

Quality of Life and New Devices in the Management of Type 1 Diabetes in Children and Adolescents

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Abstract. Insulin therapy is the cornerstone in treatment of type 1 diabetes in children and adolescents. In order to prevent long-term complication multiple daily injections (MDI) are required. Quality of life is clearly affected by the administrations of 3-4 daily injections with syringe. Insulin pens are new devices realized with the aim of simplifying insulin administration. More recently continuous blood sugar monitoring has become available for clinical studies and its role for better metabolic control and quality of life is now under investigation. The aim of this paper is to review published data on the significance of insulin pen and continuous blood sugar monitoring on quality of life in diabetic children and adolescents.

Key words: Type 1 diabetes, insulin pen, continuous blood sugar monitoring, quality of life

Treatment of type 1 diabetes in children and adolescents has greatly improved in the last decades with the introduction of human insulin and its analogues. The Diabetes Control and Complication Trial has underlined the importance of strict metabolic control in order to prevent micro and macrovascular complications.

With optimised insulin therapy diabetic children have now a long expectancy of life and the onset of late complications is delayed.

On the other side the burden of treatment with multi-daily injections or continuous subcutaneous insulin infusion and of blood sugar monitoring can worsen the quality of life.

To improve the degree of metabolic control most patients have increased the number of insulin injections to 3-4 or more.

Insulin pen injectors are simpler automatically preset device for self-injections that have been introduced in the eighties as more comfortable method that makes patients' life easier and since then their use has been chosen by a large number of patients.

In one of the first reports Czernichow and colleagues studied a group of 15 C-peptide negative insulin dependent diabetic children using an injector pen (Novopen) to deliver soluble insulin before meals in association with an insulin syringe for long acting insulin administration at bedtime for a period of 17 months. Despite frequent daily injections (4-5) long-term patients acceptability was excellent.

Novopen was experienced as a progress (100%) which made a multiple injection regimen acceptable and provided an improvement in the quality of life (77%), as recorded by questionnaires answered at the end of the study. Twelve out of 15 patients chose to continue this treatment. No significant change in glycaemic control was observed in the group as a whole. An improvement in glycosylated haemoglobin (HbA1c) was noticed only in the previously "poorly-controlled" children (n = 8) with initial HbA1c greater than 7%. In this group HbA1c decreased from $8.4 \pm$ SD, to $7.3 \pm 1.2\%$ (P less than 0.05) within the first 6 months of Novopen therapy. The authors conclude that in this group of diabetic children no long-term

metabolic improvement was obtained, despite excellent acceptability of the multiple injection regimen with Novopen (1).

Similar observations have been obtained by Hornquist and colleagues in a study that investigated whether quality of life and metabolic control improve and whether insulin requirements change subsequent to multiple injection-pen treatment. The study group comprised 72 consecutive outpatients with IDDM. Thirty-eight subjects had an initial daily regimen of one or two injection, and the remaining 34 subjects had three or more injections. All patients had four of five injections per day during pen treatment. Perceived changes in quality of life attributed to pen treatment were assessed retrospectively at follow-up 9-13 months after the changeover. Data on metabolic control (HbA1c) and insulin dose were collected at base line and follow-up. The life quality of the IDDM-patients improves consistently, a finding corroborated by recent studies with other designs and methods. The insulin requirements did not change. In conclusion, the pen contributes to a better life for the IDDM patient. The quality of life changes due to treatment intervention appear to be assessable (2).

A second study of the same authors concerns the re-examination of 65 patients of them after 3 years. Their HbA1c level was recorded yearly. After an enhancement of metabolic control in the first year, exhibited primarily by patients with fewer syringe injection before pen treatment, control up 3 years was found to have regressed to about baseline level or to have gradually declined. Patients who perceived their ability to self-test blood glucose to have decreased exhibited the least satisfactory course of metabolic control. This seems to indicate that maintaining self-testing in multiple injection insulin treatment is a very real challenge to this regimen (3).

Pen treatment in itself ought to give considerable practical benefits. In addition, patients may experience increased opportunities to live a more flexible life due to the multiple-injection therapy provided by the pen treatment, i.e., experience greater freedom. They may also actually lead a less restrictive life than before, i.e., eat, exercise physically and participate in ordinary social life in a manner that differs from the conventional diabetic. Also, a possibly improved metabolic con-

trol obtained with the multiple-injection therapy may in itself give rise to an improved quality of life (4) (Tab. 1).

