The "Ups" and "Downs" of a Bike Race in Type 1 Diabetes: Dramatic Differences in Strategies and Blood Glucose Responses from the Paris to Ancaster Spring Classic

Jane E Yardley^{1,2} PhD, Dessi P Zaharieva³ MSc, Chris Jarvis⁴ BSc, and Michael C Riddell³ PhD

¹Manitoba Institute of Child Health, University of Manitoba, Winnipeg, Manitoba, Canada, ²University of Alberta, Augustana Campus, Camrose, Alberta, Canada ³School of Kinesiology and Health Science, York University, Toronto, Ontario, Canada, ⁴I Challenge Diabetes, Toronto, Ontario, Canada

Running title: Athletic competition in type 1 diabetes

Address for correspondence:

Jane Yardley, PhD Department of Social Sciences Augustana Campus University of Alberta 4901 – 46 Avenue Camrose, AB T4V 2R3 Phone: +1 (780) 679-1688 Fax: +1 (780) 679-1590 Email: jeyardle@ualberta.ca

Word Count (excluding abstract): Abstract: 224 Main text: 2411 Tables and Figures: 2 tables, 2 figures

Abstract

Objective: Recommendations for insulin adjustments and carbohydrate intake exist for individuals with type 1 diabetes undertaking moderate exercise. Very few guidelines exist for athletes with type 1 diabetes competing in higher intensity and/or longer duration events. This observational study reports the strategies adopted by 6 habitually active men with type 1 diabetes (HbA_{1c} = $8.3\pm2.0\%$) undertaking a relatively intense endurance cycling event.

Methods: Participants wore continuous glucose monitoring (CGM) sensors for 24 hours before competition, while racing and overnight post-race. They were asked to eat their regular meals and snacks, and make their usual insulin adjustments before, during and after competition. All food intake and insulin adjustments were recorded in detail.

Results: Participants used a variety of adjustments for exercise. Four of 6 participants decreased their insulin dosage, and all participants consumed carbohydrate during the race (mean= $87\pm57g$). In spite of these strategies, three of the six participants experienced mild to moderate hypoglycemia (not requiring assistance) during the event. Hyperglycemia was seen in all participants three hours post-exercise. There were no incidents of nocturnal hypoglycemia.

Conclusions: Individuals with type 1 diabetes can compete in intensive long-distance athletic events using a variety of nutritional and insulin adjustment strategies. In addition to finely tuned insulin adjustments and increased carbohydrate intake, vigilance will always be required to maintain some semblance of glycemic control during extended duration events.

Key words: blood glucose control, insulin adjustment, hypoglycemia, diabetes

INTRODUCTION

Physical activity is a common challenge to blood glucose control in individuals with type 1 diabetes. Moderate aerobic exercise is known to cause rapid declines in blood glucose (1), thereby increasing the risk of hypoglycemia both during and after exercise. Meanwhile, short periods of high intensity activity have been associated with increases in blood glucose concentration in early recovery with the potential for hyperglycemia both during and after activity (2-4). Some recent studies have attempted to duplicate the physical stresses of intense field sports by examining how short, high intensity bouts of exercise affect blood glucose levels when combined with moderate aerobic activity (5-7). Unfortunately, controlled laboratory conditions likely fail to truly reflect the physical and psychological stresses of competition, leaving athletes with type 1 diabetes with little information on how to manage blood glucose levels for competitive events where exercise intensity and duration will be variable in nature.

Several organizations offer guidelines related to managing blood glucose during exercise for individuals with type 1 diabetes (8, 9). Recommendations include decreasing insulin dosage, increasing carbohydrate intake, or using a combination of both of these strategies (8, 9). Unfortunately, most of these guidelines assume that individuals will be performing moderate exercise for a relatively short time (30 to 60 minutes) and at a fairly constant intensity. In actuality, many team (e.g. basketball, volleyball, soccer, etc.) and individual sports (e.g. cycling, running, cross-country skiing, etc.) involve both training sessions and competitions of extended duration (>90 minutes) where periods of high intensity work may be interspersed with slightly less intense activity. Finding the right balance of insulin reductions and increased carbohydrate intake is essential for preventing both hypo and hyperglycemia, both of which can influence sport performance. Having too much insulin or insufficient carbohydrate intake prior to/during exercise often results in hypoglycemia (10), which can lead to decreases in performance at best (11), or to serious medical problems requiring medical assistance (12) at worst. Conversely, hyperglycemia can result from withholding insulin, consuming excess carbohydrate (13) or from intense activities above the anaerobic threshold (14). Prolonged hyperglycemia can lead to the production of ketones, which can

