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CONFERENCE REPORT

Blood glucose changes in diabetic children and adolescents engaged in most common sports activities

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Abstract. Circulating insulin levels decrease and substrate glycogenolysis-mediated conversion into glucose increases just a few minutes after normal subjects start exercising, but during sustained physical activity muscles massively utilize blood glucose, thus causing glycogenolysis to increase further until the end of the session. After that, in order to get liver and muscle glycogen stores up to pre-exercise levels again, blood glucose is mostly utilized, thus causing late-onset hypoglycaemia in the absence of any extra carbohydrate supply and rebound hyperglycaemia after a while. This and other patho-physiological mechanisms are dealt with in the present paper, and practical hints are provided to the clinician to cope with children-specific adaptation phenomena to exercise in t1DM. (www.actabiomedica.it)

Key words: Type 1 diabetes mellitus, sports, children, hypoglycaemia

Diabetes mellitus type 1: overview of pathophysiology

Circulating insulin levels decrease and substrate glycogenolysis-mediated conversion into glucose increases just a few minutes after normal subjects start exercising (1). This mechanisms protect the organism against hypoglycaemia and at the same time allow for continuous glucose flow into the muscles to replace molecules removed by continuous metabolic breakdown. This is how circulating glucose levels keep within the normal range even when exercise lasts for hours. In patients with Type 1 Diabetes Mellitus (T1DM) - also known as Insulin-Dependent Diabetes Mellitus (IDDM) -peripheral hormone concentrations depend only on insulin injected amount and pharmacological formulation as well as on time elapsed since the last administration. Patients have to progressively acquire the ability to effectively reduce insulin dosage to mimic physiological adaptations as close as possible.

Nevertheless, due to the fact that the subcutaneous route of administration is not close to physiology, T1DM subjects inevitably get higher insulin levels than their non-diabetic counterparts. As a consequence of that, insulin levels keep inappropriately high during exercise, thus increasing the risk for hypoglycaemia by decreasing glucose output through inhibited glycogenolysis. This explains why it is necessary to provide exercising T1DM individuals with a "wisely" tailored glucose supply. Conversely, in the case of metabolic failure due to low insulin levels, exercising muscles are unable to utilise glucose and therefore resort to circulating fatty acids and to freshly produced ketones. At the same time, as insulin levels are low, liver glucose output through glycogenolysis is enhanced and therefore circulating glucose – being unable to enter the muscles - become inappropriately high, thus endangering patients through severe hyperglycaemia and ketosis (2).

Nutrient metabolism during sports activities

The main oxidised substrate during at least 30 to 60 min non-strenuous exercise (60-70% VO_2 max) is represented by carbohydrates (CHO). Clinical evidence has progressively accumulated in favour of the need of a high CHO supply in order to have DM patients keeping at good nutritional standards and preventing hypoglycaemia. In fact, adult endurance athletes utilize up to 8-10 grams CHO per Kg body weight per day, i.e. 560 grams or more CHO per day.

Secondarily, CHO body content in human adults is just less than 300 grams. This includes muscle and liver glycogen (summing up to 79% and 14%, respectively) plus free and intra-globular circulating glucose (7%, i.e. 20 to 21 grams). Such consideration shows that CHO stores theoretically allow for only moderate exercise (EX) activities lasting up to 3 hours at most.

A generous CHO supply is indicated in diabetic athletes (DA) also to preserve liver and muscle glycogen stores, which prevent fatigue and muscle weakness from causing the discontinuation of effective sports performances. Adequate glycogen stores in fact, are essential for liver and muscle glycogenolysis to prevent and/or immediately counteract hypoglycaemic attacks as well as to assure DA's a fast recovery from it (3).

Protein metabolism supports total energy expenditure (TEE) only by a limited amount during Physical Activity (PA). During one hour EX at 60% VO_2 max, protein oxidation has been calculated to contribute to TEE by 4 to 5% at most, but may increase to 8 to 10% when glycogen stores are depleted, thus causing protein waste, which – in turn - negatively affects performance. This is another reason for maintaining and rebuilding appropriate liver and muscle glycogen stores (4).

