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Modern Methods Of Glucose Monitoring In The Context Of Physical Activity - Review Study

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ABSTRACT:

Introduction: In the last few years, with over 422 million cases of diabetes worldwide and with an overload of healthcare, the development of new glucose monitoring approaches has become a crucial subject. This paper set out to explore the effectiveness of current glucose monitoring methods, their usage in the context of physical activity, and prospects for the future.

Review methods: We conducted our study as a literature review, with data being gathered via PubMed and Embase.

The state of knowledge: Currently, the two most popular methods of glucose monitoring are self-monitoring (SMBG) and continuous glucose monitoring (CGM) with real-time devices such as Dexcom G6, and Medtronic Guardian Connect System, and intermittent devices such as Freestyle Libre 2. Both approaches are invasive and can cause allergic reactions and dermatitis. As a result, many researchers propose non-invasive methods including optical coherence tomography, spectroscopy, and fluorescence. The growing accessibility leads to the usage of CGM devices in everyday life not only by patients with diabetes melitus.

Conclusions: Advancements in diabetes technologies allow patients to maintain glucose homeostasis and improve their Quality of life. CGM devices are constantly developed to be more accessible and easy to use, which may help in adjusting the training programs and diets for individual needs.

KEYWORDS: CGM; diabetes mellitus; physical activity; freestyle libre; dexcom

INTRODUCTION:

In recent years diabetes mellitus has emerged as one of the most important health problems, with over 422 million cases worldwide.[1] The World Health Organization characterizes this condition as a metabolic disease with hyperglycemia (that is elevated blood glucose levels), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys, and nerves.[1] There are several types of diabetes, which can be caused by defects in insulin secretion, insulin action, or both.[2] In type 1 diabetes mellitus, the body cannot produce insulin; therefore, people with this type are treated with insulin. Typ 2 is caused by resistance to insulin. In both cases maintaining glucose homeostasis is necessary to prevent short- and long-term complications and improve Quality of life. To do that, especially in type 1 diabetes mellitus, patients need to check their blood glucose levels often. Therefore, new technologies such as continuous glucose monitoring (CGM), have been instrumental in the management of this disease.[3]

Some of the health issues that predispose to diabetes mellitus type 2 are overweight and obesity. In the last few years, these conditions have become a central topic with more than 2.6 billion people aged five years and older worldwide being overweight or obese[4] With growing awareness physicians can choose different strategies to help patients with these conditions. Currently, bariatric procedures are considered effective, and safe and are known to reduce obesity-related comorbidities and improve Quality of life significantly.[5] There is also a wide range of medications, that are registered to treat obesity, some of them, like semaglutyd, are also used in diabesity management.[4] Regardless, lifestyle modifications, especially physical activity, remain the most important aspect of treatment.

Physical activity is the key factor in maintaining health, however, in patients with diabetes mellitus, it may cause dangerous episodes of hypoglycemia. Consequently, glucose monitoring during training is very important for patients with insulin resistance and diabetes mellitus, especially those with hypoglycemia unawareness. CGM may help in selecting the best insensitivity and type of physical activity for patients. It also may reduce the frequency of hypoglycemia episodes and raise the safety of training.

REVIEW METHODS:

This study was conducted in the form of a literature review, with data being gathered via PubMed and Embase, and it set out to explore the effectiveness of current glucose monitoring methods and their usage in the context of physical activity.

THE STATE OF KNOWLEDGE:

Continuous Glucose Monitoring (CGM)

In 1999, the FDA gave the green light to the first CGM system.[6] Since then innovations in technology have revolutionized diabetes management.[6] Nowadays most of the CGM devices consist of a sensor, transmitter, and wireless receiver.[3,7,8] The sensor is a small device inserted into the subcutaneous tissue via a thin needle and can measure blood glucose levels in the surrounding fluids.[7] Then the transmitter transports the information to the receiver, which then processes the signal and calculates the glucose level.[8] As an output, the patient receives the real-time glucose status in the interstitial fluid. It is important to note, that this reading is not the exact extension of glucose level in the blood. The delay time between the glucose level in interstitial fluid in comparison to the serum is about 6-12 minutes.[3,9,] The glucose concentration in interstitial fluid is the reflection of local metabolism, it shows the glucose that diffuses to the local tissues and cells, while the blood glucose represents the whole currently available glucose.[9] The delay is most noticeable during periods of rapid glucose level fluctuations, such as during exercise or after meals.[3,9] Patients should be informed about these differences and referred to SMBG in cases of low glucose levels.