The Diabetes Control and Complications Trial (DCCT) and other studies have clearly demonstrated the importance of self-monitoring of blood glucose (SMBG) in maintaining intensive insulin therapy and achieving tight control (5,6). Patients undergoing intensive therapy had a 39-76% reduced occurrence of long-term complications as compared to patients treated with conventional therapy (7). However, SMBG has its limitation. The DCCT demonstrated also that a primary drawback of intensive insulin therapy was a threefold increase in the occurrence of severe hypoglycaemia (especially during sleeping hours) despite performing four or more SMBG test each day. Though the night blood glucose measurement is not practical for most patients, and the commitment of patients to daily self-monitoring varies. Further, type 1 diabetes most often emerges in children, who may not readily observe blood glucose testing and insulin administration protocols. Good glycemic control may prove elusive and this lack of control can be unsafe (8) (Tab. 2).

Table 1. Injection Devices: what we need?

Injection Devices What We Need
<ul style="list-style-type: none"> • Reliable • Easy to learn and use • Reduced weight and size • Modification by 1 or _ unit • Able to mix 2 different insulins • Injection without needle

Table 2. Blood Glucose Meter: what we need?

Blood Glucose Meter What We Need
<ul style="list-style-type: none"> • Reliable • Reduced weight and size • Quick results • Easy to learn and use • Small sample size • Not invasive • Alternative site testing

Continuous glucose monitoring system (CGMS) provides blood glucose reading continuously, without patient effort for each individual reading, every 3-5 min around the clock for 48-72 h.

Two devices are currently available. In the first one the sensor is inserted subcutaneously and is capable of reliable operation for up to 3 days. The assay method is based on electrochemical detection of glucose through its reaction with glucose oxidase. Data are collected once every 3-5 min by a pager-sized monitor device and can be periodically downloaded into a computer for analysis and interpretation.

The other system consists of a measuring device, a microdialysis fibre to be implanted in the periumbelical region of the patient and a perfusion solution. The amperometric sensor used for measuring the subcutaneous glucose concentrations consists of an enzymatic membrane with immobilised glucose oxidase and a platinum electrode.

Information obtained from continuous glucose monitoring will allow patients and their healthcare providers to better understand how to adjust their amounts of calories, exercise, and medications in order to maintain glucose levels within a target range. CGMS gives an unprecedented degree of coverage in monitoring glucose levels. By getting a fuller view of the time between fingersticks, it becomes much easier for the clinician to identify patient-specific patterns of blood glucose variation. When this data are coupled with information from the daily diaries patients keep while undergoing monitoring, it is possible to uncover problems in the current management plan that could not have been identified by SMBG alone (9). Nocturnal hypoglycaemia and postprandial hyperglycaemia are being discovered in many patients who utilize CGMS (10). Recent research demonstrates that both hyperglycaemia and hypoglycaemia can be associated with patient experiences of physical, affective and cognitive symptoms as well as cognitive-motor disruption. These effects can lead to impaired functioning and quality of life (11).

In a multiple regression model, lower HbA1c was significantly associated with better adolescent-rated QOL and with lower perceived family burden as assessed by parents and health professionals (12). HbA1c levels may be decreased by using the informa-

tion obtained with the CGMS. Three glucose profiles are representative of the overall glucose control, because the glucose area values correlate with HbA1c levels. Therefore, to improve metabolic control, it is necessary to lower the whole mean 24-h glycaemia and not just the postprandial glucose values (13).

Non-invasive CGMS is method of choice, particularly in children. Glucowatch is the first commercially available method for non-invasive glucose monitoring.

In our experience we tested 74 young patients, children and adolescents randomly selected from the Out Patient Diabetes Clinic at San Raffaele Hospital, Milan (Italy).

The average age of the patients was 18.5 years, (range 7 and 25 years); mean diabetes duration was 7.8 years (1-18), mean HbA1c of $8 \pm 0.9\%$ (DCA 2000 Bayer Diagnostic, normal value $< 6\%$) and all subjects were treated with 3-4 insulin injections daily.

