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Discrete and Continuous Glucose Monitoring Systems: The Point of View of a Patient Affected by Type-1 Diabetes

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Abstract: This work represents the point of view of a diabetic patient with an indirect experience in this specific field of research. As a chemical engineer and researcher in drug carrier production, he has always approached type-1 diabetes (T1D) in a scientific manner. Therefore, this work represents a description of almost 20 years of this illness treatment using a multi-injection insulin system, compared with the experience acquired with a newly adopted micro-infusion system, allowing automatized insulin administration. The use of the continuous system reduced significantly the Hb1Ac average values, from 8.8% to 6.6%, in less than 2 years. Moreover, a full 24 h control guaranteed the almost total elimination of the hypoglycemia risk, thanks to the automated control system, that can stop insulin administration in order to prevent critical situations. It is also important to note that the point of view underlined in this work does not presume to be that of a doctor or of a researcher who works closely in the field of medicine or diabetology. However, the author wants to highlight that doctors could try to educate patients to a scientific approach to treat illnesses correctly. The author experienced the very common difficulties related to the use of insulin with multi-injection administration for many years; then, he was proposed to start treatment with the automated pump mechanism. In this work, the author provides comments on the physical and psychological advantages and disadvantages of both insulin release systems, in order to define their impact on a patient's daily life. This work may also represent a vademecum for patients during the beginning of diabetes treatment, helped by the constant support and advice of a medical doctor.

Keywords: glucose levels; insulin administration; glycosylated hemoglobin; carbohydrates; continuous glucose monitoring; delivery systems

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1. Introduction

As a researcher in the fields of chemical, process and material engineering, the author has always had a scientific approach to drug release systems, with the aim of producing optimized drug carriers for the efficient treatment of illnesses. Type-1 diabetes (T1D) is defined as an autoimmune disorder, characterized by the own immune cells attacking pancreatic beta cells, that are responsible for insulin production. This results in a partial and, then, total stop of insulin secretion and circulation [1–6].

The author was diagnosed with type 1 diabetes on 9 June 2003, at the age of 15. The main side effects of untreated diabetes (in the first period) included, in his specific case, the triad of polyuria, polydipsia and weight loss [7]; therefore, he experienced a significant weight loss from 65 kg to 55 kg in a few months, from winter to spring [8]. In details, the specific author's case was characterized by the need to urinate that occurred almost 5 times per hour, even at night; this also led to a not negligible urinary tract infection, strongly indicated as a principal symptom for this diagnosis [9–12]. As millions of people affected by non-diagnosed diabetes can confirm, the sense of thirst was always unsatisfied; and, for this reason, also the need to urinate was never satisfied. This period lasted approximately 2 months in springtime, during which the author was occasionally involved in some sessions of physical activity. Then, following a capillary blood glucose check, a value of

507 mg/dL was obtained, much higher than the optimal glucose value for non-diabetic patients (generally, between 70 and 110 mg/dL). These conditions were almost close to those that usually require hospitalization for young people affected by type-1 diabetes. Fortunately, soon after this diagnosis, the author urgently started the common therapy, consisting in the administration of rapid insulin before each meal and basal long-lasting (about 24 h) insulin at night, before the usual sleeping hours.

The weight loss of about 10 kg, from the initial 65 kg, was still a macroscopic sign of physical not recovered conditions, also reported in the literature as a side effect of untreated illness [13]. Furthermore, the first blood tests reported that all the values were perfectly in line with a male patient of 15 years of age. This consideration confirmed that diabetes had not caused any irreversible damage or side effects yet. Of course, the only value significantly above the required limits was that of glycosylated hemoglobin (HbA1c). The first value of HbA1c measured using High-Performance Liquid Chromatography was 12% (June 2003). According to current scales, this value corresponded to about 108 mmol/mol. This high value, after the following summer and several episodes of hypoglycemia, fell back to a value of 4.9%.

