

Mortality of Patients with Diabetic Acidosis in a Large City Hospital

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INTRODUCTION

Despite marked improvement in the prevention and treatment of diabetic acidosis, it is estimated that 2 per cent of diabetic patients continue to die during acidosis.¹ During the years 1930 to 1951, reports of decreasing mortality rates appeared, with that of Harwood approaching 1.5 per cent.^{2,3} Though the groups studied in these reports were not necessarily drawn from comparable populations, the conclusion is inescapable that survival during diabetic ketosis in general has increased.

Various reasons have been offered to explain this decline in mortality. Unquestionably the employment of larger amounts of insulin, a better understanding of fluid and electrolyte derangements, and the "team" approach, have aided in the management of acidosis. Furthermore, measures such as the use of more efficient antibiotics and improved surgery have benefited the treatment of nonacidotic complications. On the other hand, the lessened mortality could be related also to a decrease in the severity of the admission state.

Ten years ago the mortality of patients with diabetic acidosis at the Cincinnati General Hospital approached 50 per cent. This dismal record prompted one of the authors to institute a program of close observation and elaborate documentation of treatment of each patient admitted with this condition. Over a ten-year period 312 cases were studied. Virtually every patient was seen by at least one of the authors, who advised the ward physicians in the management of the case. During this time there was a decrease in the yearly death rate. In the first five years the mortality was 31.4 per cent whereas in the second five years it had significantly declined to 14.5 per cent (figure 1).

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% MORTALITY IN DIABETIC ACIDOSIS

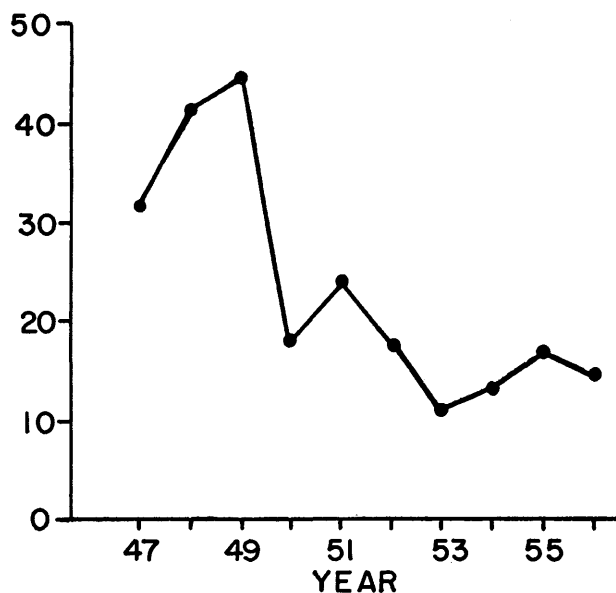


FIG. 1. Mortality in diabetic acidosis in a ten-year period.

This report is an attempt to account for the lessened mortality in a large city hospital population. The findings suggest that though improved management brought about survival in some cases, a decrease in the incidence of nonacidotic complications was equally, if not more, responsible for the decline in mortality.

METHODS

Observations were made on all patients admitted to the Cincinnati General Hospital during the ten-year period 1947-1956 in whom the serum CO₂ content was 14 mM./L. or less due to ketosis, and who lived for at least three hours following institution of insulin therapy. A patient was considered to have survived from acidosis if he was alive thirty days after admission.

Because the mortality was significantly lower in the second half of the time of study, comparisons were made

between the two five-year periods. Data were obtained from each patient concerning his condition at onset of therapy as well as therapy received. One hundred and forty, and 172 patients were observed in the first and second periods, respectively.

An over-all index of severity of each patient was not devised to evaluate his condition at admission. Rather, the individual characteristics, including age, degree of depression of the sensorium, blood pressure, nonacidotic complications, and the concentrations of blood glucose, blood urea nitrogen, and serum CO₂ content were averaged separately for each group. The degree of depression of the sensorium was graded 1 to 4, as follows:

1. Awake.
2. Drowsy, but oriented and responsive.
3. Stuporous. Spontaneous movement or phonation only.
4. Comatose. No spontaneous movement or phonation.

Considerable difficulty was encountered in the evaluation of nonacidotic complications noted at the time of admission. Any system devised to grade these is crude at best, as the actual severity of a complication in a diabetic patient and its effect on insulin action cannot be gauged with accuracy. Nevertheless, complications are so commonly associated with diabetic acidosis that they must be taken into account in any group comparisons. It is likely, however, that many errors in evaluation were nullified because of the large numbers of patients.