Also lipids, especially non-esterified fatty acids (NEFA's) and triglycerides, undergo oxidation in non-diabetic as in IDDM subjects during EX.

During low intensity PA (40 to 50% VO_2 max) NEFA's contribute to TEE by about 40% for the first hour and up to 70% thereafter, at least until the 4^{th} hour (5) (Fig. 1). As exercise intensity increases, more glucose is preferentially oxidised by muscles instead of NEFA's, but this holds true especially in the untrained athlete, as NEFA's become the favourite energy source in trained subjects.

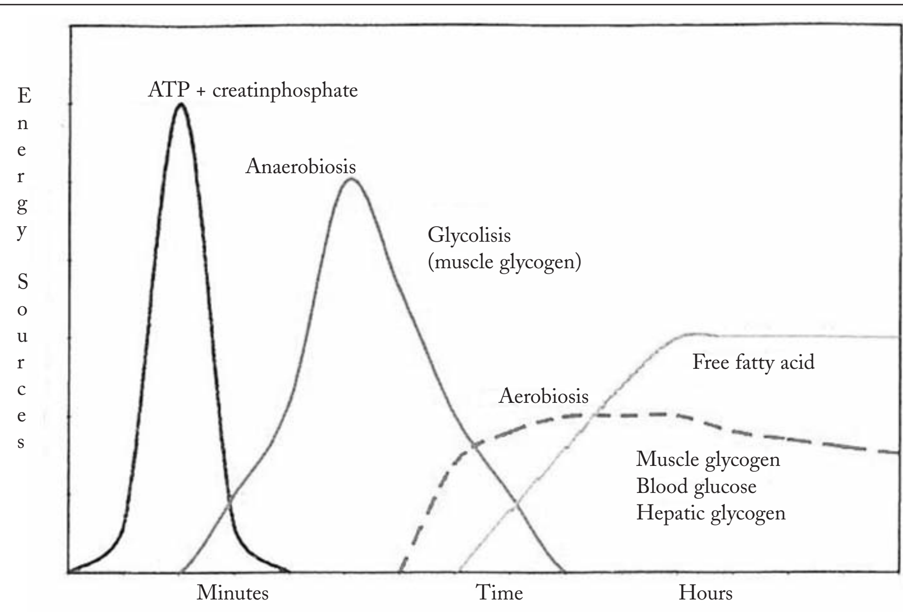

Figure 1. Preferential nutrient utilisation with respect to sports event duration

That's why T1DM patients are typically advised to choose low intensity and long duration EX regimens: this way they utilise glucose slowly and gradually, thus running a lower risk for hypoglycaemia, and exploit the benefits of full NEFA oxidation, provided they keep under totally aerobic conditions. The effects of preferential NEFA oxidation with respect to glucose are:

1. high energy yield
2. high ATP production
3. low glucose fluctuations
4. glycogen store saving with consequent fatigue prevention
5. lower circulating NEFA and triglyceride levels, which decrease insulin resistance and needs.

Due to the above mentioned reasons, endurance sports activities are recommended for DM patients, provided they keep under anaerobic threshold (Table 1).

Table 1.

Aerobic sports activities	Anaerobic sports activities
Jogging	Soccer
Skating	Tennis
Low speed running	Volley
Slow speed country skiing	Basketball
Slow speed swimming	Downhill skiing
Slow speed cycling on the flat	Body building
Aerobic dance	High speed or competition track cycling

Energy Expenditure (KCal/h) associated with main sports activities is shown in Table 2.

