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RESEARCH LETTER

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Comparable glycemic outcomes with insulin glargine and insulin degludec during exercise in adolescents with type 1 diabetes using a standardized management protocol

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1 | INTRODUCTION

Managing physical activity in adolescents with type 1 diabetes (T1D) remains a significant clinical challenge, primarily due to the risk of exercise-induced hypoglycemia. To mitigate this risk, the dose of basal insulin is usually reduced. Insulin degludec is a second-generation, ultra-long-acting insulin analog with a more stable and predictable glucose-lowering profile and a longer duration of action compared to its first-generation predecessor, insulin glargine U100.[1] While this profile is associated with reduced risks of overall and nocturnal hypoglycemia, its long half-life has important implications for dose adjustments around exercise, as it takes 2 to 3 days to reach a new steady-state dose after dose changes.[2,3] Data on how to best manage insulin degludec during physical activity, particularly in paediatric populations, are scarce but urgently needed.[4] To meet this need, here we compared the effects of insulin degludec and insulin glargine on glycemic outcomes after structured exercise in adolescents with T1D managed with a standardized protocol.

2 | METHODS

This was an observational, real-life study conducted during a four-day educational summer camp organised to evaluate the effect of different long-acting basal insulins on exercise management. The study timeline is shown in Figure 1.

Inclusion criteria were adolescents aged 13–17 years with T1D for at least 1 year treated with a basal-bolus multi-dose insulin (MDI) regimen with either insulin glargine U100 or insulin degludec. Participants were recruited from paediatric diabetes centres in Turin and Milan. Main exclusion criteria were insulin pump use, significant comorbidities, or the use of drugs affecting glucose metabolism other than insulin. The ethical committee of Turin approved the study protocol, and informed consent was obtained from all participants and their guardians.

Two weeks before the camp, cardiorespiratory fitness was assessed at baseline using a submaximal incremental exercise test on a cycle ergometer to estimate maximal oxygen uptake (VO2 max). All

