Liječenje dijabetesa tipa 1 hibridnom zatvorenom petljom

Management of diabetes type 1 with hybrid closed-loop

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Sažetak

Uvod: Kod dijabetes mellitus tipa 1 (T1DM), gušterača uopće ne proizvodi inzulin potreban za prirodnu regulaciju šećera u krvi, što stvara mnoge poteškoće kod oboljelih. Hibridni sustav zatvorene petlje djeluje na način da kontinuirano isporučuje inzulin s ciljem jednostavnijeg kontroliranja T1DM-a, a ujedno doprinosi smanjenju komplikacija za korisnike, odnosno oboljele.

Cilj: Utvrditi kako hibridni sustav zatvorene petlje pomaže u kontroliranju bolesti dijabetesa tipa 1 i poboljšanju kvalitete života oboljelih.

Ispitanici i metode: Istraživanje se temeljilo na neeksperimentalnoj kvantitativnoj metodi s upitnikom konstruiranim za potrebe istraživanja. Upitnik je bio proslijeđen u grupe namijenjene oboljelima od dijabetesa tipa 1 na društvenoj mreži Facebook, u kojima su pozvani korisnici hibridnog sustava zatvorene petlje. Za statističku obradu prikupljenih podataka pomoću upitnika korištena je deskriptivna i inferencijalna statistika. Korišten je program IBM SPSS Statistics (verzija 20).

Rezultati: Hibridni sustav zatvorene petlje ispitanicima omogućava lakše kontroliranje T1DM-a, a time i bolju kvalitetu života. Ukupno 82,9 % ispitanika bilježi manje učestale hipoglikemije nego prije korištenja hibridnog sustava zatvorene petlje. Nadalje, 65,7 % ispitanika zbog ovog sustava ranije prepoznaje znakove hipoglikemije i samim se time njihov strah od hipoglikemije smanjuje. Kod 70,3 % ispitanika zahvaljujući korištenju hibridnog sustava zatvorene petlje smanjena je zabrinutost zbog dijabetesa zbog čega se osjećaju mnogo slobodnije.

Zaključak: Istraživanje je potvrdilo pretpostavku da su ispitanici koji boluju od T1DM-a zadovoljni hibridnim sustavom zatvorene petlje te također potvrđuju da bilježe manje oscilacija šećera u krvi. Najnovija metoda liječenja hibridnim sustavom zatvorene petlje doprinosi boljoj kvaliteti života oboljelih. Zbog svih prednosti koje donosi korištenje hibridnog sustava zatvorene petlje, ispitanici preporučuju korištenje ovog sustava.

Ključne riječi: hibridni sustav zatvorene petlje, dijabetes tipa 1, inzulinska pumpa, kvaliteta života

Kratak naslov: Hibridna zatvorena petlja

Abstract

Introduction: Type 1 diabetes mellitus (T1DM), in which the pancreas is no longer able to produce insulin to naturally control blood sugar, can be a major problem for the patient in terms of disease management. Closed-loop hybrid systems are designed to automate insulin delivery to improve T1DM outcomes and reduce the burden and distress for the user. The hybrid closed-loop makes an important contribution to reducing the difficulties of disease, also its control and management.

Research goal: The goal is to examine how the closed hybrid loop system has contributed to the management of T1DM and improved the quality of life of patients.

Participants and Methods: The survey was based on a non-experimental quantitative method with a questionnaire developed for the study. The surveys were distributed on Facebook in groups dedicated to patients with T1DM. The survey covered hybrid closed-loop users in Slovenia. Descriptive and inferential statistics were used for the statistical processing of the obtained data. IBM SPSS Statistics (version 20) was used.

Results: The hybrid closed-loop system provides respondents with better management of T1DM and a better quality of life. 82.9% of respondents have fewer hypoglycaemic episodes than before using the hybrid system, 65.7% of respondents detect signs of hypoglycaemia earlier and fear of hypoglycaemia is reduced. 70.3% of respondents say they have less worries about diabetes.

Conclusion: The study confirmed the prediction that respondents with T1DM are satisfied with the hybrid closed-loop system and notice fewer fluctuations in their blood sugar. The latest treatment method also helps to improve the quality of life. Because of its benefits, respondents recommend using a hybrid closed-loop system.

