J Diabetes Clin Res. 2023;5(1):11-14.

Journal of Diabetes and Clinical Research Commentary

A Commentary on "Better TIR, HbA1c, and Less Hypoglycemia in Closed-loop Insulin System in Patients with Type 1 Diabetes: A Meta-analysis"

Xiaojuan Jiao[1], Yunfeng Shen[1,*]

[1]Department of Endocrinology and Metabolism, the Second Affiliated Hospital of Nanchang University, Nanchang, 330006, China

[*]Correspondence should be addressed to Professor Yunfeng Shen, syf92@live.com

Received date: July 18, 2023, **Accepted date:** July 27, 2023

Citation: Jiao X, Shen Y. A Commentary on "Better TIR, HbA1c, and less hypoglycemia in closed-loop insulin system in patients with type 1 diabetes: a meta-analysis". J Diabetes Clin Res. 2023;5(1):11-14.

Abstract

Our team's previous meta-analysis aimed to evaluate the efficacy and safety of closed-loop insulin system (CLS) in non-pregnant individuals with type 1 diabetes mellitus (T1DM). In this study, we aim to discuss the broader application of CLS in a more diverse population and address the current challenges and future development directions. Through a comprehensive review of relevant literature, our findings indicate that CLS not only effectively lowers glucose levels in T1DM patients but also demonstrates greater effectiveness and safety when utilized in pregnant women with T1DM, patients with type 2 diabetes mellitus (T2DM), those undergoing hemodialysis, or individuals requiring surgery. Recent studies have also explored the impact of CLS therapy on quality of life, neurological function, and C-peptide levels. Nevertheless, despite these promising results, CLS still encounters challenges in clinical practice, such as technological maturity, cost-effectiveness, and personalized treatment approaches. Therefore, further research and development of CLS technology are imperative to facilitate its broader adoption among diverse populations and address the current obstacles to its implementation.

Keywords: Closed-loop insulin system, Type 1 diabetes mellitus, Type 2 diabetes mellitus

Commentary

Closed-loop insulin system (CLS) is a remarkable innovative technology that has brought new hope to diabetes patients. In a meta-analysis published by us in 2022, we evaluated non-pregnant type 1 diabetes patients (T1DM) with a study duration of ≥ 8 weeks, and significant results were achieved. The analysis included ten articles [1-10], covering 11 studies with 817 participants. Our research findings demonstrated a significant improvement in glycemic control with a long-term CLS treatment compared to conventional treatment methods. Specifically, the CLS increased the time spent within the target glucose range (3.9-10 mmol/L) by 2.5 hours, corresponding to an improvement of 10.32 percentage points. Additionally, there was a reduction of approximately 15.7 minutes per day in hypoglycemia time (<3.9 mmol/L), equivalent to a decrease of 1.09 percentage points. The time spent in hyperglycemia (>10 mmol/L) decreased by approximately 128 minutes per day, equivalent to a reduction of 8.89%. Glycated hemoglobin (HbA1c) levels decreased by 0.30%. Furthermore, our analysis indicated no significant difference in the risk of adverse events between the closed-loop system and conventional treatment methods [11]. Through a comprehensive review of relevant literature, this study aims to explore the broader application of CLS in a more diverse population and discuss the current challenges and future development directions.

In addition to non-pregnant individuals with T1DM, CLS delivery systems have also been evaluated in other diabetes patients. For adults with onset type 1 diabetes (ADAPT), the use of CLS has shown more significant benefits compared to multiple daily injections of insulin with sensor-augmented pump (SAP) therapy, supporting the broader adoption of CLS in T1DM with suboptimal glycemic control [12]. In pregnant women with T1DM, CLS can achieve better glycemic control and maintain stable glucose levels [13-15]. However, a 28-

day study published in 2018 indicated that the day and night CLS was safe and effective in pregnant women, effectively controlling glucose levels in a wide range of T1DM pregnancies. However, the study did not observe any differences between groups regarding the target glucose range, average glucose levels, or glycated hemoglobin (HbA1c) levels. However, the group using the day and night closed-loop system experienced a lower frequency of maternal hypoglycemic events and reduced overall exposure to hypoglycemia and nocturnal hypoglycemia [16]. The results of this study suggest potential advantages for the day and night closed-loop insulin delivery system in pregnant women with type 1 diabetes. It can provide more stable blood glucose control, reduce the occurrence of hypoglycemic events, and offer better health outcomes for both mother and baby. However, further research is needed to evaluate the long-term effectiveness and safety of closed-loop treatment during pregnancy and conduct more extensive studies on its impact on newborns.

