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ORIGINAL ARTICLE

Effectiveness of a hybrid closed-loop system for children and adolescents with type 1 diabetes during physical exercise: A cross-sectional study in real life

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KEYWORDS
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Abstract
Objective: The aim of the study was to describe how physical exercise affects metabolic control, insulin requirements and carbohydrate intake in children who use hybrid closed-loop systems.
Methods: Cross-sectional study design. The sample included 21 children and adolescents diagnosed with type 1 diabetes. During the study, participants were monitored for a period of 7 days to gather comprehensive data on these factors.
Results: Nine participants (42.9%) had switched to exercise mode to raise the target glucose temporarily to 150 mg/dL. The HbA1c values ranged from 5.5% to 7.9% (median, 6.5%; IQR, 0.75). The percentage of time within the target range of 70—180 mg/dL was similar; however, there was an increased duration of hyperglycaemia and more autocorrections on exercise days. The time spent in severe hyperglycaemia (>250 mg/dL) increased by 2.7% in exercise compared to non-exercise days (P = .02). It is worth noting that hypoglycaemic episodes did not increase during the exercise days compared with non-exercise days.
Conclusion: The hybrid closed-loop system was effective and safe in children and adolescents with type 1 diabetes during the performance of competitive sports in real life.

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PALABRAS CLAVE
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Efectividad de un sistema híbrido de circuito cerrado en pacientes con diabetes tipo 1 durante el ejercicio físico: un estudio descriptivo en la vida real

Resumen
Objetivo: El objetivo de este estudio es describir cómo el ejercicio físico afecta el control metabólico, las necesidades de insulina y el consumo de carbohidratos en niños usuarios de un sistema híbrido de circuito cerrado.
Métodos: Diseño de estudio transversal. Se reclutaron veintiún niños y adolescentes diagnosticados con diabetes tipo 1. Durante el estudio, los participantes fueron monitoreados durante un período de 7 días para recopilar datos completos sobre estos factores.
Resultados: Nueve participantes (42,9%) habían activado el modo de ejercicio, para elevar temporalmente la glucosa objetivo a 150 mg/dL. La HbA1c osciló entre 5,5% y 7,9% (mediana 6,5%, IQR 0,75). El porcentaje de tiempo dentro del rango de 70—180 mg/dL fue similar; sin embargo, hubo una mayor duración de la hiperglucemia y más autocorrecciones en los días en que se realizó ejercicio. El porcentaje de tiempo en hiperglucemia grave (>250 mg/dL) fue 2,7 mayor durante el ejercicio versus los días sin ejercicio (p = 0,02). En particular, los episodios de hipoglucemia no aumentaron durante los días de práctica de ejercicio, en comparación con los días sin ejercicio.
Conclusiones: El sistema híbrido de circuito cerrado fue efectivo y seguro en niños y adolescentes diagnosticados con diabetes tipo 1 durante ejercicios físicos competitivos en la vida real.

Introduction

Type 1 Diabetes continues to be one of the most prevalent chronic diseases in childhood and adolescence. In 2022, 1.52 million children and adolescents under the age of 20 had type 1 diabetes worldwide.[1]

Numerous studies have demonstrated the positive impact that exercise has on the management of type 1 diabetes. When combined with an optimal insulin dosage and a balanced diet, regular exercise contributes significantly to good glycaemic control in children with type 1 diabetes. Exercise increases insulin sensitivity, with an effect during physical activity that often persists for some time after.[2] However, glucose levels can vary depending on the amount, type, and intensity of physical activity. In high-stress situations, like sports competitions, the secretion of counterregulatory hormones can elevate glucose levels. On the other hand, once stress decreases, glucose levels drop significantly, which makes participation in competitive sports even more challenging for athletes with type 1 diabetes.[3] Thus, new treatment strategies are needed to alleviate the burden of diabetes management.

