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Short Report: Treatment

Algorithm that delivers an individualized rapid-acting insulin dose after morning resistance exercise counters post-exercise hyperglycaemia in people with Type 1 diabetes

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Abstract

Aims To develop an algorithm that delivers an individualized dose of rapid-acting insulin after morning resistance exercise to counter post-exercise hyperglycaemia in individuals with Type 1 diabetes.

Methods Eight people with Type 1 diabetes, aged 34 ± 7 years with HbA_{1c} concentrations 72 ± 12 mmol/mol (8.7 ± 1.1%), attended our laboratory on two separate mornings after fasting, having taken their usual basal insulin the previous evening. These people performed a resistance exercise session comprising six exercises for two sets of 10 repetitions at 60% of the maximum amount of force that was generated in one maximal contraction (60% 1RM). In a randomized and counterbalanced order, the participants were administered an individualized dose of rapid-acting insulin (2 ± 1 units, range 0–4 units) immediately after resistance exercise (insulin session) by means of an algorithm or were not administered this (no-insulin session). Venous blood glucose concentrations were measured for 125 min after resistance exercise. Data (mean ± SEM values) were analysed using ANOVA ($P \leq 0.05$).

Results Participants had immediate post-resistance exercise hyperglycaemia (insulin session 13.0 ± 1.6 vs. no-insulin session 12.7 ± 1.5 mmol/l; $P = 0.834$). The decline in blood glucose concentration between peak and 125 min after exercise was greater in the insulin exercise session than in the no-insulin session (3.3 ± 1.0 vs. 1.3 ± 0.4 mmol/l: $P = 0.015$). There were no episodes of hypoglycaemia (blood glucose <3.9 mmol/l).

Conclusions Administration of rapid-acting insulin according to an individualized algorithm reduced the hyperglycaemia associated with morning resistance exercise without causing hypoglycaemia in the 2 h post-exercise period in people with Type 1 diabetes.

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Introduction

Despite the recommendation that people with Type 1 diabetes should incorporate resistance exercise into a physical activity programme [1] for long-term benefits to health and well-being [2], it has been reported in research studies [3,4] (and anecdotally) that individuals experience significant hyperglycaemia soon after performance of resistance exercise sessions of different volumes and/or intensities. This acute disruption of glycaemic control resulting from exercise is of concern because a loss of control over diabetes has been found to be a barrier to physical activity participation and adherence in people with Type 1 diabetes [5].

One strategy that might help people with Type 1 diabetes to counter the rise in blood glucose associated with exercise would be to administer rapid-acting insulin exogenously [3,4]. Insulin and exercise act independently and synergistically to increase tissue glucose uptake. This suggests a potential for a protective effect of exogenous insulin administration in tempering post-resistance exercise elevations in blood glucose levels. Physical exercise provides a complex environment where large changes in counter-regulatory

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What's new?

- Regular performance of resistance exercise can improve the health and well-being of people with Type 1 diabetes, but there is currently no systematic and/or validated method of correcting the post-exercise hyperglycaemia associated with acute resistance exercise, leaving people with Type 1 diabetes vulnerable to poor glycaemic control.
- The results from the present study show that the administration of a single dose of a rapid-acting insulin analogue, calculated using a simple algorithm, can reduce the amount of post-exercise hyperglycaemia occurring after morning resistance exercise in people with Type 1 diabetes, without causing early post-exercise hypoglycaemia.

hormones and tissue blood flow may influence tissue sensitivity and glucose kinetics [6,7]. One way to avoid hyperglycaemia after resistance exercise would be to administer exogenous insulin before the exercise session; however, the combination of an exogenous insulin dose and the immediate muscle-mediated increase in glucose uptake at the start of exercise could predispose to hypoglycaemia, which might reduce exercise tolerance and compromise patient safety. An alternative is to administer a dose of rapid-acting insulin at the end of a resistance exercise session. This will allow any insulin dose that is used to correct exercise-induced hyperglycaemia to be guided by the actual glucose rise observed. Up to now, no method has existed to guide the calculation of insulin doses in this scenario.

