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Соотношение дозы инсулина и массы тела как предиктор эффективности помповой инсулинотерапии у пациентов с сахарным диабетом 2 типа: пилотное исследование

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Цель. *Оценить эффективность инсулинотерапии в режиме постоянной подкожной инфузии инсулина (ППИИ) для лечения пациентов с сахарным диабетом 2 типа (СД2) при длительном наблюдении. Определить предикторы эффективности ППИИ в отношении улучшения показателей гликемического контроля (снижение HbA_{1c}) в этой группе пациентов.*

Материалы и методы. *В исследовании приняли участие 18 пациентов с СД2, переведенных на ППИИ в Институте диабета больничной кассы Маккаби (Петах-Тиква, Израиль). До перевода на ППИИ все пациенты получали интенсифицированную базисно-болюсную инсулинотерапию в режиме множественных ежедневных инъекций генно-инженерными аналогами человеческого инсулина. Длительность инсулинотерапии к моменту перевода на ППИИ составила 54,9±51,4 мес.*

Результаты. *Длительность наблюдения пациентов после перевода на ППИИ составила 42,2±27,0 мес. К концу исследования показатели глюкозы в крови натощак снизились (в среднем с 10,5±2,9 ммоль/л до 7,6±1,9 ммоль/л, p=0,007), однако изменения HbA_{1c} не были статистически достоверными (p=0,064). За период наблюдения не отмечено значимого изменения массы тела пациентов и частоты эпизодов тяжелой гипогликемии. После завершения исследования пациенты были разделены на 3 группы – в зависимости от изменений HbA_{1c}: A – значимое снижение (5 человек); B – значимое повышение (8 человек); C – незначимые изменения (5 человек). При анализе причин различий результатов инсулинотерапии в режиме ППИИ было обнаружено, что группы значимо отличались по соотношению дозы инсулина и массы тела (И/М) к моменту окончания исследования: 0,41±0,12 ЕД/кг и 0,93±0,6 ЕД/кг в группах A и B соответственно (p=0,011). У пациентов в группе A за время исследования соотношение И/М значимо снизилось и составило 0,81±0,29 ЕД/кг и 0,41±0,12 ЕД/кг до и после перевода на ППИИ соответственно (p=0,043). При этом за время наблюдения отмечена тенденция к увеличению массы тела у пациентов из группы B и снижению – у пациентов из группы A.*

Заключение. *ППИИ может быть эффективным способом инсулинотерапии у некоторых пациентов с СД2. Вероятно, одним из ранних предикторов эффективности ППИИ у пациентов с СД2 может быть снижение соотношения И/М. Представленная работа, в то же время, может служить очередным доказательством преимущественной роли мероприятий по контролю веса в эффективности лечения пациентов с СД2. Однако требуются дальнейшие более масштабные проспективные контролируемые исследования для изучения отдельных аспектов эффективности и безопасности применения ППИИ у пациентов с СД2.*

Ключевые слова: *инсулин; масса тела; ожирение; инсулиновая помпа; сахарный диабет 2 типа; пилотное исследование*

Insulin/weight ratio may serve as a predictor of success during insulin pump therapy in type 2 diabetes patients: a proof-of-concept study

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Aims. *To evaluate long-term efficacy of CSII for treating type 2 diabetes patients. To make an attempt to predict which patient would be more likely to reduce HbA_{1c} levels (success) on CSII.*
Methods. *18 Type 2 diabetes patients who began insulin pump therapy in our institute were included. All patients were previously treated by insulin with a mean duration of 54.9±51.4 months.*
Results. *Mean duration of follow-up with CSII was 42.2±27.0 months. No significant changes were seen in HbA_{1c} in total cohort (p=0.064), but fasting plasma glucose was reduced from 10,5±2,9 to 7,6±1,9 mmol/l, p=0.007. No weight gain and no severe hypoglycemia were noted. All patients were divided to three groups according to their HbA_{1c} levels: those whose treatment was successful (A), failed (B) or neutral (C), (5, 8, 5 patients respectively). A difference was found in insulin/weight (IWR) ratio within the group A: 0.81±0.29 U/kg before vs. 0.41 ±0.12 U/kg on CSII, p=0.043. There was a difference in IWR on CSII in group A compared to group B (0.41 ±0.12 U/kg vs. 0.93±0.6 U/kg respectively, p=0.011). We also noted a trend of weight reduction in the group A vs. weight gain in the group B.*
Conclusions. *CSII is a viable tool in insulin – requiring type 2 diabetes persons, since the insulin dosing and release it provides are much more physiological. CSII is safe and effective for improving glycemic control, but not in all diabetes patients. We suggest IWR reduction may serve as an early predictor of success on CSII. This work may serve as a "proof-of-concept" study, demonstrating once again the fundamental role of strict weight control in type 2 diabetes. More studies are needed to explore and confirm our experience.*
Keywords: *insulin; weight; obese; pump; type 2 diabetes; concept*

