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The effect of timing of remotely supervised exercise on glucose control in people with type 1 diabetes during Ramadan: A randomised crossover study

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A R T I C L E I N F O

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A B S T R A C T

Aim: The aim of the current study was to compare glucose responses when remotely supervised exercise was performed before or after breaking the fast, during Ramadan, in people with type 1 diabetes.

Methods: People with type 1 diabetes were recruited to this randomised cross over design study, which took place in Kuwait during Ramadan in 2021–2022. Interstitial glucose was measured using continuous glucose monitors during a baseline week of normal activity and during weeks where remotely supervised exercise was performed, three times per week, either before (afternoon) or after (evening) breaking the fast, in a randomised crossover design. Exercise involved resistance and aerobic exercise and was supervised during a video call.

Results: Thirty-two participants were recruited to the study (age 34(9) years and BMI 26(4)kg/m^2). Mean interstitial glucose levels were lower on exercise days, compared to equivalent days in the baseline week, during both afternoon (8.6(1.8) mmol/L vs 9.1(1.4) mmol/L, $p = 0.035$) and evening (8.7(1.8) mmol/L vs 9.6(1.8) mmol/L, $p < 0.001$) exercise weeks. Mean glucose levels were lower the day after exercise, relative to both baseline ($p < 0.001$) and exercise ($p = 0.011$) days, in the evening exercise week only.

Conclusions: Remotely supervised exercise performed during Ramadan can safely reduce interstitial glucose levels and may be of greater benefit when performed in the evening, further work is required to confirm this in a larger trial.

1. Introduction

It is well established that physical activity and exercise have wide ranging benefits in people with type 1 diabetes. This includes a reduction in macrovascular risk, mortality, insulin resistance and blood lipids alongside improvements in cardiorespiratory fitness, endothelial function and wellbeing [1], although evidence for beneficial effects on HbA1c are less clear [2]. Exercise and physical activity are, therefore, recommended for general health in people with type 1 diabetes [3]. Care must, however, be taken as blood glucose responses to exercise and physical activity are highly variable [4] and there is the potential to increase the risk of hypoglycaemia. Indeed, an increase in risk of hypoglycaemia is often cited as a barrier to participation in exercise and physical activity in people with type 1 diabetes [5,6].

The variability in blood glucose responses can make standardised recommendations for adjustments in food intake and insulin dosing prior to exercise difficult [3], which can also be complicated further by the time of day at which exercise, or physical activity, is performed [7,8]. For example, previous work in people with type 1 diabetes has shown that resistance exercise performed in the morning results in higher glucose variability and hyperglycaemic events, compared to afternoon resistance exercise [9]. This can be a particular issue during periods of fasting, such as during Ramadan. In this period around 1.6 billion Muslims worldwide fast from sunrise to sunset for 29–30 days and the risks of both hypoglycaemia and hyperglycaemia are high [10]. Whilst there are no widely accepted guidelines for exercise in Ramadan for people with type 1 diabetes, excessive physical activity is often advised again due to risk of hypoglycaemia [10]. Exercise is, however, still recommended due the aforementioned benefits. Currently there are no studies which have investigated the optimal time to perform exercise, with respect to glucose control around fasting, during Ramadan in people with type 1 diabetes.

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The aim of the current study was, therefore, to explore interstitial glucose responses, during Ramadan, when remotely supervised exercise was performed before or after breaking the fast in people with type 1 diabetes. With the COVID-19 induced shift to remote delivery of exercise classes this pragmatic mode of exercise delivery was used in the current study.