subsequently cause dehydration (15), thereby increasing the risk of muscle cramp and heat stress during intense activity (16).

As a great deal of inter- and intra- individual variability exists in terms of the hormonal responses to various types and intensities of training and competition, it is difficult for general insulin adjustment and carbohydrate supplementation recommendations to be made. In these situations, athletes must often adopt a trial-and-error approach in devising a strategy appropriate for the duration and intensity of exercise they are about to undertake, based on past experience of their blood glucose responses to similar activities. Very few of these strategies have been documented in the literature, leaving novice athletes with type 1 diabetes with very few resources at their disposal. This observational study follows six athletes, varying from recreational to elite in their competitive experiences, during a long-distance on- and off-road cycling race, in order to document how different insulin and carbohydrate strategies influence blood glucose outcomes during competition.

METHODS

This study was approved by the York University Human Participants Review Committee. Six male athletes with type 1 diabetes participated in the 2013 Paris to Ancaster Bicycle Race (Ontario, Canada) in order to take part in this observational study. All participants were habitually active in endurance-based sports. Four participants took part in regular cycling or triathlon competition, with two of these participating at an elite level. Participants ranged in age $(36.3 \pm 9.3 \text{ years}, \text{ range} = 24-46 \text{ years})$ and diabetes duration $(15.7 \pm 11.8 \text{ years}, \text{ range} = 2-31 \text{ years})$. All participants had moderate to excellent blood glucose control (Table 1). Two of the participants were using multiple daily insulin injections (MDI), three were using continuous subcutaneous insulin infusion (CSII), and one participant used a combination of both MDI and CSII. For comparison purposes, one non-diabetic athlete agreed to be monitored during competition. Subjects were provided with instruction on the experimental procedures and provided informed consent in agreement with York University ethics policies.

On the day before the race, participants were provided with continuous glucose monitoring (CGM) sensors. Data was recorded by a separate CGM device for individuals using MDI, while participants using CSII recorded the CGM data on their insulin pumps. Participants were asked to take at least four capillary glucose readings each day of sensor wear, during periods of relative glycemic stability, for CGM calibration purposes. The athletes did not perform any exercise or consume any alcohol in the 24 hours prior to the race. While participants were asked to follow their regular pre-race routines with respect to insulin dosage and food intake, they were also asked to record their food intake before, during, and after competition on race day with as much detail as possible. On the day following the race, CGM data and capillary glucose values for participants were uploaded using a website associated with the CGM devices.

OBSERVATIONS

The event took place the morning of Sunday, April 15th, 2013. The course consisted mixed terrain including asphalt, dirt or gravel roads, as well as off-road single and double-track trails involving a substantial amount of deep mud (i.e. cyclo-cross style racing). Four participants and the non-diabetic control participant completed the ~70 km route from Paris, Ontario to Ancaster, Ontario while the other two participants took part in the ~40 km route from St. George, Ontario to Ancaster, Ontario. All participants completed the event successfully, with completion time for the participants ranging from 176 minutes to 244 minutes for the 70 km route, and from 123 to 135 minutes for the 40 km route.

