CONTINUOUS SUBCUTANEOUS INSULIN INFUSION (CSII)

Manja Prašek, Tomislav Božek, Željko Metelko

SUMMARY

Intensive diabetes management can be achieved in children, adolescents and adults either with the use of continuous subcutaneous insulin infusion (CSII) or with multiple daily injections (MDI). The goals of intensive diabetes management established by the Diabetes Control and Complications Trial are to achieve near normal glycemia, to avoid short-term crises such as hypoglycemia requiring third part assistance or intervention, to minimize long-term complications, and to improve the quality and length of life in persons suffering from diabetes. The importance of tight metabolic control in patients with diabetes was also demonstrated by the results of United Kingdom Prospective Diabetes Study, and emphasized in the Saint Vincent Declaration. Disadvantages of MDI are the need for patients to take three or even more injections per day by syringe or pen, resulting in poor compliance, and to use modified insulins, intermediate or long-acting insulins (NPH, Lente, Ultra-lente) that must be injected to reach basal concentration of insulin to keep blood glucose within normal limits between meals. It has been clearly shown that absorption of modified insulins vary from 19% to 55% in the same individual, which could be the reason for blood glucose variability. Conversely, the absorption of soluble, short-acting insulins that are used in continuous subcutaneous insulin infusion varies by less than 3% daily. As the result of continuous subcutaneous insulin infusion – insulin pump therapy and use of a continuous glucose sensor, achievement of the main goals in diabetes treatment could rather become a matter of fact. During recent years continuous subcutaneous insulin infusion has reached widespread recognition, as it has become the mode of intensive diabetes treatment for more than 200 000 diabetic patients worldwide.

HISTORICAL OVERVIEW AND PRESENT WORLDWIDE SITUATION

Intensive diabetes management can be achieved in children, adolescents and adults either with the use of continuous subcutaneous insulin infusion (CSII) or with multiple daily injections (MDI). The goals of intensive diabetes management established by the Diabetes Control and Complications Trial (DCCT) (1) are to achieve near normal glycemia, to avoid short-term crises such as hypoglycemia requiring third part assistance or intervention, to minimize long-term complications, and to improve the quality and length of life in persons suffering from diabetes. The importance of tight metabolic control in patients with diabetes was also demonstrated by the results of United Kingdom Prospective Diabetes Study (UKPDS) (2), and emphasized in the Saint Vincent Declaration (3). Disadvantages of MDI are the need for patients to take three or even more injections per day by syringe or pen,
resulting in poor compliance, and to use modified insulins, intermediate or long-acting insulins (NPH, Lente, Ultra-lente) that must be injected to reach basal concentration of insulin to keep blood glucose within normal limits between meals. It has been clearly shown that absorption of modified insulins vary from 19% to 55% in the same individual, which could be the reason for blood glucose variability (4,5). Conversely, the absorption of soluble, short-acting insulins that are used in CSII varies by less than 3% daily (5,6). As the result of continuous subcutaneous insulin infusion (CSII)-insulin pump therapy and use of a continuous glucose sensor, achievement of the main goals in diabetes treatment could rather become a matter of fact. During recent years CSII has reached widespread recognition, as it has become the mode of intensive diabetes treatment for more than 200 000 diabetic patients worldwide (7).

The use of CSII was first reported in 1978 by John Pickup et al. (8). This new technology was devised and developed as a research procedure to enable testing of the connections between diabetes control and diabetes related complications. In the following years, its efficacy and beneficial effect on the development of most of the late diabetic complications were in a short time confirmed by many studies (8-25).

In the early insulin pump era, serious side effects were reported, such as ketoacidosis, hypoglycemia and mortality (26). As the result of these findings, the use of CSII decreased or was stagnant. In 1993, the Diabetes Control and Complications Trial (DCCT) reported significant reduction in the rate and severity of complications in type I diabetics due to the achievement of glucose control to near normal values (1). DCCT pointed to CSII as a slightly but significantly better method in maintaining strict glycemic control compared to other modes of intensified treatment (27). Since the publication of DCCT; in the last 10 years there has been an increase in the use of CSII, especially in the USA as well as in many other countries. Today there are more than 200,000 diabetic patients using CSII as a daily mode of their intensive diabetes treatment (7).