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Iintroduction

Exogenous insulin is the longest established blood-glucose-lowering therapy. It produces large reductions in blood-glucose levels and can be life-saving for patients that absolutely require insulin-replacement therapy, such as those with type 1 diabetes. Nevertheless, there is a clear need to review the way in which exogenous insulin is used in people with type 2 diabetes and to establish a detailed risk–benefit profile of different therapeutic schemes and facilities [1].

The use of intensive insulin therapy in type 2 diabetes is a controversial and widely discussed topic. Indeed, the rules implemented in the treatment of type1 diabetes, cannot be simplistically extrapolated to type 2 diabetes therapy [2]. Furthermore, contrary to treatment algorithms accepted in type 1 diabetes, several studies failed to find any benefits to strict adherence to "Bolus calculation". They found that only basic manipulations and optimizations of insulin doses, exerted on basal rates or on simple boluses, are feasible and effective in type 2 diabetes [3].

The evidence regarding the superiority of CSII over MDI, is currently uncertain, pending results of a large randomized control trials [4,5]. Moreover, the growing number of type 2 diabetes patients treated with MDI and CSII worldwide, presents new challenges for health care providers and opinion leaders. In addition to an improvement in the glycemic status of the patients [6], many studies on CSII in type 2 diabetes have showed an increased treatment satisfaction among patients, favoring CSII [7, 8]. However, the majority of these studies are short term, ranging from merely a few weeks to several months. Only a small number of publications deal with a long-term effect of CSII on type 2 diabetes persons [3, 14], attempting to define the optimal patient and treatment protocol. Our current investigation summarizes the clinical experience of prolonged (more than 3.5 years on average) CSII use in type 2 diabetes. This provides us a unique opportunity to look at the effect of therapy from a time-continuum perspective. We attempted to analyze separately patients who succeeded or failed on CSII. This is also the first survey to study patients' compliance on pump therapy. The data obtained in this "real-life" clinical situation gives a new understanding not only of the role of insulin pump therapy, but also of insulin per se in type 2 diabetes. This study may be considered as a proof-of-concept survey reflecting and confirming our "Gravicentric" concept regarding the key role of strict weight control in type 2 diabetes persons [2, 18] and the necessity of physiological insulin dosing [9].

Materials and methods

Study Design

This study consists of an almost 12-year period during which subjects were treated with CSII (Medtronic Paradigm). Twelve patients (67%) were treated with Metformin before CSII and continued their prior treatment on pump therapy. Most patients were also on statin therapy from the beginning of their illness. Patients' usual treatment protocol consisted of