2. Materials and methods

2.1. Study setting and participants

The study recruited people with type 1 diabetes at the Dasman Diabetes Institute in Kuwait from April 2021 to May 2022. Inclusion criteria were: physician diagnosed type 1 diabetes for at least 1 year with c peptide and autoantibodies, age 21–60 years, stable insulin therapy for 3 months prior to the study, participating in fasting during Ramadan. Exclusion criteria were: BMI ≥45 kg m^{-2}, blood pressure ≥160/100 mmHg, autonomic neuropathy, hypoglycaemia unawareness, admission to hospital within the past 3 months with DKA, any severe hypoglycaemia requiring third party help, severe proliferative retinopathy, joint or limb injuries preventing weight-bearing activity or any other medical condition that prevents participants from exercising safely. This study was fully explained to participants, both orally and written, before obtaining written informed consent. This study was approved by the Ethical Review Committee of Dasman Diabetes Institute and followed the tenets of the Declaration of Helsinki.

2.2. Trial design

The current study is a randomised crossed over study undertaken during Ramadan. Participant first underwent a week of continuous glucose monitoring (CGM) before taking part in any exercise (baseline week). Following this participants performed one week of remotely supervised exercise training with exercise sessions ~1 h before (afternoon) or ~1 h after (evening) breaking the fast at around 6pm. These exercise weeks were performed in a randomised order, with a one week wash out period between. The randomisation sequence was generated by an independent statistician. Due to the study design it was not possible to blind participants or investigators, but data analysis was carried out blinded to time of exercise.

2.3. Exercise classes

Exercise classes were carried out remotely by an exercise trainer via video call, with 3 exercise classes per week. Classes began with a 5 min warm up of walking/jogging on the spot followed by 15 min of aerobic activity (2 sets of jumping jacks, high knee running, burpees, mountain climbs, jogging boxers 45s of activity and 45s rest) and then 15 min of strength exercises (2 sets of squats, press ups, calf raises, lunges, and plank 45s of activity and 45s rest). Participants were asked to exercise to an intensity of 16–18/20 on the rating of perceived exertion scale. A 5 min cool down of walking/jogging was then performed. Exercises were adapted to patients' abilities where necessary and replicated across sessions. Participants were instructed to follow the "Dose adjustment for normal eating" (DAFNE) advice around adjustments in insulin/carbohydrate usage.

2.4. Outcome measures

2.4.1. CGM

The primary outcome of the current study was CGM derived time in range (3.9–10 mmol/L) with freestyle libre or CGM pumps used by participants throughout the month of Ramadan. We also calculated mean glucose, time in hypoglycaemia (<3.9 mmol/L), time in hyperglycaemia (>10 mmol/L), standard deviation (SD) and coefficient of variation (CV).

2.5. Statistical analysis

CGM data were processed in R with mean blood glucose, time in hypoglycaemia (<3.9 mmol/L), time in range (3.9–10 mmol/L), time in hyperglycaemia (>10 mmol/L) standard deviation (SD) and coefficient of variation (CV). The mean of these variables was calculated on the days on which exercise was performed, the day following exercise, and the equivalent days during the baseline week (i.e. if exercise was performed on a Tuesday then the Tuesday in the baseline week was used as a comparison), in the afternoon and evening conditions. Data were compared via a two-way (condition (afternoon, evening) and day (baseline, exercise or post exercise days)) ANOVA with post-hoc t-tests with Bonferroni correction to compare between and within conditions, where appropriate. A p value less than 0.05 was accepted as statistically significant.

3. Results

3.1. Participant characteristics

Forty participants were included in the study but during the second period 8 participants dropped out due to not being able to attend the exercise session. The final analysis included 32 participants (Fig. 1) with general demographics presented in Table 1. There were no differences in insulin use across the different conditions or days (Table 2) (all $p < 0.05$).

3.2. Glucose data

Glucose profiles comparing conditions are visualised in Fig. 2 and summary data presented in Table 2. Condition (afternoon, evening), day (baseline, exercise, post-exercise days) and interaction effects from our models are presented.

A condition ($p = 0.007$), but not day ($p = 0.100$) or interaction ($p = 0.092$), effect was seen for time in range. Due to the significant condition effect and a trend for interaction effect exploratory post-hoc tests were performed to compare time in range within and between conditions. Within the afternoon week, there was no difference between exercise and post-exercise days ($p = 0.267$), post exercise and baseline days ($p = 0.425$), or baseline and exercise days ($p = 0.800$). Within the evening week, time in range was higher on post-exercise days compared to exercise days ($p = 0.045$), and on post-exercise compared to baseline days ($p < 0.001$). No differences between baseline and exercise days were noted ($p < 0.068$). Post-hoc tests comparing conditions found no differences on any days between afternoon and evening weeks.