A year later, in June 2004, even though the level of glycosylated hemoglobin stabilized in the range between 6% and 7% (considered preferable for type-1 diabetic patients), there was no significant recovery of the body weight. Following further analysis, carried out between May and June 2004, the author was also diagnosed with celiac disease. To that date, there were various theories and schools of thought on the possible links between celiac disease and diabetes [14–16]. In particular, celiac disease could be due to viral or bacterial infections, genetics, autoimmunity, or even the simple introduction of gluten in the daily patient diet [17]. Indeed, a link between the two diseases is considered highly probable, but it is not yet clear, in this specific case, which of the two diseases could have triggered the other. However, a recent study found that almost 6% of patients affected by celiac disease are also affected by type-1 diabetes [18].

The transition to a gluten-free diet required a remodeling of the insulin doses administered, also because gluten-free foods, on average, have a higher fat and carbohydrate content than traditional foods [19]. After the first 2 months of the gluten-free diet, there was a significant recovery of weight, which reached about 67 kg and, after 1 year, a plateau value of almost 70 kg. Today, at the age of 34, he has reached an ideal weight in the range between 72 and 74 kg, having a height of about 1.76 cm, which corresponds to a Body Mass Index between 23.2 and 23.9.

In this work, the intent of the author was to describe the advantages and disadvantages of the drug delivery systems commonly employed for the treatment of type-1 diabetes. The comments and opinions here reported should be considered as the point of view of a patient with a scientific background, describing the advantages and disadvantages of using the traditional administration process with syringes and the novel automatized pumping system. To support these comments, the author used data obtained from his first treatment period of type-1 diabetes, which ran from 2003 (the year of his diagnosis) to March 2021, the year in which he started the use of the automatized pump, coupled with a glucose sensor monitoring system. Both physical and psychological features deriving from the use of insulin with multi-injection administration were analyzed. This modality was then compared with the automated administration modality, implemented by the patient starting from March 2021.

2. Description of the HbA1c and Cholesterol Values Monitored over Time

In order to support the opinions proposed in this work, data related to the patient's glycosylated hemoglobin are provided, from June 2003 to December 2022 (see Figure 1). The value of 12%, which was measured in a public hospital when the disease was first diagnosed, is omitted in Figure 1 in order to avoid the presentation of an out-of-scale diagram. Therefore, all the data shown in Figure 1 concern the measurement of HbA1c during the whole period of treatment with insulin therapy. In all other cases, the measurements were carried out in private centers with proper instrumentation.

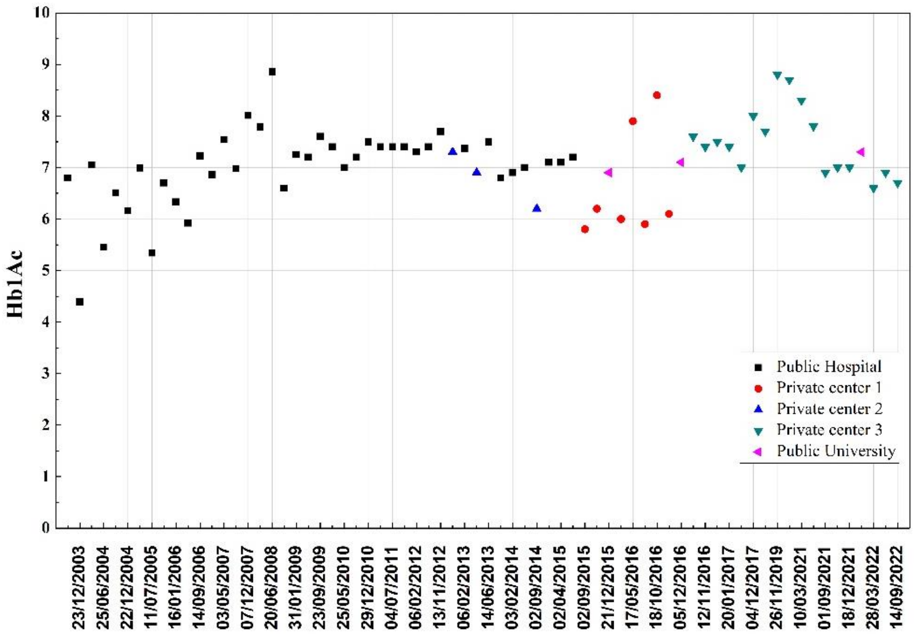

Figure 1. Evolution of the Hb1Ac values during the patient's 21 years of insulin therapy.