Hybrid closed-loop systems that facilitate the control of type 1 diabetes may offer a promising management strategy in children and adolescents.[4] This type of system, also known as an artificial pancreas, uses algorithms that adjust insulin delivery in real-time based on continuous glucose monitoring (CGM) data. Developed to maintain glucose levels within the target range (70—180 mg/dL), these systems minimize the risk of hypoglycaemia and hyperglycaemia.[5] Although these systems use CGM combined with automated insulin administration guided by glycaemic levels, they are referred to as *hybrid* because they are not fully automatic. Manual administration of insulin boluses before meals based on the estimated carbohydrate intake is still required.[6]

Even hybrid closed-loop systems are suitable for prolonged aerobic exercise, provided a higher glycaemic target (150 mg/dL) is set 45—90 min before the start of physical activity.[2] Despite considerable evidence in adult athletes,[2,7] there is insufficient scientific evidence on the use of these systems in the paediatric population, which has given rise to debate regarding their use during physical activity. However, Ekhlaspour et al.[8] reported positive results in a study on children and adolescents ($n = 48$) aged 6–18 years with type 1 diabetes, describing improved glycaemic control and a decreased frequency of hypoglycaemic episodes with the use of Control-IQ technology (an advanced hybrid closed-loop system) during high-intensity winter sports. Building upon these findings, a review by Boughton et al.[9] suggested that hybrid closed-loop systems may offer advantages over conventional therapies in glycaemic control, although further research is required due to the limitations intrinsic to the study design and the participant characteristics. Experts have also emphasized the benefits of the advanced MiniMed 780G system compared to earlier hybrid closed-loop systems,[10] highlighting its ability to adapt insulin requirements for children and adolescents.[11] Despite these promising features, there is still a dearth of robust evidence specifically addressing the potential benefits of hybrid closed-loop systems for children and adolescents with type 1 diabetes during physical activity. Therefore, the aim of our study was to characterize the impact of physical activity on metabolic control, insulin requirements and carbohydrate consumption in children with type 1 diabetes using hybrid closed-loop systems in real-world settings.

Methods

Participants

A sample of children and adolescents diagnosed with type 1 diabetes was recruited from the paediatric endocrinology and childhood diabetes unit of a Spanish tertiary care teaching hospital. The inclusion criteria were: (i) age less than 18 years; (ii) having been using the MiniMed 780G closed-loop hybrid system in automatic mode for at least 1 month; (iii) practice of extracurricular sports; (iv) ability to provide informed consent or having a legal guardian provide consent in the case of patients aged less than 16 years. The exclusion criteria were: (i) having used an automated system for less than a month.

The sample consisted of all the patients managed at the paediatric endocrinology and childhood diabetes unit that met the inclusion criteria that consented to participation.

The study was approved by the Research Ethics Committee of the Principality of Asturias (file 2022.086).

Study design

The study had a cross-sectional design. All children or adolescents with type 1 diabetes managed in the unit who met the inclusion criteria were invited to participate either during a routine visit or through a telephone call by a diabetes nurse educator (October 2021 to June 2022). We obtained the signed informed consent from parents for children aged younger than 16 years. For adolescents aged 16–18 years, we obtained signed consent from the parents and signed assent from the patients before carrying out the baseline assessment.

Study variables

The primary objective was to assess impact of exercise on metabolic control, insulin requirements and carbohydrate consumption in children with type 1 diabetes who use hybrid closed-loop systems in real-world settings. We collected baseline data from the health records of participants on the following: demographic variables (age and sex), anthropometric variables (weight, height and fat mass), disease-related variables (time from diagnosis of diabetes, time using the hybrid closed-loop system device and type of insulin) and annual variability in the venous glycated haemoglobin level (HbA1c). We also collected information on the characteristics of the extracurricular sport, such as the type of physical activity (aerobic, anaerobic or mixed),[12] its duration and its weekly frequency. Participant behaviours, including whether they removed the pump during exercise and whether they set the temporary blood glucose target (150 mg/dL) before, during and/or after exercise, were documented in reference to current consensus recommendations.[13] In addition, participants underwent a 7-day monitoring period after the baseline assessment during which they maintained their routine insulin treatment and usual extracurricular sports activities. At the end of the 7 days, we downloaded detailed reports on the total daily insulin dose (TDI), bolus proportion, time in range (TIR), time in mild and severe hypoglycaemia, time in mild and severe hyperglycaemia, coefficient of variation (CoV), mean glucose levels, insulin autocorrections and consumed carbohydrates from the Medtronic data platform (CareLink^{TM}).

