

Hyperinsulinism-Hypoglycemia in the Postgastrectomy Patient

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SUMMARY

Patients who had undergone gastric resection were studied with blood glucose and serum insulin levels during oral glucose tolerance testing. The symptoms which appear two to three hours after a glucose load follow a marked rise in serum insulin and are accompanied by hypoglycemia. By appropriate elevation of the blood glucose, high serum insulin levels and a similar secondary hypoglycemic syndrome can be produced in normal individuals. *DIABETES* 14:526-28, August 1965.

Symptomatic hypoglycemia may be a problem in patients who have undergone gastric surgery. Weakness, sweating and palpitations may occur one to three hours after a meal. This is not to be confused with the early dumping syndrome which characteristically begins within a few minutes after eating and is not associated with hypoglycemia.

The postgastrectomy patient may have symptoms several hours after a meal, especially after ingestion of soluble carbohydrate foods. Symptoms may be mild with only a feeling of uneasiness or may be severe with loss of consciousness. The condition is common, occurring in 15 to 50 per cent of the patients reported in series in the medical literature.¹⁻¹⁰ The importance of carbohydrate in indirectly producing these symptoms has long been recognized.^{11,12} Conn has suggested that alimentary functional hypoglycemia represents a normal response of a normally sensitive pan-

creas to an abnormal insulogenic stimulus—marked hyperglycemia.¹³ Evensen⁷ demonstrated alimentary hypoglycemia in normal individuals to whom glucose was administered by intraduodenal tube.

This study was undertaken to evaluate the insulin response to glucose in the postgastrectomy patient.

METHODS

Five patients who had previously undergone subtotal gastric resection with gastrojejunostomy and ten normal subjects were studied. Whole blood glucose and serum insulin values were determined fasting and at one-half, one, one and one-half, two and three hours after ingestion of 100 gm. of glucose. Three additional normal subjects without family history of diabetes were studied during a modified glucose tolerance test. Following 100 gm. of oral glucose, 100 gm. of glucose as a 10 per cent solution was given intravenously during the next hour. The whole blood was precipitated immediately and blood glucose determined by a modified Somogyi-Nelson procedure. The blood was refrigerated until serum was removed and frozen. Insulin assay was done by immunoassay^{14,15} using a pork insulin standard* and I-125-labeled insulin.†

RESULTS

The individual glucose tolerance curves of the five postgastrectomy patients (figure 1) show marked variation. The average curve is similar to the control group at two and three hours.

Three patients developed symptoms of hypoglycemia at blood glucose levels of 24, 47 and 53 mg. per 100 ml. The lowest blood glucose occurs later in some patients. Two of the five had elevated blood glucose levels at two

Presented at the Fifth Congress of the International Diabetes Federation, Toronto, Ontario, Canada, on July 22, 1964.

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*Kindly supplied by Dr. Mary A. Root, Eli Lilly and Company, Indianapolis, Indiana.

† Abbott Laboratories, Oak Ridge, Tennessee.

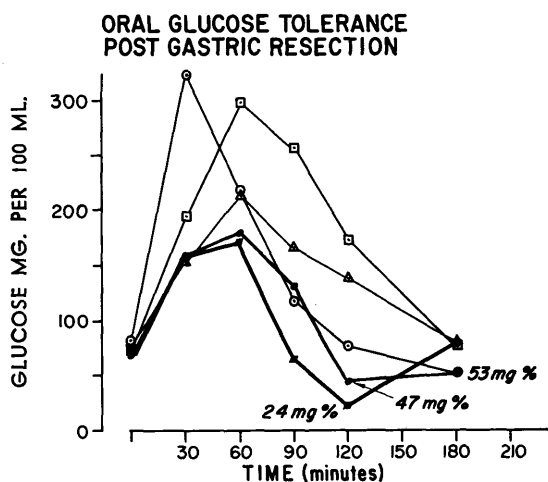


FIG. 1. Oral glucose tolerance study of five patients with gastric resection and gastrojejunostomy. Three patients developed symptoms of hypoglycemia at 24, 47 and 53 mg. per 100 ml.