As it is possible to see in Figure 1, there is a huge variability of HbA1c values between the year 2003 and the year 2006. Therefore, in the following Table 1, the author excluded the HbA1c values measured before 2006; this is explained by the fact that the first years of insulin-therapy require to find a new metabolic balance for the patient. This causes a significant variation of HbA1c during the first years of treatment.. After finding a metabolic equilibrium, starting from the year 2007, the values measured in different centers were compared. In particular, the values of mean size and standard deviations of HbA1c are reported, corresponding to the different instruments used for their determination or the centers where they were obtained. Assuming that the average HbA1c level became stable with an average global value of 7.08 $\pm$ 0.78 %, it appears evident that in public institutes, more accurate measurements are made than in private centers. However, a general trend can be easily detected.

Table 1. Comparison of the mean values and standard deviations of HbA1c measured in different institutions.

Center	Mean Value, %	Standard Deviation, %
Public hospital	7.35	0.42
Private center 1	6.61	0.99
Private center 2	6.80	0.45
Private center 3	7.49	0.65
Public university	7.10	0.16
Total average	7.08	0.78

Figure 1 reports collection of data from one single patient. Therefore, this diagram does not represent a general trend for type-1 diabetic patients, but a report of a case study, useful to support the author's opinion and comments about the traditional and novel insulin delivery systems. However, this data may represent a guideline to achieve a good treatment of type-1 diabetes; moreover, diagrams and trends may be shared with other patients in order to discuss and compare the physical implications of different treatments and measurement devices.

Medical doctors could share or criticize these opinions, finding possibly some inspiration in order to show patients what they should do and what they should avoid during the therapy; this work could be also a support to teach patients how to approach this illness scientifically and without panic.

The first 3 years of diabetes treatment (between 2003 and 2006) were characterized by a not negligible variability, with an average HbA1c value of 6.29 ± 0.79 %. On the one hand, this fell perfectly within the suggested range of HbA1c for diabetic patients; on the other hand, it denoted a clear settling phase, characterized by both several hyperglycemia and hypoglycemia episodes, probably due to a still unconscious management of the disease, but also to a difficult control of the glucose level using the traditional syringe delivery system.

A value of HbA1c of about 9% was also reported in a trimester of the year 2008, when a study period was spent in another Italian city, lasting 1 year. This resulted in a poor glycemic control, essentially due to a type of unregulated and different diet compared to that of the previous years. After this year, diabetes control returned to quite good levels. In the subsequent period, from the end of 2008 to 2015, the average value of glycosylated hemoglobin was approximately 7.08 ± 0.43%, corresponding to an average value higher than that measured in the previous period, but with a lower variability.

On average, with reference to the period of high school (2003–2007) and the period of study at the University (2008–2015), glycosylated hemoglobin was kept relatively under control, due to a moderate lifestyle and very few diet excesses. Then, starting from 2015, the beginning of the working life led to an increase in stress due to new responsibilities, which inevitably had an impact on the average HbA1c values. Furthermore, the lack of time due to the reduced spare time and to the subsequent work commitments, led the patient to neglect the daily reflections on the amount of insulin to administer, meal by meal. Often, the described situation led to the choice to perform HbA1c levels checks in private laboratories, where sometimes the accuracy seemed to be quite lower than that achieved in public institutes (see Table 1). In these last cases, the measurements were not always carried out using High-Performance Liquid Chromatography (HPLC), which is the most appropriate instrument and method (see Private center Nr. 1 in Figure 1). However, this first period of stress increase was overcome, with HbA1c mean values of 6.94 ± 0.79%.