The '100-rule' is an algorithm that has been derived for correcting patient-specific hyperglycaemic excursions with bolus insulin in a non-exercise environment [8], and this tool offers a logical starting-point from which to develop a protocol for understanding how to restore euglycaemia after morning resistance exercise. This individualized approach would allow for potential inter-individual variability in glycaemic responses to exercise [9], but this algorithm could also be adapted to provide an insulin dose based on the individuals' real-time glycaemic response to the exercise session. However, the 100-rule might present too severe a response to correcting blood glucose in a post-exercise, insulin-sensitized state. We were interested, therefore, in piloting a study that explored a conservative determination of exogenous insulin dose whilst remaining cognisant of the insulin-sensitized post-exercise environment. The aim of the present study was to develop an algorithm that delivered an individualized dose of rapid-acting insulin after morning resistance exercise to counter post-exercise hyperglycaemia in people with Type 1 diabetes.

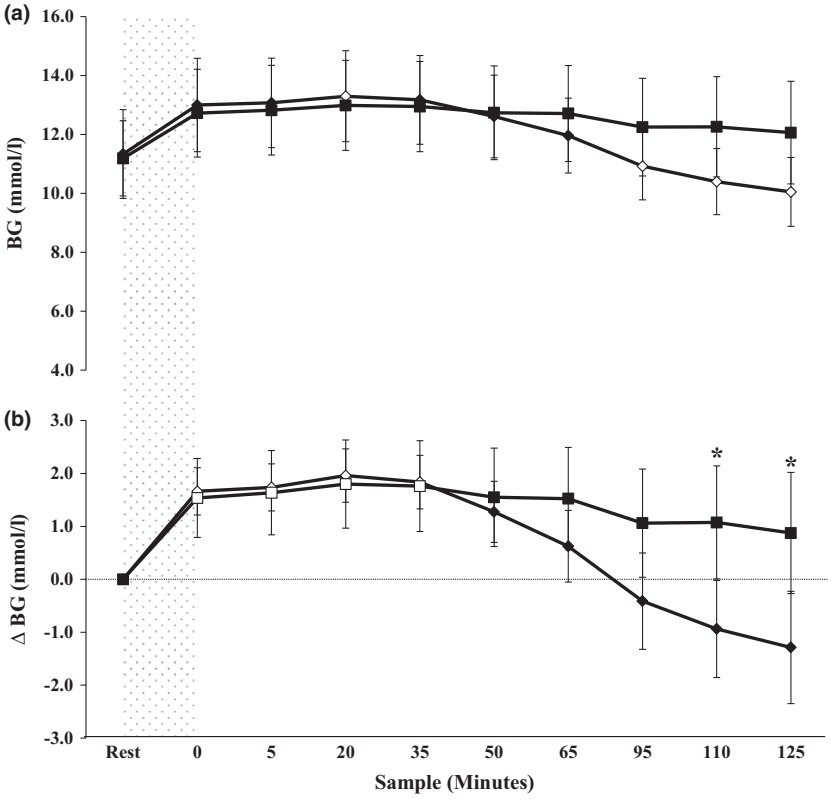
Participants and methods

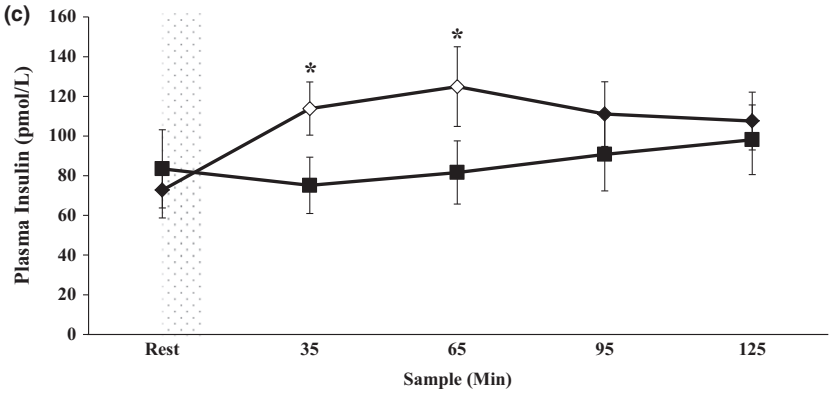
After obtaining UK National Health Service Research Ethics Committee approval (Ref. 12/WA/0049), eight people with Type 1 diabetes [six men and two women, mean ± SEM age 34 ± 7 years, HbA_{1c} concentration 72 ± 12 mmol/mol (8.7 ± 1.1%), BMI 25.7 ± 1.6 kg/m^2, body fat 23.0 ± 2.7% and diabetes duration 18 ± 5 years] volunteered and provided written informed consent for the study. The participants were regularly physically active (participating in exercise for at least 30 min, three