We considered the following dependent variables: TDI, bolus proportion, TIR, time in mild (69−54 mg/dL) and severe (<54 mg/dL) hypoglycaemia, time in mild (181−250 mg/dL) and severe (>250 mg/dL) hyperglycaemia, mean glucose level, insulin autocorrections and consumed carbohydrates.

Statistical analysis

We have expressed baseline data as absolute frequencies and percentages or as median and interquartile range (IQR), as appropriate. For quantitative variables, we assessed the normality of the distribution with the Kolmogorov-Smirnov test and used the applicable nonparametric tests. We conducted a univariate analysis using the Wilcoxon test to assess differences in median values in relation to the ''exercise'' variable.

The analyses were performed with the software package IBM SPSS Statistics, version 27.0. For all tests, statistical significance was set at $P \leq .05$.

Results

Characteristics of participants

We contacted 40 children and adolescents with type 1 diabetes who used insulin continuous subcutaneous infusion (ISCI) systems. Of this total, 35% ($n = 14$) did not meet the inclusion criteria and 12.5% ($n = 5$) declined to participate. The final sample consisted of 21 patients (52.4% female) with a median age of 11.0 years (IQR, 3.5 years). The time elapsed from diagnosis of type 1 diabetes ranged from 0.8 to 13.3 years. Nine participants (42.9%) switched to exercise mode to temporarily raise the target glucose to 150 mg/dL: 3 during exercise, 3 after exercise and 3 both during and after exercise. Five participants disconnected their pumps during exercise practice. The HbA1c level ranged from 5.5% to 7.9% (median, 6.5%; IQR, 0.75). Table 1 presents an overview of the baseline characteristics.

Characteristics of physical activity

The physical activities reported by the patients were basketball (4), athletics (2), gym (2), volleyball (2), skiing (1), dance (2), soccer (2), synchronized swimming (1), swimming (1), figure skating (1), handball (1), paddle tennis (1) and judo (1).

We ought to highlight that in 90.5% of patients, the exercise was mixed in nature, combining aerobic and anaerobic activity. Only 2 participants reported exclusively aerobic exercise. Participation in competitive sports was reported by 38.1% of the sample. The median frequency of exercise

Table 1 Demographic and treatment characteristics of the study sample (*n* = 21).

Variable	Participants
Age in years, median (IQR)	11.0 (3.5)
Sex	
Male, % (*n*)	47.6% (10)
Female, % (*n*)	52.4% (11)
Weight status (BMI)	
Underweight, % (*n*)	4.8% (1)
Normal weight, % (*n*)	71.4% (15)
Overweight, % (*n*)	23.8% (5)
Obesity, % (*n*)	0% (0)
Type of Insulin	
Insulin glulisine, % (*n*)	9.5% (2)
Insulin lispro, % (*n*)	19.0% (4)
Insulin aspart, % (*n*)	42.9% (9)
Fast-acting insulin aspart, % (*n*)	28.6% (6)
Years since diagnosis, median (IQR)	6.0 (5.0)
Months using MiniMed 780G, median (IQR)	12.0 (5.5)
Use of MiniMed 780G during exercise, % (*n*)	76.2% (16)
% HbA1c, mean over last 6 months (IQR)	6.5 (0.8)
% GMI, median (IQR)	6.7 (0.4)
TDI in units/day, median (IQR)	31.0 (24.5)
Bolus, median (IQR) (%)	63.0 (11.5%)
Basal, median (IQR) (%)	37.0 (11.5%)
Percent TIR, median (IQR)	75.0 (9.5)
Percent mild hypoglycaemia, median (IQR)	2.0 (2.5)
Percent severe hypoglycaemia, median (IQR)	0 (1.0)
Percent mild hyperglycaemia, median (IQR)	17.0 (7.5)
Percent severe hyperglycaemia, median (IQR)	4.0 (4.5)
Percent CoV, median (IQR)	37.0 (5.5)
Glucose level, median (IQR) (mg/dL)	144.0 (18.0)
Insulin autocorrections	19.0 (13.0)
Carbohydrate intake in g/day, median (IQR)	166.0 (59.0)

