

# Assess the Beta-Cell Reserve of Obese Diabetic Patients Who are Taking Insulin Using the C-Peptide to Glucose Ratio, Before Starting A Diet Program that is Low in Sugar, Starch, Saturated Fat, and Sodium

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## BACKGROUND

The global type 2 diabetic rate is on the rise. The medical community suggested that the A1C value is correlated to the diabetic complications and proposed that the A1C should be kept as close to below 7% when possible. Hence more patients have put on insulin and started on insulin earlier than before. One of the risk factors for type 2 diabetes development is insulin resistance. Adding insulin to the treatment regiment can improve glycemic control. However, insulin does not improve insulin resistance. The opposite may happen. Insulin can cause weight gain, which worsens insulin resistance. Since insulin causes weight gain, it is very difficult in helping this group of patients to lose weight. Patients who are taking insulin always have the phobia of hypoglycemia which can be an uncomfortable experience. This is especially true for those patients who need to drive an automobile for living such as school bus drivers and truck drivers. To avoid hypoglycemia, these patients will rather risk hyperglycemia rather than hypoglycemia. So these patients tend to increase their intake, especially the high-carbohydrate food items. Some patients might even eat a carbohydrate-rich meal before going to bed to prevent hypoglycemia during sleep. Insulin plus carbohydrate equals to fat gain. Using medication that can worsen the patient's insulin resistance does not make sense. However, if the patient's glycemic control is poor while already on the maximum oral medication, the physician will have no choice but to initiate insulin treatment. The best way to lower the patient's insulin resistance is through weight loss, especially the fat weight at the abdomen. To help the patient to lose

weight, the most important goal to achieve is to eliminate the medications that cause weight gain and the associated insulin resistance. If the doctor can establish that the patient's beta-cell reserve is still within the guideline, it will be safe to wean the patient off insulin as long as glycemic control is still good. As the patient is controlling the blood sugar with diet, exercise and other lifestyle management skills, it can prevent the deterioration of the beta-cell function. When diabetic patients who are on insulin already when referred to our clinic, we will first assess the beta-cell function to determine if the patient is safe to go on our program which is very low in sugar and starch. It was proposed that the random c-peptide to glucose ratio (C/G) is a good marker to assess the beta-cell function of the pancreas.<sup>1</sup> This paper is written to explain how do we go about assessing this group of patients before starting the patients on our lifestyle management program.

## METHOD

A group of obese diabetic patients on insulin were referred to one of our four centers. Before starting the patients on the diet, a set of blood work was ordered. They include creatinine, urea, magnesium, random glucose, and its corresponding c-peptide level. The C/G was calculated. In Canada, the c-peptide is reported as pmol/L and glucose is reported as mmol/L.

In the United States, the c-peptide to glucose ratio is calculated by dividing the c-peptide in nmol/L by glucose in mg/dL and multiply by 100. To convert the Canadian units to correspond to the United States units, divide the c-peptide result with the glucose result and multiply it by a factor of 0.055.

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All centers utilize the same Tanita Body Composition Analyzer 310 to assess the patients weigh and total fat percentage.

### RESULT

As shown in Table 1, there were a total of 63 patients and they all have a BMI of over 30. The average age was 58 (20-76) years old with 24 males and 39 females. The average random glucose level was 10.5 (3.7 to 22.6) mmol/L and the average c-peptide level

was 1820 (102 to 5660) pmol/L. The normal range of c-peptide as reported by the laboratory (LifeLabs Medical Laboratory Services) was 320 to 1470 pmol/L. The average C/G was 10.33 (1.51-37.92). The cutoff value of C/G for the patient who needs insulin treatment was reported as less than 1.5 (specificity of 80%).<sup>1</sup> Only patient #15 had a serum creatinine level higher than the upper limit of normal (161 mmol/L). This patient was accepted to the program and her subsequent serum creatinine lever monitored.

