

REVIEW PAPER

Advanced hybrid closed loop on the Polish market

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ABSTRACT

Since 1921, when Frederick Banting and Charles Best discovered insulin, we have observed rapid development in the field of diabetology. On the one hand, it is associated with clinical research on the aetiopathogenesis of metabolic disorders, and on the other hand, with the development of new technologies such as devices for insulin delivery and glycaemia monitoring. Since December 2020, the Medtronic MiniMed™ 780G system has been available in Poland. This is the first advanced hybrid closed loop personal insulin pump on the domestic market. It uses advanced algorithms to maintain glucose levels at a predetermined threshold by combining information from continuous glucose monitoring, which enables automatic estimation of basal insulin dose and automatic correction combined with manual initiation of meal boluses.

KEY WORDS:

diabetes, advanced hybrid closed loop, MiniMed™ 780G, AHCL.

INTRODUCTION

Even though type 1 diabetes has been known since ancient times, it was not until 1921, after the discovery of insulin by Frederick Banting and Charles Best, that it became a chronic rather than fatal disease [1]. Since then there has been continuous development of diabetology. On the one hand, related to clinical research on metabolism, and on the other hand, to the development of new technologies such as insulin preparations, insulin delivery devices, and glycaemic monitoring. A milestone in the view of therapy in type 1 diabetes was the Diabetes Control and Complications Trial (DCCT) study (1993), which proved the advantage of intensive insulin treatment aimed at maintaining "perinormal glycaemia" in minimizing complications. Unfortunately, at that time, tight metabolic control was associated with a 3-fold increased risk of hypoglycaemia [2].

PERSONAL INSULIN PUMPS

Effective intensive insulin therapy is greatly facilitated by personal insulin pumps, significantly extending

the lives of people with diabetes. Due to their adjustable basal infusion rate and meal boluses, they better reflect the physiological action of the pancreas [3]. Although their origins date back to the 1960s, it has only been since the 1980s that they have been available to patients with type 1 diabetes. Since the publication of the DCCT study in 1993, the number of pump users has increased dramatically worldwide. In the United States, the number has grown from 15,000 patients in 1993 to more than 81,000 patients by the end of 2000 [4]. A ground-breaking change in diabetes care also occurred with the development of continuous glucose monitoring (CGM). The use of CGM in patients with diabetes has been proven in studies to improve metabolic compensation by reducing HbA_{1c} values [3] and the number of hypoglycaemic episodes.

The first personal insulin pump with CGM available in Poland was Medtronic's MiniMed™ REAL-Time (722) pump (2006). Initially, the monitoring record did not affect insulin delivery. This was followed by the MiniMed™ Veo™ (2010) > (2009), a personal insulin pump with low glucose suspend, which automatically stopped insulin

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delivery and resumed insulin infusion 2 hours after glucose levels fell below a predefined threshold between 40 and 110 mg/dl [5]. The next MiniMed™ 640G pump (2015) available in our country was enriched with a further technological step, i.e. SmartGuard™ technologies – suspension of insulin infusion before a low glycaemic threshold and automatic resumption of base supply. This prediction feature requires that two conditions are met: the sensor glucose level is a maximum of 70 mg/dl above the lower limit, and if the glucose level within 30 minutes reaches a level of 20 mg/dl above the lower limit or falls below it, insulin delivery is automatically stopped [6]. Automatic basal restart is possible if 2 conditions are met: insulin delivery has been stopped for at least 30 minutes, and the sensor glucose value is at least 20 mg/dl above the lower limit and is expected to exceed the lower limit by more than 40 mg/dl within 30 minutes.

The MiniMed™ 670G pump, the first commercially approved HCL hybrid closed loop system in the world (2017) [7], has not been introduced to the Polish market. It was initially available to treat patients with type 1 diabetes from the age of 14 years and from 2018 also for children as young as 7 years old. The system can operate in 2 modes: “automatic” and “manual”. In automatic mode, it uses an algorithm to automatically adjust the basal insulin dose in response to CGM readings. The user still performs meal and correction boluses manually; however, the major change also applies to “standard” meal/correction insulin dose entry. Currently, in the automated system, the user initiates a meal bolus by entering the number of carbohydrates consumed and a correction bolus by entering the blood glucose. These boluses are automatically calculated and administered by the pump. When the system is in automatic mode, there are 2 baseline blood glucose target options: 120 and 150 mg/dl; the higher target is only an option for use during physical activity. In studies, use of the MiniMed™ 670G has been shown to significantly lower HbA_{1c} and increase the time spent in target blood glucose. Although the system in automatic mode has many benefits, it also has several limitations, including a fixed lowest target threshold of 120 mg/dl and a lack of options such as a combination bolus and extended bolus [7, 8].

MEDTRONIC MINIMED™ 780G ADVANCED HYBRID CLOSED LOOP

The Medtronic MiniMed™ 780G system is the first advanced hybrid closed loop (AHCL) pump available in Poland. On the global market, the AHCL system is also represented by Tandem control-IQ. The hybrid closed-loop system is designed to maintain glucose levels at a predetermined threshold by combining information from CGM with an algorithm that enables automatic insulin dose estimation combined with manual initiation of meal boluses [9]. In June 2020, it received the Conformité