Indeed, in addition to the use of closed-loop systems (CLS) in patients with type 1 diabetes (T1DM), recent studies have explored the effectiveness and safety of CLS in patients with type 2 diabetes (T2DM). The latest research indicates that CLS is a safe and effective approach to improve glycemic control in T2DM patients during outpatient settings over eight weeks. Compared to standard insulin therapy, the CLS increased the proportion of time spent within the target blood glucose range by 35 percentage points (equivalent to an additional 8 hours per day). It reduced average glucose levels without increasing the duration of hypoglycemia [17]. In addition to outpatient settings, CLS has also been found to improve glycemic control and reduce the occurrence of hypoglycemic events in hospitalized patients with T2DM [18,19] and in T2DM patients undergoing hemodialysis [20,21]. For patients undergoing elective surgeries and pancreatic surgeries, CLS has also been demonstrated as an effective method for improving glycemic control without increasing the risk of hypoglycemia during the perioperative period [22,23].

In addition to improving glycemic control, closed-loop insulin pumps have also shown other effects. One study compared the impact of closed-loop treatment and standard insulin therapy on C-peptide secretion in newly diagnosed T1DM patients. Although the study results showed no significant difference in the area under the curve (AUC) for C-peptide levels between the CLS group and the control group at 12 and 24 months, the CLS group had significantly lower levels of HbA1c with reductions of 4 mmol/mol and 11 mmol/mol, respectively, compared to the control group [24]. Another study investigated the impact of hybrid CLS on neurodevelopmental and cognitive outcomes in adolescents with tT1DM. The study found that the CLS significantly improved specific neurodevelopmental indicators, such as cortical surface area, regional gray matter volume, and fractional anisotropy [25]. In addition, CLS therapy has been found to improve the quality of life in children, adolescents, and elderly patients with type 1 diabetes by improving sleep, reducing diabetes-related psychological burden, and simultaneously improving blood glucose levels [26-28].

However, the widespread adoption of CLS faces several challenges. These include technical issues such as sensor accuracy, pump malfunctions or connectivity problems, device burden, and complexity, cost considerations, user training and support, psychosocial factors, and limitations imposed by healthcare insurance and policies. A comprehensive approach involving technological improvements, cost-effectiveness, education support, and policy support is necessary to overcome these challenges.

There are numerous potential directions for the development of closed-loop insulin pumps. Technological advancements will enhance the accuracy, stability, and reliability of continuous glucose monitors and insulin pumps. Devices will become smaller, more portable, and more accessible for patients to wear and use. Data integration and artificial intelligence will enable more accurate blood glucose predictions and insulin adjustments. Remote monitoring and support will allow real-time monitoring of patients' glucose data and provide personalized support and guidance. Smartphone applications and connectivity will enable patients to conveniently monitor and control their blood glucose levels and facilitate communication with healthcare teams. Automation and human-computer interaction will minimize patient intervention and operation while providing a more intuitive and user-friendly control interface. CLS may also incorporate additional functionalities, such as activity monitoring, diet management, medication administration, etc., to provide comprehensive diabetes management support for patients.

In conclusion, the prospects for developing closed-loop insulin pumps are promising. Through continuous technological improvements and innovations and addressing relevant challenges, CLS will provide diabetes patients with more effective and convenient tools for glucose management, improving their quality of life and reducing the risk of complications.

Acknowledgments

This study was supported by the National Natural Science Foundation of China (Grant No. 82160170) and the National Key R&D Program of China Synthetic Biology Research (No. 2019YFA0904500).

Competing Interests

The authors declare that they have no competing interests.