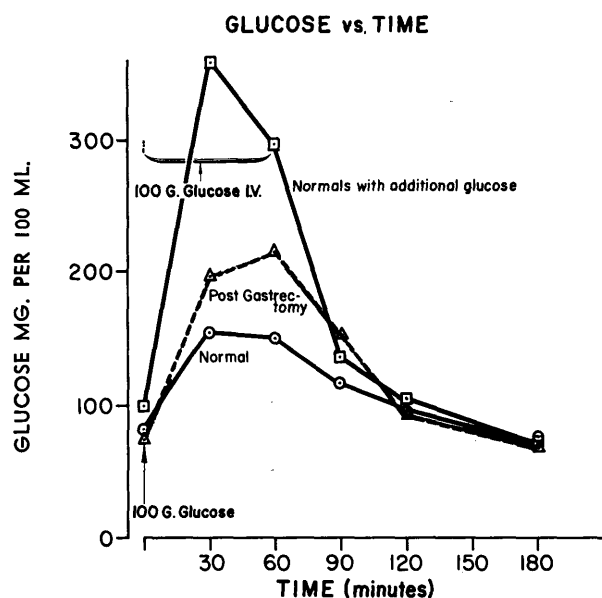


FIG. 2. Three-hour oral glucose tolerance curves showing average glucose concentration for ten normal subjects, five postgastroectomy patients and three normal subjects, given 100 gm. of glucose both orally and intravenously.

The average blood glucose concentrations during a three-hour glucose tolerance test are shown in figure 2 for ten normal subjects and five postgastroectomy patients. In addition, three normal individuals were given both oral and intravenous glucose to simulate the rapid glucose absorption of the patients. The maximum blood glucose averaging 370 mg. per 100 ml. in this latter group is higher than desired. Nevertheless, the insulin response of the three subjects given additional glucose closely resembles that of the postgastroectomy patient (figure 3). Note that the serum insulin curve is rela-

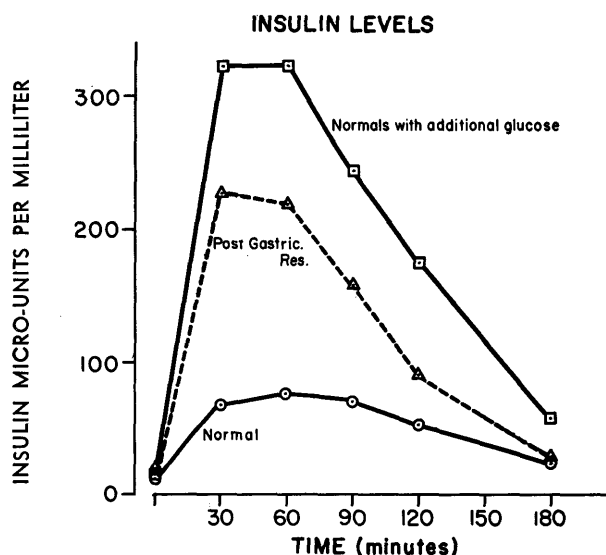


FIG. 3. Serum insulin levels corresponding to the blood glucose concentrations during glucose tolerance test depicted in figure 2. The curve of the insulin levels of the normal subjects stressed with additional glucose resembles that of the postgastroectomy patients.

INSULIN RESPONSE TO HYPERGLYCEMIA FOLLOWED BY HYPOGLYCEMIA IN NORMAL SUBJECTS

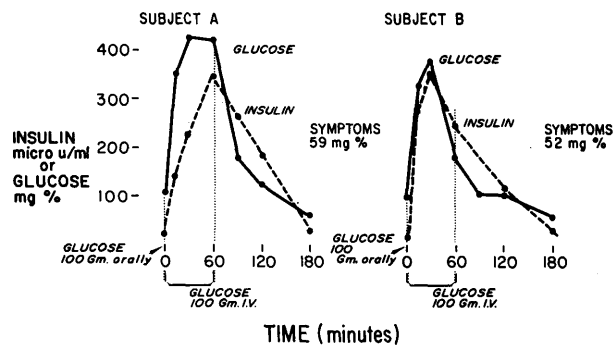


FIG. 4. Blood glucose and serum insulin levels of two normal subjects after a 200 gm. glucose load. Both experienced symptoms of hypoglycemia two hours after the end of the infusion of glucose.

hours. These two patients had been referred for evaluation of diabetes because of glycosuria. Incidentally, a postprandial blood glucose may erroneously "confirm" diabetes under these circumstances. The patient with a level of 24 mg. per 100 ml. blood glucose during the glucose tolerance study had been admitted to the hospital for evaluation of a possible brain tumor because of blackout spells.

tively flat for the normal or control group but rises promptly to high levels in both groups in which the blood glucose has reached abnormally high concentrations.

Two of the three normal subjects experienced symptoms of hypoglycemia two hours after the 200 gm. glucose load. Typical symptoms of weakness and sweating were relieved by oral carbohydrate. The slight lag in the insulin response curve (figure 4) which remains high as the blood glucose drops precipitously contributes to the hypoglycemia. Both subjects experienced headache and anxiety during the rapid fall of the blood glucose and noted weakness and sweating immediately prior to the minimum level of 52 and 59 mg. per 100 ml.