BMI, body mass index; CoV, coefficient of variation; GMI, glucose management indicator; IQR, interquartile range; TDI, total daily insulin; TIR, time in range.

was 3 days a week (IQR, 2), and the median time devoted to physical activity was 4 h a week (IQR, 2.9).

Differences between days with and without physical activity

The percentage of time spent in severe hyperglycaemia was 2.7 times greater ($P = .02$) and the percentage of insulin delivered in the form of autocorrections was 5.9 greater ($P = .03$) in days when patients exercised. Conversely, the carbohydrate intake decreased by 22.2 g on exercise days ($P = .002$). We found no differences in the percentage of time spent in hypoglycaemia or in any other variables (Table 2).

Discussion

The findings of our study demonstrate the benefits of hybrid closed-loop systems in children and adolescents with type 1 diabetes during physical activity. The results highlight the benefits of their use in children and adolescents who exercise or practice sports, particularly in terms of metabolic control, insulin requirements and carbohydrate intake. A randomized trial involving physically active children and adolescents with type 1 diabetes found similar results using a hybrid closed-loop system, irrespective of the type of insulin administration.[14] It is important to take into account that these benefits extend beyond controlled experiments, as demonstrated in our study, where variables such as the intensity of physical activity and self-report measures (e.g., carbohydrate intake) inherently lack a strict control.

The frequency of hypoglycaemic episodes did not increase in exercise days compared to non-exercise days, which is a crucial finding in terms of safety. The time in range (TIR) was similar on both exercise and non-exercise days. In contrast, on exercise days there was a decreased carbohydrate intake yet an increase in the time spent in hyperglycaemia and in insulin autocorrections. Overall, irrespective of physical activity, these results align with data described in previous literature for children diagnosed with type 1 diabetes using a hybrid closed-loop system.[15–17]

The high TIR observed in our patients on both exercise and non-exercise days was noteworthy. This finding is consistent with the previous literature and may be the most relevant outcome for children and adolescents, particularly in comparison to sensor-augmented pump therapy with predictive low glucose suspend.[18] Other studies support these results. Bassi et al.[19] observed similar improvements in TIR in a study of children and adults using the MiniMed 780 compared to the Tandem Control-IQ system. Additionally, a study that focused on a similar age group found a high TIR in MiniMed 780 users, with an increase of approximately 5% after just 28 days of use.[20] Also of note is the significant improvement in TIR found in adolescents in another study from 42.1% at baseline to 78.8% after 12 weeks with a hybrid closed-loop system.[15] Given that no prior studies have explicitly analysed real-world physical activity as an independent variable, comparisons are limited. Notwithstanding, based on our results and the current evidence, it is reasonable to hypothesise that the MiniMed 780 system can achieve an greater TIR in children and adolescents.

Worry about hypoglycaemia, a major barrier cited by children, adolescents and their parents, often restricts their engagement in physical activity or sports.[3,21,22] Our study, however, did not find significant differences in the time spent in hypoglycaemia time between exercise and, non-exercise days. This suggests that using hybrid closed-loop systems during physical activity, as suggested by previous research, could be a key solution in addressing this fear and encouraging physical activity.[17,23] The promotion of physical activity is crucial in children and adolescents with type 1 diabetes due to its well-documented benefits. For instance, a review by Aljawarneh et al.[24] concluded that exercise can enhance insulin sensitivity, reduce insulin requirements and regulate glucose levels. Furthermore, King et al.[25] demonstrated that regular physical activity improves HbA1c values in children. Customarily, people with type 1 diabetes consume extra carbohydrates before exercise to prevent hypoglycaemia, a major barrier to physical activity.[26] However, our findings suggest that using a hybrid closed-loop system significantly reduces the frequency of hypoglycaemic episodes during exercise. This is probably due to the highly adaptable algorithm of the system, which constantly adjusts insulin delivery (and therefore, carbo-

Table 2 Differences between days with and without exercise.