The patients were classified in three groups: those without nonacidotic complications on admission, those with moderate, and those with severe nonacidotic complications potentially lethal in themselves. A point system of grading was not used because of the errors in summation of points in a patient with several mild complications. Instead, grouping was made entirely by clinical estimation. Insofar as possible, grouping was also carried out without knowledge of the patient's outcome. This method was believed the most valid for this study inasmuch as almost all patients were followed by one or more of the authors. The nonacidotic complications listed as moderate or severe were as follows:

1. *Moderate nonacidotic complications:* Abscess (thigh, skin, Bartholin's gland, orbit, subungual, rectal, scalp, dental), abortion, acute alcoholism, congestive heart failure without pulmonary edema, hepatic cirrhosis, cerebral thrombosis, epileptiform convulsion, non-suppurative cholecystitis, gastroenteritis, hemochromatosis without hepatic failure, gross hemoptysis (cause unknown), rheumatic valvulitis, recent morphine administration, myxedema, otitis media, bronchopneumonia, pulmonary infarction, chronic pancreatitis, acute pyelo-

nephritis, acute nonspecific pericarditis, pregnancy, serum sickness, pheochromocytoma, salpingitis, Shigella dysentery, minimal or moderately advanced pulmonary tuberculosis, upper respiratory infection, and Vincent's stomatitis.

2. *Severe nonacidotic complications:* Multiple abscesses of the kidney, anaphylaxis, severe amebic colitis, congestive heart failure with pulmonary edema, cerebral hemorrhage, empyema of the gall bladder, Friedlander's pneumonia, gangrene of an extremity, lateral sinus thrombosis, necrotizing renal papillitis, metastatic carcinoma of the pancreas, myocardial infarction, phlegmonous esophagitis, pneumococcal lobar pneumonia (severe), hemorrhagic pancreatitis, chronic renal failure, basal skull fracture, staphylococcal septicemia, far advanced active pulmonary tuberculosis, thyroid "storm," and hemochromatosis with liver failure and bleeding varices.

Treatment followed a standard regimen sufficiently flexible to meet individual patient needs. Penicillin and Vitamin B complex were given to all patients. The management of nonacidotic complications was believed to be similar in general in the two periods. However, tetracycline drugs were used more frequently in the second period. Studies were made of treatment variables to include the amounts of insulin, glucose, water and electrolytes given in the first six hours of therapy, and of the subsequent administration of norepinephrine and parenteral potassium. It was not believed worth while to estimate therapy other than that with norepinephrine or potassium after six hours because of the deaths or recoveries that occurred between the sixth and eighteenth hours. Methods of analysis of data included the use of the *t* distribution for making group comparisons, and the use of the chi-square distribution for determining significance of differences between mortalities and between distributions of severities.¹

RESULTS

In table 1 are listed the admission characteristics related to ketosis of the two groups. There were no significant differences in the mean ages or degrees of depression of the sensorium. Nor was there a difference in the incidence of sustained hypotension not responsive to the administration of fluids or plasma expanders. The mean concentrations of blood urea nitrogen and serum CO₂ content were the same. Though the blood glucose concentration was probably decreased by 49 mg. per cent in the second period ($P < 0.05$), this small difference was not believed to be clinically significant. However, it is in the analysis of nonacidotic complications that a significant difference is noted between the two periods.

TABLE 1

The characteristics related to ketosis of the patients on admission, in the five-year periods

Characteristic	1947-1951 (140)	1952-1956 (172)	P
Age* (years)	40.2 (13-72)	42.4 (15-84)	—
Depression of sensorium* (grade)	2.66 (1-4)	2.64 (1-4)	—
Sustained hypotension (number)	15	17	—
Blood glucose* (mg.%)	556 (133-1390)	507 (197-1180)	<0.05
Serum CO ₂ content* (mM./L.)	8.07 (2.7-14.0)	8.87 (3.5-14.0)	—
Blood urea nitrogen* (mg.%)	29.7 (3-124)	29.6 (4-104)	—

*Data given as mean and range.

In table 2 are listed the distribution of cases according to severity of complications. The distribution in the second period is significantly shifted away from the severely complicated class.

