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Advances in Automated Insulin Delivery Systems

Technology has been a significant advancement in the management of type 1 diabetes (T1DM), not only by improving glycemic control but also enhancing the quality of life and other psychosocial aspects for people with diabetes.

An **Automatic Insulin Delivery (AID) system** consists of a continuous glucose monitor or sensor (CGM), an insulin pump, and a control algorithm, which is the key component connecting them.

The current generation of automated systems has been a major advance in the automation of decisions, improving glycemic control and reducing (though not eliminating) the daily burden of people with diabetes and the time they spend managing it. All systems have demonstrated improvements in glucometric parameters and time in range in real life, beyond clinical trials, even surpassing expected results in different population groups and age ranges.

However, these systems cannot be considered fully automated, as they require patient interaction, such as indicating the amount of carbohydrates (CHO) they will consume during a meal (with sufficient time in advance) or signaling that they will engage in physical exercise, so the algorithm can act in a more flexible way (avoiding hypoglycemia).

Accurate CHO counting can be challenging and significantly increases the daily control burden of diabetes. This can negatively affect quality of life, making people with T1DM feel restricted in their food choices and more socially anxious.

Recently, clinical trial results have been published with automatic systems that do not require CHO intake to be anticipated, known as **fully closed-loop** insulin delivery systems **(Fully Closed-Loop, FCL)**. These systems are an innovation in diabetes treatment, designed to function fully automatically, adjusting insulin delivery in response to real-time glucose levels. These systems use advanced machine learning algorithms and predictive control to optimally adjust insulin doses, minimizing fluctuations in glucose levels and offering more advanced adaptability (4, 5).

Among these closed-loop systems, **CamAPS HX** *(Figure 1)* has demonstrated its efficacy in a clinical trial with people with T1DM and suboptimal metabolic control (HbA1c > 9%) vs insulin pump therapy with CGM. In this study, the CamAPS HX system showed improved glucose control, increasing time in range (TIR) 70-180 mg/dL (50% vs 33%), improving mean glucose levels (192 mg/dL vs 216 mg/dL), and decreasing time in hyperglycemia > 180 mg/dL (49% vs 63%) without increasing time in hypoglycemia.

» FULLY CLOSED-LOOP SYSTEMS ARE AN INNOVATION IN THE TREATMENT OF DIABETES, DESIGNED TO OPERATE FULLY AUTOMATICALLY, ADJUSTING INSULIN DELIVERY IN RESPONSE TO REAL-TIME GLUCOSE LEVELS

FIGURE 1

CURRENTLY, SYSTEMS CAPABLE OF INFUSING BOTH INSULIN AND GLUCAGON SIMULTANEOUSLY, KNOWN AS BIHORMONAL ARTIFICIAL PANCREAS, ARE BEING STUDIED

» Additionally, a psychosocial sub-study showed that using a fully closed-loop insulin delivery system had significant benefits in quality of life and improved the perception of the daily demands of living with diabetes.

The **Omnipod** system is another complete AID system; in this case, it is a patch pump that delivers insulin without the need to anticipate CHO intake, along with the advantages of the discretion of a patch that adheres to the skin. This pump is small and discreet, similar to an adhesive patch that is placed directly on the skin, delivering continuous insulin 24 hours a day, simulating the function of a pancreas. Preliminary results from a small clinical trial with people with T1DM have demonstrated the viability of this system in an outpatient setting, as well as an improvement in time in range (a mean improvement of 4.8 hours of time in range per day).

Beyond single-insulin delivery systems, systems capable of infusing both insulin and glucagon simultaneously, known as **bihormonal artificial pancreas**, are currently being studied. These systems have already demonstrated significant progress in the management of T1DM. The bihormonal approach to diabetes management provides a more complete and potentially more effective view for glucose level control. By using both insulin and glucagon, the system can respond more dynamically to glucose fluctuations, minimizing both hyper- and hypoglycemia.

The **iLet** Bionic Pancreas (Beta Bionics) *(Figure 2)* is a fully integrated device specifically designed to receive a signal from a continuous glucose monitor and contains autonomous and continuously learning mathematical dosing algorithms. It only requi- »

FIGURE 2

» res the user's weight to begin functioning, without the need to input or anticipate the CHOs the person with diabetes will consume.

Data from a recent study show that users of this device experienced a mean 2.6 more hours of time in range and a 0.7% reduction in HbA1c. The psychosocial impact has also been evaluated with these systems, demonstrating acceptability, reduced burden, and positive psychosocial outcomes, regardless of the age group of the person with diabetes. Despite the positive impact on glycemic control parameters and others like diabetes-related burden, fear of hypoglycemia, or treatment satisfaction, many aspects still need to be resolved and improved to optimize these devices. It may be necessary to enhance control algorithms, the use of ultra-rapid insulins, and expand the number of clinical trials to eventually commercialize these devices and achieve real-life results similar to those currently seen with commercially available AID systems. D

CONCLUSIONS

Fully automated insulin delivery systems, as well as bihormonal systems, represent a significant advancement in the treatment of diabetes, achieving a more balanced and precise control of blood glucose levels while relieving the psychosocial burden that managing diabetes can sometimes entail. These systems completely automate insulin delivery without the need to anticipate carbohydrate intake from meals and achieve optimized glycemic control compared to standard treatments, even reducing the risk of hypoglycemia.

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