On the other hand, there are countries like the United Kingdom where insulin pump technology was developed but the use of CSII is still quite uncommon (28), considering the advantages or benefits of CSII. According to the study conducted by Noergaard, approximately 0.5% of type I diabetic patients in Denmark are treated with CSII (29). In contrast, in the USA approximately 16% of type I diabetic patients are estimated to use CSII as a mode of intensive treatment (30), whereas in Sweden the rate of CSII treatment is about 8% (29). In Germany, as many as 10% of patients with type 1 diabetes use insulin pumps (31).

Figure 1. History of pumps: (A) early insulin pump designed by Arnold Kadish; (B) early portable insulin pump; (C) modern insulin pump.
delivered to the body through an infusion set. A thin flexible plastic tube is attached to the pump, and at the other end of the tube there is a catheter. The catheter is inserted under the skin, near the abdomen to deliver insulin to the body. The insulin pump is about the size of a deck of cards, weighs about 100 grams (3 ounces), and can be worn on a belt or carried in a pocket. The pump is programmed to deliver small amounts of insulin continuously throughout the day and night (‘basal’ dose in the range of 0.1-1.0 U/h) to meet nonprandial insulin requirements. Extra doses of insulin (‘bolus’ doses) are delivered at meal times and at times when blood glucose is too high based on the user’s programming to cover mealtime or snack time insulin requirements. Patients can choose to receive a bolus of rapid acting insulin before, during or after the meal, and so called square-wave bolus – a bolus released evenly over a preset period of time, commonly 30 minutes to 2 hours.

Most of the currently used pumps have an opportunity for setting several basal rates (average patients require 4-6 different rates). Frequent blood glucose monitoring is essential to determine insulin dosages and to ensure that insulin is delivered. Insulin pumps manufactured by five different companies are currently available on the market: Animas, Deltec, Disetronic Medical Systems, Medtronic MiniMed, and Sooil Corporation Ltd.

INDICATIONS FOR USE OF CSII (PREREQUISITES FOR CSII)

CSII is used in selected type 1 diabetic patients to achieve strict blood glucose control. To achieve favorable CSII outcomes it is essential to identify appropriate candidates.

Indications for CSII (30):

- history of hypoglycemia unawareness or history of unpredictable, recurring hypoglycemic events requiring assistance
- hemoglobin A1c levels greater than 7%
- failure of maintaining strict glycemic control with MDI
- dawn phenomenon: glucose levels exceeding 8-9 mmol/L in the morning
- pronounced day-to-day blood glucose level variability
- pregnancy (strict glycemic control is obligatory before conception to prevent the occurrence of fetal anomalies and spontaneous abortion, and therefore it is recommendable to start insulin pump therapy even before pregnancy)
- need of flexibility in lifestyle (necessary for shift workers, business travelers, workers in a safety-sensitive job, etc.)
- low insulin requirements, below 20 U/day

Indications for use of CSII in children and adolescents

- hypoglycemia
- dawn phenomenon
- hemoglobin A1c greater than 7%
- failure of maintaining strict glycemic control with MDI
- pronounced day-to-day blood glucose level variability
- flexibility in lifestyle (skipping or delaying meals, sleeping late on weekends)
- low insulin requirements, below 20 U/day
Candidates for CSII (as well as children’s parents) should be motivated to achieve near normal glucose level, willing to perform frequent blood glucose self-testing and to learn about pump therapy, need to have technical skills and precision on performing blood glucose monitoring and handling insulin pump device. Patients must have realistic expectations about the influence of insulin pump device on their life (4-6 blood glucose measurements a day). They need to be aware that CSII is not a cure, it is a tool in achieving strict blood glucose control, to minimize the risk of acute diabetes complications, and to prevent or delay the onset of late diabetes related complications.

