Ambient temperature-related exaggerated post-prandial insulin response in a young athlete: a case report and implications for climate change

Sophie Antoine-Jonville, Cécile Faure, Olivier Hue, Stéphane Henri

Ambient temperature-related exaggerated post-prandial insulin response in a young athlete: a case report and implications for climate change

RUNNING TITLE: A case of post-prandial hyperinsulinemia

Sophie Antoine-Jonville[1], PhD-HDR✉ - conception and design, experimental work, data analysis and interpretation, preparation of draft manuscript

Cécile Faure[1], PhD - cecilefaure2203@gmail.com- conception and design, experimental work, data analysis and interpretation, critical revision of the manuscript.

Olivier Hue[1], PR – olivier.hue@univ-ag.fr- overall scientific management, critical revision of the manuscript.

Stéphane Henri[1,2], MD, MSc - stephanehenri7@hotmail.com - clinical work, critical revision of the manuscript

1. Adaptation to Tropical Climate and Exercise Laboratory, EA3596, University of the French West Indies, Guadeloupe, France

2. Orthopedics and trauma center, Academic Hospital of Pointe-à-Pitre-Abymes, Guadeloupe, France

Conflict of interest: none

This manuscript is original.

Trial registration: EudraCT (2013-003206-25); ClinicalTrials (NCT02157233)

CORRESPONDENCE: Dr. Sophie ANTOINE – JONVILLE
Laboratoire ACTES, Université des Antilles
BP 250
97157 POINTE A PITRE Cédex
GUADELOUPE
s_antoine@ymail.com sophie.jonville@univ-ag.fr
Tel: **(+ 590) 590 48 31 75** Fax: **(+ 590) 590 48 31 79**
Tel (cell): **(+ 590) 690 07 77 27**

ABSTRACT

The objective is to present the case of a 21-yr-old athlete observed with non-physiological immediate post-prandial insulin response (1162pmol/l; normal glucose excursion: 6.6mmol/l), in a warm environment. No suspicion or evidence of any underlying pathology was found in this well-trained Afro-Caribbean male runner. He never reported any hypoglycemic episode. When performing the same protocol performed in a cooler environment (21.0°C *vs.* 30.3°C), only physiological responses were observed. We conclude that 1) youth, leanness and regular exercise training are not absolutely protective against glucose metabolism impairment in apparently healthy subjects; 2) ambient temperature should be regarded as a potential source of glucose metabolism impairment.

Key words: environment; heat; diabetes; case study; exercise training

Odd post-prandial insulin response in a young athlete: a case report

INTRODUCTION

Insulin resistance is a metabolic condition known to be associated with diabetes and its macro- and microvascular complications**.** Although exact causes are not completely understood, experimental and epidemiological evidence incriminates excess weight and physical inactivity as major contributors to insulin resistance development.[1] Here we divulge the unexpected case of a fit middle-distance runner considered as healthy who presented non-physiological insulinemia.

CASE REPORT

An athlete who had been included in one of our nutrition studies presented exaggerated post-prandial insulin response (1162pmol/l; electrochemiluminescence immunoassay method; sample double-checked) during his participation in a protocol research in nutrition with published results.[2] Plasma glucose remained normal (6.6mmol/l). After approximately 10 hours of fasting, he arrived at 6.45AM at the lab deliberately heated (30.3°C) for the purpose of the experiment. He had to rest down in a semi-recumbent position during 90 minutes. Then, he sat 30 minutes alone in a non-stimulating environment for an *ad libitum* meal of small ham and cheese sandwiches (799kcal, 25.7% proteins, 33.2% carbohydrates, 41.0% lipids), widely appreciated in Guadeloupe. He finished his meal within 20 minutes. The food was proposed in abundant quantity, on a plate weighted before and after the meal, the participant being unaware of the fact that food intake was a study outcome. The water intake during the meal was 275mL (4ml/kg). He had blood sampling at different

time points of the session before the meal, and 35 minutes after starting the meal.

The patient is a healthy 21-yr-old Afro-Caribbean middle-distance runner (800m-1500m) performing at the regional level. He is 1.84m tall, 68.8kg body mass and 9.5% body fat mass (Multi-frequency bioelectrical impedance analysis: InBody S10®, Biospace Inc, Japan). He had met all eligibility criteria of the study: absence of identified chronic or acute pathology, any other limitation to exercise, absence of any food allergy or eating disorder (normal score at the three-factor eating questionnaire), acclimation to tropical climate, regular physical activity (3650METs/min/week), normal birth weight, <2kg body mass variation in the previous 6 months. For the purpose of the study, he underwent a cardiopulmonary exercise test and a general dietary investigation. He had been training regularly and his maximal oxygen uptake is normal (52.3mlO_2/min/kg, 108.3% of the predicted maximal in sedentary) with excellent endurance objectivized by the ventilatory threshold (67.3% of the maximal oxygen uptake). His dietary pattern is characterized by a daily intake of processed energy-dense food high in fat and low in fiber, and large amounts of carbohydrates – in particular with a high glycemic index.

Further biological and clinical explorations were performed. All values for blood pressure, fasting glucose, insulin, lipid profile, lactate, CRPus, cortisol, IL6, glucagon, leptin, ghrelin, CCK, PP, body water distribution were normal. There was no evidence of *acanthosis nigricans* nor any hepatic or thyroid disease. The athlete reported no episode of hypo or hyperglycemia. He denied doping and was not aware of direct ascendant with diabetes. Other markers and determinants of insulin and glucose metabolism and function such as serum c-peptide or HbA1c were not evaluated and the athlete was not interested in undergoing an oral glucose tolerance test to further investigate potential metabolic disturbance. However, he was re-interviewed 2 years later and declared good health and performance status.