times per week), were free from any diabetes complications, including hypoglycaemia unawareness [10], and were treated with a stable insulin regimen composed of once-daily insulin glargine or detemir and rapid-acting insulin aspart for a minimum of 3 months before the study began. Participants did not exercise for 24 h before or after an experimental session, and testing was rescheduled if a participant experienced a symptomatic hypoglycaemic episode during the previous 24 h. Participants maintained a similar diet and insulin regimen for 24 h before each experimental session and avoided alcohol and caffeine consumption.

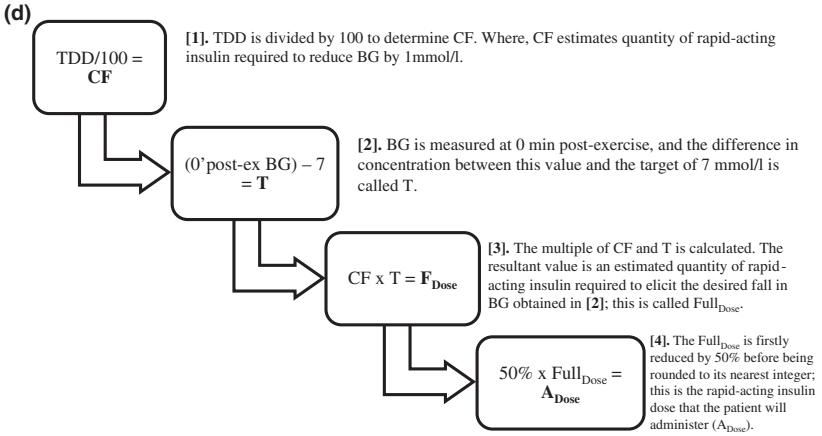
The study was registered under the Clinical Trials Registration number: ISRCTN60407046.

After a preliminary testing day, on two occasions separated by >3 days participants arrived at the clinical research facility between 06:30 and 09:00 h, having fasted for 8–10 h, and having taken their usual basal insulin dose (31.3 ± 3.8 units) the night before but omitted rapid-acting insulin on the morning of testing. On a multi-gym Smith machine (Bodymax CF380 Total Smiths System; BodyMax Powerhouse Fitness, UK), participants performed a 30-min resistance exercise session comprising six exercises (lateral pull-down, squat, bench press, leg extension, shoulder press and split-leg squat) for two sets of 10 repetitions at 60% of their pre-determined maximum one repetition score obtained during the preliminary testing session. A 2-min passive rest interval was taken between successive exercises and sets. Exercise repetitions were performed to a metronome at a fixed pace (2 s concentric-phase and 2 s eccentric phase). In a randomized and counterbalanced order, participants were