CONTRAINDICATIONS – CSII
NONELIGIBLE PATIENTS

Patients who are not ready to perform 4-6 blood glucose measurements daily and are not willing for close cooperation with the diabetes health care team consisting of a physician, a nurse and a dietitian, are not eligible for CSII. Patients with notable psychologic disturbance have a tendency to worse glycemic control using CSII. Patients with major psychiatric disorders such as psychosis and severe depression should be excluded from screening procedure for initiation of CSII. CSII should be avoided in patients who are concerned and worried even after education and counseling about daily activities such as sexual relationships, contact sports as well as in patients who would feel physically and emotionally uncomfortable wearing insulin pump device (7).

STARTING INSULIN PUMP THERAPY – BASAL INFUSION AND PREPRANDIAL INFUSION

The best candidates for CSII are individuals who are practicing diabetes self-management, including frequent monitoring of blood glucose level, recording blood glucose and insulin levels in a logbook, visiting medical team on a regular basis, and counting carbohydrates. Besides, patients who show poor control using MDI, and become frustrated and discouraged resulting in tendency to develop poor habits of monitoring and medical follow up, may be very succesful with CSII (30).

When pump therapy is initiated, the total daily insulin dose should be reduced by 25%-30%, and 50% be used as basal dose and 50% as total bolus dose (32). Children and adolescents may begin with 40% as basal and 60% as bolus dose (33). The basal dose is divided by 24 to get units per hour (U/h). The recommendation is to start with a single basal rate, and if needed to add second basal rate according to glucose self-monitoring values. The monitoring pattern indicates proper timing and rate of insulin to be administered. To determine bolus doses, the patient’s meal content must be taken in consideration: the patient is given either fixed-meal diet on which to adjust the bolus doses or the carbohydrate-to-insulin ratio for use in calculating meal boluses according to food intake. For the first 2-4 weeks, until basal rates are established, snacks are avoided. Adjustments of basal and bolus doses are based on blood glucose measurement taken before meals, 2 hours after meals, at bedtime, at midnight, and at 3 a.m. The basal rate is increased or decreased by 0.1 U/h to keep the premeal and overnight blood glucose levels within a 2-mmmol/L glucose excursion from baseline. If the glucose level rises by more than 2 mmol/L at prebreakfast measurement compared to 3 a.m. measurement, a second basal rate must be established (about 1.5 times the first basal rate that starts at 00.00 h) for 4 to 6 hours, and is started 2-3 hours before the usual breakfast time. The basal rate is adjusted during the day only if there are significant glucose excursions occurring in case of delaying meals or not eating. To perform a fine basal rate adjustment, the patient should delay or skip a meal and keep monitoring of blood glucose every 2 hours in fasting state. It is very common for people with diabetes to require a higher basal infusion of insulin in the predawn hours. Many people are more active in the late afternoon and more sedentary after dinner, requiring downward and upward adjustments, respectively (30,33).

Bolus doses are adjusted on the basis of glucose measurements performed 2 hours postmeal. The patients must be well educated to adjust his or her insulin boluses or carbohydrate-to-insulin ratio every 2 days in order to keep glucose levels within reasonable excursions (<10 mmol/L) 2 hours postmeal (30).
CALCULATING INSULIN REQUIREMENTS

It is essential for patients on CSII to know how to count carbohydrates before starting pump therapy, because the insulin pump device delivers bolus doses to compensate for the carbohydrate intake at each meal. To define a meal bolus – the amount of insulin that must be taken to compensate for the eaten carbohydrates, the patient has to calculate his insulin-carbohydrate ratio. The insulin-carbohydrate ratio tells the patient how much insulin he has to administer to compensate for a specific amount of carbohydrates. The ratio will vary from meal to meal and is under the influence of patient’s weight, age, physical activity, insulin sensitivity as well as of the presence of other diseases or diabetes related complications. There are several methods of calculating insulin-carbohydrate ratio. This ratio varies from 1U/5 g carbohydrate to 1U/25 g carbohydrate (33).

