ORIGINAL RESEARCH

DYSGLYCEMIA: A MISUNDERSTOOD FUNCTIONAL ILLNESS

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ABSTRACT

The disease entities diabetes mellitus (including NIDDM) and hypoglycemia are widely recognized. Another form of blood sugar dysregulation with attending symptomatology is dramatic "peaks and troughs" in serum glucose levels, particularly post prandial. The author proposes that such difficulties, sometimes discussed under the name reactive hypoglycemia, be termed "dysglycemia" for the purposes of clarification, further study, and most importantly, preventive treatment. This article outlines the impact of carbohydrate metabolism in women particularly, and how to assess and naturopathically correct dysglycemia.

INTRODUCTION

Two to four hours after ingesting a meal high in simple carbohydrates one may end up with blood glucose levels below preprandial levels. (1) If this excessive drop in blood glucose is associated with symptoms the patient may be suffering from reactive hypoglycemia (RH). Patients may complain of symptoms such as nervousness, hunger cravings, headache, or mental lethargy. The concept of RH has been discussed for many years in the world of natural (complementary) medicine. Since there is no well-established diagnostic criterion and no real organic lesion, RH has been mainly ignored by the medical community at large. Besides experiencing acute symptomology people who routinely eat high sugar foods may also be dramatically increasing their risk for adult onset diabetes (most frequently non-insulin dependent diabetes - NIDDM). (2) The coffee and donut type of very high simple carbohydrate (CHO) meal poses a particular physiological challenge to the individual who has poor blood glucose regulation. (3) Despite the apparent fact that the medical community largely ignores RH, there are those researchers who appear to understand that people may have poor blood glucose regulation without actually being diabetic. (2) Perhaps a better, more appropriate term for poor blood glucose regulation is dysglycemia, or difficulty regulating blood glucose.

Long term consequences of poor blood glucose regulation have mainly been related to the degree of hyperglycemia as studied in diabetic patients. What may be most important in the short term is the rate at which blood glucose fluctuates, especially in proportion to insulin fluctuations. This statement has some preliminary support by the author's own, unpublished pilot research, in which ten female subjects were asked to fill out a dysglycemia scale (see appendix A) to rate their current clinical symptoms and then submit to a glucose and insulin four hour tolerance test. The author's observations suggested that those subjects who were the most symptomatic had the greatest rate of blood glucose fluctuations. Until the final analysis of all the blood glucose and blood insulin values obtained following a 75 gram sugar load and further study, the previous statements remain speculative. Interestingly, in Davidson's medical textbook in the chapter on diabetes mellitus the authors suggest that an important dietary management strategy of diabetes is to eat in such a way as to prevent glycemic peaks and troughs, i.e., prevent dysglycemia. (4) Taken together the above information suggests that dysglycemia may need to be further explored, rather than just paying attention to absolute levels of blood glucose.

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Diabetes mellitus, especially Type II or NIDDM is an extremely common disorder with a prevalence of 6.2% in Caucasians and as much as 13% of the Mexican American population. (5) Vascular complications are the leading problems in NIDDM patients which significantly contribute to morbidity and mortality in this patient population. The only cost-effective way to treat NIDDM is by prevention. (4) Recognizing and naturopathically treating dysglycemia may well be an important step in preventing "full-blown" dysglycemia, namely NIDDM. (2)

PHYSIOLOGICAL REGULATION OF BLOOD GLUCOSE

The symptoms most readily associated with dysglycemia are central nervous system related, including but not limited to anxiety, irritability, extreme hunger, carbohydrate cravings, fatigue, and poor concentration two to four hours following a high carbohydrate meal (see appendix A for further associated symptoms). These symptoms are not surprising in light of the fact that approximately two-thirds of daily blood glucose is taken up by the brain. (1) Although glucose is not the only fuel source the brain can oxidize it is the main way in which the brain's very high energy needs are met. Given that glucose is a favored fuel substrate by all cells of the body it is important to ensure that blood glucose be maintained in order to prioritize meeting the metabolic needs of the brain, even when metabolic demands of non-CNS cells are increased: A number of hormones are critically important in regulating blood glucose. Besides insulin these include cortisol, glucagon, epinephrine, and to a lesser extent growth hormone. (1)