Européenne mark of approval for consumer marketing in the European Union [10]. According to the product characteristics, it targets people with type 1 diabetes aged 7–80 years with a total daily insulin dose of 8 units per day or more [9]. The system consists of a water-resistant (IPX8) insulin pump, Guardian Link 3 transmitter (CGM) (Guardian Link 4 transmitter and new sensors since April 2022 [10]), and a proprietary PID (proportional integral derivative algorithm) [11]. Like the Medtronic MiniMed system, the 670G can operate in manual and automatic modes but unlike its predecessor it has 3 blood glucose target thresholds: 100, 110 (additional, lower), and 120 mg/dl, a temporal target of 150 mg/dl (like the HCL model) [11]. An important and effective feature has also been added, the so-called automatic correction bolus, which can be activated (administered every 5 minutes) in an effort to reach a glucose threshold of 120 mg/dl when the continuous supply of basal insulin (base) has reached its maximum value [11]. The entire operation of the system is programmed and designed to achieve the greatest safety (minimizing hypoglycaemic episodes) and effectiveness of insulin therapy (the longest possible period of time within the target range of 70–180 mg/dl). Another new feature is the Bluetooth connectivity that the MiniMed™ 780G system is equipped with [12]. The use of this type of technology represents a significant step forward for Medtronic insulin pumps. The MiniMed™ 780G system offers 2 applications. The MiniMed™ Mobile app is used by the patient, and the CareLink™ Connect app is used by therapy partners [12]. This solution increases safety, especially in children with type 1 diabetes, by allowing their caregivers real-time collaboration with the child, e.g. in an educational institution. In addition, it allows for easy access to data from the pump and CGM for health care professionals. Thus, it is an essential element in the holistic care of a person with diabetes using telemedicine.

DISCUSSION

All hybrid systems are associated with a significant reduction in fingertip blood glucose testing because therapeutic decisions are made automatically by the system based on the CGM blood glucose record (system calibration usually twice a day, compared to an average of 12 meter readings/day [12], and with Guardian 4 only once a week) [13]. The obvious and indispensable fact is the remaining need for proper, personalized programming of the system by a medical professional and further constant modifications to the system with respect to the changing needs of the person with diabetes in diabetes holistic care. In early publications, the use of the Medtronic MiniMed™ 780G System resulted in a significant increase in the time spent in target glycaemia (TIR time in range) without increasing the time spent in hypoglycaemia (time below range – TBR), particularly at bedtime [14–18].

CONCLUSIONS

The use of advanced hybrid closed-loop systems allows the improvement of metabolic compensation, safety of therapy, and above all quality of life of people with diabetes by extending the time spent in target glycaemia. On the global market of pump insulin therapy this is a remarkable, dynamic step in technological solutions. It is important that also Polish consumers have gained the chance to use these revolutionary solutions in modern diabetes care.

DISCLOSURE

The authors declare no conflicts of interest.

REFERENCES

- Poretzky L. Principles of diabetes mellitus. Princ Diabetes Mellit. <https://link.springer.com/book/10.1007/978-0-387-09841-8>.
- Diabetes THEA. Implications of the diabetes control and complications trial. *Diabetes Care* 2003; 26: 25-27.
- McAdams B, Rizvi A. An overview of insulin pumps and glucose sensors for the generalist. *J Clin Med* 2016; 5: 5.
- Alsaleh FM, Smith FJ, Keady S, et al. Insulin pumps: from inception to the present and toward the future. *J Clin Pharm Ther* 2010; 35: 127-138.
- MiniMed * Veo™ Paradigm™ System user guide 11.03.2022.
- MiniMed TM 640G Podręcznik użytkownika systemu. 11.03.2022.
- Petrovski G, Al Khalaf F, Campbell J, et al. 10-day structured initiation protocol from multiple daily injection to hybrid closed-loop system in children and adolescents with type 1 diabetes. *Acta Diabetol* 2020; 57: 681-687.
- Knebel T, Neumiller JJ. Medtronic MiniMed 670G Hybrid Closed-Loop System: 94-95.
- O'Neill S. Update on technologies, medicines and treatments including Libre 3, MiniMed 780G and Glucomen Day continuous glucose monitoring. *Diabet Med* 2021; 38:
- <https://www.medicaldevice-network.com/news/medtronic-ce-sensor-inpen/> 09.06.2022.
- McVean J, Miller J. MiniMed™ 780G insulin pump system with smartphone connectivity for the treatment of type 1 diabetes: overview of its safety and efficacy. *Expert Rev Med Devices* 2021; 18: 499-504.
- Medtronic User Guide MiniMed 780G 11.02.2022.
- Christiansen MP, Garg SK, Brazg R, et al. Accuracy of a fourth-generation subcutaneous continuous glucose sensor. *Diabetes Technol Ther* 2017; 19: 446-456.
- Lepore G, Battelino T, Arrieta A, et al. Real-world performance of the MiniMed™ 780G system: first report of outcomes from 4120 users. *Diabetes Technol Ther* 2022; 24: 113-119.
- Petrovski G, Al Khalaf F, Campbell J, et al. The effect of advanced hybrid closed loop system on glycated hemoglobin (HbA1c) in a young male with type 1 diabetes mellitus and growth hormone treatment: a case report. *Clin Case Reports* 2021; 9: 1-5.
- Petrovski G, Campbell J, Almajali D, et al. Virtual training on advanced hybrid closed-loop system MiniMed 780G in a teenager with type 1 diabetes previously treated with multiple daily injections: A case report. *Clin Case Reports* 2021; 9: 1-5.
- Beato-Víborá PI, Gallego-Gamero F, Ambrojo-López A, et al. Rapid improvement in time in range after the implementation of an advanced hybrid closed-loop system in adolescents and adults with type 1 diabetes. *Diabetes Technol Ther* 2021; 23: 609-615.
- Boughton CK, Hovorka R. New closed-loop insulin systems. *Diabetologia* 2021; 64: 1007-1015.