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ADVANCES IN THE MANAGEMENT OF DIABETES MELLITUS TYPE 1; A REVIEW OF MOST RECENT EVIDENCE

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Abstract:

Introduction: *Management and treatment of diabetes mellitus type 1 and diabetes mellitus type 2 have been continuously developing and advancing. However, they are still not satisfactory enough.*

Aim of work: *In this manuscript, we will review most recent development and advances in the field of diabetes mellitus type 1 management and treatment.*

Methodology: *We did a systematic search for diabetes mellitus type 1 management using PubMed search and Google Scholar search engine. The terms used in the search were: diabetes mellitus type 1, management, treatment, and advances.*

Conclusions: *Despite continuous research, management and treatment of diabetes mellitus type 1 is still not satisfactory and convenient to patients, leading to relatively high rates of incompliance, especially in children. Therefore, it has been essential to continuously develop methods that improve treatment and glucose control, and thus increase compliance to treatment. To achieve this, several analogues of insulin have been develop including different types of short-acting and long-acting insulin analogues. The methods of insulin administration have also been developing with the increased use of insulin pumps.*

Keywords: *diabetes mellitus type 1, management type 1 DM, advances in therapy*

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INTRODUCTION:

Almost 100 years have passed since the discovery of insulin by Banting and Best in 1923, which revolutionized the management and treatment of diabetes mellitus [1]. Since then, management and treatment of diabetes mellitus type 1 and diabetes mellitus type 2 have been continuously developing and advancing. However, they are still not satisfactory enough. For example, most diabetes mellitus type 1 patients still find it inconvenient that they must balance between hypoglycemia and hyper glycemia episode, take several injections daily, and watch their food and diet strictly, which are even harder in children and younger patients. Therefore, research is still continuing in aims to find better, more convenient treatments and modalities.

Incidence of diabetes mellitus type 1 differs among different areas and depends on several environmental and genetic factors that affect the expression and the prevalence of the disease. In Finland, for example, the incidence of diabetes mellitus type 1 can reach 57.4 cases per 100,000, whereas the incidence of diabetes mellitus type in India is about 0.6 cases per 100,000 [2]. Recent studies have been reporting a significantly increasing incidence of the disease among children [3].

These increasing incidences, especially among children, make it more important to improve treatment modalities, and find more satisfactory modalities that will improve compliance to treatment and thus outcomes of the disease. In this manuscript, we will review most recent development and advances in the field of diabetes mellitus type 1 management and treatment.

METHODOLOGY:

We did a systematic search for diabetes mellitus type 1 management using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). Our search also looked for recent treatments of diabetes mellitus type 1. All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: diabetes mellitus type 1, management, treatment, and advances.

Advances In Insulin:

Many researchers around the world have been trying to discover the best modality to administrate insulin in the most ideal ways. This research has resulted in discovering several insulin analogues have been discovered to improve stability and absorption of normal insulin. We will discuss in this section the most important analogues:

Short acting insulin:

Short acting insulin (also called lispro) has been used to control hyperglycemia that is caused following meals. Lispro has a relatively rapid onset and extremely short action, so it only acts to prevent hyperglycemia during the meal without risking the late developing of hypoglycemia [4].

Later, the short acting insulin known a glulisine was introduced to become the most recent addition to this type of insulin. Glulisine was approved for use in children older than four years. However, many concerns about its use are still present including its tumorigenic effects [5].

Long acting insulin:

Glargine is considered the most widely used long acting insulin, with duration of activity that can last up to 24 hours. Some concerns are present regarding its mitogenic effects, but no solid evidence is present yet [6].

Insulin detemis is another long acting insulin that has an onset of about an hour, with a duration of about 24 hours. It was approved by the FDA for the use in children older than six years [7].

Albulin is the most recently discovered long acting insulin that was synthesized using human insulin genes and albumin genes to create this long acting insulin analogue. Albulin will potentially provide the best long-term control of glucose levels. Moreover, it has less risk of having mitogenic effects than other insulin analogues [8]. However, evidence supporting its use in clinical practice is still lacking, making it necessary to perform more clinical trials on it.