TABLE 2

The distribution of patients with nonacidotic complications between periods

Period	Uncomplicated	Moderately Complicated	Severely Complicated	Total
1947-1951	51 (36%)	62 (44%)	27 (19%)	140
1952-1956	77 (45%)	83 (48%)	12 (7%)	172

 $\chi^2=10.9$ d.f.=2 P<0.01

In table 3 the treatment given in the first six hours is listed for the two periods. The mean amount of insulin administered in the second period was 64 units greater than in the first period. There were no differences in the quantities of water and sodium given. However, less glucose, amounting to 50 gm. per patient, was given in the second period. Bicarbonate averaging 150 mEq. per patient was given to 116 patients in the second period, in contrast to thirty-two in the first period. The potassium administered parenterally in the first period was not only infrequent but was also less in amount, averaging 35 mEq. per patient in the first period as compared to 49 mEq. per patient in the second period. Norepinephrine for sustained hypotension was not available in the first period but was given to seventeen patients in the second period.

TABLE 3

Parenteral therapy given in the five-year periods

Therapy	1947-1951 (140)	1952-1956 (172)	P
Insulin (units)	392 (100-950)	456 (65-1,200)	<0.01
Water (liters)	3.01 (1.00-5.00)	3.07 (0.20-6.50)	—
Sodium (mEq.)	449 (0-450)	417 (0-317)	—
Glucose (gm.)	142 (0-450)	88 (0-375)	<0.01
Number of patients receiving:			
Bicarbonate	32	116	
Potassium	13	76	
Norepinephrine	0	17	

The factors believed responsible for death are presented in table 4. It is of interest that in the first period twenty-three of the forty-four who died had demonstrable nonacidotic complications potentially lethal in themselves, whereas nine of the twenty-five who died were similarly afflicted in the second period. However, little significance can be attached to this finding as autopsies were not done on all patients, and the observations are few.

TABLE 4

The incidence of nonacidotic complications in those who died

Complication	1947-1951 (140)	1952-1956 (172)
Infection:		
Pneumonia	5	1
Septicemia	2	1
Necrotizing renal papillitis	2	
Massive skin gangrene	1	
Lateral sinus thrombosis	1	
Amebiasis	1	
Phlegmonous esophagitis		1
Total	12	3
Vascular:		
Myocardial infarction	3	2
Cerebrovascular accident	2	1
Cardiac failure	2	
Gangrene of leg	1	
Total	8	3
Miscellaneous:		
Carcinoma of pancreas	1	
Thyroid storm	1	
Skull fracture	1	
Hemochromatosis		1
Acute pancreatitis		1
Uremia		1
Total	3	3
No demonstrable complication	21	16
Total Deaths	44	25

DISCUSSION

From the foregoing, it is evident that between the two five-year periods there were differences in the characteristics of the groups as well as the types of therapy carried out. If the mortality rate in the second period had been similar to that of the first, fifty-four deaths would have been expected. Inasmuch as only twenty-five patients succumbed in the latter period, there was a theoretical salvage of approximately twenty-nine cases. Doubtless, the changes both in patient condition and therapy were concerned with the decreased mortality.

With respect to the characteristics of the patients on admission, the significant difference between the periods lay in the distribution of the nonacidotic complications. If the distribution had been the same in the second period as in the first, thirty-three severely complicated cases would have been expected. Since the mortality of this class was very little different between the periods, twenty-six deaths would have been expected instead of the observed nine. Accordingly, it is very likely that a large part of the increased salvage was due to the presence of less severely complicated cases. Undoubtedly the more prevalent use of antibiotics prior to admission eliminated many of the more serious infectious complications.

To evaluate the role of altered management is more difficult. When the severely complicated cases are excluded, there is no significant difference between period mortalities of the uncomplicated and moderately complicated cases either separately or collectively (table 5). Furthermore, if the difference in severity distributions between periods is eliminated by adjusting that of period II to that of period I, and the mortality rates of period II remain unchanged, the resulting mortality of 23 per cent in period II is not significantly different from that of period I. Accordingly, it is not possible to conclude from these observations that change in treatment alone was effective in increasing survival. Nevertheless, it is believed that the use of norepinephrine and massive parenteral potassium was lifesaving in certain instances.

In the first period there were fifteen patients who developed sustained hypotension unresponsive to therapy with ordinary fluids or plasma expanders. Fourteen of these died. In the second period there were seventeen instances of similar hypotension. Norepinephrine was administered in all, with recovery in nine. In four of these cases the amounts employed ranged from 26 to 96 mg. over periods ranging from seventeen to ninety-six hours. The recovery of three of this latter group was believed to be uncontestedly related to the norepinephrine therapy.

Parenteral potassium was given infrequently and in small dosage in the first period, with what was believed to be beneficial effect in one patient only. It is certain that many examples of severe potassium deficiency were not recognized at the time. In the second period there were five patients without nonacidotic complications in whom severe or acute potassium deficiencies occurred. Intravenous potassium in amounts ranging from 240 to 480 mEq. were administered up to the thirty-sixth hour of treatment. These large amounts were necessary to correct and prevent the recurrence of respiratory paralysis. It is believed that death would have occurred in the absence of this measure.

