Diabetic Ketosis: Elevated Serum Glutamic-Oxaloacetic Transaminase (SGOT) and Other Findings Determined by Multi-channel Chemical Analysis

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SUMMARY

Twelve-channel chemical analysis (sodium, potassium, chloride, CO_2, total protein, albumin, calcium, alkaline phosphatase, total bilirubin, urea nitrogen, glucose, and glutamic-oxaloacetic transaminase [SGOT] was performed on sera from fifty-five of sixty-one cases of diabetic ketosis hospitalized over a two-year period. The cases represented consecutive admissions and were not selected for severe ketoacidosis. Abnormalities of the serum sodium, potassium, chloride, CO_2, calcium, urea nitrogen and glucose generally conformed to recognized patterns, and abnormalities of the total protein, albumin, alkaline phosphatase, and total bilirubin were noted in a minority of cases. In contrast, the SGOT was elevated in 69 per cent of all cases and in 82 per cent of those in whom the determination was performed on the day of admission. Elevation of the SGOT in ten of eleven patients with hepatomegaly and the relationship between elevations of the SGOT and elevations of the serum glutamic-pyruvic transaminase and lactic dehydrogenase, as well as the recognized occurrence of fatty infiltration of the liver in uncontrolled diabetes, are consistent with an hepatic origin for the elevated SGOT found in patients with diabetic ketosis. DIABETES *18*:781-85, November, 1969.

The routine performance of multiple chemical determinations on the sera of hospitalized patients has provided unanticipated diagnostic information in as many as 12 per cent of patients.[1] Routine qualitative testing for ketonemia[2] in patients with uncontrolled diabetes mellitus permits the definition of a group of patients encompassing mild to severe diabetic ketoacidosis. The frequent clinical observation of an elevation of the serum glutamic-oxaloacetic transaminase (SGOT) in such ketotic diabetes prompted a review of the twelve-channel chemical profiles of patients with diabetic ketosis.

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METHODS

The records of all patients hospitalized on the medical service of Barnes Hospital from July, 1966 through June, 1968 with final diagnoses of diabetic ketoacidosis, diabetic acidosis, diabetic ketosis, or diabetic coma were reviewed. Sixty-one episodes of diabetic ketosis, all ketonemic as evidenced by a strongly positive qualitative nitroprusside test (Acetest, Ames) form the basis of this report. All of the patients were ketotic on admission to the hospital and none of the female patients was pregnant. The sixty-one episodes of diabetic ketosis occurred in forty-one patients (thirty-one female, ten male) ranging in age from fifteen to sixty-seven years.

Precipitating factors were not apparent in thirty-four of the sixty-one cases of diabetic ketosis. Infection was present in eleven, and nine were newly diagnosed diabetics. Acute alcoholism was the precipitating event in five instances. A major change in the mode of therapy, such as conversion from insulin to an oral hypoglycemic agent or from an oral agent to diet alone, overt emotional stress and a perforated duodenal ulcer, completed the recognized causes of decompensation. Four patients had two potential precipitating factors. Vomiting was a particularly common symptom occurring in 84 per cent of the cases; hepatomegaly was detected in 20 per cent. The initial systolic blood pressure was below 100 mm. Hg in only one instance. None of the patients was comatose and there were no deaths.

A twelve-channel chemical profile (sodium, potassium, chloride, CO_2, total protein, albumin, calcium, alkaline phosphatase, total bilirubin, urea nitrogen, glucose, and glutamic-oxaloacetic transaminase), performed on a Technicon AutoAnalyzer (SMA-12), is routinely obtained on patients admitted to Barnes Hospital. The details of this procedure, as well as the 2.5 per cent and 97.5 per cent limits for the normal hospital population, have been described.[1] Serum is generally obtained at the time of admission in patients admitted before

6 p.m., and the following morning in patients admitted after 6 p.m.

Chemical profiles were performed on fifty-five of the sixty-one cases of diabetic ketosis; forty were obtained at the time of admission (Day 1), eleven were obtained the following morning (Day 2), and four were obtained on the third hospital day (Day 3). In tabulation of the data, pretreatment values for the sodium, potassium, chloride, CO_2, urea nitrogen, and glucose were used in those instances in which the chemical profile was obtained after the initiation of therapy.

RESULTS

The available chemical findings in sixty-one episodes of diabetic ketosis are summarized in figure 1. The percentage of values which were normal, high, or low are listed in table 1.