Table 1

Basal characteristics and main results of the 18 patients on CSII

Measure	Mean Before ± SD	Mean on CSII ± SD	p
Total number of patients	18	-	-
Men	12	-	-
Women	6	-	-
Mean age (years)	63.5	-	-
Mean age on first Diabetes diagnose (years)	46.3	-	-
Average time on pump therapy (months)	42.2±27.0	-	-
Average time on insulin before CSII (months)	54.9±51.4	-	-
HbA_{1c}%	8.4±1.6	7.8±1.2	0.064
FPG mg%	189.7±51.6	136.8±34.8	0.007
Total Cholesterol mg/dl	172.2±31.8	162.8±30.8	NS
LDL mg/dl	98.9±32.3	88.9±28.6	NS
HDL mg/dl	45.6±11.7	44.3 ±9.2	NS
TG mg/dl	177.46 ± 96.7	149.8 ± 65.4	NS
Weight kg	89.3 ±15.8	89.9±15.7	NS
BMI kg/m^2	31.7 ±4.9	32.0 ±5.2	NS
Sys BP mmHg	130.4 ±20.1	136.7±14.1	NS
Diastolic BP mmHg	82.4 ±18.0	74.1±8.3	NS
Daily Insulin Units/day	86.7 ±72.0	63.5±50.1	NS
Insulin/Weight Ratio U/kg	0.88 ±0.56	0.68 ± 0.48	0.093
% Basal	64.2±14.6	62.78± 17.8	NS
% Bolus	35.8±14.6	37.2 ± 17.8	NS
Total compliance score	0.8±1.1	0.9±1.2	NS
Freq. Hypo score	0.63±1.2	2.8±2.9	0.0313

SMBG measurements with glucose meter at least with every main meal and before sleep. Patients were also requested to calculate carbohydrates and insert the data into the pump's memory before each meal to be used as diary data points. Insulin doses were adjusted at least once in three months. Treatment target was to achieve HbA_{1c} of less than 7% (53 mmol/mol) and there were no limitations for insulin dosing.

Patients and Methods

All 18 type 2 diabetes patients who were treated with CSII and diagnosed with type 2 diabetes for at least 12 months before starting insulin pump therapy, were followed in the Institute of Diabetology, at the Maccabi Health Fund in Petah Tiqwa. Insulin pump therapy was implemented from January 2001 and data collection was closed in August 2012. The follow-up ranged between 6 months and 11 years. For this study, we have reviewed the medical records of all 18 patients. Prior to pump therapy all patients were on MDI, using premixed insulin analogs or basal-bolus regimens (also analog insulins). Mean duration of injection-based insulin therapy was 4.6 years (Table 1).

CSII was initiated because of poor glycemic control, as observed by an average HbA_{1c} of 8.4±1.6 % (68±17 mmol/mol) before pump therapy or/and wide glucose variations with frequent hypoglycemia. Mean age of first diabetes diagnosis was 46.3 years; none of the 18 patients had positive Anti-GAD and Anti- Islet Cell antibodies, which makes type 2 diabetes diagnosis most reasonable.

In all 18 patients TDI dose was automatically reduced by 20 – 25% on average, while switching from MDI to CSII. As regarding investigated measures, in each parameter, the mean value of three last measurements just before switching to CSII was compared to the mean value of three last measurements on CSII (See table 1).

Statistics

Pre- and on-pump measures were compared using a paired samples t-test. Due to the small sample size, the Wilcoxon signed-rank test was applied to compare measures that resulted in small values and noticeably deviated from normality. Pearson correlation coefficient was performed to estimate the strength of correlation between several measures.

Compliance Assessment

When at least two of the four following parameters were met, the patient was considered incompliant:

Table 2

Hypoglycemia assessment score	
Score	Hypoglycemia frequency
0	No hypoglycemia episodes
1	Less than 1 episode/month
2	1-3 episodes/month
3	1 episode/week
4	2-4 episode/week
5	5 or more episodes per week

- Patient has missed two or more appointments at the diabetes clinic in the last year.
- Patient has not provided SMBG results at least twice in the last year.
- Low compliance for diet and physical activity.
- Patient has not used carbohydrate counting and "bolus calculation" in the last 6 months.

Hypoglycemia Assessment

All hypoglycemia events were divided to severe (a patient was in need of assistance) and non-severe. A non- severe hypoglycemia was assessed according to the following score (Table 2).

Results

Following a statistical analysis of the total cohort, no significant reduction of HbA_{1c} was found. Nevertheless, when every patient's file was analyzed separately, there was clear evidence of improvement in some patients, while no improvement or even deterioration was noted in others. Post Hoc, we categorized the patients into 3 groups according to their HbA_{1c} changes: A – successful treatment (significant mean HbA_{1c} reduction, 5 patients); B – failed treatment (mean HbA_{1c} elevation, 8 patients); and C – treatment achievements were neutral, (HbA_{1c} didn't change, 5 patients).