CGM is particularly useful for children, for patients with frequent hypoglycemia episodes, and hypoglycemia unawareness, for pregnant women, and for patients with poorly controlled diseases.[3,10] However, every patient may observe benefits from using CGM devices.

There are two types of CGM instruments, real-time devices that continuously measure glucose levels and intermittent devices that capture it when the sensor is in proximity to the receiver.[3,10] In the first group, the most popular devices are the Dexcom G6, Medtronic Guardian Connect System, and Eversense CGM System.[3] The second group consists of Freestyle Libre 2, which reads glucose levels when swiped by a reader or smartphone. The intermittent devices are in most cases more affordable alternatives, Medicare mainly covers them, and their sensor life is longer (approximately 2 weeks).[3]

Table 1. presents the comparison between the most popular systems, which are Dexcom and FreeStyle Libre.[3,11,12] They have similar functions and characteristics and are widely used by patients worldwide. Both devices' groups are highly accurate, but a recent study by Kevin Hanson et al. revealed that the FreeStyle Libre 3 was more precise than the Dexcom G7 in all metrics evaluated throughout the study period.[12] However, more studies are needed to surely evaluate the accuracy and the best group of patients for both devices.

	Dexcom CGM	**FreeStyle Libre CGM**
Devices and Users	Dexcom G6 - adults and children above 2 years Dexcom G7 - adults and children above 2 years	FreeStyle Libre 14-Day - adults 18 years and older FreeStyle Libre 2 - adults and children above 4 years FreeStyle Libre 3 - adults and children above 4 years FreeStyle Libre 2 Plus - adults and children above 2 years
Frequency of Glucose Readings	Continuously throughout the day, obtaining data as often as every five minutes. Glucose readings update	Systems automatically report readings up to every minute (except for the FreeStyle Libre 14 Day).

	automatically.	The FreeStyle Libre 2 requires the sensor to be scanned for readings to update.
Sensor Characteristics	A sensor is attached to the skin with a small electrochemical probe inserted into the underlying tissue.	A sensor is attached to the skin with a small electrochemical probe inserted into the underlying tissue.
Sensor life	Up to 10 days	Up to 15 days
Compatibility with insulin pumps	All Dexcom systems can be programmed to work with insulin pumps.	Only the FreeStyle Libre 2 Plus system is compatible with an insulin pump.

Table 1. Comparison between Dexcom and FreeStyle Libre CGM Systems

Numerous benefits can be observed regardless of the CGM type. Nowadays, with wide accessibility to smartphones, they can be used to capture and analyze data and send the results to physicians. This is both convenient and cost-saving and allows doctors to easily monitor the patient's treatment. One of the most important features is the possibility to set alarms for high and low glucose levels. This is particularly crucial in cases of hypoglycemia, where the patient presents no symptoms and is unaware of the low glucose values.[10] Another important characteristic is the possibility of creating an ambulatory glucose profile and checking the time in the target range (TIR), which is extremely useful after any treatment modifications when the patients need to be monitored more closely. Some systems even provide data transmission to insulin-delivery devices. Furthermore, the devices may evaluate the potential level of HbA_{1c} . Lastly, real-time data and predictive algorithms allow the patients to closely monitor the fluctuations of their glucose levels and gain awareness of how food and lifestyle choices affect their glucose values.[3,10]

Having discussed the advantages of CGM devices, the disadvantages also need to be addressed. The accuracy of the measurements was already discussed in this article. Another important problem is the potential risk of contact dermatitis.[10] Sensors that are applied to the skin may cause irritation and in some cases allergic reactions. Finally, some users experience information overload because of the continuous data stream. The psychosocial impact of CGM according to many studies may lead to stress and anxiety.[3,8,10] Because of the above-mentioned problems, there is a constant need for non-invasive, safe, and easy-to-use devices.[8]

Non-invasive methods

The two most popular methods of glucose monitoring are SMBG and above mentioned CGM. Both of them are invasive and can cause irritation and dermatitis after repeated use.[8] This section of the article gives a brief overview of the recent non-invasive methods, that are gaining popularity.

