Controversy continues to surround the treatment of diabetes mellitus, particularly with the oral hypoglycemic drugs. A committee of biostaticians reviewed the data originally reported in the University Group Diabetes Program study.\textsuperscript{1} They found the conclusions of that study basically sound, namely that there is an increased risk of mortality from cardiac causes in some patients treated with either oral sulfonylurea or phenethylbiguanide drugs.

These conclusions, however, must be contrasted with several other reports purporting to show either no effects of the sulfonylurea drugs on mortality from cardiac causes or a decrease in “cardiovascular events” in patients with mild diabetes treated with an oral sulfonylurea drug.\textsuperscript{2} Because of this potential for serious toxicity and the lack of definite evidence for any positive benefit of these agents on the vascular complication of diabetes, oral hypoglycemic agents must be used with caution in patients with symptomatic diabetes mellitus.

Concern about the use of these agents has led to two important observations: (1) a small but significant percentage of patients receiving oral hypoglycemic agents have been found to have no definite evidence of diabetes mellitus after discontinuation of the drug and (2) perhaps as many as 50\% of patients treated with oral sulfonylurea agents can be treated successfully with diet alone after discontinuation of the drug. Therefore, before considering the use of oral hypoglycemic agents, the diagnosis of diabetes mellitus should be carefully confirmed.\textsuperscript{3} If the diagnosis is made, dietary control of hyperglycemia should be attempted before moving automatically to drug therapy.

Treatment of Ketoacidosis

In the treatment of diabetic ketoacidosis, new approaches to therapy have received a great deal of attention in the past year. Careful control of fluid balance to avoid rapid correction of hyperosmolality and the potential for cerebral edema has been emphasized, as has the continued careful monitoring of serum potassium levels. Hypokalemia remains a serious complicating problem in the treatment of patients with diabetic ketoacidosis. Alkali therapy for the acidotic state is potentially dangerous in these patients and must be administered carefully and only when arterial blood pH is below 7.1. Several potential problems from the use of alkali have been suggested. They include “overshoot” alka-
losis, a too-rapid fall in serum potassium; a paradoxical fall in the pH of the cerebrospinal fluid, and the possibility of increasing the affinity of hemoglobin for oxygen because of low 2,3-diphosphoglycerate concentrations in erythrocytes.

In general, administration of insulin in patients with ketoacidosis has been carried out by intravenous bolus injections of 50 to 100 units every 1 to 2 hours; the total amount of insulin required has been approximately 500 units in the first 24 hours. Recent reports of continuous intravenous infusion of low doses of insulin have suggested that much smaller doses of insulin are needed for control of ketosis and hyperglycemia. These reports raise serious questions about the presence of insulin resistance in patients with ketoacidosis. In these studies, correction of hyperglycemia and ketosis was achieved with a total of 40 to 70 units of insulin. Similar results have been obtained by some investigators using frequent intermittent intramuscular injections of small doses of insulin. It is not yet possible to determine if complications of insulin treatment, such as hypokalemia and hypoglycemia, are less frequent with these low-dose methods than with the high-dose intermittent regimens. One word of caution—delay in bringing hyperglycemia and ketosis under control in the rare patient with insulin resistance must be considered a potential hazard of these low-dose methods of insulin administration in patients with ketoacidosis.

Control of Hyperglycemia

The discovery of the hypothalamic inhibitory peptide, somatostatin, and its administration to patients with diabetes has raised interesting questions about the control of hyperglycemia in the diabetic patient. This small molecular weight polypeptide hormone inhibits secretion of a number of pituitary hormones as well as other nonpituitary hormones such as gastrin and glucagon. When somatostatin was administered to patients with insulin-requiring diabetes, the suppression of glucagon secretion by somatostatin prevented the development of ketoacidosis for 18 hours after insulin withdrawal.

This finding has implicated glucagon as a significant factor in the development of diabetic ketoacidosis. Administration of somatostatin to diabetic subjects has also abolished postprandial hyperglycemia, apparently through its ability to suppress postprandial increases in glucagon. These fascinating studies should lead to a better understanding of the control of hyperglycemia in diabetes and may eventually assist in the development of more rational treatment programs.

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