At first, the group A consisted of six patients, but in order to prevent bias, one patient was moved to the group C, because of a very small dose of insulin at the beginning (in spite of negative Anti-GAD antibodies and Anti-Islet cell antibodies ,we couldn't exclude other types of diabetes in this patient). Groups A and B were analyzed and compared separately.

The Total Cohort Analysis

HbA_{1c}: CSII seemed to be effective in terms of HbA_{1c} reduction in a whole cohort: 8.4±1.6 % (68±17 mmol/mol) at the beginning vs. 7.8±1.2% (62±13 mmol/mol) at the end of the study, but the difference wasn't statistically significant (p=0.064), most likely because of the small number of patients.

FPG: In consistence with the difference obtained in HbA_{1c} levels before and during CSII, there was clear evidence of FPG reduction from 189.7±51.6 mg% before, to 136.8±34.8 mg% on CSII, p=0.007.

The Basal – Bolus ratio: It is of note that the Basal-to-Bolus ratio was 64.2 %-to-35.8 % respectively, thus determining probable physiological demand in patients with type 2 diabetes. This finding also may justify the use of "low-mixed" insulins, such as Mix 70/30 and possibly shows that "high-mixed" insulins, such as Mix 50/50 or 30/70, are less appropriate in type 2 diabetes.

Hypoglycemia: No case of severe hypoglycemia was observed. However, the frequency of mild hypoglycemic episodes slightly increased: 0.63±1.2 vs. 2.8±2.9 points, p = 0.03.

Compliance: The total compliance score didn't change on CSII therapy.

Weight: No significant changes were noted in the total cohort after initiating CSII: 89.3 ± 15.8 kg before vs. 89.9 ± 15.7 kg during CSII, p value is non-significant. This is in concordance with our previous work where no weight gain was found on long-term therapy

Table 3

Between and Intra-Group Comparison of "Successful" and "Failed" Groups					
Measure	Successful-treatment group (N=6)	Failed-treatment group (N= 8)	P value Successful vs. Failed	P value Successful-treatment group: Before vs. On CSII	P value Failed-treatment group: Before vs. On CSII
I/W ratio before CSII	0.81 ±0.29	1.02±0.8	0.4852	0.043	0.67
I/W ratio On CSII	0.41 ±0.12	0.93±0.6	0.011		
Weight before CSII	88.0±21.1	94.6±15.1	0.572	0.08	0.017
Weight On CSII	83.7±19.2	98.6±14.1	0.307		
BMI Before CSII	31.3 ±4.6	33.7±5.6	NS	0.14	0.017
BMI On CSII	29.8±4.4	35.2±5.8	NS		
HbA_{1c} Before CSII	8.2 ± 1.8	8.9± 1.8	0.435		
HbA1c On CSII	6.9 ± 0.7	8.5 ± 1.1	0.065	0.042	NS

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Table 4

HbA_{1c}, TDI, Weight and IWR in Success-group on first HbA_{1c} improvement								
Patient's N	TDI (U) Before CSII	TDI (U) within 1/2 year on CSII	Weight (kg) before CSII	Weight (kg) within 1/2 year on CSII	IWR (U/kg) before CSII	IWR (U/kg) within 1/2 year on CSII	HbA_{1c} (%) before CSII	HbA_{1c} (%) within 1/2 year on CSII
Patient1	134	100.5	106.3	96	1.261	1.047	6.8	6.3
Patient2	56	42	99.5	97	0.563	0.433	8.0	7.5
Patient3	89	57.1	104	96	0.856	0.595	7.3	6.3
Patient4	34	25.5	63.5	64.3	0.535	0.397	7.4	7.0
Patient5	56	42	66.5	66.5	0.842	0.632	9.8	7.3

with pre-mixed insulins [9]. Reasons and explanations for this phenomenon are to be discussed.