Insulin adjustments and carbohydrate intake

Details of each participant's insulin adjustments and carbohydrate intake both before and during the race can be found in Table 1. CGM tracings for the race, 12-hours post-race and overnight post-race for all six participants with diabetes, along with the control participant without diabetes can be found in Figure 1. Two (one MDI, one CSII) out of the six participants did not make any adjustments to insulin dosage and chose instead to rely solely on "extra" carbohydrate intake (i.e. Ex carbs, without insulin administration) during the race to prevent hypoglycemia. The other two participants using a long-acting insulin injection decreased their evening injection by 20% and 33% respectively on the evening before the race and consumed Ex carbs. Of the three remaining participants using CSII, two decreased their basal insulin infusion rate approximately one hour prior to the race, while one chose to suspend the basal insulin infusion completely at the start of the race. All three also used a modified Ex carb approach, which takes into account reductions in insulin administration (17). The different insulin adjustment strategies and the resulting blood glucose outcomes of all participants, along with the CGM glucose profiles can be found in Figure 2.

As mentioned above, all participants consumed additional carbohydrate both before and during competition. Pre-race carbohydrate intake varied from 33 to 120 grams (Table 1), while carbohydrate intake during the race varied greatly from as little as 7 grams in one participant who struggled with severe hyperglycemia during the race, to 165 grams in another participant who struggled with hypoglycemia. Four out of the six participants with diabetes consumed over 100 grams of carbohydrate during the event, in line with the 30 to 60 grams of carbohydrate per hour that are generally recommended for athletes during endurance events (18).

Blood glucose levels

Interstitial glucose levels as measured by CGM show that two participants (Participants 4 and 5 in both Figure 1 and Figure 2) experienced mild to moderate hypoglycemia during the event. While interstitial glucose levels for participant 6 were measured between 6 and 12 mmol/l during the race, the participant performed a capillary glucose test with a handheld meter after 60 minutes due to feeling unwell and found that his glucose levels had dropped below 3 mmol/l. Conversely, participant 2, who was hyperglycemic (~20 mmol/l) before the event, experienced an increase in blood glucose levels throughout the first two hours of competition, and eventually delivered a bolus of insulin to bring his glucose levels under control. The final two participants (Participants 2 and 7) managed to complete the event with their blood glucose

levels in a "safe" glycemic range (between 6 and 10 mmol/l) from start to finish. All participants experienced some level of hyperglycemia ranging from very mild (~8 mmol/l) to severe (>22.2 mmol/l) in the six hours following the race. There were no instances of nocturnal hypoglycemia post-race.

DISCUSSION

This observational study monitored interstitial glucose concentration by means of CGM in six athletes with type 1 diabetes (ranging from recreational to elite) during a long distance intense cycling race. As they were all taking part in the same endurance event (a cyclocross bike race), the timing, environmental conditions, and race terrain were comparable for all involved. In spite of this, the six monitored athletes showed a great deal of inter-subject variability in their approach to competition in terms of reducing insulin intake and increasing carbohydrate consumption. All six athletes managed to finish the race successfully, albeit not without some difficulty (mild hypo- and hyperglycemia).

A number of guidelines exist for insulin adjustments and nutritional strategies for exercise and sport for patients with type 1 diabetes (8, 9, 17). To date, only a handful of field studies have been published evaluating strategies of individuals with type 1 diabetes during competition (19, 20). In a group of type 1 diabetes marathoners, participants reduced both basal insulin (~23 and 20%) and pre-race breakfast insulin (~30 and 15%) when followed in the same race for two consecutive years. Carbohydrate ingestion was increased from a mean of 50 g to a mean of 60 g during the race from one year to the next in order to prevent hypoglycemia (19). In a 75km cross country ski race, excessive pre-race carbohydrate loading (65g) and a dramatic reduction in short-acting insulin (by 58%) resulted in pre-race hyperglycemia, while in the following year hyperglycemia was attenuated by dropping the pre-race carbohydrate to 40g with less of a reduction in short-acting insulin (by 35%) (20). In that cross country ski field study, ~40g of carbohydrate per hour of exercise appeared to prevent hypoglycemia in a majority of subjects (8 of 9) in both years (20). Similarly, we found that a combination of reduced circulating insulin levels, via reductions in either basal insulin 60 to 90 minutes before the start of the race or by reducing pre-race

bolus insulin, and the consumption of carbohydrates at a rate of about 40-60g/hour of cycling helped to reduce the occurrence of hypoglycemia and did not result in hyperglycaemia during the race.

