Diabetes Management: Devices, ICT Technologies and Future Perspectives

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Abstract. Diabetes, a metabolic disorder, has reached epidemic proportions in western countries. Contextualized continuous glucose monitoring measurements to control directly the insulin delivery can provide optimum management of the disease and could provide diabetes patients with insulin profiles close to that of the normal patient, however problems related to delivery systems, control algorithms and safety of the system have to be properly solved for realizing a long term accurate continuous monitoring systems. In this paper we describe the current status of diabetes management and insulin administration and the future perspectives and aspects to support long term management of diabetes based on wearable continuous blood glucose monitoring sensors.

Keywords: Diabetes management, Blood glucose measurement, Insulin delivery devices, Continues glucose monitoring, Close loop control.

1 Introduction

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia (high blood sugar) resulting from defects in the production or response to insulin [1]. The disease has two main forms: type 1 and type 2. Type 1 disease is characterized by diminished insulin production resulting from the loss of beta cells in the pancreatic islets of Langerhans, in most cases caused by immune-mediated cell destruction. Disease management entails administration of insulin in combination with careful blood glucose monitoring. Type 2 diabetes patients, usually over 50 years old with additional health problems, especially cardiovascular disease (CVD), exhibit reduced insulin production and resistance or reduced sensitivity to insulin. Earlier stages of type 2 diabetes are characterized by high plasmatic insulin concentration due to the insulin resistance and the capability of beta-cells to secrete insulin. In later stages of type 2 diabetes, beta-cells are unable to produce enough insulin and in such cases type 2 becomes more similar to type 1 diabetes. Management principally involves the adjustment of diet and exercise level and the use of oral anti-diabetic drugs (OADs) and, eventually, insulin to control blood sugar. Diabetes type 2 is one of the faster growing chronic conditions in the developed world and it is closely linked to the emerging epidemy of obesity and bad life style, which is now a major cause of preventable health problems.

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2 Glucose Control in Diabetes Therapy for Insulin Dependent Patients

Blood glucose is typically measured in a drop of capillary blood using a disposable dry chemical strip and reader device, an uncomfortable and slow process. Tight Glucose Control (TGC) requires almost continuous measurements and different sensors for continuous blood glucose measurement have been under development in the last two decades. Minimally invasive sensors able to measure glucose in interstitial fluid, more suitable for self-monitoring, have also been developed. To date, however, none of these has delivered a level of performance sufficient for use in routine glucose monitoring. Robust, clinically acceptable devices are however widely expected to become available in the near term.

Although several guidelines for treatment regimen for management of diabetes have been defined [2, 3, 4], no clear definitions of treatment regimen have been found for the establishment of glycaemic control of patients [5, 6]. Hyperglycaemia and insulin resistance are common in severe illness and are often associated with physical and mental stress. Studies have shown that frequency of hyperglycaemia in surgical ICU’s (Intensive Care Units) can amount to –50-70 % of all admitted patients [7].

Management of diabetes has to be performed at 360^o in hospital and outside healthcare premises. Based on the emerging clinical evidence from several clinical studies, there are increasing efforts world-wide to establish tight glycaemic control in critically ill and hospitalized patients [8, 9, 10, 11]. One of the major differences between inpatient and outpatient control of glycaemic levels is the fact that tight glycaemic control in hospitalized patients has to be provided by healthcare physicians and/or nurses. Achieving the goal of tight glycaemic targets requires extensive nursing efforts, including frequent bedside glucose monitoring, training to handle control algorithms or guidelines with intuitive decision taking and most importantly additional responsibility to prevent hypoglycaemic episodes. In summary, there is an urgent need for a safe method to establish tight glycaemic control without any risk of hypoglycaemia for patients in intensive care units and the general ward.

Traditional diabetes therapies for insulin dependent patients try to achieve normal glycaemia by administrating synthetic insulin to control patient’s blood sugar level. Given that insulin cannot be taken orally patients must turn to special type of devices to administer insulin. The overall insulin the body needs is covered with the administration of “basal insulin” and “bolus insulin”. Using a continuous delivery device it is possible to deliver continuously the “basal insulin” at a “basal rate”.

3 Insulin Delivery Devices

During the last years a number of new insulin delivery systems have become available making insulin administration much more easily. Many factors influence the choice of the appropriate device for each patient including patient conformance and self-care capacity. Most commonly, insulin is delivered, into the fat under the skin (subcutaneous) or into the blood (intra-venous), using a needle injection or a syringe, an insulin pen, an insulin pump.

A syringe is the simplest device used for the injection of insulin. To administer insulin, the patients typically use disposable units to prevent contamination and infection. An insulin pen is composed of an insulin cartridge and a dial to measure the dose. There are two different types of insulin pens: a durable pen using a replaceable insulin cartridge allowing the disposal and replacement of an empty insulin cartridge with a new one; and an entirely disposable prefilled pen, where the pen comes pre-filled with insulin, and when the insulin cartridge or reservoir is empty the entire unit is discarded. Insulin pens are convenient and may cause less pain than syringes for the injection of insulin.

The advantage of insulin pens over insulin syringes is that they are much more convenient and easier to transport and use than traditional vial and syringe. They can repeatedly administrate more accurate dosages (especially for patients with visual or motor skills impairments). Insulin pens usually cause less pain to the patient. One of the disadvantages of insulin pens over insulin syringes is that unlike traditional syringe two different insulin solutions cannot be mixed in an insulin pen. Also using pens needles is usually more expensive than using the traditional vial and syringe method.