Between and Intra-Group Comparison of "Successful" and "Failed" Groups

Changes in weight and BMI. Patients from group A exhibited a tendency to reduce body weight: 88.0 ± 21.1 kg before and 83.7 ± 19.2 kg during CSII, p=0.08 with a BMI of 31.3 ± 4.6 before CSII and 29.8±4.4 on CSII, although the differences were not statistically significant.

On the other hand, there was a significant weight gain in patients from group B: 94.6±15.1 kg before and 98.6±14.1 kg on CSII, p= 0.017, with a BMI of 33.7±5.6 before and 35.2±5.8 on CSII, p= 0.017.

Insulin/Weight ratio (IWR). This is the only measurement where significant differences were detected between the two groups: 0.41 ±0.12 U/kg on CSII in the Successful-treatment group A, vs. 0.93±0.6 U/kg on CSII in the Failed-treatment group B, p=0.011 (Table 3). Causes and explanations to these findings are explored later.

The cohort in Group A was characterized by a significant reduction in IWR from 0.81 ±0.29 U/kg at baseline to 0.41 ±0.12 U/kg on CSII, p= 0.043. There was a parallel reduction of HbA_{1c} from 8.2 ± 1.8% (66 ± 20 mmol/mol) at baseline, to 6.9 ± 0.7% (52 ± 8 mmol/mol) on SCII, p= 0.042.

Correlations

Because IWR was the only measurement where significant between – group differences were detected, the question was asked regarding possible correlations between IWR and other parameters.

Indeed, a directly proportional connection was found between IWR and BMI, before and on CSII. The more weight (BMI) was before CSII therapy, the bigger was the IWR ($p < 0.001$). The less weight (BMI) was on CSII therapy, the smaller was the IWR (p=0.011). Another correlation was a directly proportional dependence between IWR and HbA_{1c} on CSII (p=0.029). Specifically: the less the IWR was, the smaller was the HbA_{1c} value.

A strong connection was also found between IWR and triglyceride (TG) levels on CSII. The smaller was the IWR, the lesser were the TG levels. Unlike cholesterol levels, which may be influenced by statin therapy, triglycerides are much less statin-dependent and thus, may reflect a true improvement in the metabolic status of our patients.

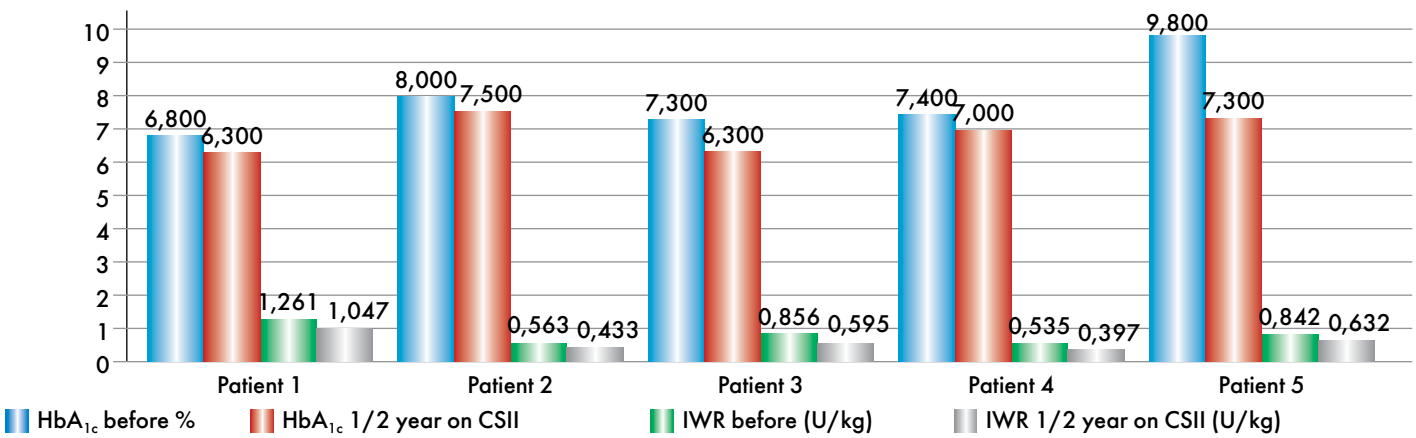

Рис. 1. Figure 1. HbA1c and IWR in Success-group on first HbA_{1c} improvement.