Presumably, if the aforementioned hormones are regulated properly, blood glucose will remain in balance. Insulin is considered to be the main hormone in control of blood glucose. Insulin has a net effect of decreasing blood glucose by promoting the uptake of glucose into all kinds of muscle cells, adipocytes, and indirectly hepatocytes. (6) Insulin will also increase the cell's oxidation of glucose and promote glycogen synthesis by activating a number of the rate limiting enzymes in these pathways. Epinephrine, cortisol, glucagon, and growth hormone (the counter-regulatory hormones) have the net effect of increasing blood glucose by either stimulating gluconeogenesis, hepatic glycogenolysis, or decreasing peripheral (skeletal muscle) use of blood glucose. (7) When a person is correctly regulating blood glucose, insulin is released when blood glucose increases (i.e., post-prandial) in amounts appropriate to bring blood glucose back to pre-meal levels, but not below. The counterregulatory hormones would be released when blood glucose begins to drop so that blood glucose would never be allowed to drop too low. In other words appropriate sensitivity of the endocrine cells which secrete these regulating hormones to blood glucose levels should dictate good glycemic regulation. It seems plausible that if the endocrine organs which release the aforementioned hormones, including the pancreas, the adrenal cortex, the adrenal medulla, and the anterior pituitary are overtaxed then regulating the output of these hormones may be impaired. Repeated or chronic high levels of stress (physical and mental) may overwork the adrenal glands whereas repeated challenges of high simple carbohydrates may overwork the pancreas. (8) Interestingly, chronic recurrent stress (physical or mental) is known to lead to increased chromium loss, and chromium is especially important for normal blood glucose regulation. (9, 10)

RISK FACTORS/WOMEN AND DYSGLYCEMIA

There are a number of well-established risk factors for NIDDM: obesity, overeating, age, sedentary lifestyle and a genetic predisposition. (4) Mexican Americans and native Americans are considered high risk groups for NIDDM. (11) These factors are also considered risk factors for hyperinsulinemia. (12) Hyperinsulinemia or insulin resistance is now well established as a factor in obesity, hypertension, atherosclerosis, and NIDDM. (13) Insulin resistance is a condition where the blood insulin levels are normal or high, yet the metabolic actions of insulin are diminished due to a probable defect in the sensitivity of the insulin receptor. (14) Possibly the controversy of whether hyperinsulinemia precedes or follows insulin resistance would become clinically unimportant if the focus was rather on the functional problem of dysinsulinemia. It may be that dysinsulinemia and dysglycemia are simply two aspects of the same metabolic problem.

Those risk factors established for NIDDM should probably also be considered risk factors for developing dysglycemia. Other factors common in the American lifestyle may also pose a challenge to maintaining good glycemic control; high alcohol consumption, high stress, inadequate micronutrient intake, low intake of dietary fiber, and possibly being female. People who currently consume alcohol, or are recovering alcoholics, frequently have symptoms which may be remedied by improving blood glucose regulation. The mechanism to account for this association may be based on high sugar intake, a common practice in recovering alcoholics, or possibly their liver function is compromised by overworking to metabolize large quantities of alcohol. Since gluconeogenesis and glycogenolysis happen in the liver, this organ is intimately involved in regulating blood glucose. High recurrent stress, like over-exercising or excessive psychological stresses, can lead to impoverished adrenal gland function and therefore inadequate regulation of cortisol and epinephrine. Appropriate micronutrient intake (e.g., a number of B vitamins) is needed both for the metabolism of glucose and for the normal function of insulin (see natural treatment section for further elaboration). Dietary fiber is also important to slow down the absorption of carbohydrates and therefore help prevent significant blood glucose fluctuations. (15)

If women were really at a greater risk for developing dysglycemia the epidemiological data regarding incidence of NIDDM would report a greater number of women than men developing NIDDM. Two studies have been reported; one found a greater incidence of NIDDM in women, while the other found no difference. (4) It is important to note that a large number of cases of NIDDM may go unreported, thus confounding the possibility of obtaining accurate epidemiological information. (4) As part of a pilot study on dysglycemia the author administered the dysglycemia scale to forty-five naturopathic medical students. The top five scorers were female (well over 100) and the average score for females was 86.5 compared to 62.5 for males. Further evidence that females may be at a

greater risk of developing dysglycemia is gestational diabetes. Normal pregnancy is always accompanied by a hyperinsulinemia and for those susceptible women this extra pancreatic stressor may lead to gestational diabetes (the onset of Type II diabetes coincident with pregnancy). The actual mechanism accounting for gestational diabetes is unclear, but the aforementioned theory is at least a way to understand that certain female hormones which are high during pregnancy can negatively impact insulin and therefore glucose metabolism. The placental hormones, lactogen and progesterone are known insulin antagonists. Further information regarding various female hormones suggest that because of a women's hormonal milieu they are at a greater risk of developing dysglycemia than their male counterparts. Progesterone appears to be able to impair insulin's ability to suppress endogenous hepatic glucose production. (16) A number of studies have found impaired glucose metabolism in women who are taking birth control pills containing synthetic estrogens and progestins or progestins alone. (17,18) Taken together it appears that female hormones, especially progesterone, have a potential to poorly influence insulin and therefore blood glucose regulation.