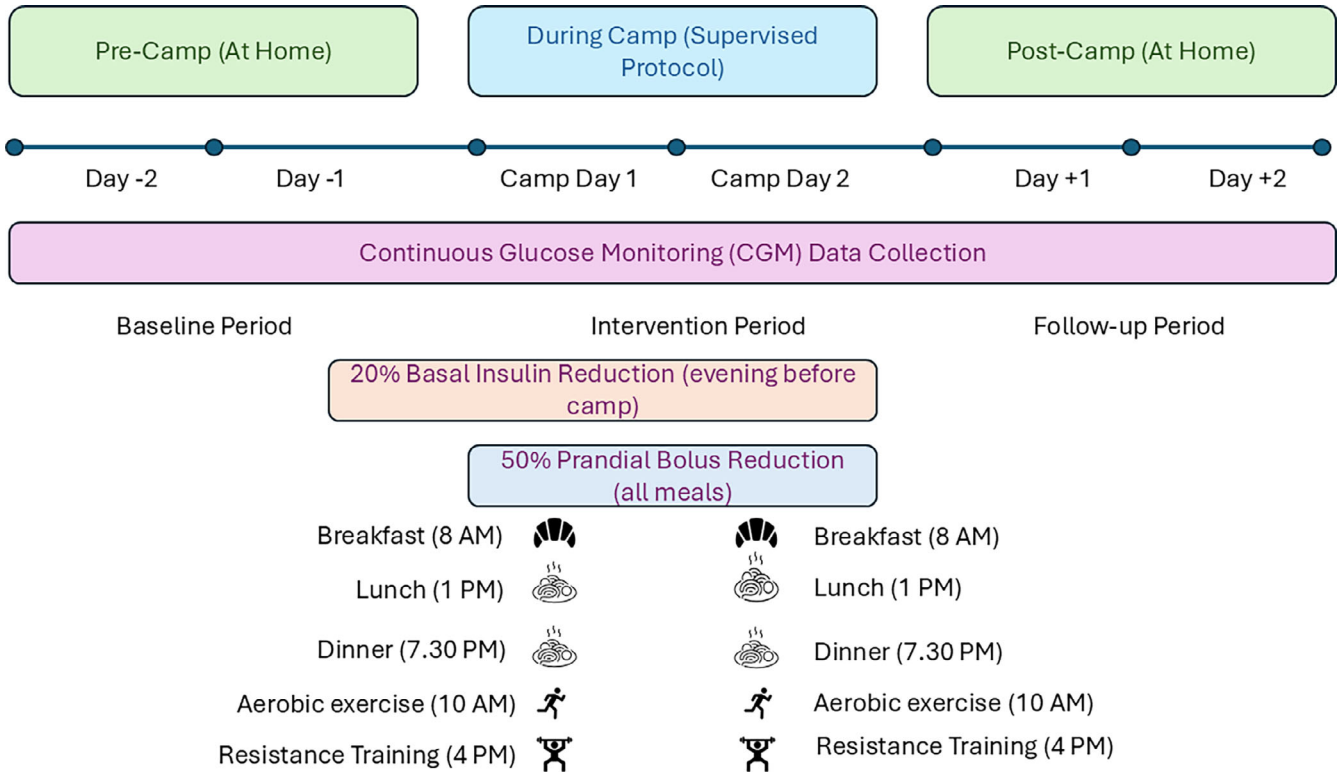

FIGURE 1 Visual timeline of the study design. The study included a two-day pre-camp baseline, a two-day structured camp intervention, and a two-day post-camp follow-up. During the camp, participants followed a protocol of reduced basal (20% reduction, pre-camp) and prandial (50% reduction) insulin. The daily schedule featured standardized meals and structured aerobic and resistance exercise sessions, while CGM data was collected continuously.

27 participants (16 on glargine, 11 on degludec) wore a Dexcom G6 continuous glucose monitoring (CGM) system.

To ensure comparability, all participants followed a standardized management protocol throughout the camp:

1. *Insulin adjustments*: On the evening prior to the camp, all participants were instructed to reduce their usual basal insulin dose by 20%. Throughout the camp, prandial insulin doses were uniformly reduced by 50% for all meals, consistent with consensus guidelines for mitigating hypoglycemia risk during prolonged, strenuous activity.[5]
2. *Glycemic management*: Participants were instructed to check CGM data frequently. Preventive strategies for hypoglycemia included the consumption of 15 to 30 g fast-acting carbohydrates if glucose levels were <90 mg/dL before starting exercise. Hypoglycemic episodes (<70 mg/dL) were treated with 0.3 g/kg glucose to a maximum of 15 g (Glucosprint Plus, Harmonium Pharma, Milan, Italy), with glucose re-checked after 15 min. To manage potential pre-exercise hyperglycemia (>250 mg/dL), a 50% reduced correction bolus was planned following a negative ketone check; however, no participant required pre-exercise corrective doses during the camp.
3. *Meal standardization*: Meals were standardized and supervised by a dietitian to ensure consistent carbohydrate intake and macronutrient balance. Mealtimes were fixed at 8:00 am (breakfast, ~70 g carbohydrates), 1:00 pm (lunch, ~80 g carbohydrates), and 7:30 pm (dinner, ~70 g carbohydrates). Fat and protein intake during the camp was the same for each participant, since all consumed their meals together.

The exercise protocol is detailed in Box 1. The physical activity program consisted of four sessions of monitored aerobic and resistance exercises conducted over two consecutive core days. Each day included both modalities, with aerobic activity in the morning followed by resistance training in the afternoon, separated by a recovery and meal period (Figure 1). This pairing was designed to reflect adolescents typical activity patterns and create a significant metabolic challenge. During all exercise sessions, heart rate was continuously monitored using POLAR H10 chest-strap monitors (Polar Electro, Kempele, Finland) and visualized in real time through the Polar Team iPad app to quantify and ensure comparable exercise intensity across participants.

CGM data were analysed for three periods: 2 days pre-camp (at home), 2 days during camp, and 2 days post-camp. Calculated metrics included mean glucose, maximal glucose, time in range (TIR, 70–180 mg/dL), time below range (TBR, <70 mg/dL and <54 mg/dL), time above range (TAR, >180 mg/dL), time very high (TVH, >250 mg/dL), and the coefficient of variation (CV) for glycemic variability.

BOX 1 Structured exercise protocol.

