

Plasma Insulin Response to an Oral Carbohydrate Solution

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SUMMARY

Plasma insulin responses to an oral carbohydrate solution were determined in twenty-one normal subjects. Mean insulin values at fasting, 30, 60, and 120 minutes after the carbohydrate load were 13, 109, 90, and 62 μ U. per ml., respectively. Twelve subjects retested with 100 gm. of oral glucose had equivalent insulin responses. In nineteen subjects with moderate diabetes, blood glucose and plasma insulin responses to the carbohydrate solution and to 100 gm. of glucose were also equivalent. It is concluded that this form of carbohydrate loading is an effective and reliable challenge to the pancreas. *DIABETES* 18:434-36, June, 1969.

Any new form of carbohydrate tolerance testing traditionally has been judged according to its ability to discriminate between normal and diabetic subjects on the basis of blood glucose levels. With the advent of technics for measuring blood insulin levels, a new dimension has been added to the usefulness of carbohydrate tolerance testing. It has now become desirable to know whether a modified carbohydrate tolerance test provides a quantitatively and qualitatively adequate challenge to the pancreas. Recently, Leonards et al.¹ introduced a new carbohydrate solution for test purposes consisting of a cola-flavored carbonated partial hydrolysate of corn starch. Because its palatability is greater than that of pure glucose solutions, it has been especially useful for epidemiological studies.^{2,3} An extensive evaluation by Leonards et al. showed no appreciable differences in the blood glucose levels obtained with this mixture when compared to 100 gm. of oral glucose in normal or diabetic subjects.¹ The purpose of the present communication is to report that the plasma insulin responses to this carbohydrate solution are appropriate in their promptness, magnitude and duration. Furthermore, they do not differ significantly from the responses observed after oral administration of 100 gm. of glucose in either normal subjects or diabetics.

MATERIALS AND METHODS

Normal subjects were twenty-one laboratory personnel without obesity or immediate family history of diabetes. Diabetic patients had adult onset disease never treated with insulin (FBS 89-295, two-hour blood glucose values 152-493 mg./

100 ml.). If taken, oral hypoglycemic agents were discontinued at least three days prior to testing. All subjects were given in the fasting state either the commercial preparation of cola-flavored carbohydrate,* 75 gm. in 210 cc., or 100 gm. of pure glucose in 250 cc. None of the subjects had emesis, although several complained of nausea with the 100 gm. glucose load. Heparinized venous blood was drawn at 0, 30, 60, and 120 minutes and immediately chilled. Glucose levels were determined by a glucose oxidase procedure⁴ on barium-zinc filtrates of whole blood. The remaining blood was centrifuged in the cold, and plasma insulin levels were determined in duplicate by a double antibody radioimmunoassay.⁵ Human insulin standards were kindly supplied by the Eli Lilly Company.

RESULTS AND DISCUSSION

Table I lists the glucose and insulin values obtained in normal subjects who received the new carbohydrate solution. As has been noted in other studies,^{6,7} carbohydrate tolerance in the normal young subjects was excellent. In nineteen of twenty-one subjects the glucose levels reached a peak at thirty minutes, and two-hour levels were below 100 mg./100 ml. Plasma insulin levels rose in all subjects tested. The peak response was seen at thirty minutes in thirteen subjects and at one hour in seven subjects; in only one subject was the highest value obtained at two hours. The magnitude of insulin response was well within the wide ranges for normals following pure glucose loads reported by many investigators using several variations in immunoassay technic.⁸⁻¹⁰ The fasting insulin levels were significantly correlated with fasting glucose levels ($r = .472$, $p < 0.05$). Significant correlation was also noted between glucose and insulin values following the administration of carbohydrate at one hour ($r = .522$, $p < .025$) and at two hours ($r = .663$, $p < .005$). Glucose and insulin values were not significantly correlated at thirty minutes ($r = .329$, p NS) however. In several of the subjects impressive insulin rises were seen despite virtually flat glucose curves. Although an earlier rise in blood glucose may have been missed, it is also possible that much of the early insulin response might be due to the gastrointestinal insulin releasing mechanism.¹¹⁻¹³

Twelve of the normal subjects had repeat tests with 100 gm. of glucose. In figure 1 are plotted the mean glucose and insulin responses of these twelve subjects to the two loads. The increments in blood glucose levels were comparable in the two tests as reported by Leonards et al.,¹ though in this instance slightly higher absolute levels predominated during

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*Glucola, Ames Company.