How to Assess

Clinical presentation together with looking at the risk factors is probably the most accurate and cost-effective determination of who has dysglycemia. Although the author is unaware of any previously published or standardized questionnaire, the dysglycemia scale in appendix A was developed using unofficial publications from medical practitioners who have spent many years in their own practice correlating symptom improvement with naturally treating dysglycemia.[1] Laboratory tests that may be helpful are 2 hour post-prandial blood glucose, a 4 or 6 hour glucose tolerance test, and most appropriately a 4 or 6 hour glucose and insulin tolerance test. A fasting blood glucose is a single, static measurement of blood glucose and therefore cannot provide any information on how someone might be regulating blood glucose. A single fasting blood insulin may be helpful because serum insulin can be used to judge the degree of insulin resistance (hyperinsulinemia). Eades and Eades have suggested that published laboratory normals are not accurate enough and that reference ranges for insulin should be: less than 10 mU/ml = good, 10 -15 mU/ml = mild degree of dysinsulinemia, 15 -20 mU/ml = moderate degree of dysinsulinemia, >20 mU/ml = high degree of dysinsulinemia. (19) Dysinsulinemia would correlate directly with dysglycemia.

Because of the costs, time constraints, and difficulty interpreting glucose tolerance tests, they are probably not necessary to diagnose dysglycemia. However these "tolerance" (better labeled "challenge") tests can be extremely helpful for the patient to see how they respond to a simple sugar load. The interpretation of these tests has varied, including; total area under the curve, an H-index, and the ratio of the level of glucose to insulin in an effort to assess glycemic control. (20, 21, 22) Obviously more research needs to be conducted in order to understand the clinical usefulness of these challenge tests, beyond using them to simply diagnose diabetes. A challenge test is always a better assessment of a functional rather than lesional impairment. Possibly a more relevant sugar challenge is to give the patient a normal dietary sugar load such as a fruit drink rather than the standard, but dietarily unrelated load of pure glucose.

At this time it may be most useful and convenient to do a fasting blood glucose, a 2 hour post-high carbohydrate meal and measure blood glucose and insulin at these same time points. Although these tests may not be necessary for the clinician to diagnose dysglycemia, they may be helpful to 1) monitor progress, 2) motivate the patient to make important dietary changes, and 3) get some more information as to degree of dysglycemia. If glucose and insulin are measured perhaps the interpretation of Eades and Eades could be useful. They suggest that the "normal" glucose to insulin ratio should be over 7 (glucose in mg% units and insulin mU/ml units). (19)

Natural Treatment Options

A large variety of micronutrient and herbal preparations have been reported which can improve glycemic control in NIDDM patients and even treat a number of the vascular complications. A recent review of these natural treatments was published in the *Herb Quarterly*, Spring 1996. (23) The chapter on diabetes mellitus in the *Textbook of Natural Medicine* also has a good review on natural treatments for diabetes. (24) Suffice it to say that an adequate intake of micronutrients is important for both optimal insulin function and appropriate glucose metabolism, especially chromium, magnesium and zinc. (25-28) The intakes of these micronutrients are often low in people consuming the standard American diet. Women consuming low or moderately low calorie diets (1000 - 1300 Kcal/d) in an attempt to lose weight are especially vulnerable to inadequate intake of the minerals noted above. Magnesium can easily be obtained from the diet if intake of fresh fruits, nuts and seeds is increased. The most reliable way to increase dietary zinc and chromium is via eating seafoods (both plant and flesh) and adding nuts and seeds to the diet.

Instead of reviewing all the natural treatments which can be effective in full blown diabetes this article will focus on those natural treatments which may be especially helpful and simple to implement to treat dysglycemia/dysinsulinemia. In other words the focus will be on dietary changes rather than on product supplementation. Possibly one of the most helpful short and long term treatments of dysglycemia is altering the proportion of macronutrients in the diet. Several studies using Australian Aborigines found that blood glucose is better controlled in both diabetic and non-diabetic subjects when these people went back to live in the Australian back country and returned to their native diets. (29, 30) The main difference between the modern diets that the aborigines had adopted living in the cities compared to their native diets was the proportion of protein relative to the amount of total carbohydrates. Analysis of diets of hunter-gatherer populations suggest that the macronutrient proportions they consumed were about

[1] The author obtained a symptom list of Dr. Paavo Airola (from his book entitled; *Hypoglycemia: A Better Approach*) and Dr. William Mauer at the Oxidative Medicine Conference in March of this year in St. Louis, Missouri where Dr. Mauer gave a presentation on his many years experience of treating "carbohydrate metabolism imbalance."