Adequate calorie intake is best evaluated by taking into account daily food nutritional supply and

Table 2. Hourly Energy Expenditure (EE, Kcal/h) (according to Kesterer and Knipping)

Sports activity	Hourly EE	Sports activity	Hourly EE
Running on flat			
short distance	500	Weight lifitng	450
mid-distance	930		
long-distance	750		
Discus throwing	460	Boxing	600
Shot putting			
on track	220	Fencing	600
on the road	360		
on the road against the wind	600		
Cycling		Basketball	600
high speed	450		
long distance	700		
Jump			
high/long	400	Handball	600
Skiing			
downhill	960	Football	400
country	750		
Skating			
figure	600	Rugby	500
speed	720		
Speed walking	350	Swimming	450
Tennis			
single	800	Water polo	500
twin	350		
All-in wrestling	900	Rowing	500

monitoring body weight and usual hanger sensation; nevertheless, when glucose metabolism is not kept at optimal levels, any additive food intake is useless, as extra glucose gets lost in the urine.

Peculiarities of energy metabolism in T1DM children (6)

- alactacidic-anaerobic metabolism (ATP + Phosphocreatine [PC]) is very active
- NEFA and CHO oxidation is often only partial, like in anaerobic lactacidic metabolism
- aerobic alactacidic metabolism is delayed (being specific enzyme systems still immature)
- children performances are therefore excellent in short duration activities requiring mostly muscle elastic tension and explosive strength
- the consequences of all above-mentioned phenomena are:
  - immediate or late onset hypoglycaemic attacks (due to glycogen rather than glucose or NEFA preferred utilisation)
  - hyperglycemia (due to huge adrenergic counter-regulation typical of explosive efforts)

Cardio-circulatory adjustment mechanisms may be classified as central (involving mainly the heart) or peripheral (involving mainly large and small vessels). During pre-pubertal age stroke volume (SV) is lower, so that maximal cardiac output (CO) is maintained at appropriate levels by a proportional increase in maximal heart rate (HR), eventually reaching as hìgh as 205-210 beats per minute. Cardiovascular adaptation to physical strain involve mainly district muscle blood flow, which reaches up to 80% whole body blood flow levels from starting 15% values. Children cardio-circulatory adaptation mechanisms are strikingly different from those occurring in adults. First of all, the former have a lower CO, due to the inability of HR to compensate for lower SV. This, together with lower haemoglobin levels and higher artero-venous oxygen discrepancy causes a reduced aerobic power in children than in adults. From 6 years on, maximal aerobic power corrected by body weight exponentially increases until the age of 18 in males and until the age of 10 or so in females. Then latter phenomenon depends on the fact that between 10 and 14 years of age girls undergo puberty, which causes an increase of their percent body fat mass, known to be functionally inactive (7).

When taking into account the above reported considerations, matches or any competitive sports activities may become a further factor perturbing glucose homeostasis in children and adolescents with T1DM. In fact, circulating insulin is not easily kept at as low and decreasing levels as those required to just allow glucose to enter muscle cells in T1DM subjects and young people metabolic / cardiovascular features make such aerobic alactacidic activities much more difficult – despite more useful – than anaerobic lactacidic and alactacidic ones. This is why glucose fluctuations will be more evident and frequent in the young T1DM, often leading to “hypo’s” and “hyper’s”.

Exercise hypoglycaemia

Exercise hypoglycaemia is due to enhanced insulin sensitivity combined with reduced glycogen stores as a consequence of increased energy expenditure.

Some children may wrongly interpret hypoglycaemic symptoms as exercise fatigue, thus easily running into a severe hypoglycaemic attacks immediately after exercise. Conversely, due to the fear of a “hypo”, some other take excess food as snacks or even refrain from exercising (8). “Hypo’s” may be easily prevented by taking a snack before, during or even after exercise, depending on the kind of activity (prevalently aerobic, anaerobic or mixed) and on its timing with respect to meal and insulin dosage/formulation.

When choosing the kind and amount of a snack, it is important to take into account exercise intensity/duration, how much insulin is expected to be active during and after it, and finally when the meal has taken place.