With the exception of the participant who started the race with severe hyperglycemia (blood glucose ~ 20 mmol/L), all race participants with type 1 diabetes experienced a decline in blood glucose concentration throughout the race in spite of taking in Ex Carbs and/or decreasing insulin dosage. Even the patient who had hyperglycemia initially experienced a dramatic decline in blood glucose once a small insulin correction was taken. In addition to the expected declines in glucose concentration during the race, five out of six participants experienced a steady increase in glucose levels upon completing the race, with peak glucose concentration being reached approximately three hours post-exercise. A similar trend towards post-exercise hyperglycemia was also found after 45 minutes of aerobic exercise in a study comparing aerobic and resistance exercise in individuals with type 1 diabetes where glucose levels were monitored by CGM for 12 hours post-exercise (1). As no study to date has collected hormonal and/or metabolic data related to this post-exercise period in individuals with type 1 diabetes, it is difficult to ascertain the cause of this phenomenon. The concentrations of plasma non-esterified fatty acids (NEFA) as well as the levels of lipid oxidation are both elevated post-exercise, with levels increasing in proportion to exercise intensity (21) and duration (22). The exercise-induced increase in free fatty acid mobilization peaks within two to three hours of exercise cessation, and can persist for up to 24 hours (23). Elevated lipid oxidation is known to suppress carbohydrate metabolism. When combined with elevated epinephrine levels stimulating glycogenolysis for up to two hours post-exercise (22), this could result in an increase in blood glucose concentration in individuals with type 1 diabetes unless a bolus of insulin is delivered. Consistent with this theory, the only participant who did not experience significant post-exercise hyperglycemia delivered frequent insulin correction boluses in the hours following exercise.

In addition to an increase in glucose uptake into the muscles during exercise, physical activity can increase insulin sensitivity for several hours post-exercise (24), thereby increasing the risk of post-

exercise hypoglycemia. The DirecNet consortium found that when children exercised for 75 minutes at moderate-intensity the number of nights where nocturnal hypoglycaemia (blood glucose < 3.3 mmol/L) was experienced was more than double (42 versus 16%) compared to a day without exercise (25). Conversely, there is evidence to indicate that in regularly active individuals with well-controlled type 1 diabetes, the frequency of nocturnal hypoglycemia is not increased after days where exercise has been performed as compared to relatively sedentary days (26), presumably due to having developed effective prevention strategies. Participants in the present study were all habitually active with relatively well-controlled type 1 diabetes (mean HbA_{1c} 8.3±2.0%), which may explain why no nocturnal hypoglycemia was seen post-race. It should also be noted that the observed post-exercise hyperglycemia, caused either by a transient reduction in insulin sensitivity or because of increases in energy intake that were not properly matched with appropriate insulin delivery, may help prevent post-exercise hyperglycemia corrective insulin administration has been linked to at least one death in a patient with type 1 diabetes (27).

In summary, athletes with type 1 diabetes are capable of taking part in high level athletic competition successfully. While the tools for managing and monitoring blood glucose have improved over the years, a knowledge and understanding of one's own responses to exercise intensity and competition stress is essential in the decision-making processes required for adjusting insulin dosage and carbohydrate intake. Frequent testing of capillary glucose can be used as an adjunct to real-time CGM to ensure that blood glucose levels remain in a healthy range before, during and after competition.

ACKNOWLEDGEMENTS

Author Disclosure

M. Riddell has received speakers' fees from Medtronic Canada. J. Yardley is supported by a Canadian Institutes of Health Research Post-Doctoral Fellowship.

Contributions

The manuscript was drafted by J. Yardley and D. Zaharieva. C. Jarvis assisted in participant recruitment and data collection. J. Yardley and D. Zaharieva performed the data collection and presentation. M. Riddell provided support and guidance in data collection, and reviewed and edited the manuscript.