The serum glutamic-oxaloacetic transaminase (SGOT) was elevated in thirty-eight of fifty-five cases (69 per cent). Of the forty cases in which the chemical profile was drawn immediately upon admission, the SGOT was elevated in thirty-three (82 per cent) (figure 2). The elevations were generally mild with only one initial value off the profile scale (greater than 250 KU) and that on a second day chemical profile. The

TABLE 1

Abnormalities in the chemical findings expressed as a percentage of the number of cases in patients with diabetic ketosis

	Number of cases	Percentage of cases		
		Normal	High	Low
Sodium	61	72	0	28
Potassium	61	64	36	0
Chloride	60	78	12	10
CO_2	61	4	0	96
Total protein	55	75	16	9
Albumin	55	82	5	13
Calcium	55	80	9	11
Alkaline phosphatase	55	76	24	0
Total bilirubin	55	87	13	0
Urea nitrogen	61	64	34	2
Glucose	61	0	100	0
SGOT	55	31	69	0

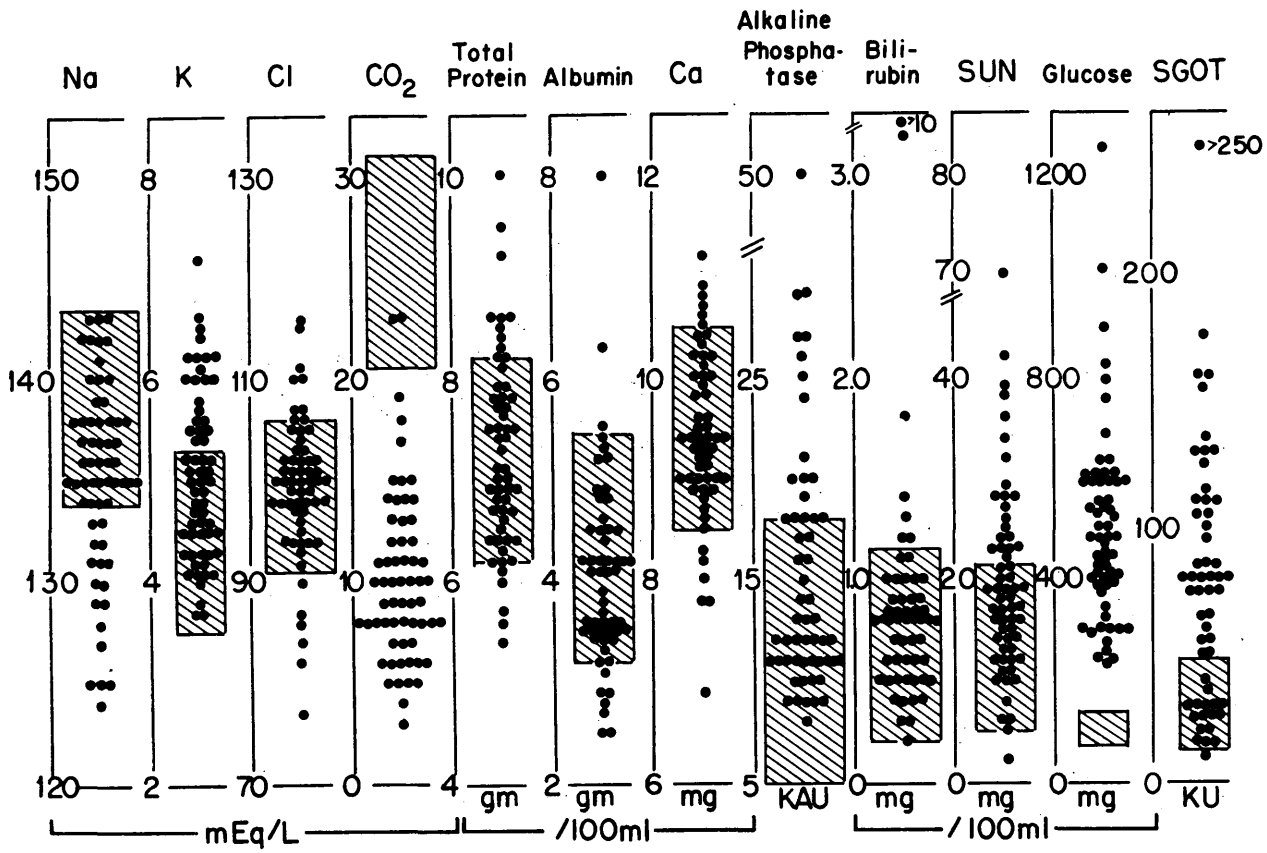

FIG. 1. Chemical findings in patients with diabetic ketosis. The shaded areas represent the 2.5 per cent and 97.5 per cent limits for the normal hospital population.[1]