To determine whether the pancreas of the postgastrectomy patient responds normally to a glucose stimulus the "insulogenic index" of these patients and the three normals was compared. The insulogenic index as used by Seltzer¹⁶ is obtained by dividing serum insulin levels (microunits per milliliter) by blood glucose (mg. per 100 ml.). These values are most meaningful when greatest stimulation is obtained so are only shown for the first sixty minutes. The results (figure 5) suggest that during marked hyperglycemia, the insulin response of the postgastrectomy patients was normal.

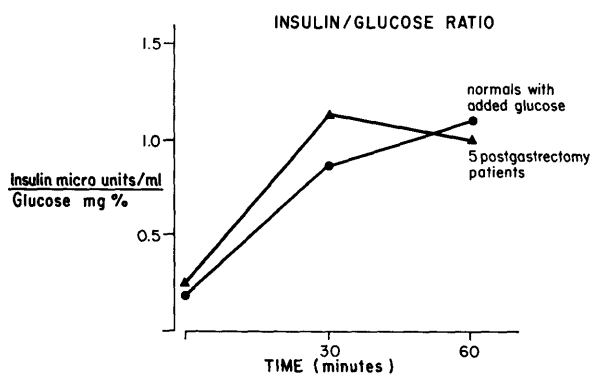


FIG. 5. Insulogenic index (Insulin μ U./ml. \div glucose mg. per 100 ml.) plotted for five postgastrectomy patients and three normal individuals during hyperglycemia. The similarity of the curves suggests a normal pancreatic response in the postgastrectomy patients.

DISCUSSION

It has long been recognized that, following total or subtotal gastrectomy, a dumping syndrome followed by secondary hypoglycemia may occur. The early dumping syndrome is due to rapid passage of ingested food causing distention of the jejunum. The rapid absorption

of carbohydrate produces marked hyperglycemia which is an excessive stimulus to the pancreatic islets. The sudden cessation of absorption coupled with high serum insulin levels produces a precipitous fall in blood glucose which exceeds the rate of insulin degradation. When the blood glucose falls below 100 mg. per 100 ml. the serum insulin is still elevated to values up to ten times normal. This results in continued decline in blood glucose, and secondary hypoglycemia may result before the insulin can decrease to a normal value. The same mechanism can be demonstrated in normal individuals given adequate glucose stimulus.

REFERENCES

- Adlersberg, D., and Hammerschlag, E.: The postgastrectomy syndrome. *Surgery* 21:720-29, 1947.
- Adlersberg, D., and Hammerschlag, E.: Mechanism of the postgastrectomy syndrome. *JAMA* 139:429-37, 1949.
- Barnes, C. G.: Hypoglycaemia following partial gastrectomy. *Lancet* 2:536-39, 1947.
- Zollinger, R. M., and Hoerr, S. O.: Gastric operations: Troublesome postoperative symptoms with special reference to carbohydrate ingestion. *JAMA* 134:575-79, 1947.
- Gilbert, J., and Dunlop, D.: Hypoglycaemia following partial gastrectomy. *Brit. Med. J.* 2:330-32, 1947.
- Wells, C., and Welbourn, R.: Postgastrectomy syndromes. *Brit. Med. J.* 1:546-54, 1951.
- Evenson, O. K.: Alimentary hypoglycemia after stomach operations and influence of gastric emptying on glucose tolerance curve. *Acta Med. Scand. Supp.* 126:1-388, 1942.
- Smith, W. H., Fraser, R., Staynes, K., and Wilcox, J.: Causes of postprandial attacks of palpitation and weakness after gastric operation. *Quart. J. Med.* 22:381-404, 1953.
- Azina, M. A.: Hypoglycemia in the symptom complex of patients with peptic ulcer having sustained gastric resection. *Soviet Medicine* 9:35-40, 1962.
- Sullivan, M., and Boshell, B.: Aetiological factors and therapeutic approach to the dumping syndrome. *Brit. Med. J.* 1:414-16, 1964.
- Conn, J. W.: The advantage of a high protein diet in the treatment of spontaneous hypoglycemia. *J. Clin. Invest.* 15:673-78, 1936.
- Conn, J. W., and Newburgh, L. H.: The glycaemic response to isoglycogenic quantities of protein and carbohydrate. *J. Clin. Invest.* 15:665-72, 1936.
- Conn, J. W., and Seltzer, H. S.: Spontaneous hypoglycemia. *Amer. J. Med.* 19:460-78, 1955.
- Meade, R. C., and Klitgaard, H. M.: A simplified method for immuno-assay of human serum insulin. *J. Nuclear Med.* 3:407-16, 1962.
- Yalow, R. S., and Berson, S. A.: Immunoassay of endogenous plasma insulin in man. *J. Clin. Invest.* 39:1157-75, 1960.
- Seltzer, H. S., and Harris, V. L.: Exhaustion of insulogenic reserve in maturity-onset diabetic patients during prolonged and continuous hyperglycemic stress. *Diabetes* 13:6-13, 1964.