No condition ($p = 0.545$), day ($p = 0.801$) or interaction ($p = 0.739$) effects were seen for time in hypoglycaemia.

A condition ($p = 0.004$), but no day ($p = 0.100$) or interaction ($p = 0.092$), effect was seen for time in hyperglycaemia. Due to the significant condition effect and a trend for interaction effect exploratory post-hoc tests were performed to compare time in hyperglycaemia within and between conditions. Within the afternoon week, there was no difference between exercise and post-exercise days ($p = 0.249$), post-exercise and baseline days ($p = 0.286$), or baseline and exercise days ($p = 0.832$). Within the evening week, time in hyperglycaemia was lower on post-exercise compared to exercise days ($p = 0.027$), and on post exercise compared to baseline days ($p < 0.001$). No differences between baseline and exercise days were noted ($p = 0.068$). Post-hoc tests comparing conditions found no differences between afternoon and evening weeks on any days.

The two-way repeated measures ANOVA demonstrated a significant effect of condition ($p < 0.001$) and an interaction effect ($p = 0.004$), with no effect of day ($p = 0.912$) noted, for mean glucose levels. Post-hoc tests comparing conditions found no differences between afternoon and evening weeks on any days. Within the afternoon week, there was no difference between exercise and post-exercise days ($p = 0.841$),

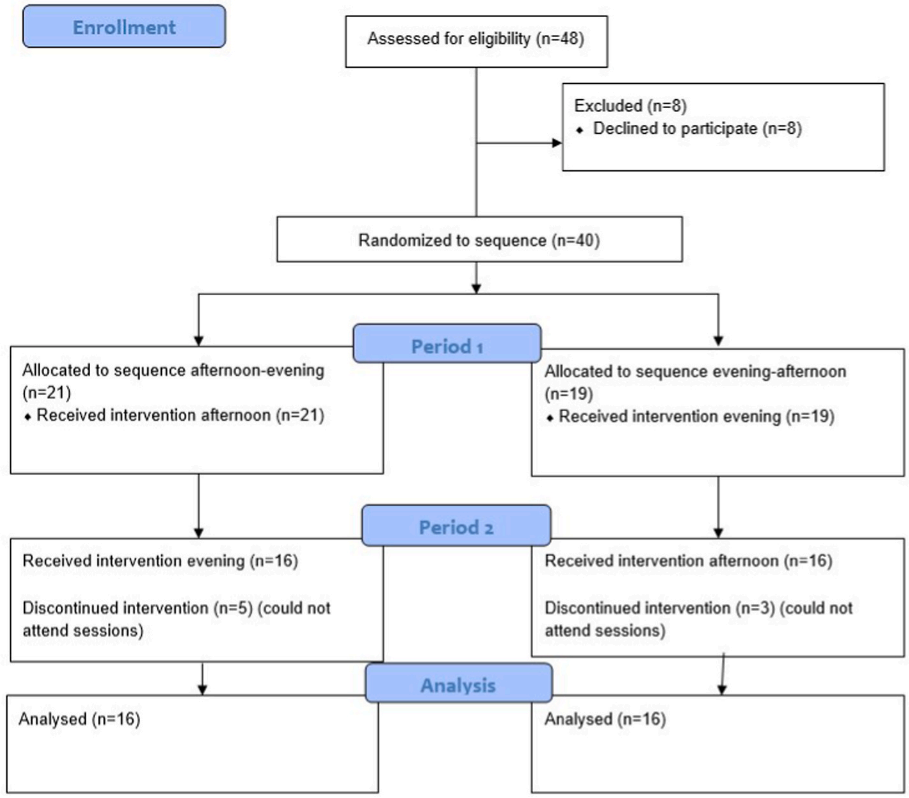

Fig. 1. Participant flow diagram for the current study investigating glucose responses to remotely supervised exercise performed, during Ramadan, before and after breaking the fast in people with type 1 diabetes.