Aerobic activities

On Day 1, participants completed a 2-hour high-altitude trekking session that involved a 260-meter positive elevation gain, performed at a consistent pace to maintain their heart rate within Zone 2 (60–70% HRmax) and Zone 3 (70–80% HRmax). If participants exceeded these thresholds and entered Zone 4 (80–90% of their maximum heart rate), they were instructed to pause and recover until their values returned to the target range.

On Day 2, following a 20-minute full-body dynamic warm-up (mobility and muscle activation), participants performed a 30-minute interval training session on treadmills. The session included a 3-minute familiarisation phase at 6.0 km/h, followed by five 3-minute bouts at progressively increasing speeds (9.5, 10.0, 10.5, 11.0, and 11.5 km/h), each separated by 3 minutes of walking recovery at 5.5 km/h. The session concluded with a 20-minute cool-down that involved static stretching of the major muscle groups.

Resistance training

Resistance exercises were performed in the gym on both days, using Technogym isotonic machines. On Day 1, following a 20-minute full-body warm-up (including joint mobility and muscle activation), participants engaged in a 60-minute circuit focusing on major muscle groups (pectorals, abdominals, quadriceps, calves, hamstrings, lumbar muscles, dorsal muscles, biceps, and triceps). Each participant completed 3 sets of 10 to 12 repetitions at a constant load equal to 50% of their estimated one-repetition maximum (1RM), with 90 s of recovery between sets.

On Day 2, the same muscle groups were targeted with a progressive overload approach. After a similar warm-up, participants performed 3 sets of 12–10–8 repetitions at increasing loads ranging between 50% and 60% of their estimated 1RM. As on Day 1, exercises were performed on isotonic machines under supervision, with a focus on technical precision and safety, and 90 s of rest was allowed between sets.

The primary endpoint was mean TIR during the 2-day camp. As data were not normally distributed according to the Shapiro–Wilk test, continuous variables are expressed as medians and interquartile ranges (IQR). All other reported endpoints and time periods were considered exploratory. The Mann–Whitney *U* test was used for between-group comparisons and the Wilcoxon signed-rank test for within-group comparisons. Categorical variables were compared using the chi-square or Fisher's exact test. A *p*-value <0.05 was considered statistically significant. It is critical to note that all analyses are unadjusted for baseline characteristics (e.g., baseline glycemic control, sex). Given the observed baseline differences between groups, the unadjusted *p*-values should be interpreted with significant caution and are presented as hypothesis-generating.

3 | RESULTS

The glargine ($n = 16$) and degludec ($n = 11$) groups were comparable for baseline age, BMI, HbA1c, and estimated VO2 max (Table 1), but a significantly greater proportion of males in the glargine group (93.8% vs. 63.6%; $p = 0.045$). Exercise intensity was comparable between groups, confirmed by similar average heart rates during sessions (Table 1).

In the pre-camp period at home, the degludec group had significantly poorer glycemic control than the glargine group in terms of TIR (median 54% vs. 67%; $p = 0.036$), TAR (42% vs. 30%; $p = 0.039$), and TVH (15% vs. 8%; $p = 0.048$).

During and after the camp, following implementation of the standardized protocol, these inter-group differences were eliminated, with no statistically significant differences for any glycemic metric (all $p > 0.05$). The protocol proved highly effective at preventing clinically significant hypoglycemia: time spent below 54 mg/dL was 0% in both groups. The amount of supplemental glucose required for corrections was also similar (median 30 g for each group; $p = 0.88$).

However, there was a significant difference in glycemic metrics pre-camp vs. during-camp. Participants in the glargine group experienced a significant shift in their glycemic profile, including a decrease in TIR (from 67% to 54%; $p = 0.021$), an increase in TAR (from 30% to 44%; $p = 0.008$), and an increase in glycemic variability (CV from 35% to 40%; $p = 0.035$). In contrast, the degludec group's glycemic profile remained remarkably stable, with no significant changes observed in any key glycemic metric between the pre-camp and during-camp periods (all $p > 0.05$). For both groups, the protocol was effective at reducing time spent in clinically significant hypoglycemia (TBR <54 mg/dL), with the reduction statistically significant for the glargine group ($p = 0.045$).

In the 2 days post-camp, glycemic metrics for both groups began returning to their baseline values, with no significant differences between them.