**Table 1.** C-peptide to Glucose Ratio of Obese Type 2 Diabetic Patients on Insulin

Patient #	Gender	glucose mmol/L	c-peptide pmol/L	c-pep ÷ glu X 0.055	BMI	Body Fat %	% of Body Fat Over the Upper Limit
1	M	3.7	102	1.51			
2	F	4.9	1568	17.58	37.6	31.9	145
3	M	5.2	545	5.76			
4	F	5.6	487	4.78			
5	F	5.8	1415	13.40			
6	M	6	1814	16.61	39.7	34.2	155
7	M	6.1	173	1.56			
8	F	6.3	1583	13.80			
9	F	6.5	494	4.17			
10	M	6.8	375	3.03			
11	F	6.8	3340	26.98	60.4	56.5	134
12	F	7	865	6.79			
13	F	7.1	3626	28.05			
14	M	7.3	1048	7.89			
15	F	7.4	752	5.58			
16	F	7.6	1823	13.18			
17	F	7.8	1491	10.50			
18	F	8.1	1095	7.43			
19	M	8.2	2420	16.21	41.6	62.3	283
20	M	8.2	5660	37.92	44.4	41.1	187
21	F	8.4	2630	17.20	52.8	56	165
22	M	8.5	2474	15.99	41.5	43.3	197
23	M	8.5	750	4.85			
24	M	8.8	1862	11.62			
25	F	8.8	3084	19.25	38.6	53.7	158
26	F	8.9	3896	24.05	56.6	51.3	151
27	M	9	1537	9.38			
28	M	9	402	2.45			
29	F	9.2	1361	8.13			
30	M	9.2	4641	27.71	28.6	33.4	152

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31	F	9.4	1754	10.25			
32	M	9.6	2307	13.20			
33	M	9.7	986	5.58			
34	F	9.7	1747	9.89			
35	F	10.1	1956	10.64			
36	F	10.3	1637	8.73			
37	M	10.3	4655	24.83	39.9	42.8	195
38	F	10.4	1265	6.68			
39	F	10.6	1834	9.50			
40	F	11.3	2245	10.91			
41	F	11.3	2245	10.91			
42	F	11.3	1712	8.32			
43	F	11.5	2530	12.08			
44	F	11.7	1792	8.41			
45	M	12	408	1.87			
46	M	12.1	2211	10.04			
47	F	12.1	530	2.41			
48	F	12.5	1048	4.61			
49	F	13.4	1310	5.37			
50	F	13.6	1983	8.01			
51	F	14.1	979	3.81			
52	F	14.1	1626	6.33			
53	M	14.5	2898	10.98			
54	F	14.6	2485	9.35			
55	M	14.8	1895	7.03			
56	F	15.2	2536	9.16			
57	F	15.3	598	2.15			
58	M	15.5	1945	6.89			
59	F	16.6	1813	6.00			
60	F	18.2	2396	7.23			
61	M	18.7	2247	6.60			
62	F	21.1	2074	5.40			
63	F	22.6	1684	4.09			

**DISCUSSION**

A commonly quoted study is the UKPDS study that suggested that despite lifestyle treatment and medications, blood glucose will continue to go up with time.<sup>2</sup> Beta-cell reserve will deteriorate and most patients will need to go on insulin replacement treatment in about twelve. Hence, when the patient's glycemic control is sub-optimal, insulin treatment is initiated. The patient was told by the clinician that to no fault of the patient, the pancreas no longer able

to produce enough insulin and it is pertinent that the patient starts insulin to get to better glycemic control. In most cases, there is no investigation on the beta-cell reserve done before starting on insulin treatment. Most type 2 diabetic is overweight or obese and suffering from insulin resistance. Insulin treatment can cause weight gain and can worsen the patient's insulin resistance. With the worsening of the patient's insulin resistance, a higher dosage of insulin will be needed which in turn causes further weight gain

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and insulin resistance. Weight reduction and not by insulin treatment is the best way to lower the patient's insulin resistance. More recent studies had raised the possibility that declining beta-cell function in type 2 diabetic patients can be arrested or reversed with intense treatment.<sup>3</sup>

In our diet clinics, there are many obese type 2 patients using insulin who were referred to our clinic for weight reduction and better glycemic control. The patient was given a list of food items that are suitable to consume and a list of food items that have to be avoided. In short, avoid sugar, starch, bad fat and sodium. Eat a diet mainly of good quality protein, omega-3 and omega-6, and vegetables with high fiber contents. The patient does not have to measure or count the calories but to eat until full. Include protein and good fats at each meal. It is not how much but what the patient consumes to achieve the weight loss goal and to obtain better glycemic control.

Putting a patient who has good beta-cell reserve but is taking insulin, on a low sugar and starch diet, this patient is at risk of developing hypoglycemia. Hence, insulin dosages have to be adjusted before starting on the diet. The goal is to achieve weight reduction and good glycemic control by lowering or eliminate the use of insulin. On the other hand, if the patient's beta-cell reserve is gone, then the patient will be considered as insulin-dependent. This patient is prone to develop ketoacidosis if the clinician lowers the insulin dosage to help the patient to weight reduction.