TABLE 1

Blood glucose (mg. per 100 ml.) and plasma insulin (μ U./ml.) following the administration of 75 gm. carbohydrate to normal subjects

Subject No.	Fasting		30 min.		60 min.		120 min.	
	Glucose	Insulin	Glucose	Insulin	Glucose	Insulin	Glucose	Insulin
1	69	1	85	102	57	25	57	19
2	77	5	102	41	89	57	87	30
3	80	12	96	91	71	48	80	52
4	84	18	117	142	91	99	70	50
5	71	13	87	68	67	84	71	62
6	68	10	99	165	78	102	64	53
7	72	12	100	113	73	95	67	58
8	66	9	108	80	95	89	69	55
9	66	1	84	83	68	84	70	48
10	76	11	108	94	110	140	74	63
11	87	21	84	62	72	73	68	64
12	70	8	114	223	81	186	72	84
13	77	12	110	69	77	53	91	49
14	70	17	94	200	54	60	57	34
15	72	26	121	234	90	218	75	121
16	74	16	96	112	74	90	68	44
17	66	17	86	83	59	42	74	48
18	81	17	137	100	92	66	100	50
19	75	12	107	88	105	138	84	85
20	68	8	101	91	119	99	109	207
21	80	19	104	55	61	42	81	32
Mean	74	13	102	109	80	90	76	62
S.E.M.	1.3	1.4	2.9	11.7	3.9	10.4	2.8	8.7