Starting from July 2017, monitoring with a glucose sensor [20] began, allowing the patient to move from the classic fingertip sampling for measuring capillary glucose to the continuous (24 h) measurement of interstitial glucose. On the one hand, a more accurate and increased number of data could be acquired, with the possibility to observe the precise value of the maximum glucose peak, reached after meals; however, on the other hand, the use of sensors triggered a psychological fear of reaching a low level of glucose concentration, feeling the classic symptoms of hypoglycemia [21]. This resulted in an average reduction in the insulin volumes administered before meals and in a consequent considerable glycemic decompensation. Starting from the second half of 2017, and until April 2020, HbA1c was measured in a different private laboratory, which ensured a proper measurement using the High-Performance Liquid Chromatography (HPCL) method (see Private center Nr. 3 in Figure 1). Therefore, in the period from 2017 to 2020, a significant worse glycemic control was recorded, which resulted in an average value of 8.30 ± 0.41%, with dangerous peaks of 8.8% and 8.7%, measured, respectively, in November 2019 and April 2020.

Aware that the problem was essentially psychological [22] and having to continue to carry out the same working activity, with all the associated stress, the author decided to contact the diabetes center of the Secondo Policlinico di Napoli (University of Naples Federico II, Naples, Italy), specialized in innovative techniques for diabetes care and insulin delivery. In this department, the author was proposed to use a new continuous glucose-monitoring device (Dexcom G6, Dex Com Inc., San Diego, CA, USA), coupled with an insulin pump (Tandem Diabetes Care, San Diego, CA, USA). In that case, the sensor would not simply record and display data continuously, it would also communicate constantly with the pump, taking constant therapeutic decisions in order to improve the management of type-1 diabetes. With this system, the only patient's decision is related to the insulin units of volume to be administered. This delivery system is constantly controlled by an algorithm that also allows the patient to automatically correct high glucose concentrations in the blood by calculating a correction bolus, taking into account the active insulin already administered to the body and also considering the glucose target, set (generally) at 110 mg/dL. When using the continuous system, another element could cause fear of hypoglycemia. This kind of fear could be due to the possibility of the system failure, causing the administration of hundreds of insulin units stocked in the pump's pot. Fortunately, this automated pump has a safety system. Therefore, the infusion set is separated from the insulin pot by a camera of micrometric volume; in case of failure, this camera only administers a negligible insulin volume, eliminating the tubing communication with the main pot. This avoids the risk of hypoglycemia due to a failure of the infusion system.

Moreover, the pumping delivery system simulates the normal body release rate, administering micro-volumes of insulin per unit time and avoiding the on-shot administration of insulin permeating the adipose tissues, in order to be absorbed by the body. This guarantees the elimination of the traditional administration of basal insulin, which is generally characterized by a huge volume of insulin that lasts around 24 h.

Following the use of the insulin pump, the glycosylated hemoglobin value slowly decreased from May 2021 (7.8%) to March 2022 (6.6%). Considering the peak reached in November 2019 (8.8%), the benefits of the new delivery systems were particularly evident (see Figure 2). In the period of treatment using the insulin pump (from March 2021 to the present), an average value of 7.1 ± 0.37% was recorded, indicating a clear improvement of the glycosylated hemoglobin control, with respect not only to its decreased average values, but also to its reduced variability.