Table 1
General demographics of participants. Data are mean (SD).

	N = 32
Age	33.8 (9.1)
Height (cm)	166 (9)
Weight (kg)	74.5 (13.9)
BMI (kg/m^2)	26.4 (4.0)
Duration of diabetes (years)	19.6 (9.2)
Systolic blood pressure (mmHg)	122.1 (11.9)
Diastolic blood pressure (mmHg)	73.3 (8.0)

or between post-exercise and baseline days ($p = 0.103$) but mean glucose levels were lower on exercise compared to baseline days ($p = 0.035$). Within the evening week mean glucose levels were lower on post-exercise compared to exercise days ($p = 0.011$), post-exercise compared to baseline days ($p < 0.001$), and on exercise compared to baseline days ($p < 0.001$). A condition ($p = 0.009$), but no day ($p = 0.948$) or interaction ($p = 0.170$), effect was seen for SD. Post-hoc tests comparing conditions found no differences between afternoon and evening weeks on any days. No condition ($p = 0.246$), day ($p = 0.653$) or interaction ($p = 0.880$) effects were seen for CV.

4. Discussion

The current study has demonstrated that in people with type 1 diabetes, remotely supervised performed during Ramadan lowers glucose levels on the days on which exercise is performed, regardless of whether being performed before or after breaking the fast. On the days following remotely supervised exercise a decrease in glucose levels was seen when exercise was performed following the breaking of the fast (evening). A

Table 2
Insulin use and glucose variables measured via CGM on days of exercise and days post exercise during weeks where exercise was performed in the afternoon or evening, and equivalent days at baseline (no-exercise week). Data are mean (SD).

	Afternoon Evening					
	Baseline	Exercise	Post Exercise	Baseline	Exercise	Post Exercise
Daily Insulin Dose (U/day)	41.9 (9.6)	42.1 (10.7)	40.8 (11.4)	41.9 (11.2)	41.5 (12.1)	40.4 (9.8)
Mean glucose (mmol/L)[1,2]	9.14 (1.38)	8.62 (1.76)[a]	8.67 (1.77)	9.57 (1.79)	8.71 (1.79)[a,b]	8.12 (1.42)[a,c]
Time in Hypoglycaemia (%)	3.22 (2.16)	3.59 (4.59)	3.71 (5.60)	3.14 (2.12)	3.13 (4.32)	3.91 (4.16)
Time in Hyperglycaemia (%)[1]	41.59 (15.83)	41.11 (19.18)	37.85 (21.90)	43.47 (16.46)	38.86 (21.04)[b]	31.60 (17.48)[a,c]
Time in Range (%)[1]	55.81 (12.73)	55.29 (17.67)	58.44 (21.05)	53.57 (12.43)	58.01 (19.65)[b]	64.50 (17.14)[a,c]
SD[1]	2.92 (0.67)	2.81 (0.75)	2.77 (0.81)	3.07 (0.70)	2.73 (0.78)	2.68 (0.79)
CV	31.65 (4.94)	30.15 (6.48)	30.38 (6.99)	31.07 (4.91)	29.60 (6.13)	30.46 (7.03)

[1] denotes a significant ($p < 0.05$) effect of condition (afternoon, evening) in the two-way repeated measures ANOVA.
[2] denotes a significant ($p < 0.05$) condition*day (baseline, exercise, post-exercise) interaction effect in the two-way repeated measures ANOVA.
[a] denotes a significant ($p < 0.05$) difference from baseline in the same condition from post-hoc t-tests with Bonferroni correction.
[b] denotes a significant ($p < 0.05$) difference from post exercise in the same condition from post-hoc t-tests with Bonferroni correction.
[c] denotes a significant ($p < 0.05$) difference from exercise in the same condition from post-hoc t-tests with Bonferroni correction.