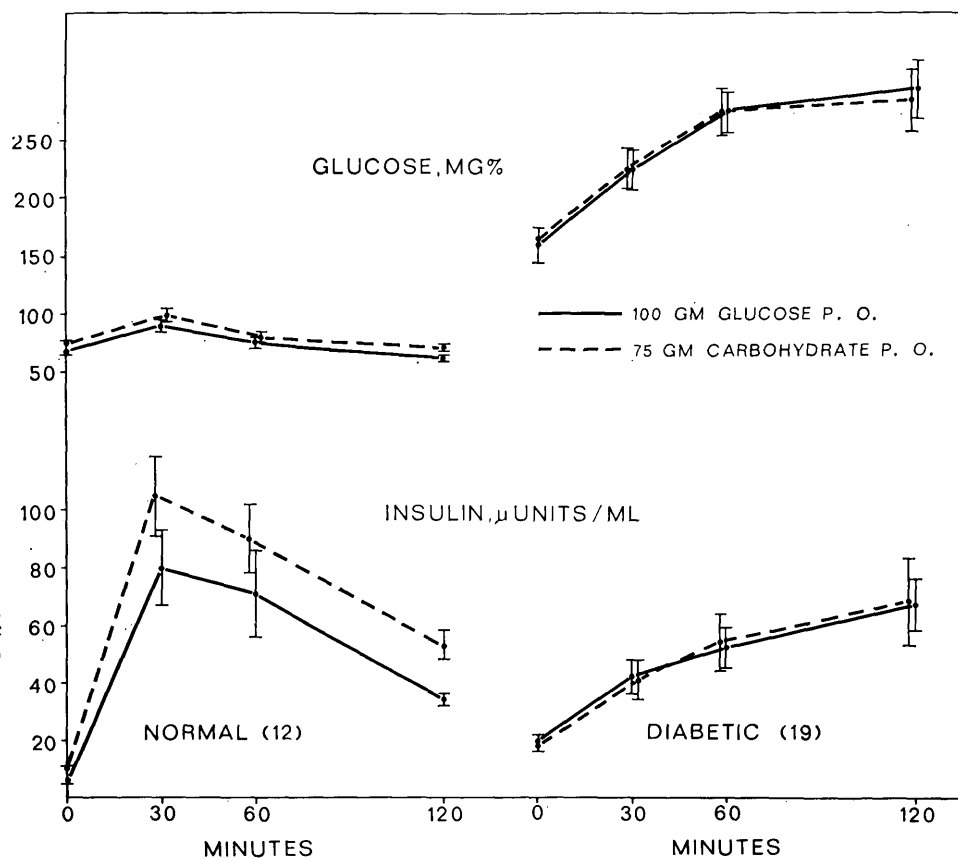


FIG. 1.
Blood glucose and plasma insulin after administration of 75 gm. carbohydrate or 100 gm. glucose orally to normal or diabetic subjects. Mean \pm S.E.M.

the tests with the new carbohydrate solution. The plasma insulin levels were also slightly higher following the new carbohydrate solution but this was of statistical significance only at two hours.

The nineteen diabetic subjects were tested with both the carbohydrate solution and the standard 100 gm. glucose load. As seen in figure 1, mean glucose values were virtually identical during both tests. Plasma insulin responses were likewise indistinguishable. When compared with normal subjects, these moderate diabetic patients had a significantly reduced early plasma insulin response at thirty minutes (41 μ U. per ml. vs 109 μ U. per ml., $p < .001$) and a delayed peak value at two hours. This pattern reported by other investigators is typical of moderate diabetics¹⁴⁻¹⁵ and was reproduced as well by the carbohydrate solution as by a pure glucose challenge. When the diabetic patients were divided by FBS into two groups, total insulin response (as estimated by the sum of plasma insulin increments at 30, 60, and 120 minutes) tended to be less in the more severe group regardless of which load was given (figure 2).

The present data substantiate the validity of using a complex carbohydrate solution with distinctly greater palatability as a convenient challenge to the pancreas. Though 70 per cent of the carbohydrate is present as saccharides requiring digestive hydrolysis prior to absorption as glucose, blood glucose and plasma insulin responses were substantially the

same as those produced by a 100 gm. glucose load in both normal and diabetic subjects. Although it is possible that an occasional individual might have impaired digestion of the complex carbohydrate, the present experience suggests this is uncommon. There should be no hesitation in employing this carbohydrate solution as a pancreatic challenge, particularly in epidemiological studies when large numbers of subjects are to be tested repeatedly and patient acceptance is at a premium.

ACKNOWLEDGMENT

The author is grateful for the technical assistance of Mrs. Helen Hughes and Mr. David Mattern.