Interestingly, a few weeks after the occurrence of the odd post-prandial response, the athlete performed the same session with 21.0°C ambient temperature (similar time pattern, similar food intake for the last meal of the day preceding the test). His post-prandial response was completely normal in terms of insulin (416pmol/l) and blood glucose (5.5mmol/l), despite the ingestion of a larger quantity of sandwiches (1182 kcal) during the meal.

DISCUSSION

Fitness and leanness are considered as protective against insulin resistance. Here is described a counterexample, in which post-prandial insulinemia is not physiological in a young well-trained athlete with low percent body fat.

None of the criteria used to define the metabolic syndrome were met, whatever the chosen definition.[3] In this patient, the exaggerated post-prandial insulin response does not occur concomitantly with isolated hypoglycemia. Hypoglycemia is listed in the differential diagnosis of most insulin-secreting islet cell tumors and other pathological conditions leading to hyperinsulinism. Acute and chronic diseases that affect the pancreas, liver, kidneys, thyroid and adrenal glands would be compatible with transient exaggerated post-prandial insulinemia. In particular, insulinoma and other endocrinopathies could be suspected. However, none of the conditions to consider their diagnosis was present given the convergence of normal values for the biomarkers and the absence of symptom. For example, fasting glycaemia and insulinemia was measured at rest 12 times on 4 separate days. Only physiological values were observed (minimum and maximum were 3.7 and 4.6 mml/l and 34 and 179pmol/l for glucose and insulin, respectively). Based on available data and on the absence of development of later observable disease, our interpretation is to discard

underlying pathology. We are not aware of any bias that would explain the observation. Subsequently, environmental temperature is the only identified factor likely to contribute to the abnormal profile described here. Increased glycaemia and/or insulinemia, specifically in ambient temperature above 25°C have been previously reported in healthy subjects[4,5] and pregnant women.[6] Also, this athlete participed in a study which evidenced higher postprandial glucose and insulin levels with heat exposure.[2] Although he was the only one to present a quasi-pathological insulin response in the session performed in a warm environment, the increase in insulin and glucose was observed in most subjects. In the same study but with another group of participants performing a standard glucose tolerance test, the glucose load elicited an exaggerated increase in blood glucose in a warm environment. We therefore suggest that this case is an additional piece of evidence supporting that a warm environment is likely to impair glucose metabolism. This point is of potentially wide clinical relevancy since it could contribute to explain the diabetes burden in warm regions like India or the Pacific islands, where the overprevalence of metabolic pathologies is mostly attributed to genetic factors, jointly with poor diet and physical activity behaviors. Also, if confirmed, this phenomenon calls for better standardization of environmental temperature to improve the accuracy of the analyses of glucose tolerance. It furthermore has to be considered in the context of climate change that has been conceptualized as a risk multiplier as well as a trigger of primary effects on global health.[7] Disturbance of glucose metabolism is a putative additional piece in the burden of disease of climate change.

In conclusion, in light of the present case, fitness and leanness appears as not systematically protective against acquired glucose metabolism impairment. The eventuality that high ambient temperature contributes to transient or even chronic glucose intolerance and/or insulin resistance deserves to be seriously explored.

ACKNOWLEDGEMENTS: This case study was made possible by the recruitment and data collection from a project supported by grants from the European Social Fund (European Commission), Region Guadeloupe (No CR/12-116), the French Ministry of Overseas Territories (No 0123-C001-D971/2013) and from the European Regional Development Fund (PO No 1/1.4/-31793).

We warmly thank Chiraz Agrebi for her excellent revision.

REFERENCES

1. Roberts CK, Hevener AL, Barnard RJ. Metabolic syndrome and insulin resistance: underlying causes and modification by exercise training. Compr Physiol. 2013; 3:1–58. doi: 10.1002/cphy.c11006.
2. Faure C, Charlot K, Henri S, Hardy-Dessources MD, Hue O, Antoine-Jonville S. Impaired glucose tolerance after brief heat exposure: a randomized crossover study in healthy young men. Clin Sci (Lond). 2016; 130:1017-25. doi: 10.1042/CS20150461.
3. Parikh RM, Mohan V. Changing definitions of metabolic syndrome. Indian J Endocrinol Metab. 2012; 16:7–12. doi: 10.4103/2230-8210.91175.
4. Dumke CL, Slivka DR., Cuddy JS, Hailes WS, Rose SM, Ruby BC. The effect of environmental temperature on glucose and insulin after an oral glucose tolerance test in healthy young men. Wilderness Environ Med. 2015; 26:335-42. doi: 10.1016/j.wem.2015.03.002.
5. Akanji AO, Bruce M, Frayn K, Hockaday TD, Kaddaha GM. Oral glucose tolerance and ambient temperature in non-diabetic subjects. Diabetologia 1987; 30:431-3.
6. Schmidt MI, Matos MC. Branchtein L, Reichelt AJ, Mengue SS, Iochida LC Variation in glucose tolerance with ambient temperature. Lancet 1994; 344:1054-5.
7. Butler CD. Climate change and global health: a new conceptual framework – Mini Review. CAB Reviews 2014; 9(27).

FIGURE LEGENDS

Time course of blood glucose (thick lines, diamond markers) and insulin (thin lines, circle markers) in warm (30.3°C, continuous line, closed markers) and cooler (21.0°C, discontinuous line, open markers) environmental temperature.