In our program, we assess the patient's dietary habits to identify if the patient was consuming a large quantity of sugar and starch routinely in the past. Instead of starting the patient on diet right away, the patient is asked to do a random serum glucose and random serum c-peptide level. The lower limit of normal according to the LifeLabs Medical Laboratory Services was 320 pmol/L. In this study, only 2 out of 63 patients (patient # 1 and 7 ) had a level lower than this lower limit. Most c-peptide was eliminated by the renal route. If the renal function is poor, the c-peptide level will be artificially over-estimated. The creatinine level of patient # 1 and patient # 7 were normal. If the clinician only relies on the c-peptide level to conclude that these two patients had a poor beta-cell reserve and denied the patient's eligibility to join this diet program, that may not be an accurate assessment.

Most of the c-peptide secretion was triggered by the serum glucose level. Even though the trigger response is blunted in the diabetic patient, this relationship is universal. Yoshifumi Saisho suggested using the c-peptide to glucose ratio as a marker of beta-cell function.<sup>1</sup> That study suggested using 1.5 as the cut off level of C/G to determine if the patient needs to start insulin treatment. That is, if the patient's C/G is less than 1.5, the patient is likely insulin-dependent. According to the c-peptide only, patients 1 and 7 will not be eligible for the diet program. Using the C/G, they were accepted to the diet program. For patient # 1, he lost 40 pounds in 12 weeks and stopped his insulin. His c-peptide increased to 662 and his serum glucose was 8.7. The C/G increased from 1.5 to 4.2. This showed an improvement of his beta-cell function. If the patient continues to lose weight and keep his new lifestyle, he will not need to return to using insulin. Patient #7 is using an insulin pump when he first saw at the clinic. Since his c-peptide to glucose ratio is above 1.5, he was accepted to the diet program. His G/C was repeated after 10% weight reduction and it was increased to 1.8. Patient # 7 had an A1C of 7.2% before joining the diet program and went down to 6.8% after 10% weight reduction.

The upper limit of c-peptide as reported by the LifeLabs Medical Laboratory Services was 1470 pmol/L. Thirty-eight patients had a c-peptide level that is over this upper limit. There were c-peptide to glucose ratio that was 10 times the limit of normal. This means that the patients had hyperinsulinemia already and yet they were treated with insulin. High insulin levels can cause an increase in appetite, hypoglycemia, weight gain and water retention. The patients with C/G that were over 15 had a percentage of body fat that was very high indicating the possibility of insulin resistance. Treatment with insulin does not improve insulin resistance. If the patient gains weight due to the extra insulin, it can worsen insulin resistance. The fastest way to improve on the patient's insulin resistance is by losing the fat weight by diet and exercise.

Type two diabetic patients usually started on oral medication and switched or add on insulin treatment eventually as the beta-cell functions deteriorated with time. It makes more sense to treat the cause of the deterioration rather than keep on adding medications. Other than genetic predisposition, the most common causes of beta-cell dysfunction are glucotoxicity and

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lipotoxicity.<sup>3</sup> Persistent hyperglycemia impairs glucose-stimulated insulin secretion and insulin biosynthesis which eventually leads to beta-cell exhaustion. Hypertriglyceridemia increases peripheral insulin resistance, indirectly increasing beta-cell demand. Most obese type 2 diabetic patient also suffers from other features of metabolic syndrome, namely high triglycerides, low HDL cholesterol, and hypertension. Not uncommonly these patients also have high serum uric acid, liver enzymes and ultrasound finding of fatty infiltrate. In designing a diet to treat this type of patient, the diet has to be low in sugar, starch, bad fat, sodium and alcohol.

Using the C/G as a guideline, the patient can safely put on a low sugar and starch diet. A sliding scale should be given to the patient to self adjust the insulin dosage as the glycemic control improves to avoid hypoglycemia. A good diet accounts for 80% of the weight reduction. Another aspect of lifestyle management should include counseling sessions on exercise, food label reading, essential nutrients, hydration, sleep hygiene, emotional eating, stress management, and food addictions just to name a few. Explain to the patient that it is going to be a marathon and not a dash to finish.

### CONCLUSION

Most obese type 2 diabetic patients who are on insulin treatment that were referred to our program have enough beta-cell reserve using the C/G guideline that they do not require to take extra insulin provided that they can improve on their insulin sensitivity by losing weight and limit their sugar, starch, and bad fat intake.

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