REFERENCES

- ¹ Leonards, J. R., McCullagh, E. P., and Christopher, T. C.: A new carbohydrate solution for testing glucose tolerance. *Diabetes* 14:96-99, 1965.
- ² Kent, G. T., and Leonards, J. R.: Mass screening for diabetes in a metropolitan area using finger blood glucose after a carbohydrate load. *Diabetes* 14:295-99, 1965.
- ³ Miller, M., Bennett, P. H., and Burch, T. A.: Hyperglycemia in Pima Indians: a preliminary appraisal of its significance. *In Biomedical Challenges Presented by the American Indian*, Scientific Publication No. 165:89-103, 1968.
- ⁴ Saifer, A., and Gerstenfeld, B.: The photometric micro-determination of blood glucose with glucose oxidase. *J. Lab. Clin. Med.* 51:448-60, 1958.
- ⁵ Morgan, C. R., and Lazarow, A.: Immunoassay of insulin: two antibody system. Plasma insulin levels of normal, sub-diabetic and diabetic rats. *Diabetes* 12:115-26, 1963.
- ⁶ Ricketts, H. T., Cherry, R. A., and Kirsteins, L.: Biochemical studies of "prediabetes." *Diabetes* 15:880-88, 1966.
- ⁷ Taton, J., Pometta, D., Camerini-Davalos, R. A., and Marble, A.: Genetic determinism to diabetes and tolerance to glucose. *Lancet* 2:1360-62, 1964.
- ⁸ Yalow, R. S., and Berson, S. A.: Immunoassay of endogenous plasma insulin in man. *J. Clin. Invest.* 39:1157-75.
- ⁹ Hales, C. N., and Randle, P. J.: Immunoassay of insulin with insulin antibody precipitate. *Biochem. J.* 88:137-46, 1963.
- ¹⁰ Samols, E.: *On the Nature and Treatment of Diabetes*. Excerpta Medica Foundation, 1965, p. 227.
- ¹¹ Elrick, H., Stimmler, L., Hlad, C. J., and Arai, Y.: Plasma insulin response to oral and intravenous glucose administration. *J. Clin. Endocr.* 24:1076-82, 1964.
- ¹² McIntyre, N., Holdsworth, C. D., and Turner, D. S.: Intestinal factors in the control of insulin secretion. *J. Clin. Endocr.* 25:1317-24, 1965.
- ¹³ Dupre, J., and Beck, J. C.: Stimulation of release of insulin by an extract of intestinal mucosa. *Diabetes* 15:555-59.
- ¹⁴ Seltzer, H. S., Allen, E. W., Herron, A. L., and Brennan, M. T.: Insulin secretion in response to glycemic stimulus: relation of delayed initial release to carbohydrate intolerance in mild diabetes mellitus. *J. Clin. Invest.* 46:323-35, 1967.
- ¹⁵ Perley, M. J., and Kipnis, D. M.: Plasma insulin responses to oral and intravenous glucose: studies in normal and diabetic subjects. *J. Clin. Invest.* 46:1954-62, 1967.
- ¹⁶ Buchanan, K. D., and McKiddie, M. T.: Factors determining the plasma insulin response to oral glucose in diabetes mellitus. *Diabetes* 16:466-71, 1967.

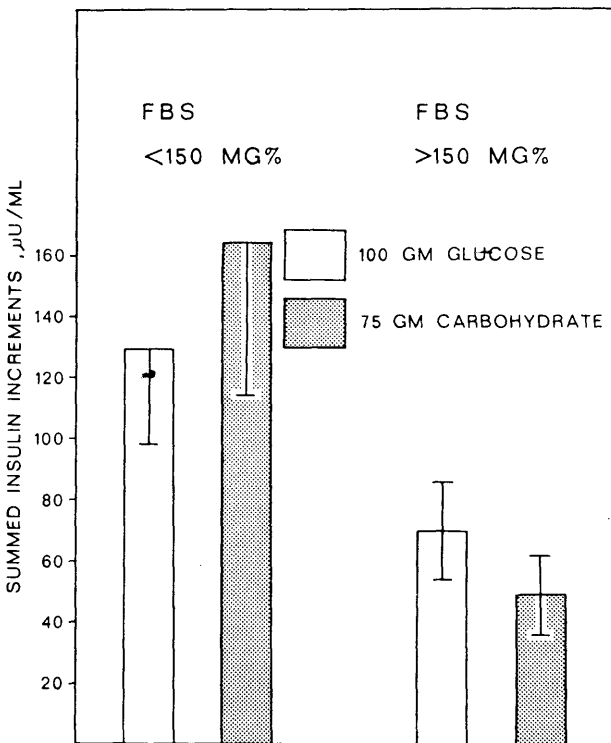


FIG. 2. Insulin responses to 75 gm. carbohydrate or 100 gm. glucose are plotted as the sum of plasma insulin increments at 30, 60, and 120 minutes in ten diabetic subjects with FBS less than 150 mg. per 100 ml. and nine diabetic subjects with FBS greater than 150 mg. per 100 ml. Mean \pm S.E.M.