REFERENCES

- Yardley JE, Kenny GP, Perkins BA, et al. Resistance versus aerobic exercise: acute effects on glycemia in type 1 diabetes. Diabetes Care 2013; 36:537-42.
- Mitchell TH, Abraham G, Schiffrin A, Leiter LA, Marliss EB. Hyperglycemia after intense exercise in IDDM subjects during continuous subcutaneous insulin infusion. Diabetes Care 1988;11:311-7.
- Sigal RJ, Purdon C, Fisher SJ, Halter JB, Vranic M, Marliss EB. Hyperinsulinemia prevents prolonged hyperglycemia after intense exercise in insulin-dependent diabetic subjects. J Clin Endocrinol Metab 1994;79:1049-57.
- 4. Fahey AJ, Paramalingam N, Davey RJ, Davis EA, Jones TW, Fournier PA. The effect of a short sprint on postexercise whole-body glucose production and utilization rates in individuals with type 1 diabetes mellitus. J Clin Endocrinol Metab 2012;97:4193-200.
- Guelfi KJ, Ratnam N, Smythe GA, Jones TW, Fournier PA. Effect of intermittent high-intensity compared with continuous moderate exercise on glucose production and utilization in individuals with type 1 diabetes. Am J Physiol Endocrinol Metab 2007;292:E865-70.
- Iscoe KE, Riddell MC. Continuous moderate-intensity exercise with or without intermittent highintensity work: effects on acute and late glycaemia in athletes with Type 1 diabetes mellitus. Diabet Med 2011;28:824-32.
- Guelfi KJ, Jones TW, Fournier PA. The decline in blood glucose levels is less with intermittent high-intensity compared with moderate exercise in individuals with type 1 diabetes. Diabetes Care 2005;28:1289-94.
- Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Physical Activity and Diabetes. Can J Diabetes 2013;37:S40-4.
- American Diabetes Association. Physical activity/exercise and diabetes. Diabetes Care 2004;27
 Suppl 1:S58-62.

- Diabetes Research in Children Network Study Group. Prevention of hypoglycemia during exercise in children with type 1 diabetes by suspending basal insulin. Diabetes Care 2006;29:2200-4.
- Kelly D, Hamilton JK, Riddell MC. Blood glucose levels and performance in a sports camp for adolescents with type 1 diabetes mellitus: a field study. Int J Pediatr 2010;2010.
 Doi:10.1155/2010/216167.
- Graveling AJ, Frier BM. Risks of marathon running and hypoglycaemia in Type 1 diabetes.
 Diabet Med 2010;27:585-8.
- 13. Galassetti P, Riddell MC. Exercise and type 1 diabetes (T1DM). Compr Physiol 2013;3:1309-36.
- 14. Marliss EB, Vranic M. Intense exercise has unique effects on both insulin release and its roles in glucoregulation: implications for diabetes. Diabetes 2002;51 Suppl 1:S271-83.
- 15. Dhatariya K. People with type 1 diabetes using short acting analogue insulins are less dehydrated than those with using human soluble insulin prior to onset of diabetic ketoacidosis. Med Hypotheses 2008;71:706-8.
- Yardley JE, Stapleton JM, Carter MR, Sigal RJ, Kenny GP. Is whole-body thermoregulatory function impaired in type 1 diabetes mellitus? Curr Diabetes Rev 2013;9:126-36.
- Perkins BA, Riddell MC. Type 1 Diabetes and Exercise: Using the Insulin Pump to Maximum Advantage. Can J Diabetes 2006;30:72-9.
- Burke LM, Hawley JA, Wong SH, Jeukendrup AE. Carbohydrates for training and competition. J Sports Sci 2011;29 Suppl 1:S17-27.
- 19. Murillo S, Brugnara L, Novials A. One year follow-up in a group of half-marathon runners with type-1 diabetes treated with insulin analogues. J Sports M Phys Fitness 2010;50:506-10.
- 20. Sane T, Helve E, Pelkonen R, Koivisto VA. The adjustment of diet and insulin dose during longterm endurance exercise in type 1 (insulin-dependent) diabetic men. Diabetologia. 1988;31:35-40.
- Mulla NA, Simonsen L, Bulow J. Post-exercise adipose tissue and skeletal muscle lipid metabolism in humans: the effects of exercise intensity. J Phys 2000;524:919-28.

