Reducing insulin degludec around regular exercise improves time spent in euglycaemia in people with type 1 diabetes: a randomised cross-over trial

O. Moser[1], M.L. Eckstein[1], A. Mueller[2], P. Birnbaumer[2], F. Aberer[3], G. Koehler[3], C. Sourij[3], H. Kojzar[3], P. Holler[4], H. Simi[4], P. Pferschy[3], P. Dietz[2], R.M. Bracken[1], P. Hofmann[2], H. Sourij[3];
[1]Swansea University, Swansea, UK, [2]University of Graz, Graz, Austria, [3]Medical University of Graz, Graz, Austria, [4]FH JOANNEUM, Bad Gleichenberg, Austria.

Background and aims: Insulin degludec (IDeg) is associated with a similar risk of exercise-induced hypoglycaemia compared to insulin glargine. Though adjustment of bolus insulin is commonly recommended around exercise with an unaltered background of IDeg, no research has explored the impact of intermittent IDeg dose reduction in patients regularly exercising on a few consecutive days. Therefore, the aim of this study was to compare the time spent in euglycaemia in people with type 1 diabetes (T1D) during 5 consecutive days of continuous moderate-intensity exercise, on either 100% or 75% of their usual IDeg dose.

Materials and methods: 9 participants with T1D (4 females, age 32.1 ± 9.0 years, BMI 25.5 ± 3.8 kg/m^2, HbA$_{1c}$ 7.2 ± 2.8 % (55 ± 7 mmol/mol)) performed a cardio-pulmonary exercise test on a cycle ergometer to determine maximum oxygen uptake (VO$_{2max}$) as well as the first (LTP$_1$) and the second lactate turn points (LTP$_2$). Afterwards, a flash glucose monitoring sensor was inserted, and participants were switched to IDeg if not running on that insulin before. 3 days before the first exercise phase participants were randomised to either 100% or 75% of their usual IDeg dose. Then participants exercised on a cycle ergometer for 55 min at a moderate intensity (midpoint between LTP$_1$ and LTP$_2$ (~ 65% VO$_{2max}$)) for 5 consecutive days in the evening at the clinical research facility. After a wash-out period of 4 weeks, participants performed the second exercise phase for 5 consecutive days with the remaining allocation. Time spent in eu- (3.9 - 10 mmol/l), hypo- (< 3.9 mmol/l) and hyperglycaemia (> 10 mmol/l), AUC for these glycaemic ranges, numbers of hypoglycaemic events, glycaemic CV and insulin as well as carbohydrate intake were compared for the entire 5 days. Data were compared between groups by paired t-test and Wilcoxon matched-pairs signed rank test, $p < 0.05$.

Results: A 25% reduction in IDeg dose around regular exercise achieved a longer time spent in euglycaemia ($p = 0.04$) with no effect on numbers of hypoglycaemic events ($p = 0.91$) or time spent in hypo- ($p = 0.07$) or hyperglycaemia ($p = 0.38$) (table 1). The amount of carbohydrates and dose of bolus insulin injections were similar between the two dosing regimens ($p > 0.05$).

Conclusion: This is the first study demonstrating that people with T1D should be encouraged to reduce IDeg dose by 25% when performing regular exercise on consecutive days.

Table 1 Comparison of groups over the 5-day period (mean ± SD)

	75% IDeg dose	100% IDeg dose	p-value
Time euglycaemia (min (%))	4008 ± 938 (62 ± 15)	3566 ± 856 (57 ± 14)	0.04
Time hypoglycaemia	270 ± 165 (4 ± 3)	240 ± 112 (4 ± 2)	0.07
Time hyperglycaemia	2187 ± 1046 (34 ± 16)	2440 ± 1094 (39 ± 18)	0.38
AUC euglycaemia (min × mmol/l)	28372 ± 6684	25187 ± 6384	0.03
AUC hypoglycaemia	1347 ± 1474	1032 ± 1017	0.05
AUC hyperglycaemia	29062 ± 15274	31749 ± 15269	0.49
Hypoglycaemic events (n)	4.8 ± 3.4	4.7 ± 2.9	0.91
CV glycaemia (%)	40 ± 7	39 ± 7	0.57
Prandial insulin used (IU)	72 ± 32	73 ± 40	0.89
Correction insulin used (IU)	20 ± 10	17 ± 10	0.31
Prandial carbohydrates (g)	739 ± 237	648 ± 115	0.10
Correction carbohydrates (g)	219 ± 112	259 ± 114	0.17