Optical Coherence Tomography (OCT)

Optical Coherence Tomography (OCT) is an imaging technology that exploits the principle of coherent radiation from low-coherence light generated by an interferometer.[13] This technique is particularly effective for achieving micron-level high-resolution detection of changes in the optical properties of biological tissues.

The operational mechanism of OCT involves predicting the glucose concentration in interstitial fluid (ISF) through the analysis of the light interferogram, which is created by backscattered light from the tissue and a reference light.[14] The refractive index of the tissue increases alongside rising blood glucose concentration and subsequent decrease in the scattering coefficient of the tissue. OCT typically uses light with wavelengths ranging from 800 to 1300 nm, which falls within the Near-Infrared (NIR) spectrum. NIR light sources are advantageous as they are relatively inexpensive and small, making them suitable for OCT technology.

Because of its high signal-to-noise ratio and substantial penetration depth, OCT technology holds significant potential for non-invasive glucose monitoring, although it carries some disadvantages. The primary challenges for the OCT technique in glucose sensing are the relatively weak measured signal for changes in the scattering coefficient and the technique's sensitivity to numerous factors.[15] These factors include motion artifacts which can alter interference patterns. Skin properties and environment, such as pH, temperature, and humidity can also hinder the OCT accuracy - these factors can impact the scattering coefficients. Consequently, personalized calibration may be essential for accurate non-invasive glucose measurement using OCT technology. [16]

Spectroscopy

Another method used to noninvasively measure the glucose level is spectroscopy. It is a scientific technique used for examining the interaction between matter and electromagnetic radiation. Spectroscopy measures the absorption, emission, or scattering of light by a sample to obtain information about its structure, composition, and physical properties.[17]

Different types of spectroscopy can be used for non-invasive glucose monitoring. The ones currently in use and under research include near-infrared spectroscopy, mid-infrared spectroscopy, Raman spectroscopy, far-infrared spectroscopy, Time of Flight (TOF), and Terahertz Time-Domain Spectroscopy (THz-TDS), thermal-emission spectroscopy and photoacoustic spectroscopy.[18] The first two methods are the most extensively studied and form the foundation for both emerging and existing devices. This is due to their high selectivity for glucose sensing, which is crucial given the complexity of blood and tissue properties.[17]

Near-infrared spectroscopy (NIRS) technology depends on the absorption and scattering of light in the 780nm to 2500nm wavelength range. Although glucose has only weak absorption in the NIR band, water also has minimal absorption of NIR radiation. Consequently, up to 95% of the light can penetrate the stratum corneum and epidermis to reach areas with higher blood concentrations, largely unaffected by skin pigmentation.[19] Components and materials for NIR spectroscopy are readily available and cost-effective, which led to the development of two non-invasive glucose measurement systems currently on the market: the Combo glucometer [20] and HELO Extense.[21]

The longer wavelengths in mid-infrared spectroscopy result in reduced scattering of radiation within tissues. This allows molecules to exhibit unique spectral signatures in the MIR range, making it excellent for molecular identification. However, the significant water absorption in this region limits MIR signal penetration to just a few micrometers into the tissue.[18] Creating a device based on MIR technology is more expensive than one based on NIR technology, but there are several being investigated, for example, LTT - light touch technology.[22]

Many other sensors utilizing different types of spectroscopy are currently under research. However, these technologies require further development to meet regulatory standards before they can be introduced to the market. The main challenge with these methods is their high sensitivity to temperature changes and motion, which are difficult to avoid during physical exercise. Additionally, there are often issues with selectivity in determining glucose, and they may not be suitable for detecting sudden changes in glucose levels.[17]

Fluorescence

Fluorescence is a process by which a substance absorbs light or other electromagnetic radiation of a shorter wavelength and subsequently emits light of a longer wavelength. Fluorescence sensing, known for its high sensitivity, can be utilized with cost-effective light sources like LEDs that produce ultraviolet (UV) or visible light.[23]

Fluorescence sensing has been explored for glucose monitoring in both biofluids and subcutaneous measurements. Research teams have developed optical sensors utilizing fluorescence detection, which have proven to be highly sensitive for determining glucose levels in human serum.[24] Additionally, fluorescence sensing is particularly promising for non-invasive glucose measurement, as small fluorescence-based devices are relatively easy to obtain, cost-effective, and can be implanted under the skin without the need for surgery.[16]