PATIENTS ON CSII NEED TO BE WELL EDUCATED AND ACQUIRE PROFICIENCY IN BASIC INSTRUCTIONS

With all candidates for insulin pump therapy, the risk of its use and risk prevention should be discussed in depth. This includes the risk of hyperglycemia and its possible development into ketosis and diabetic ketoacidosis, site infections as well as hypoglycemia awareness, prevention and treatment. The patients need to be aware of potential mechanical problems and problem solving strategies such as air bubbles, kinked infusion set, dislodged tubing that could cause lacking of expected insulin delivery, etc. Bode et al. point out that for the widespread use of CSII, an excellent educational set-up for patients and for medical staff is essential to increase favorable effects and to diminish side effects of CSII (33). All recent reports suggest that CSII shows greatest efficacy in patients who are well-trained in the management of intensive insulin treatment and who remain inadequately controlled because of frequent unpredictable hypoglycemia or a pronounced dawn phenomenon (7).

MONOMERIC INSULIN – THE PUMP INSULIN OF CHOICE

The pump insulin of choice is monomeric insulin. Several lately published studies have revealed that the use of insulin analog lispro in comparison to regular insulin for CSII significantly reduces blood glucose level and hemoglobin A1c (HbA1c) (34-38). Moreover, slightly but significantly less lispro insulin than regular insulin was required, but no difference in the incidence of hypoglycemic events was reported. Aspart insulin has recently been indicated to be as effective as buffered regular insulin and lispro when used in CSII therapy (39). In the same study the insulin analogs had an advantage over buffered regular insulin in terms of improvement of postprandial glycemic control. Postprandial glycemic control as well as fasting plasma glucose and mean plasma glucose highly correlate with HbA1c, as reported in the American Diabetes Association position statement (40). Several studies in nondiabetic and type 2 diabetic subjects have shown an increased risk of mortality and myocardial infarction to be associated with isolated postprandial hyperglycemia (41-47).

Some patients using lispro insulin in their pumps were found to have developed erratic and unpredictable glucose fluctuations because of insulin lispro precipitation in infusion catheters (48,49). Upon switching from lispro insulin to aspart insulin or buffered regular insulin, the problem resolved without repeated catheter blockages. It was confirmed that instability of lispro insulin was not in connection with any particular infusion catheter or type of insulin pump (48).

The rapid action of insulin analogs provides patients greater flexibility in their mealtime insulin needs because the bolus can be administered just before meals, resulting in improved compliance and better quality of life for patients using CSII therapy.

GLYCEMIC CONTROL DURING CSII

According to the results of DCGT, patients who used CSII had the mean HbA1c value lower by 0.2%-0.4% and improved lifestyle flexibity compared to patients on MDI therapy (50).
A recent meta-analysis of 12 randomized controlled trials (13-15,51-59), which compared CSII to intensified insulin injection regimens, shows a mean difference in blood glucose concentration of 0.9 mmol/L (95% CI 0.5-1.2) and HbA1c difference of 0.5% (0.2-0.7) in favor of CSII (7). Glycemic control according to the value of HbA1c was significantly improved after starting CSII therapy, as shown by other investigators (33,60-62). Glycemic control in patients on CSII is affected by several factors, as observed by Bode et al. (63). The frequency of blood glucose self-monitoring is the one with greatest impact on glycemic control. Other factors with a significant effect on glycemic control are: 1) recording of insulin and blood glucose values in a logbook (HbA1c 7.4% in those who record versus 7.8% in those who do not) (63); 2) dietary practices – carbohydrate counting (HbA1c 7.2% in those who count carbohydrates, 7.4% in those on a fixed-meal diet, and 8% in those on an undefined diet, p>0.001) (63); and 3) use of insulin lispro versus buffered insulin in the pump (HbA1c=7.3% versus 7.7%, p<0.001) (64).