A major disadvantage of insulin injection devices is that they are only designed to administer insulin in large boluses, which can cause peaks and valleys in the blood sugar levels in patients. A solution to that problem (insulin shots) is provided when using insulin pumps. These devices, which are worn outside of the patient's body, can be programmed to deliver a steady supply of insulin throughout the day and/or programmed to deliver larger boluses of insulin after meals. An insulin pump delivers tiny selected amounts of insulin continuously throughout the day (the basal rate) and is able to provide additional doses if necessary (bolus doses). Each basal rate can be variable since the pump can be programmed to deliver different basal rates throughout the day. The main advantage of insulin pumps is that the individuals do not need to take multiple injections or shots every day allowing them to continue with their daily activities without any problem. With a pump, continuous doses of background insulin are delivered to support the body's needs between meals and with a button press it is possible to obtain an "on demand" dose of insulin (a "bolus") to cover instant needs.

The main disadvantage of insulin pumps, apart from the obvious discomfort that a person might feel wearing it, is the cost of the pump and the cost of maintenance that can get very high. More than that, patient’s activity could force the infusion set of the pump to slide off and stop the necessary delivery of insulin to the patient’s body. It is thus very important for patients to monitor their blood glucose levels much more frequent making sure that the pump is working correctly and, thus, also avoiding risks of ketoacidosis.

Other approaches include insulin inhalers that deliver insulin by spraying a blast of insulin powder into the patient's respiratory system. They operate similarly to other kinds of inhalers but are not as efficient at delivering insulin into the body which means patients must use larger quantities of insulin. Pulsatile insulin uses micro-jets to pulse (transdermal) insulin into the patient, mimicking the physiological secretions of insulin by the pancreas. The transdermal insulin administration aspect remains even today experimental.

4 ICT Technologies in Diabetes Management

4.1 Close-Loop and Self-management of Diabetes with an ICT Platform

A possible solution would be envisioned with a state-of-art technological solution that will assist healthcare professional, patients and informal carers, to better manage diabetes insulin therapy in a variety of settings, help patients understand their disease, support self-management and provide a safe environment by monitoring adverse and potentially life-threatening situations with appropriate crisis management.

Within the REACTION project [12] we aim to support long term management of diabetes based on wearable, continuous blood glucose monitoring sensors, and automated closed-loop delivery of insulin. The platform will provide integrated, professional, management and therapy services to diabetes patients in different healthcare regimes, including professional decision support for in-hospital environments, safety monitoring for dosage and compliance.

At such purpose, the availability of glucose sensors with proper accuracy is requested for a proper functioning of the overall system.

4.2 Glucose Sensor Technology

The standard-of-care for measuring glucose levels is by “finger-stick” blood glucose meters. For these a drop of blood, usually drawn by piercing the skin of a finger, is brought in contact with a test strip. A chemical reaction, commonly mediated by glucose oxidase, glucose dehydrogenase or hexokinase enzymes, triggers an electrochemical sensor or a color reaction that is detected in a reader. The drawback of this method is that only a few measurements can be performed in the course of a day.

The development of a control system that infuses insulin on the basis of glucose measurements could permit tighter glycaemic control and improve clinical outcome without increasing workload of the health care professionals [13]. Only a few commercially available sensors, that allow continuously monitoring the blood glucose level (CGM), have been approved for use. These sensors rely on electrochemical detection of an enzymatic reaction and are minimally invasive.

A range of other sensor technologies are currently being tested for their suitability for glucose monitoring. The most promising technologies for continuous glucose monitoring can broadly be classified as follows: Enzymatic (electrochemical), Impedance Spectroscopy / Dielectric spectroscopy, Optical (IR-/NIR-Absorption, mid-IR emission, Polarimetric (e.g. anterior chamber of the eye), Refractive index, Raman spectroscopy (inelastic photon scattering), Photoacustic (pulsed light absorption dependent on glucose concentration), and other.

Moreover, alternatives for invasive sampling are being investigated for electrochemical detection, for example samples may also be collected by iontophoresis or suction blister extraction through the skin. Despite significant efforts these technologies are still in a development or evaluation phase and yet have to prove their reliability and accuracy.

Wearability for sensors for some time can help in the collection of the required measurements. For this purpose the use of the ePatch technology has been considered (see Fig. 1).

Fig. 1. Wearable health monitoring ePatch system from DELTA

The ePatch sensor is a small body sensor, which senses physiological signals and is embedded in a skin-friendly adhesive. It can contain various types of miniaturised body sensors to measure physiological parameters, microelectronics for data analysis, a wireless radio module for communication and a battery power source. The skin adhesive of the ePatch ensures optimised for wearability and bio compatibility. The basis for the adhesive will be hydrocolloid pressure sensitive adhesives. This category of adhesives is extensively used in a number of medical devices like ostomy products, blister patches, wound dressings and for other skin applications. Wireless communication between sensors and the central node in the Body Area Network BAN: off-the-shelf radio chips will be benchmarked to identify components that optimize the trade-off between bandwidth, reliability and low-power performance.

The loop has to be closed to health professionals inside hospitals or to the patients when outside the healthcare premises. Then, they will deliver the insulin using the appropriate insulin device. In case of automatic glucose management the loop will be automatically closed on an insulin pump.

5 Conclusion

There is abundant evidence, for the future diabetes management and therapy, that tight control of the blood glucose level is vital for good diabetes management and insulin therapy. Good glucose control requires frequent measurement of blood glucose levels and complicated algorithms for assessing the insulin dose needed to adjust for short term variations in activity, diet and stress. On the other hand, good control of diabetes, as well as increased emphasis on blood pressure control and lifestyle factors, may improve the risk profile of most complications and attain future good health.

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