Keywords: hybrid closed-loop, type 1 diabetes, insulin pump, quality of life

Short title: Hybrid closed-loop

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Introduction

T1DM is also known as juvenile diabetes. It is usually caused by an autoimmune reaction in which the body's defence system attacks the insulin-producing beta cells in the pancreas. The exact cause has still not been identified, but it is clear that the insulin-producing cells destroy the body's immune system. The disease can affect people at any age, but usually develops in children and young people. People with T1DM are insulin-dependent because their bodies produce little or no insulin. If they don't have access to insulin, they die [1].

The initial signs of T1DM are increased thirst, frequent urination, weight loss, hunger due to cell starvation, and fatigue. When blood glucose levels rise, the body tries to remove excess glucose in the urine and thin the blood by increasing water intake. However, many patients are initially diagnosed when they arrive at the hospital very ill with a condition called diabetic ketoacidosis. Diabetic ketoacidosis causes abdominal pain, nausea and/or vomiting, and drowsiness and is a potentially life-threatening condition. Other signs of diabetes include weight loss, fatigue, lack of interest and concentration, tingling or numbness in the hands and feet, blurred vision, frequent infections, slow wound healing, vomiting, and stomach pain [1].

Diagnosing T1DM is not too difficult. The doctor will request the following tests if patient exhibits signs of T1DM:

Blood glucose test: To determine how much sugar is in patients' blood, the doctor will do a blood glucose test. They might ask to submit to both a fasting test (no food or liquids for at least eight hours before the test) and a random test (without fasting). If the test results reveal that the patient has extremely high blood sugar, T1DM s is likely the cause. Patients' healthcare providers may do an A1C test if the results of the blood glucose test show that the patient has diabetes. This calculates three-month average blood sugar levels.

Test for antibodies: This blood examination looks for autoantibodies to identify Type 1 or Type 2 diabetes. Proteins called autoantibodies mistakenly attack the tissue in patient's body. Patients have T1DM if certain autoantibodies are present. People with Type 2 diabetes typically do not have autoantibodies [2].

T1DM accounts for 5% – 10% of diabetes worldwide. It usually occurs in childhood, but a quarter is diagnosed in adulthood. In 2015, the number of children with T1DM exceeded half a million [3]. T1DM is the rarest in China and Venezuela and the most common in Finland.

The occurrence of T1DM is increasing by 3.9% every year in Europe. T1DM used to be considered a fatal disease. However, the introduction of insulin has significantly increased people's life expectancy. Today, children and adolescents with T1DM have a life expectancy of around 65 to 69 years [4].

Dietary guidelines for people with diabetes do not differ significantly from the principles of a healthy diet. Monitoring carbohydrate intake and adjusting insulin doses properly is a key component of the diet of people with T1DM [5].

Carbohydrate counting is significant for blood glucose control and is an important step in diabetes management. This approach can be utilised for improved glycaemic control and quality of life [6].

Regular physical activity is a fundamental part of the recommendations for the treatment of T1DM and has a positive impact on cardiovascular health, insulin requirements, physical fitness, and general well-being. Data from large diabetes registries have shown a positive link between physical activity and metabolic control [7].

Treating diabetes with multi-day injections daily is the most common method of treatment. A technological alternative to this treatment method is continuous subcutaneous insulin infusion. A portable insulin pump is a mechanical medical device that offers the most physiological way to administer insulin because it simulates the normal pattern of insulin secretion [8]. A hybrid closed-loop system consists of three components: an insulin pump, a continuous glucose sensor, and an algorithm that determines insulin delivery. Based on glucose sensors, these systems deliver or cut off insulin to the body [9]. The hybrid closed-loop was launched in Slovenia in November 2018. On February 6, 2020, there were 267 hybrid closed-loop users in Slovenia. Of these, 216 are over 18 years old and 51 are under 18.

Even though the treatment of T1DM is very advanced, most patients are unable to achieve near-normal blood sugar levels and remain at risk of severe hypoglycaemia, diabetic ketoacidosis, and late complications of diabetes [10].

The Hybrid Closed Loop Automated Insulin Delivery technology uses a control algorithm to automatically increase or discontinue insulin delivery using data from a sensor for continuous measurement of glucose in the extracellular matrix, improving glucose control and reducing the burden of disease management. Most of the hybrid closed-loop systems under development are hybrid systems, which means that the user still has to enter the number of carbohydrates consumed in a meal and confirm the recommended insulin dose [11].

The Medtronic MiniMed Inc. hybrid closed-loop system is the first integrated system designed for continuous day and night control of a hybrid closed-loop system with an algorithm embedded in an insulin pump. The hybrid closed-loop system requires a meal prediction, whereby the patient estimates the carbohydrate intake and enters this number into the insulin pump [12]. The hybrid closed-loop system consists of three components: an insulin pump, a continuous glucose sensor, and an algorithm that determines insulin delivery. Such a system not only cuts off insulin delivery, but also increases insulin delivery based on sensor glucose values [9].