FIG. 2. Distribution of the SGOT (Karmen units) in the total group of fifty-five cases of diabetic ketosis (SGOT elevated in 69 per cent) and in the forty cases in which the determination was performed at the time of admission (SGOT elevated in 82 per cent). The shaded areas represent the 2.5 per cent and 97.5 per cent limits for the normal hospital population.[1]

SGOT was repeated in twenty-two cases. In five instances there was a subsequent rise in the SGOT; the values in two patients reached peaks of 2,620 and 1,480 KU with persistent elevations for nine and eight days respectively. In the remaining seventeen cases all subsequent values were lower than the initial SGOT and usually were within the normal range by the second or third day, though elevations persisting until the sixth day were noted.

There was good agreement between the SGOT and the serum glutamic-pyruvic transaminase (SGPT) in the twenty cases in which the latter was obtained. The SGPT was elevated on nine of ten occasions when measured at a time when the SGOT was elevated. Conversely, the SGPT was normal on twenty-three of twenty-five occasions when measured when the SGOT was normal. Similarly, the lactic dehydrogenase (LDH) was elevated on all eight occasions that it was measured when the SGOT was elevated. In three cases at least, three determinations of the SGOT, SGPT, and LDH were available and the enzyme changes appeared to parallel each other. An example is shown in figure 3.

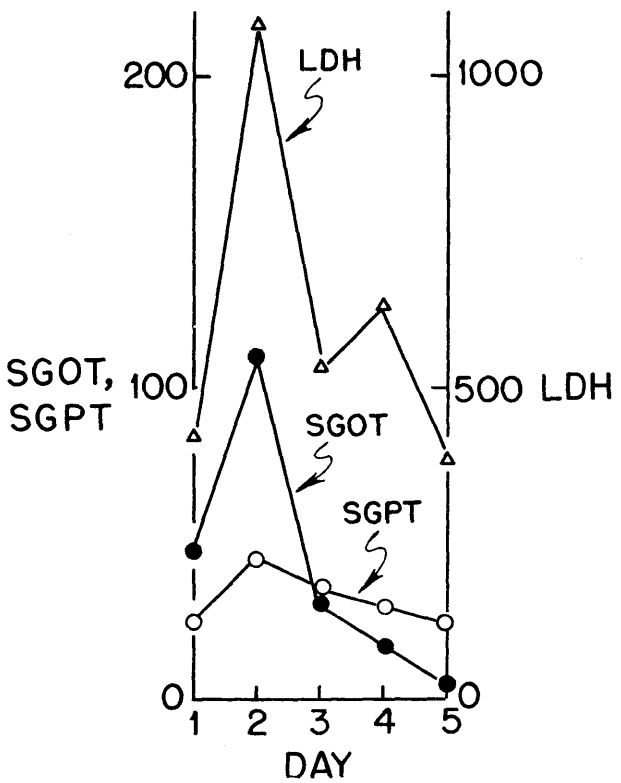

FIG. 3. Serial determinations of the SGOT (Karmen units), SGPT (Sigma units), and LDH (Broida-Bodansky units) in a patient with diabetic ketosis.

The SGOT was elevated in ten of eleven patients with hepatomegaly; the normal SGOT in one patient with hepatomegaly was drawn on the second hospital day. Of nineteen cases with hepatomegaly and/or abdominal tenderness, 89 per cent had an elevated SGOT

whereas 58 per cent of thirty-six cases with neither of these findings had an elevated SGOT. There was no correlation between elevation of the SGOT and depression of the blood pressure and elevation of the SGOT was not directly related to elevation of the urea.

The total protein was elevated in nine cases but normal on prompt repeat in three of four cases; the fourth had grossly hyperlipemic serum and the repeat determination was also on a chemical profile. Two other cases with elevated total proteins had hyperlipemic sera. The serum albumin was low in seven cases. None of the hypoalbuminemic patients had qualitative proteinuria greater than 1+ and proteinuria was not detected in the three patients upon whom quantitative studies were done. The albumin remained low in two of the three instances in which it was repeated.

The alkaline phosphatase was elevated in thirteen cases. On prompt repeat, elevated alkaline phosphatases were normal in four of six cases; in one case with gross hyperlipemia the alkaline phosphatase remained elevated on a repeat chemical profile. Three others with elevated alkaline phosphatases had hyperlipemic sera.