FIGURE 1 (a) Blood glucose and (b) plasma insulin responses to insulin group (diamonds) and no-insulin group (squares) experimental sessions. Values are mean ± SEM. Transparent sample points indicate significant changes from rest ($P < 0.05$). *Indicates a significant difference ($P < 0.05$) between the insulin group and no-insulin group. (c) Step-by-step guide to algorithm used to determine patient post-resistance exercise rapid-acting insulin dose. The interventional insulin dose was adapted from the '100-rule' [13], with the objective to return blood glucose to a target of 7 mmol/l during the 2-h recovery after exercise. The adjustment in stage [4] to convert F_{Dose} to A_{Dose} corresponded with a 53 ± 10% reduction in experimental sessions. As a practical example of the algorithm, patient 1 with a total daily dose of 40 units and a blood glucose of 9.5 mmol/l at 0-min post-exercise, was determined to require 1 unit of insulin aspart (i.e. 0.5 units rounded-up) to theoretically reduce blood glucose by 2.5 mmol/l (see Table 1 for algorithm results). BG, blood glucose; CF, correction factor; TDD, total daily dose.







administered an individualized dose of rapid-acting insulin immediately after resistance exercise (insulin session) as determined by the insulin algorithm (Fig. 1c) or were not administered insulin (no-insulin session). Participants then remained sedentary within the research facility for 125 min.

From an antecubital vein, blood was sampled at rest, and 0, 5, 20, 35 and 65, 95, 110 and 125 min after cessation of exercise, using a 21-gauge catheter in conjunction with a three-way tap. Blood was used to determine HbA_{1c} concentration (Roche Cobas Integra 800 analyser, Roche Diagnostics Corp., Indianapolis, IN, USA), and blood glucose, pH and lactate on a metabolic analyser (GEM Premier 3000; Instrumentation Laboratories, UK) for each sample. Blood withdrawn via a 10-ml syringe was immediately decanted into lithium heparinized plasma vacutainer tubes, then centrifuged at 2400 *g* for 5 min. Plasma aliquots were stored at -80°C for later determination of insulin (Invitron, Monmouth, UK). Data (mean ± SEM) were analysed with IBM PASW software version 18, using repeated-measures ANOVA on two factors (experimental session and time), with *post hoc* analysis, and statistical significance was indicated by a *P* value ≤0.05. Participants were randomized to sessions using a computer program (GraphPad Software Inc., San Diego, CA, USA). Thresholds for hypoglycaemia and hyperglycaemia were ≤3.9 and >10.9 mmol/l, respectively.

Results

There were no session differences in total weight lifted (insulin vs. no-insulin session 3675 ± 651 vs. 3675 ± 651 kg) or intensity (insulin vs no insulin session 59 ± 1 vs. 59 ± 1%1RM) during exercise ($P > 0.05$). Blood lactate and pH responses were similar between experimental sessions ($P > 0.05$).

Resting blood glucose concentrations were similar between sessions (insulin vs no-insulin session 11.3 ± 1.5 vs. 11.2 ± 1.3 mmol/l; $P = 0.900$). There was an interaction [$P = 0.011$, partial eta $(\eta)^2=0.495$] between time and experimental session for acute glucose responses (Fig. 1a). Blood glucose rose to similar concentrations during exercise (i.e. before insulin administration: insulin session 13.0 ± 1.6 vs. no-insulin session 12.7 ± 1.5 mmol/l ($P = 0.834$). For the insulin session, participants were then administered 2 ± 1 units of rapid-acting insulin within 5 min of finishing exercise (see Table 1 for patient-specific values). For plasma insulin (n = 7; Fig. 1b), there was an interaction ($P = 0.015$, partial-$\eta^2=0.475$) between time and experimental session. Peak blood glucose occurred at 20 min after exercise for both experimental sessions, and concentrations were similar in the two sessions (insulin vs. no-insulin session 13.4 ± 1.5 vs. 13.4 ± 1.6 mmol/l; $P = 0.992$). The magnitude of decline from peak blood glucose concentrations to 125 min after exercise was statistically greater for the insulin session (3.3 ± 1.0 vs 1.3 ± 0.4 mmol/l; $P = 0.015$). Individualized nadir blood concentrations were significantly lower for the insulin session than the no-insulin session (9.9 ± 1.1 vs. 12.4 ± 1.5 mmol/l; $P = 0.035$). There were no hypoglycaemic occurrences during either experimental session.