40% carbohydrates, 30% protein, and 30% fat. (31) These proportions are similar to the native Aboriginal diet.

The difference between these native diets and those currently recommended by the American Diabetes Association (ADA) is the amount of total carbohydrates (complex or simple) and the amount of protein. The Diabetes Association recommends 50-60% of total calories as carbohydrates. The reasoning behind not following the ADA recommendations, but instead having a higher percentage of protein and lower percentage of total carbohydrates is based on the hormonal changes which occur when a meal has a certain proportion of carbohydrates compared to protein. A study was conducted which suggested that if the protein/carbohydrate (g/g) ratio was .75 or higher then the release of insulin would be much lower. (32) If insulin is not being released as often or at such high levels following meals then there will be less stress on the pancreas and less fluctuation in blood glucose. In other words adequate protein can help keep blood glucose levels more even throughout the day. This concept is elaborated in more detail in both reference (19) and the book *The Zone.* (33) The author thinks that it is particularly important to maintain total protein intake in accordance with individual needs, rather than simply using a population norm such as the RDAs. An individual's protein needs can be determined by figuring out their lean body mass and factoring in their degree of physical activity. In order to maintain good glycemic control throughout the day all meals and snacks should have the protein/carbohydrate (gram/gram) proportion of .75 or above. Reference 19 and 33 can be used to help an individual estimate their protein requirement. An example is that a female who weighs 140 pounds, with 25% body fat, and who is very physically active may require 65 grams of protein daily, whereas a same sized women, but sedentary may only require 55 grams of protein daily.

One particular micronutrient that is often found to be low in the American diet and is difficult to obtain in sufficient quantities from the diet is chromium. (34) Chromium's role in the body is well-established as an enhancer of insulin function. (35) Numerous studies have found that 200 µg or 400 µg of chromium picolinate can improve glycemic control in diabetic patients. (36, 37) More specifically related to dysglycemia/dysinsulinemia, several studies have found chromium picolinate to lower fasting blood glucose in non-diabetic subjects. (38, 25)

	Before			2 weeks			4 weeks		
	CHO	Prot.	Fat	CHO	Prot.	Fat	CHO	Prot.	Fat
Total grams:	257	89	58	27	79	34	52	87	34
% calories:	54	18	28	15	43	42	30	40	30
Total calories:		1906			730			862	
dysgly. score:		109						39	

TABLE 1

Although complete analysis has not been finalized on all the subjects in the author's dysglycemia study, one female (39 years) subject was particularly compliant with the dietary changes recommended above and had some good clinical results which are reported in Table 1. The grams and percent calories of macronutrients were obtained from diet diaries which were analyzed using Nutritionist III diet software.

This patient is an excellent example of how helpful dietary changes alone can be, and she is also a good example of the importance of optimal protein to carbohydrate ratio. That is, not just increasing protein intake as a way to help regulate blood glucose, but also decreasing the total carbohydrate load. Because of this subject's especially high dysglycemia score and her very poor reaction to the fruit drink challenge test (not reported here) the author asked that she initially go on a very low carbohydrate diet. Interestingly, this subject had been aware of her blood glucose problems for some years and had increased her protein and cut out most simple carbohydrates as a way to try and remedy her symptoms. These dietary changes were apparently not enough. This subject reported that her energy was improved and more consistent throughout the day and her muscle achiness was gone. She had also lost 12 pounds over a 4 week period and did not feel hungry as before despite her low calorie intake.

CONCLUDING REMARKS

The functional illness of dysglycemia may be an overlooked problem in which physicians of natural medicine can play an especially important role. By recognizing and naturally treating dysglycemia, health problems as diverse as mental lethargy and mood swings to hypertension and difficult weight management may be helped, if not cured. Other problems which may be greatly helped by treating dysglycemia are carbohydrate cravings (39), accelerated aging (40), PMS (39), depression (39), muscle cramps (41), and possibly fibromyalgia. Diseases which may actually be prevented by treating dysglycemia are NIDDM, hypertension, obesity, and atherosclerosis. Although more studies are needed to fully understand this functional problem some simple dietary recommendations, alone or in conjunction with a variety of natural supplements, could significantly impact the health of Americans and create substantial savings in health care costs.