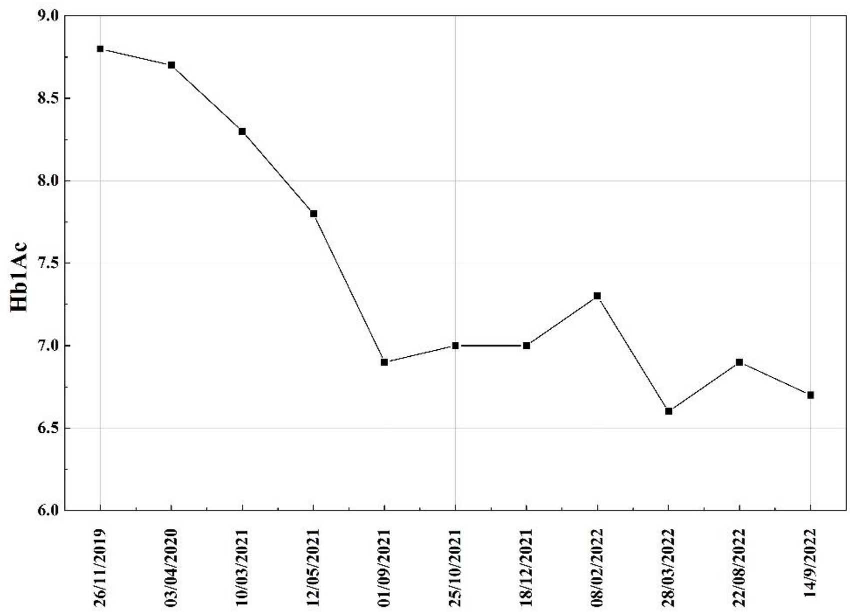

Figure 2. Evolution of HbA1c levels from November 2019 to the present day.

For the completeness of the data, Figure 3 shows the values of total cholesterol, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) measured in almost 20 years of diabetes treatment.

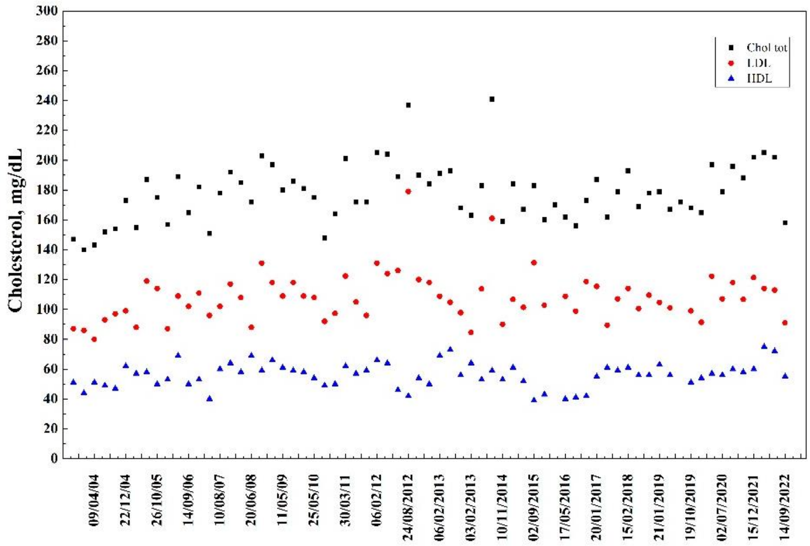

Figure 3. Evolution of total cholesterol, HDL and LDL values during the patient's 21 years of insulin therapy.

Looking at Figure 3, over the observed years, total cholesterol showed an average value of 178 ± 19 mg/dL, while HDL cholesterol had an average value of 56 ± 8 mg/dL, and LDL cholesterol of 108 ± 19 mg/dL. During the treatment period of type-1 diabetes, cholesterol monitoring recorded only two out-of-average episodes. In these two cases, the total value was close to 240 mg/dL, while the corresponding LDL value was about 180 mg/dL, probably because of incorrect compliance with the hours of fasting before carrying out these analyses. According to the most diffused guidelines, the total cholesterol level should be under 200 mg/dL; the LDL level should be under 110 mg/dL (diabetic people are suggested to keep it under 100 mg/dL); the HDL level should be less than 40 mg/dL for men and less than 50 mg/dL for women.

After listening to the point of view of the consulted medical doctors, it is also worth noting that, for the containment of cholesterol, this patient has not yet started any pharmacological cure. However, according to the guidelines for type-1 diabetes, his average levels of cholesterol are slightly above the recommended limit values. Indeed, in order to avoid serious cardiological risks in the future, the LDL value must be kept constantly under 100 mg/L.