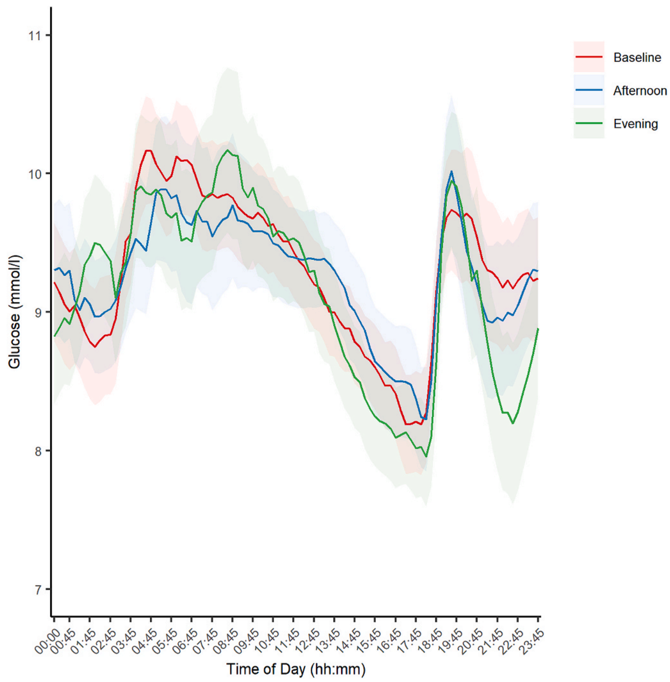

Fig. 2. Mean interstitial glucose responses recorded using continuous glucose monitors during baseline, afternoon exercise and evening exercise weeks in people with type 1 diabetes (n = 32) during Ramadan. Data are mean (95%CI). Two-way repeated measures ANOVA demonstrated a significant effect of condition ($p < 0.001$) and an interaction effect ($p = 0.004$), with no effect of day ($p = 0.912$) noted, for mean glucose levels.

tendency for an increase in the time spent in range and decrease in time spent in hyperglycaemia was also seen on these days. This occurs with no change in time spent in hypoglycaemia or measures of glucose variability (SD and CV). Whilst the current study has limitations it indicates that during Ramadan, in people with type 1 diabetes, remotely supervised exercise can safely lower glucose levels and that it may be more beneficial to perform exercise after the breaking of the fast although further work is required to confirm this.

There are several other studies which have investigated the effects of time of day on responses to exercise, in different populations. There has been no work performed during Ramadan when 1.6 billion people fast. Previous work is primarily in people with type 2 diabetes, rather than type 1 diabetes. Whilst comparing our data to data derived in people with type 2 diabetes is not perfect, we believe such comparisons are still useful. In a study in people with type 2 diabetes, there were no differences between CGM measured 24hr glucose responses to a bout of walking performed in the morning, afternoon, or evening. However, any conclusions that can be drawn from this study are limited as none of the walking sessions lowered glucose compared to control [11]. In another study, again in people with type 2 diabetes, it was found that acute glucose levels after moderate intensity aerobic exercise are lower when exercise is performed in the afternoon or evening, compared to in the morning [12]. Similarly in people with type 2 diabetes high intensity interval exercise was more effective in lowering CGM measured 24hr glucose responses when performed in the afternoon compared to when performed in the morning [13]. There are some data in people with type 1 diabetes. In one such study, an acute bout of resistance exercise performed in the morning resulted in more time spent in hyperglycaemia 6 h post exercise, compared to afternoon exercise. No differences were seen during the nocturnal period (midnight to 6am) [9]. Another study in people with type 1 diabetes found that following 60 min of moderate intensity treadmill exercise there was a lower risk of hypoglycaemia and more time in normoglycaemia when exercise was performed in the morning, compared to the afternoon [14]. The time of day at which exercise is performed does, therefore, appear to influence the metabolic responses, although with limited studies, low sample sizes, different participant demographics, and various exercise protocols employed data is not clear. Such an effect of time of day is supported by the various studies which have demonstrated the link between circadian rhythms and metabolism, and the mediating effect of exercise [15].