SUMMARY

Observations were made on 312 cases of diabetic acidosis in a city hospital during a ten-year period. The mortality decreased in this time from 31.4 per cent in the first five-year period to 14.5 per cent in the second five years. It is suggested that a lower incidence of nonacidotic complications was in large part responsible for the decline in mortality. Though it could not be shown that altered therapy caused increased survival in those without severe complications, the use of norepinephrine and parenteral potassium appeared to be lifesaving in certain instances.

SUMMARIO IN INTERLINGUA

Factores Que Influentia Le Mortalitate De Patientes Con Acidosis Diabetic In Un Grande Hospital Municipal

TABLE 5
The mortality of diabetic acidosis according to severity of nonacidotic complications

Period	Uncomplicated		Moderately Complicated		Severely Complicated	
	Living	Dead	Living	Dead	Living	Dead
1947-1951	41 (80%)	10 (20%)	50 (81%)	12 (19%)	3 (11%)	24 (89%)
1952-1956	69 (90%)	8 (10%)	75 (90%)	8 (10%)	3 (25%)	9 (75%)
	P>0.3		P>0.3		P>0.5	

In le curso de un periodo de dece annos, 312 casos de acidosis diabetic esseva observate in un hospital municipal. Durante le prime periodo de cinque annos, le mortalitate esseva 31,4 pro cento; illo decresceva a 14,5 pro cento durante le secunde periodo de cinque annos. Es suggerite que un reducite incidentia de complicationes non-acidotic esseva in grande parte responsabile pro le reduction del mortalitate. Ben que il non esseva possibile demonstrar que alterationes del therapias habeva causate un augmentate superviventia inter le patientes sin sever complicationes, il pareva que le uso de norepinephrina e de kalium parenteral esseva factores que salvava le vita del patiente in certe casos.

ACKNOWLEDGMENT

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Cholesterol in Diet and Serum

Although it is difficult at the present stage of investigation to measure the effect of cholesterol feeding on human atherosclerosis, A. Keys (*Fed. Proc.* 8:523 (1949); *Circulation* 5:115 (1952)) and Keys and J. T. Anderson (*Nat. Research Council Pub.* 338 (1954)) have previously reported briefly both survey and experimental evidence indicating that the cholesterol in ordinary human diets has substantially no effect on the concentration of cholesterol in the blood. However, these authors have more recently collaborated with others (Keys, et al., *J. Nutrition* 54:39 (1956)) in an extensive series of dietary experiments on human subjects under very rigidly controlled conditions, and also in both cross-sectional and longitudinal studies on men in Minnesota and Sardinia.

All of the subjects were men between the ages of twenty and sixty and were pronounced to be physically healthy on the basis of medical examinations, including electrocardiography. Subjects in the prolonged controlled experiments were schizophrenic patients in Hastings State Hospital, Minnesota. Men in the longitudinal surveys were professional and business men aged forty-five to fifty-five in 1947 who had cooperated with the laboratory for at least nine years. Surveys on the island of Sardinia included coal miners in the small town of Bacu Abis and moderately active men employed by the city of Cagliari and by the University of Cagliari Medical School.

Dietary cholesterol was computed from food charts. In surveys, except for those where the diets were meas-

ured by a U. S. Department of Agriculture group, the dietary intake of cholesterol-containing foods was estimated by individual interviews, with particular attention being given to the intake of eggs, cream, butter, cheese, ice cream, meats, fish and chicken. On the island of Sardinia the individual habits of eating eggs most wholly accounted for the variation in total cholesterol intake. The mean for a total of 187 men was 4.92 eggs per week with the range extending from zero to thirty eggs per week.

Results of six cross sectional surveys on men in Minnesota showed clearly that any relationship between serum cholesterol and that consumed in the diet must be very small. However, it appeared that there is a slight tendency for men who consume the least cholesterol to have concentrations of blood cholesterol slightly lower than the average while those who eat the most cholesterol have the opposite tendency, the deviations in each case being approximately 3 per cent of the mean. Complete independence prevailed over the middle range of intakes, including 60 per cent of the subjects.

Results of the two surveys in Sardinia in 1955, one on moderately active municipal employees in Cagliari and one on poor coal miners in the small mining town of Bacu Abis (representing a two-fold difference in cholesterol intake) failed to show significant differences in serum cholesterol levels.

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