- Bahr R, Hostmark AT, Newsholme EA, Gronnerod O, Sejersted OM. Effect of exercise on recovery changes in plasma levels of FFA, glycerol, glucose and catecholamines. Acta Physiol Scand 1991;143:105-15.
- 23. Magkos F, Mohammed BS, Patterson BW, Mittendorfer B. Free fatty acid kinetics in the late phase of postexercise recovery: importance of resting fatty acid metabolism and exercise-induced energy deficit. Metabolism 2009;58:1248-55.
- 24. Mikines KJ, Sonne B, Farrell PA, Tronier B, Galbo H. Effect of physical exercise on sensitivity and responsiveness to insulin in humans. Am J Physiol 1988;254:E248-59.
- Tsalikian E, Mauras N, Beck RW, Tamborlane WV, Janz KF, Chase HP, et al. Impact of exercise on overnight glycemic control in children with type 1 diabetes mellitus. J Pediatr 2005;147:528-34.
- 26. Yardley JE, Kenny GP, Riddell MC, Perkins BA, Sigal RJ. The frequency of nocturnal hypoglycemia is not increased with exercise in physically active individuals with well-controlled diabetes. Can J Diabetes 2013;37:S4-S49.
- 27. Tanenbert RJ, Newton CA, Drake AJ. Confirmation of hypoglycemia in the "dead-in-bed" syndrome, as captured by a retrospective continuous glucose monitoring system. Endocr Pract 2010;16:244.

Table Legends

Table 1 - Insulin adjustments and carbohydrate (CHO) intake before and during event

Table 2 - Insulin adjustments and carbohydrate (CHO) intake immediately post-race and in the evening after the event

Figure Legends

Figure 1. A) Continuous glucose monitoring profiles as measured during the event for one control participant without diabetes (participant 1), and six individuals with type 1 diabetes (Participants 2-7). B) Continuous glucose monitoring profiles for all participants in the 12 hours post-exercise. C) Post-race nocturnal continuous glucose monitoring profiles for all participants.

Figure 2. CGM glucose profiles for 6 participants with type 1 diabetes demonstrating different approaches to blood glucose management during competition as compared to a control participant without diabetes.

Participant	HbA _{1c}	Insulin Delivery	Pre-race CHO (g)	Pre-race insulin adjustment	Ride time (mins)	Race CHO (g)	Hypoglycemia during race (y/n)
1	N/A	N/A	68	N/A	179	102	N/A
2	11.7	MDI	120	Evening glargine \downarrow 33%	227	105	No
3	9.5	MDI	34	None	244	7	No
4	7.6	MDI +	54	$20\% \downarrow$ pre-race evening glargine,	123	53	Yes
		CSII		basal rate suspended during race			
5	6.9	CSII	115	↓ basal rate to 25% 1-hour pre-	135	165	Yes
				race			
6	7.4	CSII	33	None	177	156	Yes
7	6.6	CSII	53	\downarrow basal rate to 40% 1-hour pre-	176	103	No
				race			

Participant	Post-	Post-race insulin adjustment	Total	Evening	Total evening	Overnight	Nocturnal
	race		afternoon bolus insulin	CHO (g)	bolus insulin	insulin adjustments	hypoglycemia (y/n)
1	110	N/A	N/A	144	N/A	N/A	N/A
2	170	Regular bolus for food	9	56	3	Evening	No
3	116	(insulin lispro) Regular bolus for food (insulin lispro)	11	117	11	glargine ↓ 33% None	No
4	140	Multiple small adjustments + regular bolus for food	6.9	132	6	Regular basal	No
5	10	Multiple small adjustments + regular bolus for food	13.55	66	4.55	Regular basal	No
6	160	One large adjustment + regular bolus for food	9.5	152	4.95	Regular basal	No
7	103	Multiple small adjustments + regular bolus for food	4.9	52	6.9	Regular basal	No





7 (CSII) Race 22 20. CGM glucose (mmol/L) 18-40% basal rate 16 14 asal resumed 12 10 2 9am 12pm 3pm 6pm 9pm 12am 3am 6am 9am Time of day