On top of time of day differences our participants were also performing exercise in fasting compared to non-fasting states. The study of Toghi-Eshghi et al. [9] is particularly relevant in this regard as the morning group were fasted and the afternoon group were fed 1h prior to exercise in that study. Similarly, when comparing morning (fasted) to afternoon (fed 4h prior to exercise) moderate intensity exercise, in people with type 1 diabetes a lower rate of hypoglycaemia was seen following morning exercise [14]. These results are supported by another similar study [16]. Uncovering how much of these effects are due to time of exercise and/or the fasting/fed status remains to be established, but data do clearly suggest a role for feeding in altering blood glucose response to exercise in people with type 1 diabetes [17] and so will likely contribute to the effects seen in the current work.

The current study is the first study in people with type 1 diabetes to compare glucose responses to remotely supervised exercise performed before (afternoon) and after (evening) the breaking of the fast during Ramadan. Our study finds that remotely supervised exercise, at either time of day, did not alter time spent in hypoglycaemia. Remotely supervised exercise, therefore, is safe to perform during Ramadan from the point of view of risk of hypoglycaemia. Remotely supervised exercise either in the afternoon or evening lowered glucose levels on the days on which exercise was performed. On top of this we found that evening remotely supervised exercise lowered glucose levels on the day following exercise, with a tendency to increase the time spent in range and lower time spent in hyperglycaemia. The lowering of glucose levels, with more time in range and less in hyperglycaemia, is likely to be beneficial for people with type 1 diabetes, who are at higher risk of cardiovascular disease [18], and where better control of glucose levels has been shown to reduce long-term risk of cardiovascular disease [19]. Hyperglycaemia is also associated with an increase in the risk of other diabetic complications such as neuropathy, nephropathy and retinopathy [20] and strategies to lower time in hyperglycaemia are, therefore, a positive.

5. Clinical relevance

It would appear, therefore, that recommending exercise either before or after breaking the fast, during Ramadan, will be of benefit but exercise following the breaking of the fast may be most beneficial for people with type 1 diabetes. With no increase in risk of hypoglycaemia exercise during Ramadan appears safe and should be recommended, remembering that the benefits of exercise go beyond glucose control [1,21].

6. Limitations

The current study is not, however, without limitations which must be considered. Whilst the sample size is larger than previous studies in this area it is still relatively small, with recruitment during the short Ramadan period a challenge. Furthermore, to deliver a pragmatic trial, exercise was delivered remotely and so we cannot quantify the relative intensity and ensure this was the same in the afternoon and evening classes. We would argue that as this is a pragmatic trial and by design reflects the real-world situation.

7. Conclusions

In conclusion the current study has demonstrated that in people with type 1 diabetes remotely supervised exercise performed either before or after the breaking of the fast, during Ramadan, can lower glucose levels on the day of exercise. Remotely supervised exercise does not result in more time spent in hypoglycaemia, during Ramadan, and can, therefore, be considered safe. Remotely supervised exercise performed in the evening was also beneficial in reducing glucose levels the day after exercise and exploratory analysis indicated it may also and increase the time in range and lower time in hyperglycaemia. There findings are preliminary and further work in a larger trial are required, but do indicate that evening exercise, following the breaking of the fast, may be considered as the optimal recommendation for people with type 1 diabetes fasting during Ramadan.

Authorship confirmation/contribution statement

EAO Conceptualization, Resources, Supervision, Project Administration, Funding acquisition, Writing – Review and Editing: AE Methodology, Investigation, Writing – Review and Editing.

JAK Methodology, Investigation, Writing – Review and Editing: YH Methodology, Investigation, Writing – Review and Editing: DT Methodology, Investigation, Writing – Review and Editing.

SRG Conceptualization, Resources, Supervision, Project Administration, Funding acquisition, Writing – Original Draft.

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Declaration of competing interest

The authors declare that they have no conflicts of interest.

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