4 | CONCLUSION

Our study provides important real-world evidence that, under a supervised and proactive management protocol, adolescents with T1D on MDI therapy achieved similar glycemic outcomes with insulin degludec and glargine during intensive physical activity. A key finding is that there were no significant differences in TIR, TAR, or hypoglycaemia between the two insulin groups during the structured exercise period, despite significant differences in their at-home glycemic control.

TABLE 1 Baseline characteristics and CGM glycemic metrics before, during, and after the structured exercise camp.

	Glargine ($n = 16$)	Degludec ($n = 11$)	p-value
Baseline characteristics			
Age (years)	15 [14–17]	16 [15–17]	0.78
Male (n, %)	**15 (93.8)**	**7 (63.6)**	**0.045**
BMI (kg/m^2)	23 [22–24]	22 [20–25]	0.85
HbA1c (%)	7.4 [6.7–8.5]	7.5 [7.3–8.1]	0.91
VO2 max (ml/kg/min)	42 [38–45]	44 [40–48]	0.42
Pre-camp (2 days at home)			
Mean glucose (mg/dL)	155 [141–175]	179 [156–210]	0.15
Maximal glucose (mg/dL)	280 [250–310]	330 [300–360]	**0.041**
Coefficient of variation (%)	35 [32–38]	38 [34–42]	0.23
Time in range, 70–180 mg/dL (%)	67 [57–78]	54 [41–66]	**0.036**
Time below range, <70 mg/dL (%)	1.2 [0–4.2]	0.9 [0–5.4]	0.88
Time below range, <54 mg/dL (%)	0.2 [0–0.8]	0.1 [0–1.0]	0.95
Time above range, >180 mg/dL (%)	30 [18–40]	42 [33–59]	**0.039**
Time above 250 mg/dL (%)	8 [4–15]	15 [9–24]	**0.048**
During camp (2 days of structured activity)			
Mean glucose (mg/dL)	178 [159–191]	176 [150–213]	0.93
Maximal glucose (mg/dL)	340 [310–370]	350 [320–380]	0.65
Coefficient of variation (%)	40 [35–40]	41 [36–47]	0.58
Time in range, 70–180 mg/dL (%)	54 [36–68]	61 [29–70]	0.71
Time below range, <70 mg/dL (%)	0 [0–0.9]	0.5 [0–2.1]	0.31
Time below range, <54 mg/dL (%)	0 [0–0]	0 [0–0.2]	0.45
Time above range, >180 mg/dL (%)	44 [31–62]	38 [28–69]	0.74
Time above 250 mg/dL (%)	10 [5–18]	12 [6–20]	0.68
Average exercise HR (bpm)	145 [135–155]	148 [138–158]	0.52
Post-camp (2 days at home)			
Mean glucose (mg/dL)	162 [148–180]	168 [155–190]	0.63
Maximal glucose (mg/dL)	290 [260–320]	310 [280–340]	0.49
Coefficient of variation (%)	36 [33–40]	39 [35–43]	0.38
Time in range, 70–180 mg/dL (%)	65 [55–75]	62 [50–71]	0.69
Time below range, <70 mg/dL (%)	1.0 [0–3.5]	1.3 [0–4.0]	0.81
Time below range, <54 mg/dL (%)	0.3 [0–1.0]	0.4 [0–1.2]	0.77
Time above range, >180 mg/dL (%)	32 [22–43]	35 [27–48]	0.66
Time above 250 mg/dL (%)	9 [5–16]	11 [7–19]	0.69

Note: Data are presented as median [interquartile range] or *n* (%). Significant *p*-values are in bold from unadjusted Mann–Whitney *U* or Fisher's exact tests, and they should be interpreted with caution due to the study's limitations (see Section 2).

Abbreviations: BMI, body mass index; CGM, continuous glucose monitoring; HbA1c, glycated haemoglobin; HR, heart rate; VO2 max, maximal oxygen uptake.