References

1. Thabit H, Tauschmann M, Allen JM, Leelarathna L, Hartnell S, Wilinska ME, et al. Home use of an artificial beta cell in type 1 diabetes. New England Journal of Medicine. 2015 Nov 26;373(22):2129-40.

2. Tauschmann M, Thabit H, Bally L, Allen JM, Hartnell S, Wilinska ME, et al. Closed-loop insulin delivery in suboptimally controlled type 1 diabetes: a multicentre, 12-week randomised trial. The Lancet. 2018 Oct 13;392(10155):1321-9.

3. McAuley SA, Lee MH, Paldus B, Vogrin S, De Bock MI, Abraham MB, et al. Six months of hybrid closed-loop versus manual insulin delivery with fingerprick blood glucose monitoring in adults with type 1 diabetes: a randomized, controlled trial. Diabetes Care. 2020 Dec 1;43(12):3024-33.

4. Kropff J, Del Favero S, Place J, Toffanin C, Visentin R, Monaro M, et al. 2 month evening and night closed-loop glucose control in patients with type 1 diabetes under free-living conditions: a randomised crossover trial. The Lancet Diabetes & Endocrinology. 2015 Dec 1;3(12):939-47.

5. Kovatchev BP, Kollar L, Anderson SM, Barnett C, Breton MD, Carr K, et al. Evening and overnight closed-loop control versus 24/7 continuous closed-loop control for type 1 diabetes: a randomised crossover trial. The Lancet Digital Health. 2020 Feb 1;2(2):e64-73.

6. Kovatchev B, Anderson SM, Raghinaru D, Kudva YC, Laffel LM, Levy C, et al. Randomized controlled trial of mobile closed-loop control. Diabetes Care. 2020 Mar 1;43(3):607-15.

7. Brown SA, Kovatchev BP, Raghinaru D, Lum JW, Buckingham BA, Kudva YC, et al. Six-month randomized, multicenter trial of closed-loop control in type 1 diabetes. New England Journal of Medicine. 2019 Oct 31;381(18):1707-17.

8. Brown SA, Beck RW, Raghinaru D, Buckingham BA, Laffel LM, Wadwa RP, et al. Glycemic outcomes of use of CLC versus PLGS in type 1 diabetes: a randomized controlled trial. Diabetes Care. 2020 Aug 1;43(8):1822-8.

9. Breton MD, Kanapka LG, Beck RW, Ekhlaspour L, Forlenza GP, Cengiz E, et al. A randomized trial of closed-loop control in children with type 1 diabetes. New England Journal of Medicine. 2020 Aug 27;383(9):836-45.

10. Benhamou PY, Franc S, Reznik Y, Thivolet C, Schaepelynck P, Renard E, et al. Closed-loop insulin delivery in adults with type 1 diabetes in real-life conditions: a 12-week multicentre, open-label randomised controlled crossover trial. The Lancet Digital Health. 2019 May 1;1(1):e17-25.

11. Jiao X, Shen Y, Chen Y. Better TIR, HbA1c, and less hypoglycemia in closed-loop insulin system in patients with type 1 diabetes: a meta-analysis. BMJ Open Diabetes Research and Care. 2022 Apr 1;10(2):e002633.

12. Choudhary P, Kolassa R, Keuthage W, Kroeger J, Thivolet C, Evans M, et al. Advanced hybrid closed loop therapy versus conventional treatment in adults with type 1 diabetes (ADAPT): a randomised controlled study. The Lancet Diabetes & Endocrinology. 2022 Oct 1;10(10):720-31.

13. Stewart ZA, Wilinska ME, Hartnell S, Temple RC, Rayman G, Stanley KP, et al. Closed-loop insulin delivery during pregnancy in women with type 1 diabetes. New England Journal of Medicine. 2016 Aug 18;375(7):644-54.

14. Murphy HR, Elleri D, Allen JM, Harris J, Simmons D, Rayman G, et al. Closed-loop insulin delivery during pregnancy complicated by type 1 diabetes. Diabetes Care. 2011 Feb 1;34(2):406-11.