The benefits of the hybrid closed-loop system are following: reduced fear of hypoglycaemia, reduced anxiety, fewer needs due to diabetes, reassurance to users and family members, improved sleep, increased trust, enthusiasm and empowerment, and more freedom to engage in exercise and unplanned activity [13].

Burdens reported by users: size and appearance of devices, intrusiveness of alarms and associated sleep interruptions, increased time thinking about diabetes, technical difficulties, exercise limitations and perceptions around office work, and data obsession [13].

The algorithm is set to a target glucose level of 6.7 mmol/l. Users can enter into the insulin pump that they will exercise and increase the target glucose level to 8.3 mmol/l. User specific parameters are based on data from the previous 2–6 days. The system automatically updates the data [14]. Closed-loop insulin treatment increases the time spent in the target glucose range (TIR) (3.9 – 10.0 mmol/l), which means that it decreases the time spent in hypoglycaemia (below 3.9 mmol/l) and hyperglycaemia (above 10.0 mmol/l) [15].

Nimri et al. [16] conducted a study evaluating physician adjustments of insulin pump settings based on continuous glucose monitoring for patients with type 1 diabetes and compared them with automatic insulin dose adjustments. The study involved 26 physicians and 16 centres in Europe, Israel and South America. Significantly similar results were found between physicians and the automated algorithm.

Hybrid closed-loop insulin delivery systems (HCLs) are an emerging technology for the management of T1DM. HCLs combine an insulin pump with a continuous glucose monitor (CGM) and a computer program. Together, these use information from the CGM to automatically determine insulin needs throughout the day and keep the user within a pre-determined blood glucose range. They are called hybrid systems because users must still manually account for insulin needs before and after meals [17].

The aim of the study was to find out how the hybrid closed-loop system contributed to the management of T1DM and improved quality of life for patients.

Methods

The study is based on a non-experimental quantitative empirical research method. The study sample was purposive. People with T1DM were selected using a hybrid closed-loop system. The research instrument was a structured questionnaire developed for the purpose of our study, consisting of demographic data and statements to which the respondents gave their opinions on the basis of a five-point Likert scale. The questionnaire was published on the www.1ka.si website, and the link was shared in Facebook groups where people with diabetes are members. The study sample consisted of 64 people of different ages.

The gathered data were analysed using SPSS (version 20.0). Descriptive statistics were used for demographic data, the Mann-Whitney test to test for statistically significant differences between the two groups, and the one-sample test to test the expected mean value of each group.

Results

The study involved 64 users of a hybrid closed-loop for T1DM management. The glycated haemoglobin level was analysed using the one-sample test and is statistically significantly lower than 7%, as the test showed a mean value of 6.71% for the variable glycated haemoglobin level. Differences in mean rank values between the sexes were tested using the Mann-Whitney test, which indicates that there is no statistically significant difference between the sexes in terms of life limitations, as both significance values are bigger than 0.05 (0.232>0.05 and 0.304>0.05, respectively). The average rank values also vary between the ages of the respondents. For the statement *The thought of living with diabetes is a problem for me*, the rank value for respondents in the 18–35 age group is 30.12, while it is slightly higher for respondents aged 35+ (32.80).

There was very little difference in the mean rank values in terms of the duration of diabetes. For the statement *I have fewer blood sugar fluctuations with the hybrid closed-loop*, the rank value for respondents with 1–15 years of diabetes is 32.39, while for respondents with 15 or more years of diabetes, the rank value is almost the same (32.56).

Most respondents, 48.4%, disagreed with the statement *The thought of living with diabetes is a problem for me*. 57.8% of respondents have excellent control of their diabetes, 43.8% of respondents fear the possibility of late complications, and 51.6% of respondents say they are not deprived of food and drink. 70.3% of those surveyed are regularly physically active, and 59.4% of the diabetics surveyed who use a hybrid closed-loop have full confidence in the insulin pump and its judgements on insulin supplementation. 68.8% of respondents are satisfied with the hybrid closed-loop system, 82.9% report fewer hypoglycaemic episodes since using the hybrid loop, and 65.7% detect signs of hypoglycaemia earlier. 70.3% of respondents who use a hybrid closed-loop have fewer concerns about diabetes. 70.3% of respondents believe they are freer with a hybrid closed-loop. 67.2% of respondents are satisfied with the glycaemic limits set in the hybrid closed-loop. 51.6% of respondents do not report higher blood sugar at night, 59.4% of respondents feel they have reached their glycated haemoglobin targets, 67.2% have fewer blood sugar fluctuations since using a hybrid closed-loop, and 56.2% of respondents report that they can no longer live without a hybrid closed-loop.