Degludec is recent long acting insulin that got its approval in 2012. It has an extremely long half-life allowing for duration of action that could reach three days, with less variability in glucose levels. Moreover, it was found to decrease the risk of nocturnal hypoglycemia by up to 25% when compared to other types of insulin [9]. However, an important limitation of its use is the increase in cardiovascular diseases risk, which has prevented it from being approved in pediatric [9].

Inhaled insulin:

The inhaled insulin Exubera was first introduced and approved for use in clinical practice in the year 2006. However, studies found it to have a bioavailability of less than 10% leading to significantly increased doses. Moreover, this bioavailability varied with

degrees of absorption, and was affected by age, smoking status, and the presence of respiratory diseases. All this made inhaled insulin inconvenient and led to the withdrawal of it from markets due to poor popularity among patients [10].

Insulin Pumps:

Apart from efforts to improve insulin and its analogues, significant effort was made in improving insulin delivery modes. The concept of using a device to pump insulin to the body was first introduced in the year 1963. However, back then the pump was huge and was associated with significant inaccuracy in the rate of pumping insulin. However, recent programming techniques have led to the designing of more advanced pumps that achieve accurate pumping of insulin according to the body's need with the ability of adjustment according to the conditions [11].

Continuous Glucose Monitors:

The most concerning side effects that affects new treatments for diabetes mellitus type 1 is the development of hypoglycemia, which could be fatal. Therefore, a system that continuously monitors blood glucose will provide significant help in the management and everyday treatment of diabetes mellitus type 1.

Since their introduction, Continuous Glucose Monitors (CGMs) have provided a convenient way to monitor glucose. In fact, they have been proven to improve hypoglycemia attacks, and reduce their time, when compared to normal self-monitoring [12].

Continuous glucose monitors use a sensor that measure glucose levels in the blood continuously using an electrode and a membrane layer. The sensor then will pass the measurement to the receiver through a transmitter [12]. Sensors are designed to detect the concentrations of glucose in the interstitial tissues. Older monitors used to store the values of blood glucose and make them available for later download and retrospective assessment. This limitation was overcome in more recent monitors, which have sensors to measure glucose and send it immediately to the receiver which will display it. In addition, recent monitors can send alarms to the patient when glucose concentrations are higher or lower than certain thresholds. The receivers can also be linked with insulin pumps to control insulin administration to the patient automatically [13].

Despite these significant advantages of the use of continuous glucose monitors, they still have some limitations that could raise concerns regarding their routine use. An important limitations of these monitors use is the instability against conditions like inflammation or granulation which could alter measurements [13]. To limit the effects of inflammation on measurements and improve biostability, membranes of the sensors have been developed to include oxide nanoparticles and Polyethylene Glycol[14]. Research is still continuing to further improve sensors and limit environmental effects from altering measurements.

Another crucial limitation of the use of monitors is that they measure glucose levels in the interstitial tissues which do not always reflect blood concentrations accurately. In addition, the time until the sensor measures the levels in the interstituim and display the measurement could sometimes take up to ten minutes [15].

In 1999, the Glucowatch Biographer was introduced as a wristwatch that can monitor glucose levels continuously. However, this device was associated with several mistakes and inaccuracies especially with skin irritations, leading to the failure of its use [16].

Recently, there have been efforts to manufacture glucose monitors that are based in smartphones, which could make this process easier and more convenient to patients. Moreover, applications have been created to calculate the required insulin dose based on nutritional intake, water consumption, exercise, and other patient-related factors. The most recent device, which is currently still being developed, will be implanted under the conjunctiva to measure blood glucose using a small photometer [17].

CONCLUSIONS:

Diabetes mellitus type 1 is one of the most common chronic diseases that require continuous monitoring and strict management to achieve favorable outcomes. Despite continuous research, management and treatment of diabetes mellitus type 1 is still not satisfactory and convenient to patients, leading to relatively high rates of incompliance, especially in children. Therefore, it has been essential to continuously develop methods that improve treatment and glucose control, and thus increase compliance to treatment. To achieve this, several analogues of insulin have been develop including different types of short-acting and long-acting insulin analogues. The methods of insulin administration have also been developing with the increased use of insulin pumps.

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