15. Murphy HR, Kumareswaran K, Elleri D, Allen JM, Caldwell K, Biagioni M, et al. Safety and efficacy of 24-h closed-loop insulin delivery in well-controlled pregnant women with type 1 diabetes: a randomized crossover case series. Diabetes Care. 2011 Dec 1;34(12):2527-9.

16. Stewart ZA, Wilinska ME, Hartnell S, O'Neil LK, Rayman G, Scott EM, et al. Day-and-night closed-loop insulin delivery in a broad population of pregnant women with type 1 diabetes: a randomized controlled crossover trial. Diabetes Care. 2018 Jul 1;41(7):1391-9.

17. Daly AB, Boughton CK, Nwokolo M, Hartnell S, Wilinska ME, Cezar A, et al. Fully automated closed-loop insulin delivery in adults with type 2 diabetes: an open-label, single-center, randomized crossover trial. Nature Medicine. 2023 Jan;29(1):203-8.

18. Kumareswaran K, Thabit H, Leelarathna L, Caldwell K, Elleri D, Allen JM, et al. Feasibility of closed-loop insulin delivery in type 2 diabetes: a randomized controlled study. Diabetes Care. 2014 May 1;37(5):1198-203.

19. Thabit H, Hartnell S, Allen JM, Lake A, Wilinska ME, Ruan Y, et al. Closed-loop insulin delivery in inpatients with type 2 diabetes: a randomised, parallel-group trial. The lancet Diabetes & Endocrinology. 2017 Feb 1;5(2):117-24.

20. Boughton CK, Tripyla A, Hartnell S, Daly A, Herzig D, Wilinska ME, et al. Fully automated closed-loop glucose control compared with standard insulin therapy in adults with type 2 diabetes requiring dialysis: an open-label, randomized crossover trial. Nature Medicine. 2021 Aug;27(8):1471-6.

21. Bally L, Gubler P, Thabit H, Hartnell S, Ruan Y, Wilinska ME, et al. Fully closed-loop insulin delivery improves glucose control of inpatients with type 2 diabetes receiving hemodialysis. Kidney International. 2019 Sep 1;96(3):593-6.

22. Herzig D, Suhner S, Roos J, Schürch D, Cecchini L, Nakas CT, et al. Perioperative fully closed-loop insulin delivery in patients undergoing elective surgery: an open-label, randomized controlled trial. Diabetes Care. 2022 Sep 1;45(9):2076-83.

23. Krutkyte G, Roos J, Schuerch D, Czerlau C, Wilinska ME, Wuethrich PY, et al. Fully Closed-Loop Insulin Delivery in Patients Undergoing Pancreatic Surgery. Diabetes Technology & Therapeutics. 2023 Mar 1;25(3):206-11.

24. Boughton CK, Allen JM, Ware J, Wilinska ME, Hartnell S, Thankamony A, et al. Closed-loop therapy and preservation of C-peptide secretion in type 1 diabetes. New England Journal of Medicine. 2022 Sep 8;387(10):882-93.

25. Reiss AL, Jo B, Arbelaez AM, Tsalikian E, Buckingham B, Weinzimer SA, et al. A pilot randomized trial to examine effects of a hybrid closed-loop insulin delivery system on neurodevelopmental and cognitive outcomes in adolescents with type 1 diabetes. Nature Communications. 2022 Aug 30;13(1):4940.

26. Kubilay E, Trawley S, Ward GM, Fourlanos S, Grills CA, Lee MH, et al. Lived experience of older adults with type 1 diabetes using closed-

loop automated insulin delivery in a randomised trial. Diabetic Medicine. 2023 Apr;40(4):e15020.

27. Farrington C. Psychosocial impacts of hybrid closed-loop systems in the management of diabetes: a review. Diabetic Medicine. 2018 Apr;35(4):436-49.

28. Abraham MB, de Bock M, Smith GJ, Dart J, Fairchild JM, King BR, et al. Effect of a hybrid closed-loop system on glycemic and psychosocial outcomes in children and adolescents with type 1 diabetes: a randomized clinical trial. JAMA Pediatrics. 2021 Dec 1;175(12):1227-35.