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APPENDIX A

DYSGLYCEMIA SCALE

0: never or almost never have the symptom
1: occasionally have it, effect is not severe
2: occasionally have it, effect is severe
3: frequently have it, effect is not severe
4: frequently have it, effect is severe

DYSGLYCEMIA SYMPTOM LIST

1. Afternoon headaches ..... (0) (1) (2) (3) (4)
2. Awaken after a few hours sleep—hard to get back to sleep ..... (0) (1) (2) (3) (4)
3. Aware of breathing heavily ..... (0) (1) (2) (3) (4)
4. "Butterfly stomach," cramps ..... (0) (1) (2) (3) (4)
5. Can't decide easily ..... (0) (1) (2) (3) (4)
6. Can't start in the morning without coffee ..... (0) (1) (2) (3) (4)
7. Can't work under pressure ..... (0) (1) (2) (3) (4)
8. Crave candy or coffee in the afternoons ..... (0) (1) (2) (3) (4)
9. Cry easily for no apparent reason. ..... (0) (1) (2) (3) (4)
10. Eat when nervous ..... (0) (1) (2) (3) (4)
11. Fatigue, relieved by eating. ..... (0) (1) (2) (3) (4)
12. Get "shaky" if hungry ..... (0) (1) (2) (3) (4)
13. Irritable before meals. ..... (0) (1) (2) (3) (4)
14. Lack of energy ..... (0) (1) (2) (3) (4)
15. Reduced initiative ..... (0) (1) (2) (3) (4)
16. Sleepy after meals ..... (0) (1) (2) (3) (4)
17. Sleepy during day ..... (0) (1) (2) (3) (4)
18. Weakness ..... (0) (1) (2) (3) (4)
19. Symptoms come before breakfast ..... (0) (1) (2) (3) (4)
20. Afternoon exhaustion ..... (0) (1) (2) (3) (4)
21. Depression ..... (0) (1) (2) (3) (4)
22. Insomnia ..... (0) (1) (2) (3) (4)
23. Anxiety ..... (0) (1) (2) (3) (4)
24. Irritability (general). ..... (0) (1) (2) (3) (4)
25. Headaches ..... (0) (1) (2) (3) (4)
26. Dizziness ..... (0) (1) (2) (3) (4)
27. Sweating ..... (0) (1) (2) (3) (4)
28. Internal trembling ..... (0) (1) (2) (3) (4)
29. Palpitation of heart ..... (0) (1) (2) (3) (4)
30. Muscle pain and backache ..... (0) (1) (2) (3) (4)
31. Difficulty in concentration ..... (0) (1) (2) (3) (4)
32. Chronic indigestion ..... (0) (1) (2) (3) (4)
33. Cold hands or feet ..... (0) (1) (2) (3) (4)
34. Blurred vision ..... (0) (1) (2) (3) (4)
35. Muscular twitching or cramps ..... (0) (1) (2) (3) (4)
36. Joint pain ..... (0) (1) (2) (3) (4)
37. Restlessness ..... (0) (1) (2) (3) (4)
38. Obesity ..... (0) (1) (2) (3) (4)
39. Forgetfulness ..... (0) (1) (2) (3) (4)
40. Nervousness ..... (0) (1) (2) (3) (4)
41. Indecisiveness ..... (0) (1) (2) (3) (4)
42. Craving for sweets ..... (0) (1) (2) (3) (4)
43. Moodiness. ..... (0) (1) (2) (3) (4)
44. Allergies ..... (0) (1) (2) (3) (4)
45. Sighing and yawning ..... (0) (1) (2) (3) (4)
46. Peculiar breath or perspiration odor ..... (0) (1) (2) (3) (4)
47. Noise or light sensitivity ..... (0) (1) (2) (3) (4)
48. Mood swings ..... (0) (1) (2) (3) (4)
49. Crave chocolate ..... (0) (1) (2) (3) (4)
50. Crave bread ..... (0) (1) (2) (3) (4)
51. Feeling "spacey" or unreal" ..... (0) (1) (2) (3) (4)
52. Crave alcohol ..... (0) (1) (2) (3) (4)
53. Poor exercise tolerance ..... (0) (1) (2) (3) (4)
54. Night urination ..... (0) (1) (2) (3) (4)
55. Frequent urination ..... (0) (1) (2) (3) (4)
56. Premenstrual symptoms (PMS) ..... (0) (1) (2) (3) (4)
57. Constantly hungry ..... (0) (1) (2) (3) (4)

TOTAL. ..... >_____