3. Discussion

After about 20 years of experience in the treatment of type-1 diabetes, what appears evident is the possibility of acquiring more or less information on blood sugar or glucose values, depending on the monitoring system employed. In particular, with the classic method of finger sticking to obtain capillary blood, it is necessary to reduce the blood glucose measurements to no more than 6 measurements per day, i.e., before and after each meal (breakfast, lunch and dinner). In theory, the decision to have another meal would imply two additional fingertip samplings (before and after). The reduced number of measurements is also related to the fact that each one involves the use of a single stripe (device for capillary glucose measurement), which cannot be reused and is necessarily disposed of. Moreover, increasing the number of fingertip measurements increases the cost of the treatment and its specific environmental impact, as well as the patient sufferance (see Table 2).

Table 2. Advantages and disadvantages of continuous vs. discrete glucose monitoring systems.

Type of Glucose Monitoring	Advantages	Disadvantages
Discrete	6 g of waste per day A 24 h control of the glucose levels	4+ insulin administrations per day Up to 6 fingertip samplings per day More pain for the patient High probability of hypoglycemia
Continuous	1 infusion substitution every 3 days No fingertip sampling Reduced pain for the patient Reduced risk of hypoglycemia Automated reduced administration in exercise mode	32 g of waste every 3 days A spot-like glucose control (up to 6 points per day)

In addition to this, fingertip sampling only estimates the efficacy of the administered insulin bolus only 2 or 3 h after a meal. However, according to the author's personal opinion, by using the classical capillary glucose measurement, it appears more difficult to predict information on the maximum peak reached at the apex of meal digestion. Therefore, a good glucose level in the blood before and after a meal could hide a peak of 250 mg/dL or even, in some cases, 300 mg/dL or more. Furthermore, these spot measurements performed on capillary blood cannot give precise information on the efficacy of insulin during the night hours of sleep.

In Figure 4, the red dots represent the spot analysis of capillary blood glucose concentration (only one point), and the black line represent the data obtained using the Continuous Glucose Monitoring (CGM) system, which was programmed to collect a new glucose value every 5 min. In this last case, the data are much more interesting and useful, because they allow the patients and the medical doctors to understand how long the body had to manage hyperglycemia (high level of glucose concentration), over the daily course of 24 h.

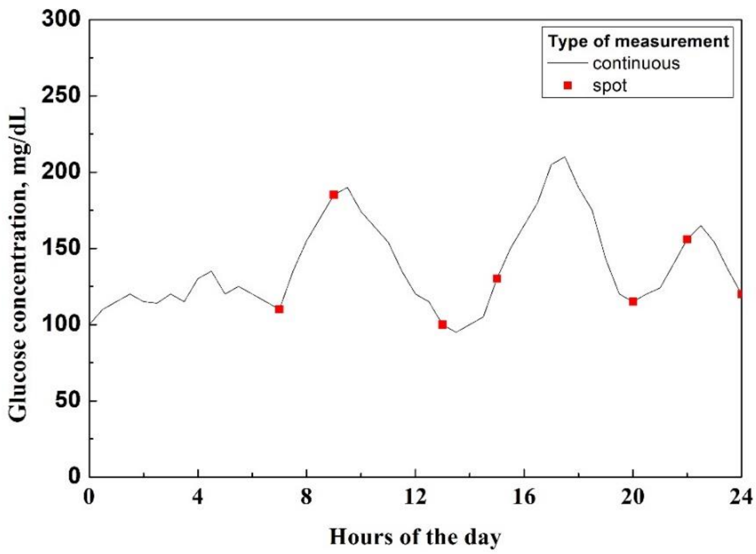

Figure 4. Comparison of type 1-diabetes continuous monitoring and spot-like monitoring.