A more nuanced finding, however, emerged from the intragroup analysis. The standardized protocol, while equalizing outcomes, induced a significant glycemic shift in the glargine group while maintaining stability in the degludec group. This suggests that responses to the two insulins may differ under the combined stress of exercise and a fixed dose reduction. For degludec, with its ultra-long and stable profile, the 20% reduction may have been appropriate. For glargine, the same percentage reduction may have been insufficient to cover the hyperglycemia that can follow anaerobic activity, such as the resistance exercise included in our program, leading to wider glycemic excursions. Alternatively, for this better-controlled glargine group, the uniform 20% basal and 50% prandial reduction protocol may have been overly aggressive, contributing to the shift in glycemic profile. It is also possible that the structured camp environment had a greater stabilizing effect on the degludec group, which started from a baseline of poorer control.

Disentangling these effects is challenging. A crucial observation is that the convergence of glycemic outcomes may be partly explained by a "levelling effect", where the highly structured intervention had a more pronounced stabilizing impact on the group with poorer baseline control, potentially masking subtle differences between the insulins.

These results have significant clinical implications, particularly for managing diabetes with degludec around planned exercise. The prolonged pharmacokinetics of degludec have led to vague recommendations for its use. For instance, ISPAD guidelines suggest a dose reduction prior to exercise that accounts for its long half-life, implying a need for adjustments to begin several days in advance, unlike for glargine.[5] Our findings challenge this theoretical concern in a real-world paediatric setting. We demonstrate that a straightforward 20% dose reduction for degludec the day before exercise was a sufficient and practical strategy, yielding outcomes indistinguishable from those with glargine and potentially alleviating the need for a more complex, multi-day titration schedule.

Our findings are consistent with and extend previous randomized trials in adults. A crossover trial by Heise et al. found a similar risk of exercise-related hypoglycaemia between degludec and glargine,[4] while a study by Moser et al. showed that a 25% dose reduction of degludec improved time in euglycaemia during exercise, consistent with our observation that a 20% reduction was safe.[3] To our best knowledge, our study is the first to extend these findings to an adolescent population in a real-world group setting.

Our findings should be interpreted in the context of several important limitations. First, the observational design and small sample size limit the generalisability of our results and increase the risk of bias. The significant sex imbalance between groups is a key potential confounder that we could not adjust for in our analysis.

A major statistical limitation is the unadjusted nature of our analysis. The degludec group entered the study with significantly poorer baseline glycaemic control. Consequently, the observed convergence of glycaemic outcomes during the camp could be partly explained by a "levelling effect" or regression to the mean, rather than a true equivalent effect of the insulins under the protocol. The ideal analytical approach would have been a mixed-effects model adjusting for baseline TIR and sex; however, this analysis was not possible. Furthermore, we did not apply multiplicity corrections for the numerous exploratory endpoints, and we were unable to report formal effect sizes with confidence intervals.

Therefore, our results must be considered preliminary and hypothesis-generating. A larger, randomized controlled trial is essential to confirm these findings, and future studies should employ adjusted statistical models to properly disentangle the effects of the insulin from baseline confounding factors.

In conclusion, despite its distinct pharmacokinetic profile, insulin degludec did not require a more complex preventive dose-adjustment strategy compared to insulin glargine for planned, intensive physical activity in this adolescent cohort. When managed with a proactive protocol involving a 20% basal insulin reduction the day before exercise, both insulins provided comparable and safe glycemic control. This provides clinical reassurance that simplified, single-day dose-adjustment strategies can be effective for both insulins in this challenging real-world scenario, potentially simplifying current guideline recommendations. Future research should build on these preliminary findings in larger, randomized controlled trials to confirm efficacy and disentangle the glycemic effects of different exercise modalities (aerobic vs. resistance). It would also be interesting to clarify the impact of macronutrients (fat, protein) on glycemic control with newer insulins during exercise, which could lead to more personalized and dynamic adjustment protocols.

AUTHOR CONTRIBUTIONS

Ivana Rabbone, Riccardo Bonfanti and Andrea Scaramuzza conceived the study, discussed the results, drafted the manuscript and critically revised and approved the final version. Davide Tinti, Andrea Rigamonti, Chiara Mossetto, Michela Trada and Carmelo Pistone collected data and supervised the camp, critically discussed and approved the final version. Luisa De Sanctis supervised the study and critically discussed and approved the final version. Federico Abate Daga and Samuel Agostino designed the exercise protocol and supervised the exercise sessions.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/dom.70108.

DATA AVAILABILITY STATEMENT

Data can be requested upon reasonable request to the corresponding author.

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