The experimental protocol was the following: each patient and / or his parents received a complete training about the use of the Glucowatch and how to wear it properly. Since the instruction guide was in English we also provided the patients with a short but comprehensive summary in Italian. The biographer was initially worn by children attending the outpatient department and then used at home. The first calibration of the biographer was always performed by the attending physician. Afterwards we asked patients to assess their capillary glucose level at least 4 times a day using a glucose meter, every time they used the Glucowatch. We processed glucose levels values in order to perform statistical evaluations and error-grid analysis.

Patients and parents were asked to fill in a questionnaire regarding compliance, potential advantages and disadvantages of the device and difficulties occurred wearing the Glucowatch.

Only 37 out 72 (51%) patients managed to obtain data from the Glucowatch, while the remaining patients either experienced an early shutting off (13/35), suffered skin irritations (4/35), error in the battery management at home and consequent impossibility to obtain glucose data (10/35), excessive sweating (5/35) or difficulty in problem-solving of the device (3/35).

The total amount of paired glucose levels obtained was 343, and it was corrected by the time delay of the biographer. The mean of capillary glucose levels was 152 ± 73 mg/dL versus 134 ± 70 mg/dL from the biographer; Gluowatch showed a lower value of the glucose levels in 73% of cases. The average difference between the two methods was -18.5 ± 51.5 mg/dL: the biographer on average underestimated the capillary glucose level value by 7.6%.

The correlation between Gluowatch values and glucose meter ones was $R=0.74$.

In the Clark error grid, the majority (95%) of values was allocated in the AB area of the grid, even though 15 values (5%) were allocated in the CDE area of the grid. Four values were allocated in C area, 11 in the D area and 0 in the E area respectively. 40% of the value in CDE area of the grid belonged to the glycaemic 0-50 mg/dl range.

Data from 44 questionnaire analyzed showed that the Gluowatch was well tolerated even if 34/44 (77%) reported skin reactions, however rapidly solved in all the patients. Eighty-four of our patients reported they would wear the biographer again and judged it particularly effective during night-time. However 48% of the subjects considered the monitor excessively big to be worn every day, while 25% judged it difficult to use.

We recorded that 50% of the patients were not able to use the device properly under usual real life conditions and reported difficulties in the calibration of the Gluowatch and premature switching off. Those problems were much more frequent in our study than reported before, were in hospitalized children and in adults, instead, malfunctions were mainly due to early shut off, skipped values for movement, excessive sweating, impossibility to calibrate the device.

Our results can be partially justified by the fact that our study was not supported by the manufacturing company and the instructions guide was in English. Moreover, some times we realized that an extensive reading of the whole guide might have been more useful for patients in solving practical problems, when using the device at home, but the language barrier prevented them from being successful.

In conclusion our study demonstrated that the biographer can measure glucose levels rather accurately and without safety concerns in children and adolescents under real life conditions. The device was well tolerated and most of the patients reported they would have used it continuously. Unfortunately the biographer was not able to obtain glucose levels in 50% of the patients so other and more extensive studies are required to get a better knowledge of the effective potential applications of the device under real life conditions (14, 15)

Of course, the positive effect of CGMS may be short-lived, but experience is that glucose sensor often give valuable informations that is not possible to get via traditional self-control of blood glucose. Even more importantly, patients can learn by using the sensor and understand that blood glucose has a continuous course – something they may not have been able to understand before. This may have profound effects on both their way of self-monitoring blood glucose and their way of living. Such insight may have long-lasting positive effect. In general, glucose sensor measurements work well, and non compliant patients often find this device useful and informative (16).

The accumulation of information can result in improved education of both the patient and the clinician and improved education alone is known to often result in significant improvements in metabolic control (Tab. 3).

Table 3. Potential Benefits in CGMS

Potential Benefits in CGMS
• “Truer” assessment of glycemic control
• Application as diagnostic tool
• Uncovering issues related to food and diet, including eating disorders
• Detection of prolonged hyperglycaemia and unrecognised hypoglycaemia
• Determination of correct amount and type of carbohydrate to treat hypoglycaemia
• Assessment of adequacy of insulin regimen
• Ability to better program insulin pump
• Evaluation of adequacy of self-monitored blood glucose timing frequency

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Received: 3 April 2003

Accepted in original form: 7 April 2003

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