Although fluorescence sensing has advanced significantly for glucose measurement, some challenges remain. For instance, in non-invasive methods, light scattering from fluorescence can be affected by various skin characteristics, such as pigmentation levels. Additionally, for minimally invasive approaches, calibration is still necessary for fluorescence-based continuous glucose monitoring (CGM) systems.[16,24] This is to address issues like signal drift and the loss of fluorophores due to photobleaching over time. Furthermore, other sugars, such as galactose and fructose, can interact with many of the same fluorophores used for glucose detection, causing interference and reducing the effectiveness of available fluorophores.

Future Development

In recent years, particularly since 2020, there has been a surge in research and development regarding non-invasive glucose monitoring (NIGM) solutions, especially continuous glucose monitoring (CGM) devices. This renewed focus includes efforts from both major tech companies like Apple and Samsung, as well as startups.

NIGM devices in the form of smartwatches or wristbands could certainly be enticing to the diabetic population, given that the only forms of CGM are painful to use and require extra time and care. As of today (the year 2024), NIGM devices are not FDA-approved [25], although it is easy to find products with such claims available for purchase.

Overall, with advancements in technology and funding, the future for NIGM devices looks promising. However, it is still largely uncharted territory, as many of these innovations face challenges related to accuracy, sample sizes and price [26]. Still the ultimate impact and feasibility of these technologies remain to be fully understood.

Glucose Monitoring in Sport

The non-invasive devices are promising, nevertheless, CGM based on invasive systems remains the basic course of management. As already mentioned above CGM is particularly useful for patients with frequent hypoglycemia episodes, hypoglycemia unawareness, and for patients with poorly controlled diseases. However, because of the growing accessibility of devices, more studies explore CGM use during physical activity. They focus not only on patients with diabetes mellitus but also on athletes and healthy people. Gaining knowledge about the influence of sport on glucose levels in individuals may help adjust the training program for their needs.

Numerous studies have demonstrated the benefits of using CGM among patients with T1DM who engage in sports, including fewer insulin-induced hypoglycemic events and the maintenance of stable glucose levels throughout the exercise period and afterward.[27] A study by Riddell et al. concluded that the ability to monitor glucose levels in real time and respond quickly to changes helps prevent significant fluctuations in blood glucose levels.[28] It also provides continuous glucose tracking during the recovery period, enabling appropriate responses and preventing hypoglycemic events. Additionally, the athlete's medical team gains increased access to glucose readings, allowing for the best response to fluctuations in glucose levels [29] Abdulrahman and colleagues evidenced that CGM helped athletes spend more time within their target glucose range. In their research, the time spent in the target blood glucose range increased from 72.4% to 88.1% during workouts after just one week of using CGM.[30] Another study by Houlder and Yardley demonstrated that an improved understanding of glucose trends with different types of training allows for better preparation.[31] Several studies have indicated that a long-term advantage of CGM is the reduced need for constant finger-prick sampling during training or competition.[28,32,33] Another benefit is that CGM enables monitoring glucose trends over time [28,30,34] and decreases the stress associated with participating in sports and avoiding hypoglycemia.[28,30,35]

CONCLUSIONS:

In recent years CGM devices have evolved as a less invasive way to optimize blood sugar control and provide real-time data. The most widely used systems are Dexcom and FreeStyle Libre, both of them effective and easy to use. The rapid pace of technological innovations allows patients to maintain glucose homeostasis and improve their Quality of life. Many researchers focus on future adjustments in diabetes mellitus treatment, especially in the context of healthcare overload. An interesting approach is presented in a study „Diabetes and technology in 2030: a utopian or dystopian future?", in which authors speculate about the use of new technology and artificial intelligence in the future management of diabetes.[36] Furthermore, the growing accessibility of CGM systems, especially non-invasive devices, engage not only patients but also athleats and healthy individuals. Currently, FDA has not authorized any smartwatch or smart ring, but it remains a possibility in the future. CGM use in sports may help adjust the training programs and diets for individual needs. However, more studies are needed to establish the accuracy and potential benefits.

DISCLOSURES:

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