Young people snack and general meal planning should reflect time dedicated to organised and spontaneously occurring physical activity every day. Those who interact with the young T1DM, namely parents, trainers, metabolic fitness operators, friends and team companions, should all be well aware of hypoglycaemic symptoms and always keep snacks, sugar, hypotonic sweet drinks (as sugar concentrations higher than

10% may cause osmotic diarrhoea) ready aside the field or in child's bag (9). This is also a good reason for parents to take part to their T1DM child's games whenever possible - or at least to keep close to the place - during his/her first sports events. On the other hand, the medical doctor (or the nurse) who takes care of the group has to reassure the child and his/her parents that any eventually occurring hypoglycaemic attacks do not force the player to stop and leave the field after the episode has been efficiently solved. Even better, it is more appropriate and reassuring to encourage game continuation after that.

In any case, it has to be stressed that T1DM children performing long-duration aerobic exercise undergo frequent hypoglycaemic attacks which are often refractory to the oral glucose supply of 15 grams supposed to be useful in the adult. Hypoglycaemia occurring during sports activities may be dangerous in children and deleterious for physical performance in young people. Despite the relevant role of exercise and sports in many young T1DM patients' lives, specific recommendations are still lacking, which might be helpful for relatives and family doctors to better face exercise-related excess blood glucose fluctuations. In such cases orally administered glucose at a dosage as high as 35 to 45 grams might result to be appropriate to efficiently treat hypoglycaemia occurring during exercise (10).

Exercise hyperglycemia

Exercise hyperglycaemia depends on insulin deficiency. When blood glucose (BG) exceeds 250 mg/dL a urine test has to be performed for ketone determination. If urinary ketone test is positive, exercise has to be delayed until it turns back to negative again. If ketones are not found in urine, then exercise can start, provided BG does not exceed 300 mg/dL. Actually, BG may sometimes be very high immediately after competitions or intensive exercise bouts as a consequence of high adrenergic output (11). Under such circumstances, in the absence of ketonuria – which suggests insulin levels to be adequate for glucose metabolism -, a good strategy might be to significantly reduce pre-exercise snacks for the future. Another possibility is to reduce snacks just a little, provided insulin dosage is re-evaluated in case of repeated hypoglycaemic events. IF PA is programmed to occur one or two hours after the meal, it might be useless to add a snack before, but it is wise to supply the child with CHO during or after the session.

Anyway, PA timing is thought to be ideal about 3 to 4 hours after regular insulin administration, 8 hours after intermediate insulin and 90 to 180 min after Lyspro or Aspart analogues, because this way insulin levels tend to be neither too high nor critically low (12, 13).

Twice a day premixed (fast- and slow-acting), slow-acting or even ultra-lente insulin regimens are seldom chosen for children: in any case they are not compatible with adequately safe EX programs.

Blood glucose changes with reference to some usual sports activities in children and adolescents with IDDM

Due to continuous developmental muscle-skeletal system changes, physical activity has to be graded according to age throughout childhood, also taking into account individual skills and metabolic enzyme maturation rate.

Table 3, which has been prepared according to the indications given by the American Alliance for Health, Physical Education, Recreation and Dance (14), shows major recommended activities with respect to age and developmental stage.

All above points to the fact that T1DM patients, even during pre-pubertal age, may reach excellence (getting Olympic medals, sometimes) in anaerobic exercises, either lactacidic or alactacidic, like art gym, horse riding, parallel bars, 100 or 200 meter swimming, but are not performing at all when engaging into aerobic alactacidic long-distance competitions.

According to the well known aphorism "fat burns completely in sugar-fed fire", a T1DM child is expected to mostly and incompletely utilize NEFA rather than glucose, if ketones are often found in his post-exercise urine specimens.