Besides lowering the levels of glycosylated hemoglobin, CSII has been shown to decrease variability in the blood glucose level (6,65) and to lower fasting glucose level (13,16,66-68).

BLOOD GLUCOSE SELF-MONITORING

As reported by Bode et al., the frequency of blood glucose monitoring is the most important factor for successful treatment with insulin pumps (63). They have found that patients who monitor blood glucose levels three or more times a day have lower mean HbA1c level compared to patients who monitor it once or twice daily (7.2% versus 8%; p<0.001). They suggest that each additional blood glucose measurement corresponds to a 0.2% decrease in HbA1c (p<0.0002). To achieve strict blood glucose control it is neccessary to perform 4 to 6 blood glucose measurements daily.

DISADVANTAGES OF CSII

Hypoglycemia (disadvantage or indication for use of CSII?)

CSII therapy has been shown to decrease the incidence of severe hypoglycemia as compared to MDI therapy as a result of greater reproducibility and flexibility of insulin administration during CSII therapy. In DCCT, the incidence of severe hypoglycemia was three times greater in the group of patients on intensive diabetes treatment, with similar rates for multiple insulin injections and CSII (27). Much of the DCCT-associated hypoglycemia may have been due to unfamiliarity with the management of strict blood glucose control. This conclusion is based on the fact that the rates of hypoglycemia halved during the study. In contrast to DCCT, according to the experience of Bode et al., CSII is associated with a lower occurrence of hypoglycemia requiring assistance (69), and in some cases with restored hypoglycemia awareness. It is important to emphasize that the number of hypoglycemic episodes remained significantly lower in years 2, 3 and 4 of pump use (26, 39 and 36 episodes per 100 patient/years, respectively), without increase in HbA1c value (69). Moreover, a reduction in hypoglycemia has been shown by other investigators (60,61). Several factors are substantial for this decrease in severe hypoglycemia: better pharmacokinetic delivery of insulin, the ability to control blood glucose over a desired although higher target range for patients prone to hypoglycemia, and markedly reduced insulin requirements compared to MDI therapy (33).

Ketoacidosis

A patient on CSII does not have a subcutaneous depot of long acting insulin. If the flow of short acting insulin is interrupted, diabetic ketoacidosis can develop more rapidly and more frequently (as it has been reported in some early studies) with CSII compared to other modes of treatment (70-73). The cause of interruption of insulin administration may be either intentional, because of some patient activities, or unintentional, caused by catheter occlusion, catheter disinsertion, battery failure, or depleted insulin supply (74-76). In many cases ketoacidosis occurs as a result of patient error and inadequate training, particularly in patients who do not perform emergency steps in the event of unexplained hyperglycemia (77). Most studies show that with proper education and pump practice, there is no difference in the frequency of ketoacidosis between CSII and injection therapy (61,62,69,78).
Infusion site infections

Infection at the infusion site is probably more common in CSII than in MDI therapy. The organisms that are mainly causing infusion site infections are *Staphylococcus aureus*, *S. epidermidis* and *Mycobacterium fortuitum* (79-81). Occasionally, the infection may lead to cellulitis or abscess formation requiring surgical treatment. The annual rate of infusion site infection has been estimated to 7.3-11.3 events per 100 years of patient follow up (50). The risk of infusion site infections can be reduced by changing the infusion set every 2-3 days, not reusing cannulas, washing hands before insertion, and covering the implanted needle with a sterile dressing.

THE COST-EFFECTIVENESS OF CSII COMPARED TO MDI IN THE MANAGEMENT OF DIABETES

It is well known that for the application and reimbursement of CSII therapy appropriately screened candidates are necessary. The ability to identify eligible candidates for CSII and to sustain their participation in therapy is a hard issue to achieve positive outcomes reported by the DCCT (1).

Many persons with type 1 diabetes mellitus are now exploring whether CSII is a treatment option for them. Unfortunately, despite the initial enthusiasm about this mode of intensive treatment, according to the literature, about 50% of these diabetics discontinue CSII within a period of 2 years of its initiation (82-84).