Discussion

This study shows that an algorithm that delivers an individualized dose of rapid-acting insulin after morning resistance exercise counters early post-exercise hyperglycaemia in people with Type 1 diabetes.

After overnight fasting and omission of morning food and rapid-acting insulin, participants started resistance exercise with a blood glucose concentration of ~11 mmol/l on both occasions. Although these baseline glycaemic levels fell within the acceptable parameters for exercise [11,12], our results show that exercise increased resting blood glucose concentration by ~2 mmol/l. In the control session, blood glucose levels remained elevated at >12 mmol/l throughout the 2-h recovery period. This exercise-induced rise in glycaemia is in line with previous work that showed that a similar resistance exercise session elicited a 2–3-mmol/l rise in blood glucose above a resting control trial [3]. The present algorithm, which was developed to estimate conservatively the dose of post-exercise rapid-acting insulin, was successful at countering a sustained exercise-induced rise in glycaemia during the 2 h after strength exercise. For instance, with the administration of 2 ± 1U of rapid-acting insulin immediately after exercise, blood glucose dropped to concentrations below baseline (pre-exercise) after the insulin session (10.1 ± 1.2 mmol/l) but not after the no-insulin session (12.1 ± 1.7 mmol/l).

Table 1 Factors used in the derivation of the post-exercise rapid-acting insulin dose for the insulin group.

	Patient ID								
	1	2	3	4	5	6	7	8	Mean ± SEM
Total daily insulin dose, units	40	60	63	35	55	70	60	53	55 ± 4
Basal insulin dose, units	20	42	48	26	18	40	28	28	31 ± 4
Correction factor	0.40	0.60	0.63	0.35	0.55	0.70	0.60	0.53	0.55 ± 0.04
Blood glucose*, mmol/l	9.5	16.1	9.8	7.5	12.6	10.5	19	19	13.0 ± 1.5
Post-exercise dose†, units	1	3	1	0	2	1	4	3	2 ± 1

*0-min post-exercise blood glucose concentration. †Post-exercise bolus: interventional dose of rapid-acting insulin.

This user-friendly insulin dose calculation seems sensitive to inter-individual variability in glycaemic responses to resistance exercise and, as such, no individuals were exposed to early (< 2 h) post-exercise hypoglycaemia. For example, participant number 4 (Table 1) finished exercise with the lowest post-exercise glucose concentration (7.5 mmol/l), and where the algorithm was applied with their data (based on their immediate post-exercise blood glucose reading) the result was administration of no rapid-acting insulin; thus, pragmatically, healthcare professionals should be aware that, in the absence of carbohydrate consumption, some individuals might not require exogenous insulin to maintain euglycaemia soon after morning resistance exercise. Future research should explore whether a dose of rapid-acting insulin, calculated in a similar way and administered before resistance exercise, could attenuate or prevent the exercise-induced rise in blood glucose level, and also whether this increases the risk of hypoglycaemia.

Overall, these findings help bridge a gap between the knowledge of post-resistance exercise glycaemia and the development of an efficacious tool to safely manage potential acute hyperglycaemia associated with pre-breakfast exercise, where the occurrence of hypoglycaemia is unlikely. Although the findings from these preliminary data reflect a reasonable statistical power (blood glucose at 125-min post-exercise, 83.6%; decline in blood glucose from 0 to 125 min post-exercise, 66.9%), the ecological validity of these findings could be improved with a larger sample size.

In conclusion, the present study shows, for the first time, that the use of an individualized algorithm by people with Type 1 diabetes performing morning resistance exercise reduced acute post-exercise hyperglycaemia without causing early hypoglycaemia. These findings serve as a foundation to improve glycaemic stability in people with Type 1 diabetes performing strength exercise.

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Competing interests

None declared.

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