Variable	Exercise days	Non-exercise days	*P*
TDI (units/day)	29.8 (25.5)	33.7 (26.1)	.737
Bolus	62.8 (13.3)	63.1 (14.1)	.179
Basal	37.2 (13.3)	36.9 (14.2)	.179
Percent TIR	71.5 (16.1)	77.8 (9.2)	.100
Percent time in mild hypoglycaemia	2.2 (3.3)	2.8 (3.5)	.062
Percent time in severe hypoglycaemia	0.3 (1.0)	0.3 (0.5)	.173
Percent time in mild hyperglycaemia	17.5 (13.6)	16.1 (10.7)	.218
Percent time in severe hyperglycaemia	5.3 (9.4)	2.6 (5.3)	.02
Insulin autocorrection	20.7 (19.5)	14.8 (14.2)	.03
Carbohydrate intake	152.8 (55.8)	175.0 (58.9)	.002

IQR, interquartile range; TDI, total daily insulin; TIR, time in range.
Values expressed as median (IQR); $n = 21$.

hydrate needs) based on individual factors like glycaemic profiles, biological rhythms, physical activity levels or food intake.[13] Furthermore, setting a temporary blood sugar target of 150 mg/dL during exercise may signal the algorithm to limit insulin boluses, proactively preventing hypoglycaemia and reducing the need for additional carbohydrates.

Closed-loop systems require strategic approaches to type 1 diabetes management, including careful consideration of exercise timing, duration, and carbohydrate intake.[27] While some strategies involve pump suspension, keeping the infusion system connected during exercise is generally recommended, as it allows the algorithm to learn and adapt.[27,28] In line with this recommendation, 76% of our patients chose to wear their devices during sports activities. Interestingly, less than half of participants reported using the temporary 150 mg/dL target to prevent hypoglycaemia, highlighting the importance of personalized recommendations based on both exercise type and individual responses. Our study found a significantly higher time spent in severe hyperglycaemia on exercise days. This likely stems from the fact that 90.5% of participants engaged in mixed exercise combining aerobic and anaerobic activities, which are known to induce an increase in counterregulatory hormone levels, potentially leading to hyperglycaemia.[29] Conversely, previous evidence demonstrates that children and adolescents using hybrid closed-loop systems experience significantly fewer hyperglycaemic events compared to other pump therapy options.[30] This suggests that, had our participants not used the hybrid closed-loop system, we might have observed a higher rate of hyperglycaemic episodes. Although it was not primary objective of our study, we confirmed that the use of hybrid closed-loop systems has additional advantages for parents. Parents have reported increased trust in allowing others to care for their children[31] when using a hybrid closed-loop system and a decreased need for health care services.[32] Finally, is also important to highlight that beyond safety and efficacy, data on patient-reported outcomes shows an increased satisfaction and improved quality of life with advanced hybrid closed-loop systems.[33]

When it comes to the limitations of our study, we ought to highlight that it was conducted in a single centre study and in limited number of participants over a short period of time. In addition, we assessed physical activity and carbohydrate intake based on self-reported data, which carries a risk of recall bias. On the other hand, it is important to highlight that the study was conducted in real-world conditions. Despite the lack of objective information on the intensity of physical activity and carbohydrate consumption, the hybrid closed-loop system effectively prevented the occurrence of hypoglycaemia.

Conclusion

In conclusion, our study demonstrated the effectiveness and safety of hybrid closed-loop systems for paediatric patients with type 1 diabetes during competitive sports. Notably, we did not observe an increase in hypoglycaemic episodes, a major barrier and fear that often limits engagement in exercise. Larger, multicentre studies with hybrid closed-loop systems would allow comparisons based on the type of physical activity performed and would open exciting new avenues for future research.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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