Last but not least, acute physical stress causes severe lactic acidosis and a more pronounced adrenergic hyper-reactivity in T1DM as compared to age-mat-

Table 3

	Early infanthood (3-5 years)	Childhood (6-9 years)	Adolescence (10-12 Years)
Guidelines	No competition. Teach through practice and amusement.	Understate scores to minimise competition. Keep rules flexible. Choose easily performed sports activities.	Start encouraging individual skills through specific training for real sports competitions.
Recommended activites	Free play, short distance walking, running, jumping, swimming, somersaulting.	Gym, biking, skating, swimming. Start supporting team games.	Football, swimming, tennis, bike, volley, art gym, dancing, sailing.

ched children (11). Consequently, when trying to cope with glucose changes in exercising children and adolescents, one should take into account the following factors:

Kind of activity	• Aerobic
	• Anaerobic
Timing of activity	• Post-meal
	• Among meals
	• Pre-meal
Activity duration	• 3 shots
Insulin regimen	• 4 shots
	• > 4 shots
	• CSII (i.e. PUMP)
	• Glargine
Spot BG levels	
Usual post-exercise BG Levels	

Aerobic alactacidic activities (30' - 60' Duration)
(long distance running or skiing, marching, cycling, long duration indoor swimming)

Energy supply from: glucose, NEFA's, glycogen

Energy expenditure: hundreds of calories

Effects upon glucose: progressive and programmed decrease

Other consequences:
- enhanced insulin efficacy (decreased requirements)
- possible weight decrease
- training effect (VO_2 max increase)
- low-impact acute cardiovascular stress (when really occurring)
- enhancing effect upon psycho-motor development

Figure 2.

Anaerobic lactacidic activities (1' - 5' duration)
(400-800 metres hurdles, anaerobic phases during team games, art gym, art dance, ice-skating, 100-200 metres swimming competitions)

Energy supply from: mainly glucose and glycogen

Waste product: lactate

Effects upon glucose: proneness to
- exercise and late onset post-exercise hypoglycaemia
- transient stress hyperglycaemia

Other consequences:
- moderate cardiovascular stress
- low energy performance

Figure 3.

Different kinds of exercise cause different effects in terms of glucose metabolism and other physiologic parameters, as shown by Fig. 2 and Fig. 3.

Let's now comment upon some clinical cases.

Sample clinical cases

Anaerobic activity

Alex, 18 years of age, T1DM since he was 8, under a 4 shot regimen (fast acting analogue plus glargine) summing up to 66 units per day, HbA1c 8.0%, plays volley and smashes as often as possible all games long. His team role requires him to perform a rather continuous series of fast-occurring, short-lasting movements within the field, which provide a typical example of anaerobic lactacidic activity, and by extremely acute movements (like jumping and smashing) requiring anaerobic alactacidic metabolism. Such exercise is therefore classified as an anaerobic mixed (lactacidic and alactacidic) activity.

Due to previously described mechanisms, Alex is always hyperglycaemic immediately after the match (recently enough his BG was 145 mg/dL before the match and 293 mg/dL after it), but he rather often experiences also post-match late onset nocturnal hypoglycaemia, probably due to the need for synthesising again liver and muscle glycogen stores depleted by anaerobic lactacidic metabolism (recent night BG as low as 52 mg/dL). Such oscillations may be at least partially flattened down by a very low pre-match insulin dose administration (e.g. 1-2 U "paradox bolus") and a reduction by up to 30% of long-acting bed-time insulin dosage. A snack is often needed two hours after the match to compensate for the lack of previously active hyperglycaemia-inducing adrenergic counterfiring, along with another snack at bed-time to prevent nocturnal hypoglycaemia.

In this case, utilised "fuel" is mainly represented by glucose and glycogen partially oxidized through anaerobic pathways, besides muscle fast-recycling ATP and phospho-creatine required for explosive activities.

Aerobic alactacidic activities

Mauro, 16 years of age, T1DM since he was 9, with a recent HbA1c of 6.9%, is under the following CSII regimen: 0.7 U/h from 24:00 to 07:00 hours, 0.3 U/h from 07:00 to 10:00 hours (0.1 U/h in case of morning exercise), 0.5 U/h from 10:00 to 24:00 hours; variable bolus intensities depending on CHO intake.