According to the protocol used in the DCCT, to initiate intensive therapy subjects were hospitalized. The estimated cost for initiating CSII in the DCCT was about 2900 USD per subject (27,85). Total estimated annual cost for sustaining CSII was about 5800 USD per subject per year (27,85). In the study performed by Sanfield et al. (86), participants were followed for 2.5 years, discontinuation rate was 3%, and the estimated cost for screening, CSII initiation and follow-up was about 2431 USD. Through the structured screening protocol 37% of patients were identified as noneligible candidates for CSII. Once the CSII has been initiated, only 3% of elected individuals discontinue this therapy within 2.5 years of initiation. The most recently published study suggests that CSII is most cost-effective in patients who had more than two severe hypoglycemic events per year and who required admission to hospital at least once a year (87).

USE OF CSII IN SPECIFIC GROUPS OF DIABETIC PATIENTS

CSII and pregnancy

A connection between maternal hyperglycemia in women with type 1 diabetes and the risk of consecutive congenital fetal anomalies is well known (88,89). Euglycemic or near euglycemic control is the goal throughout pregnancy as well as during the preconception period. One of the main indications for use of insulin pump therapy is hypoglycemia, the occurrence of which increases during the first trimester of pregnancy. In the study of Kimmerle et al. (90), a very high rate of severe hypoglycemia of 41% was recorded in pregnant women with diabetes. Severe hypoglycemia was defined as coma, seizure or incapacitation requiring third part assistance. Considering the efficacy of CSII in reducing hypoglycemia and improving glucose excursions, there is every reason for its use in pregnant women with diabetes.

In spite of the at least comparable effect to MDI (91-93), there are several advantages that suggest the use of CSII in pregnancy, i.e. increased ease of treating morning sickness and hyperemesis gravidarum, reduction in glycemic excursions and hypoglycemia, ease of treating the dawn phenomenon that increases during pregnancy, and improvement in the postpartum period when fluctuation of insulin requirements may occur (94).

CSII in children and adolescents

In the last years, there has been a dramatic increase in the use of CSII in children and adolescents suffering from diabetes. The DCCT recommendations for strict metabolic control and development in pump technology have resulted in a tremendous increase in the number of insulin pump users in the USA, from 500 in 1997 to more than 7 500 in 2001 (30). A recently published study (95) analyzed 161 patients (aged 18 months to 18 years) and has reported a decrease in HbA1c by 0.6%-0.7% as well as a decrease in the number of severe hypoglycemia episodes. The
continuation rate was 98%. In spite of lower HbA1c value, the rate of severe hypoglycemic events (seizure or coma) was significantly lower. In a lately published study that included 95 patients, mean age 12 years and median duration of follow-up 28 months, the mean HbA1c value upon starting pump therapy was significantly lower than before it (7.75% vs 8.1%, p<0.001) (96). The number of hypoglycemic events was reduced upon the introduction of pump therapy (12 vs. 17; rate ratio 0.46, CI 0.21-1.01). The incidence of diabetic ketoacidosis and emergency department visits was similar before and after the start of insulin pump therapy. According to the above mentioned results, it is to conclude that insulin pump therapy significantly improves glycemic control and reduces hypoglycemic events in children and adolescents, with no difference in the number of diabetic ketoacidosis episodes. One of the considerable benefits of CSII in infants and toddlers is reduction in the risk of severe hypoglycemia (97).