The total bilirubin was elevated in seven cases, three of which had grossly hyperlipemic sera that could have led to analytical artifacts. These three patients included the two highest elevations (greater than 10.0 mg./100 ml. and 3.2 mg./100 ml.). In one of these a repeat bilirubin on the day of admission was normal.

Hyponatremia was present in seventeen cases (28 per cent) with a minimal value of 124 mEq./L. Three of these patients had grossly hyperlipemic sera. The serum potassium was elevated in twenty-two cases (36 per cent) with a maximal value of 7.2 mEq./L. All eight cases with CO_2 of 15 mEq./L. or greater had normal potassiums, whereas the potassium was elevated in twenty-two of fifty-three cases (41 per cent) with a CO_2 of 14 mEq./L. or less. There were no instances of initial hypokalemia, though two patients had values of 3.7 mEq./L. and one had a value of 3.8 mEq./L. The serum calcium was low in six cases, with the lowest value being 6.9 mg./100 ml. In five cases the hypocalcemia was relatively mild, ranging from 7.8 to 8.3 mg./100 ml.; four of the latter were associated with hypoproteinemia and the fifth with gross hyperlipemia. Renal failure was not present in any of the hypocalcemic patients (the maximal SUN was 22 mg./100 ml.) and the only patient with abdominal pain had a normal amylase. Mild hypercalcemia, ranging from 10.6 to 11.2 mg./100 ml., was present in five cases.

The serum CO_2 was depressed in fifty-nine cases and low normal in two others. The median value was 10 mEq./L. and the range was from 3 to 23 mEq./L. The serum glucose ranged from 230 to 1,250 mg./100 ml. with a median value of 480 mg./100 ml. The glucose was 400 mg./100 ml. or less in nineteen of fifty-six (34 per cent) cases with a CO_2 of 15 mEq./L. or less and 300 mg./100 ml. or less in seven (12 per cent) of these cases. The serum urea nitrogen (SUN) was elevated in twenty-one cases (34 per cent) with a maximal value of 70 mg./100 ml. One patient had a SUN of 2 mg./100 ml.

DISCUSSION

The SGOT was elevated in 69 per cent of cases of diabetic ketosis and in 82 per cent of those in whom the determination was performed immediately upon admission to the hospital. The SGOT has been reported to be normal in large groups of patients with controlled diabetes.[3,4] Chinsky, Shmagranoff, and Sherry[5] found the SGOT to be normal in two cases of "severe diabetic acidosis." However, Seige[6] noted an elevation of the SGOT in nine of twenty-nine uncontrolled, often newly diagnosed, diabetics.

In the present series, the agreement between the SGPT and SGOT on thirty-two of thirty-five occasions when they were measured simultaneously, the elevation of the LDH on all eight determinations obtained when the SGOT was elevated, the apparent parallel patterns in the changes of the SGOT, SGPT, and LDH in three patients and the occurrence of an elevated SGOT in ten of eleven patients with hepatomegaly are consistent with an hepatic origin for the SGOT elevations noted in diabetic ketosis. In the absence of histologic study, the hepatic pathology in these patients with uncontrolled diabetes remains speculative. However, uncontrolled diabetes was the second most common underlying disorder in the series of patients with fatty liver reported by Leevy,[7] and fatty infiltration of the liver is frequently found when biopsies are obtained from patients with diabetes.[8] Abnormal liver function tests, including elevation of the transaminases, occur in patients with fatty liver,[7,9] though it has recently been suggested that factors other than diabetes may be responsible for abnormal liver function tests in diabetic patients with fatty livers.[8]

Hyperlipemia produces artifactual elevation of the total protein, albumin, alkaline phosphatase and bilirubin when these determinations are performed on the AutoAnalyzer.[1] This fact complicates the interpretation

of elevations of the total protein, alkaline phosphatase and bilirubin in the present report and may have obscured some cases of hypoalbuminemia. Recognized hyperlipemia could not account for all variations in these determinations and they may reflect underlying liver disease. However, it could be argued that lesser degrees of hyperlipemia were not detected.

Abnormalities in the serum electrolytes generally conformed to recognized patterns.[10] However, the absence of initial hypokalemia is remarkable since it was noted in 15 per cent of 145 patients with severe diabetic ketoacidosis studied by Martin, Smith, and Wilson[11] and its therapeutic significance has been emphasized.[12] Lesser degrees of potassium depletion in the present series may have been due to less prolonged and less severe ketoacidosis.

ACKNOWLEDGMENT

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