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Clinical importance of IWR

The differences in IWR gave rise to a question: would it be possible to predict the success or failure of CSII therapy at its early stages? For this purpose, IWR in the successful-treatment group was investigated as soon as first improvements in HbA_{1c} were observed. First HbA_{1c} improvement was usually noticeable three to six months after starting CSII. In all five patients, there was a parallel reduction in IWR compared to baseline (Table 4; Figure 1).

Discussion

Continuous subcutaneous insulin infusion for type 2 diabetes mellitus is a promising therapy, but the clinical evidence supporting it is mixed [6].The advantages of pump therapy in type 1 diabetes are discussed elsewhere [10], while the benefits of CSII in type 2 diabetes remain a matter of debate. Some authors claim CSII advantages [11], some remain skeptical [12], while others suggest that CSII is as good as MDI in type 2 diabetes therapy [13, 5]. When considering CSII therapy for a type 2 diabetes person, several issues have to be taken into account. The first is the fact that type 2 diabetes constantly grows younger. Given the proven convenience of insulin pump therapy and the improvement in quality of life it provides, there seems to be almost no objective medical reason against advising CSII to younger type 2 diabetes patients treated with MDI. Another point to be considered is that many studies have proved CSII benefits in type 2 diabetes persons [14, 6].

This study stands-out due to its long-term follow-up in 18 type 2 diabetes patients on CSII, and thus it can help to define the responders versus non-responders to long – term pump therapy.

Safety was achieved as there was no increase of severe hypoglycemic events in all groups assessed. The frequency of non-severe hypoglycemia, on the other hand, went up from 0.63±1.2 to 2.8±2.9 points according to our score, (p =0.03). In other words, at the beginning of treatment ,the frequency of non-severe hypoglycemia was less than once per month, while on CSII it was 1-3 per month and up to one episode per week.

There may be two explanations for this. First, as a result of a more intensive insulin therapy provided by pumps, patients had an improved glycemic control that resulted in more frequent hypoglycemic events. Additionally, considering the fact that most hypoglycemia episodes were recorded from patients' individual SMBG reports, this finding may be at least partially explained by a much more frequent and accurate use of SMBG by patients who switched from MDI to CSII, thus revealing previously "hidden" hypoglycemia events.

Overall, there was no significant weight gain.

Our concept of insulin therapy in type 2 diabetes has been applied for the last years [2,9], and consists of the following:

- Avoiding the prescription of MDI to morbidly obese patients;
- Dose of insulin should be the lowest possible, less than 0.6 U/kg of current body weight (so called, physiological doses) [9,15,18];
- Prescribing insulin therapy along with Metformin, unless the latter is contraindicated.

With this strategy, there was a trend towards HbA_{1c} reduction in total cohort, though no significant change was detected (8.4±1.6 % (68±17 mmol/mol) before vs. 7.8±1.2 % (62±13 mmol/mol) on CSII). This may indicate an overall tendency to glucose control improvement. FPG, on the other hand, was considerably reduced on CSII. This is likely due to the night basal insulin delivered much more physiologically by pumps. It is somehow counterintuitive that despite the tendency to TDI dose reduction, pump therapy improved diabetes control and FPG in particular. This data is in concordance with recent investigation [16], where impressive improvement was achieved on CSII despite a decrease in overall insulin requirements, representing one of the advantage of CSII over modern basal insulins.

All patients were treated by statins from the beginning of their illness, as part of a complex therapy in type 2 diabetes. Considering this fact, the tendency to LDL reduction from 95.7 ± 33.3 to 79.0 ± 20.4 mg/dl may only partially be explained by an overall metabolic improvement on SCII (p value was close to significant = 0.06).

No significant changes of weight, BMI and IWR were reported in total cohort.

In spite of absence of changes in IWR in total cohort, (p= 0.09), this parameter was the only significantly diverse measurement at comparison between "Group A" and "Group B" (Table 3).