Chosen sports: country skiing, which is a typical aerobic alactacidic activity characterised by rather smooth, unchanging and regularly occurring movements repeatedly synchronised with breath rate. Speed and movement frequency may be regulated while country-skiing, therefore Mauro tries to keep them within aerobic conditions, namely under the threshold leading to 60% VO_2max (in his case represented by 147 beats per minute).

This way, during a recent session he managed to keep within the following ranges: BG 141 mg/dL at wake (07:00 hours), followed by breakfast (milk, biscuits and corn flakes) and a 4 U insulin shot with a marked reduction of basal rate (0.1 U/h). Just before the training session, at 09:00 hours BG was 204 mg/dL (owing to inactivity due to car-driving from home to the field). At 10:30 hours BG was 153 mg/dL and at 11:00 hours he took a 40 gr CHO snack with an isotonic drink, stopped for 15 minutes and then started training again. At 12:00 hours BG was 134 mg/dL and at 12:30 hours it dropped again to 84 mg/dL. This was a typical case of alactacidic aerobic activity implying mainly glucose utilisation during the first 30 to 40 minutes and therefore leading to some degree of hypoglycaemia just as expected from what we reported above (10), followed by prevalent NEFA utilization. In fact, an approximate NEFA/CHO ratio of 70/30 allows complete aerobic NEFA oxidation and causes a progressive and programmed BG decrease accordingly.

References

1. Galbo H. Hormonal Adaptations to Exercise. New York, Thieme-Stratton, 1983.
2. Wasserman DH, Zinman B. Fuel Homeostasis in "The Health Professional's Guide to Diabetes and Exercise". ADA Clinical Education Series, 1995: 29-47.
3. Corigliano G. L'attività Sportiva in Atti Della Tavola Rotonda: "Diete e Diabete ai Confini Tra Fisiologia e Malattia" Abano Terme 14 Febbraio 2002 ed. D.
4. Colberg S. The Diabetic Athelete. Chap. 4. Ed. Human Kinetics 2001: 61-2.
5. Wasserman DH, Lacy DB, Goldstein RE, Williams PE, Cherrington AD. Exercise-inducet fall in insulin and the increase in fat metabolism during prolonged exercise. *Diabetes* 1989; 38: 484-90.
6. Rowland TW. Exercise and Children's Health. Champaign, IL, Human Kinetics Books, 1990: 215-33.
7. Cerretelli P. Manuale di Fisiologia dello Sport e del Lavoro Muscolare. Società Universo, Roma, 1985
8. Bhatia V, Wolfsdorf JI. Severe hypoglycemia in youth with insulin dependent diabetes mellitus frequency and causative factors. *Pediatrics* 1991; 88: 1187-93.
9. Wagenmakers AJM, Brouns F, Saris WHM, Halliday D. Oxidation rates of orally ingested carbohydrates during prolonged exercise in men. *J Appl Physiol* 1993; 64: 2774-80.
10. Tansey MJ. The effects of aerobic exercise on glucose and conterregolatory hormone concentrations in children with type 1 diabetes. *Diabetes Care* 2006; 29 (1): 20-5.

11. Yasar SA. Sympathetic-adrenergic activity and acid-base regulation under acute physical stress in type 1 (insulin-dependent) diabetic children. *Horm Res* 1994; 42 (3): 110-5.
12. Corigliano G, Turco S, Gentile S, Agrusta M, Perrelli A, Scurini C. Modificazioni Endocrino-metaboliche pre.post esercizio fisico in IDDM trattati con analogo. Atti del XII congresso AMD, Chia Laguna; 1999: 491-5.
13. Heller S. Reduced hypoglycaemia with insulin aspart :a double-blind, randomized, crossover trial in type 1 diabetic patients. *Diabetes* 2001; 50 (suppl. 2): A137
14. Green L, Adeyanju M. Exercise and fitness guidelines for elementary and middle school children. *The Elementary School Journal* 1991; 91: 437-44.

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