COMPARISON OF CSII AND MDI WITH GLARGINE

Glargine is an insulin analog proposed as long acting, peakless insulin designed to meet basal insulin requirements. The theoretical advantage of CSII is its ability to deliver insulin more physiologically resulting in greater stability of blood glucose level than it could be achieved with MDI. One of the most significant features of CSII is basal rate preprogramming to meet the physiologic insulin needs, therefore mostly several basal rates are necessary. This feature is in particular helpful during the night when insulin pharmacokinetics and the dawn phenomenon may modify basal insulin requirements (98). The study performed by King (99) showed the patients on MDI (lispro insulin and glargine) to be for a significantly longer time out of the target sensor glucose ranges (3.8-11.1 mmol/L) compared to the group of patients on CSII (50.7% vs. 20.9%, p=0.04). The patients treated with glargine had a 3-fold increase in the time exposed to glucose values below 3.8 mmol/L compared to CSII patients, and 2-fold increase in the time exposed to glucose values greater than 11.1 mmol/L. The mean number of nocturnal basal rate setting was 2.4 ± 0.7 in the CSII group. The group of patients on MDI with glargine had no possibility to change basal rates. The ideal basal insulin should be administered at a variable rate to satisfy changes in daily insulin requirements. CSII seems to be the only current method of basal insulin delivery achieving this variable rate (99).

OUR EXPERIENCE WITH THE USE OF CSII

At the end of the 1980s, we carried out a study to compare the efficacy and safety of MDI and CSII introduced in outpatient conditions during a one-year randomized crossover trial. After a 3-month run-in period, 39 type 1 diabetic patients were allocated either to MDI or CSII. During the first 6 months, HbA1c values decreased significantly in both groups (MDI from 7.2% ± 1.9% to 6.5% ± 1.0%, p<0.05; CSII from 7.4% ± 0.9% to 5.9% ± 0.8%, p<0.001). After crossover HbA1c values decreased again on CSII (from 6.9% ± 1.3% to 6.1% ± 0.8%, p<0.05), however, in the group of patients who were switched from CSII to MDI, HbA1c values significantly increased (from 6.1% ± 0.5% to 7.4% ± 1.2%, p<0.001). Although the rate of severe hypoglycemia requiring assistance was twice as high during pump therapy (0.94/patient-years) compared to MDI (0.47/patient-years), the total number of hypoglycemic coma was the same (4 both). The rate of severe episodes of ketosis was 6-fold (2.05/patient-years vs. 0.37/patient-years) and the incidence of diabetic ketoacidosis 2.5-fold in CSII compared with MDI (0.28/patient-years vs. 0.11/patient-years) (100,101).

CONTINUOUS INTRAPERITONEAL INSULIN INFUSION (CIPII) - IMPLANTABLE INSULIN PUMPS

These are insulin pumps that are located within the body to deliver insulin intravenously or intraperitoneally. Despite their use for almost 20 years now, the number of patients using this mode of intensive diabetes management remains low, about one thousand, worldwide. The advantages of implanted insulin pumps include: the pump is out of sight, there is no need for catheter insertion, and ease of insulin delivery to great veins or into peritoneal cavity. The use of implanted insulin pumps is limited by their relative invasiveness, cost and reported high frequency of complications during pump therapy (101-105).
use of implanted insulin pumps in comparison to CSII/MDI improves glycemic control (the level of HbA1c was lower by 0.6%), and the number of severe hypoglycemic events was reduced, as suggested by some investigators (106-109).

According to so-called Dutch experience, very poor glycemic control and repeated admissions to the hospital due to diabetes are indications with good reason for implantable insulin pumps (110).

CONCLUSION

The future of CSII seems to be promising. CSII in comparison to MDI has better insulin pharmacokinetics, less variability in insulin absorption, and decreased risk of hypoglycemia. The main advantages of CSII are improvement in glycemic control, reduced risk of hypoglycemic events, and lifestyle flexibility. The improvement in lifestyle is one of the most important advantages of CSII allowing patients to perform activities that would otherwise be risky, such as skipping or delaying meals, sleeping late on weekends, or engaging in vigorous exercise. Notable disadvantages of CSII include increased implementation cost, infusion site infections, and the risk of ketoacidosis.

Because of its advantages it is to expect that CSII technology may be used in 40% of type 1 diabetic patients and about 5% of those suffering from type 2 diabetes (33).

REFERENCES