As the IWR= TDI/Current weight, it is apparent there are two ways to reduce IWR: either reduce TDI while weight is stable, or elevate the weight while TDI is stable. Considering the fact that each patient was recommended to decrease TDI dose by 20-25% while switching from MDI to CSII, one might expect an IWR reduction in all 18 patients. Surprisingly, IWR did not

change in groups B and C. This is due to the fact that the TDI dose had to be elevated during the follow-up of these patients. All patients within the "failed" group B exhibited weight gain: 94.6±15.1 kg before and 98.6±14.1 kg on CSII, with a BMI of 33.7±5.6 before and 35.2±5.8 on CSII, p= 0.017. Logically, this should have reduced IWR; however, growing insulin resistance prevented it from happening. In these patients we had to increase the insulin dose from visit to visit. As a result, at the end of the study, IWR in the failed-treatment group exceeded physiological parameters: 0.93±0.6 U/kg.

We call this phenomenon the "double 'O' syndrome", a pattern of "Overeating- Overtreating" [2;18]. The kind of vicious cycle that occurs when patients gain weight and remain uncontrolled in spite of insulin dose elevation. On the other hand, there was a tendency toward weight reduction in group A: 88.0 ± 21.1 kg before and 83.7 ± 19.2 kg during CSII, p=0.08 with a BMI of 31.3 ± 4.6 before CSII and 29.8 ± 4.4 on CSII, although the differences were not statistically significant. Looking at the IWR formula, one would expect weight reduction to invariably cause IWR elevation. However, the IWR went down.

To understand this finding let us take a separate look at each "successful" patient 6 months after beginning CSII (Table 4). There was an apparent and impressive TDI reduction in each successful-treatment group patient. Three out of five patients reduced their body weight. The fourth patient gained 1 kg as the insulin dose went down, while the weight of the fifth patient remained unaffected. Although three patients reduced both their weight and their TDI, the proportion of TDI reduction exceeded the proportion of body weight reduction. This resulted in an apparent reduction in IWR. Patient 4 was the only one to slightly gain weight, but his TDI also dropped. In this patient IWR changed from the borderline-physiological 0.54 U/kg to a much more physiological 0.4 U/kg, while HbA_{1c} went down from 7.4 % (57 mmol/mol) to 7.0% (53 mmol/mol). Patient 5 didn't change his body weight, but his TDI dropped from 56 to 42 U/day, while IWR changed from supra-physiological 0.84 U/kg to a much more physiological 0.63 U/kg. It seems therefore that patients with better insulin sensitivity within type 2 diabetes tend to respond better to CSII, or that a different approach for highly insulin resistant patients should be considered.

IWR reduction was seen early, within the first 6 months of CSII therapy. This finding is remarkable, since it is likely to provide us with an opportunity to predict success in our patients (Table 3, Table 4, Figure1).

Considering the above information, a plausible explanation of the IWR reduction phenomenon is as follows: CSII is much more physiological than subcutaneous multiple injections and provides the maximal insulin effectiveness. Insulin given in physiological doses prevents overtreatment and facilitates weight reduction in compliant patients. This, in turn, results in better insulin sensitivity and further diminishment of TDI. Thus, it seems likely that we would succeed when we would be able to proceed through the following pathway:

More physiological insulin delivery > less weight (BMI) > better metabolic status > less IWR > less HbA_{1c}

Overall, these findings support our recently published "Gravicentric" concept and algorithm [2;18], showing once again that weight reduction is a key factor of success in type 2 diabetes therapies. Significant correlations, found between IWR on the one hand and BMI, TG, and HbA_{1c} on the other hand, complete this puzzle.

Conclusion

CSII is a viable tool in insulin – requiring type 2 diabetes persons, since the insulin dosing and release it provides are much more physiological; CSII is safe and effective for improving glycemic control, but not in all diabetes patients. We suggest, IWR reduction may serve as an early predictor of success on CSII. This work may serve as a "proof-of-concept" study, demonstrating once again the fundamental role of strict weight control in type 2 diabetes. More studies are needed to explore and confirm our experience.

Competing interests

The authors declare that they have no conflict of interest.

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