Moreover, hypoglycemia (low level of glucose concentration) can be easily avoided by the use of sensors coupled with an insulin pumping system. If the glucose level tends to the minimum accepted value (generally below 60–70 mg/dL), the sensor sends warnings (also acoustic) to the patient and suggests assuming sugars, while communicating to the pump to stop insulin administration. The stop of insulin administration helps the body to increase the glucose concentration up to an average 80 mg/dL, establishing a new balance of normal values. In details, Figure 4 shows that, working with the spot metering system, all information on blood glucose fluctuations in the early morning would have been lost. Furthermore, from the finger stick sampling before lunch, a good glycemia level would have been recorded, followed by another good measurement (2 h later). Indeed, the blood glucose spiked at around 220 mg/dL, returning to a normal average level at 8:00 pm before dinner.

The advantages and the disadvantages deriving from the use of discrete or continuous glucose monitoring systems are listed in Table 2:

As it is possible to see, the continuous monitoring system introduces a significant innovation in the treatment of diabetes, since it provides a 24 h continuous control of the glucose level, with the possibility to obtain information on the glucose increase or decrease speed.

Moreover, the patient suffers less, since he/she needs to provide only one substitution of the infusion set every 3 days, on average. This means that the patient does not have to perform needle administration up to 4 times per day (breakfast, lunch, dinner and basal insulin), without taking into account any eventual corrections.

The use of conventional needles causes suffering. Often, it also causes fear in children affected by diabetes. In some cases, research in microneedles administration could make a difference in terms of pain reduction [23].

One specific disadvantage may be the overall environmental impact of the continuous monitoring system, since it creates about 32 g of waste materials every 3 days, compared with 18 g of waste (6 g per day, on average) for the conventional monitoring system. These materials are not reusable and not recyclable, nowadays; therefore, this waste weight reducing issue should be taken into account in future research.

Regarding the performance of physical activity by diabetic patients, the automated system gives the possibility to activate the "exercise mode" using the pump, inducing the system to reduce the amount of continuously administered insulin while physical activity is performed, as reported for fully automated systems [24]; this is of course not possible with the conventional spot-like glucose measurements.

4. Conclusions

To the eyes of a patient with a scientifically assisted approach, the spot monitoring system appears obsolete with respect to the loss of information on diabetes management and the effectiveness of administered insulin boluses.

Continuous monitoring, on the other hand, provides full awareness of the variations and trends of blood sugar, making the patient also much more aware of diabetes management and therapeutic choices. Of course, continuous monitoring has its beneficial effects if coupled with an insulin micro-infusion system, which regulates the delivery of the bolus according to the variation in blood sugar over time.

By eliminating the administration of basal insulin, the pump delivers only rapid insulin, emitting micro-boluses that continuously balance the glucose value around the set point (generally 110 mg/dL). Ultimately, a modern monitoring system is certainly the one resulting from the use of a sensor coupled with an insulin pump. Thanks to this system, the author has almost forgotten the problem of diabetes; this new treatment method guarantees the possibility for a diabetic patient to live a quiet life, almost totally free from the psychological implications of carrying out continuous checks and corrections of the blood glucose concentration with the use of syringes.

Indeed, the insulin pump almost perfectly replaces the human pancreas. However, there is still a lot to improve with this kind of insulin delivery; process engineers together with biotechnologists and researchers in medical fields can further optimize these systems. A synergistic approach would generate a system available to predict the amount of insulin to administer just before meals. In this last case, the patients will leave to the pump not only the possibility to monitor glucose level, releasing insulin constantly and correcting high glucose levels, but also the therapeutic choice of managing meals from their beginning. So far, the physical and psychological benefits of the actual system seem to be clearly significant and give us the hope of creating a fully automated pancreas-like working device, in the future.

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Conflicts of Interest: The author declares no conflict of interest.

Abbreviations

T1D: Type-1 Diabetes; CGM: Continuous Glucose Monitoring; HbA1c: glycosylated hemoglobin; HPLC: High-Performance Liquid Chromatography; HDL: High-Density Lipoprotein; LDL: Low-Density Lipoprotein.

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