treated with the pump were infections of the gastrointestinal tract (2 cases), the dislocation of the catheter at night-time (2 cases) and the damage of the pump (1 case). In the case of two patients the pump therapy was interrupted because of a marked allergic skin reaction observed a few hours after the connection of the catheter and fixation of the plaster.

Both the patients were treated earlier for atopic allergy. Due to a short time of the pump treatment (aproximately 1 month) the results of these patients were not taken into account in this report.

All the patients treated with CSII were satisfied with the therapy. First of all, they emphasised the freedom in planning meals and other everyday activities. The main advantage of the CSII therapy is the normalization of the postprandial glycemia and during the second half of the night.

Discussion

The imitation of the physiological diurnal profile in insulin secretion through the β cell of the pancreas and proper changes in the regulation of the activity of this hormone during 24 hours is the main aim of the diabetes therapy. The DCCT investigations proved that the intensive insulin therapy with a personal insulin pump contributed to a decrease of the development of chronic diabetic complications and their progression [11]. The CSII treatment with Lys-Pro resulted in a near-normoglycemia, not only in the around-meal but also preprandial period, with a simultaneously decrease of the hypoglycemia. With the pump therapy it is possible to obtain a good balance between the inflow of insulin into the tissues and its outflow, limiting not only the catabolism of insulin in the tissues but, what is of the principal significance the cumulation of insulin at the place of infusion [14]. The results of research of many authors prove that postprandial glycemia is the most significant atherogenic factor responsible for the development of diabetic microangiopathy. The CSII therapy enables a good metabolic control of diabetes, decrease of HbA_{1c} level [1, 5, 7, 8, 15, 16]. In presently analysed group, in the majority of patients the level HbA_{1c} before the CSII therapy was < 8.0%, which testifies a good metabolic diabetic control at that time. This was obtained with an intesive therapy with insulin Lys-Pro in 56% of the patients and with multiple daily doses of short acting insulin in 44%. The analysis of individual patients has shown that the decrease of the HbA_{1c} levels during the CSII therapy was more significant in the patients who had an insufficient diabetic control before this treatment. Described observations are similar to the observations of other authors [1, 12, 17]. During the CSII therapy in one patient with obesity a 22% decrease of the insulin requirement was observed. This observation is also convergent with the data of other authors. The insulin requirement is conversely proportional to the sensibility of the peripheral cells and increases in individuals with obesity. The CSII therapy in obese patients with diabetes lead not only to a decrease of the insulin dose but, first of all, to the reduction of the body mass [4, 18, 19]. The comparison of the insulin inflow carried out for Actrapid and Lys-Pro insulin shows that the risk of ketoacidosis was bigger in the case of the pump therapy with Humalog [3, 17, 20, 21].

In the examined group, ketoacidosis was observed during a viral infection of the gastrointestinal tract, after the dislocation of the catheter during the night, and in case of the pump damage. The most serious complication observed in children is hypoglycemia, especially during the night. The cause of hypoglycemia in the patients treated with short acting insulin during the day and with intermediate insulin before bed time may be hyperinsulinemia resulting from the pharmacokinetic and pharmacodynamic of their action [22–24].

The application of insulin Lys-Pro in a pump significantly decreased the occurrence of this complication. The risk of hypoglicemia is especially high in patients performing physical activities and the cause may be hyperinsulinemia resulting from the overlap of short acting insulin (Actrapid or Regular) given in a bolus and the basal insulin dose. Sonnenberg et al. claim that in order to avoid hypoglycemia during physical activities, it is necessary to reduce to 50% the insulin dose in the bolus before and to reduce by 25% the insulin dose after physical activities [24].

The cause of severe hypoglycemia during the CSII therapy in described patient was most probably the fact, that the basal insulin was not reduced during and after the physical activity.

Mild, clinically diagnosed and confirmed with a glukometer hypoglycemia was uncommon in the examined patients. This may be the evidence of an appropriate therapy of diabetes and of proper self-control.

It was emphasised that the success of the CSII therapy is a result of patient's motivation, a correct monitoring of glycemia, observing dietary rules and physical activity [16]. The investigated patients emphasise that the CSII therapy caused normalisation of glycemia during the day and night and significantly improved the quality of their lives. The therapy enabled the patients to plan freely their daily activities and to adjust the insulin dose to the quantity of consumed carbohydrates. Some authors stress that the liberalization of meal planning and daily activities planning are for many patients the most important advantages of CSII [12, 14]. They also emphasise that appropriate education and monitoring of the glycemia are the best ways to prevent chronic diabetic complications [23]. Thanks to the pump therapy occurrences of hypoglycemia during the night – particulary dangerous in children – could be avoided in the patients altogether.

The allergic reactions at the place of the catheter, which caused the interruption of the therapy, were observed in two girls. The girls had been treated for some years because of atopic allergy. Skin complications in form of reddening in the area of catheter fixation, abscesses or thickening described by other authors are mostly the result of insufficient hygiene and not frequent enough changes of the place of infusion, but the possibility of allergic reactions to the fixing plaster cannot be excluded [25].

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