Discussion

A study involving people with T1DM who use a hybrid closed-loop showed us how respondents manage their diabetes, the difference in their disease management since using a hybrid closed-loop, and how satisfied they are with their disease management.

In Slovenia, we started using hybrid closed-loop systems in November 2018. In 2020, there were 267 hybrid closed-loop users in Slovenia. Of these, 216 users are over 18 years old. Although such an instrument was subject to a surcharge, many people chose this option. The insurance company later denied the payment.

While closed-loop systems can make a significant difference to the quality of life of users by making people feel unencumbered in their eating, there is the potential for misuse of the technology in the sense that unhealthy eating can occur over time [18].

Our study results show that 51.6% of respondents answered that they do not feel deprived of food and drink and do not feel guilty when they "sin" when it comes to food. More than half, 59.4%, do not feel overwhelmed by the constant worry about food and drink.

Fear of hypoglycaemia is crucial for the quality of life. The results of our study showed that less than half of the respondents, 45.3%, experience a fear of hypoglycaemia. How this fear affects diabetes performance, fitness management and mental health is something that experts believe will require further research. The ongoing problem of fear of hypoglycaemia, especially at night, and the possibility of sleep disturbance is an extremely important problem that affects the risk of both short-term and long-term complications [19].

Our study found that the hybrid closed-loop system gave respondents a better quality of life, with 82.9% having fewer hypoglycaemic episodes than before using the hybrid system and 65.7% detecting signs of hypoglycaemia earlier. That, in turn, has reduced the fear of hypoglycaemia.

In September 2016, the U.S. Food and Drug Administration approved the first hybrid closed-loop system that automates insulin delivery but requires user input to treat T1DM. This study aimed to investigate the benefits, expectations, and opinions of individuals with a hybrid loop following a clinical trial of the system. Thirty-two individuals with a hybrid loop (17 adults, 15 adolescents) participated in the focus group study. Some participants felt misled by terms such as "closed loop" and "artificial pancreas". The perceived benefits for users were improved glycaemic control, an expected reduction in long-term complications, improved quality of life, and reduced mental burden of diabetes management. Problems and limitations included unexpected tasks for the user, difficulty wearing the system, concerns about controlling high levels, and diabetes alerts. They state that users are willing to accept some difficulties and limitations if they perceive health and quality of life benefits that go beyond the current self-management. To help manage expectations, clinicians need to provide a balanced view of the positives and negatives [20]. A study conducted by Adams et al. [21] among fourteen adults and fifteen adolescents showed that this system holds promise for improving attitudes towards technology and reducing user anxiety. Psychosocial factors such as coping distress can negatively affect glycaemic outcomes and should be a priority area for further investigation. The psychosocial aspects of users' usage of closed-loop systems are crucial. User feedback is valuable to help manufacturers and researchers improve systems and develop additional features to be implemented. If closed-loop is to be widely accepted as the standard management of T1DM in the future, it is imperative that healthcare providers explore the real-life experiences of users using this technology in order to adequately meet their expectations.

This study identifies significant positive benefits of closed-loop therapy for glycaemia and quality of life. The perceived benefit of night-time monitoring achieved with this technology has reduced anxiety and improved sleep quality. The system has also been able to reduce the burden of diabetes by reducing the time spent on daily diabetes management.

Bally, Thabit & Hovorka [22] wrote in their paper... Although the ideal situation would be a biological cure for T1DM, where damaged beta cells could be replaced by healthy and viable ones, the intermediate but rapidly innovative role of an artificial pancreas could act as a "bridge" to finding a cure. Rapid progress from "bench to bedside" over the last decade has made the artificial pancreas a reality and may lead to better care for people with T1DM in the near future.

Conclusion

The study aimed to find out how the hybrid closed-loop system contributed to the management of T1DM and improved the quality of life for patients.

The study contributes to a better understanding of the latest hybrid closed-loop therapy used among T1DM patients. It is also encouraging that hybrid closed-loop users have fewer hypoglycaemic episodes and a better quality of life.

In conclusion, the results of our study showed general satisfaction with the unrestricted use of the hybrid closed-loop. Further longitudinal studies are needed to better understand the closed-loop experience in this age group.

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