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UNIVERSIDAD NACIONAL AUTONOMA DE MÉXICO

FACULTAD DE MEDICINA

HOSPITAL DE ESPECIALIDADES CENTRO MEDICO NACIONAL "SIGLO XXI"

DIABETIC KETOACIDOSIS IN ADULTS: CLINICAL AND LABORATORY FEATURES

TESIS

QUE PARA OBTENER EL CURSO DE ESPECIALIZACION EN

E N D O C R I N O L O G I A

PRESENTA

RITA ANGELICA GOMEZ DIAZ

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Original Article

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KEY WORDS: Diabetic ketoacidosis; Epidemiology in adults; Infections; Serum electrolytes.

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Table 3
Acid-Base Disturbances on Admission

	Hyperchloremic acidosis	Mixed acidosis	Normochloremic acidosis
$\Delta Gap/\Delta HCO_3$	<0.4 %	0.4 - 0.8 %	>0.8 %
Adrogue	11	43	46
INNSZ	8	25	67

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Table 1 shows the distribution of the episodes of DKA according to the age at onset and type of treatment described previously. Recurrent DKA was more common in the groups of late onset IDDM (7/22 patients) and early onset NIDDM (1/4 patients) - average age range 20 - 40 years old - 8 of the 26 patients had three or more episodes.

Precipitating factors were as follows: 40 episodes of DKA (41%) were precipitated by an infection, the urinary tract being the most common site. Of the 19 patients with urinary infections (47.5% of all infected patients); 6 had pyelonephritis, 12 had urinary tract infections (UTI), and one had a renal abscess. Eight patients (20% of all infections) had respiratory infections, upper respiratory tract in four and pneumonia in the other four. Seven patients had soft tissue infections (17.5% of all infections), two had a dental abscess, and the other four patients had enterocolitis, parotiditis or sepsis. In most cases there was no bacteriologic reports or they were negative because antimicrobial treatment had already been started. *E. coli* was the most common microorganism isolated in urinary tract infections.

Although currently accepted antimicrobial therapy guides are usually followed in our setting, specific drugs are not registered in many cases of infection precipitated DKA. Twenty nine episodes of DKA (30%) were precipitated by omission of insulin administration and nine more (9%) by dietary transgressions. DKA was the initial manifestation of diabetes in seven patients. Other precipitating causes like pancreatitis, ischemic heart disease, alcohol ingestion, immunological resistance to insulin or steroid use were present in 8% of cases. No precipitating event could be identified in 5% of cases. On admission, patients were alert in 72 cases (72%), lethargic in 20 (20%) and stuporous in 8 (8%). The average duration of hospitalization was 7 days.

Table 2 shows the biochemical abnormalities upon admittance, compared with previous reports from Kitabchi (6) and Foster (7). Table 3 shows the type of acidosis according to the $\Delta Gap/\Delta HCO_3$ quotient upon admittance, compared with the results reported by Adrogue (8). The average anion gap found in our series was 30.4. When we compare series, we can see that metabolic disturbances show a different pattern, the percentage of normochloremic acidosis being higher in our cases (67%) and mixed acidosis being lower (25%). On admission, serum electrolytes were found as follows: sodium levels were normal (138 - 145 mEq/l) in 44.3%, high in 14.4% and low in 41.2% of reported episodes; potassium was normal (3.5 - 5.3 mEq/l) in 70%, high in 16.4% and low in 13.4%. Finally, chloride was found to be normal in 71.4%, high in 18.3% and low in 10.2% of all cases.

Most patients were managed according to accepted recommendations, they had isotonic solutions during the first hour of admission, then according to electrolyte losses, hypotonic or isotonic fluids and potassium (20 - 40 mEq/l) were continued for the next eight hours. Insulin therapy with an initial I.V. bolus of 10 units is started at the beginning of treatment, then 5 I.V. units are given each hour until the glycemia reaches 250 mg/dl (0.1 U/kg of body weight). Insulin doses are then reduced to 2 units/h and subcutaneous administration of insulin is simultaneously started; I.V. administration is stopped 1 - 2 h later. Saline solutions are changed to 5% glucose solutions at this moment.

Bicarbonate is given when plasma pH is less than 6.9 (44 mEq/l as a single dose). This conduct was adopted when we found similar results when bicarbonate was not used in a controlled study (9). Phosphate and magnesium are used only when their levels are low.

Reported complications corresponded to hypokalemia (five cases), hypoglycemia (four cases), hypernatremia (four cases), pulmonary edema (one case), ventricular fibrillation (one case), cerebro-vascular apoplexy (one case) and coma (one case). The great majority of deaths in DKA are due to complications of treatment itself, although they can be prevented by a careful follow-up of the patient's condition. There were three deaths (6.5% mortality); two cases were attributed to bronchoaspiration (a 39-year-old man and a 35-year-old woman) and one case to acute pulmonary edema (a 61-year-old patient who also developed multiple cerebral infarctions documented by CAT scan).

Discussion

Lack of epidemiological, clinical and biochemical data of DKA in our country is noteworthy. Available information from two or three centers refers, mainly, to crude statistic data, without reference to such important aspects as some of the clinical or biochemical features previously mentioned (1-4). This is one of the reasons why we consider of great importance that all centers involved in the attention of diabetic patients report regularly all new cases of DKA and their characteristics.

Patients in our institution are exclusively adults. This is why our series does not include diabetic patients younger than 15 years of age. The average age of our

Table 3
Acid-Base Disturbances on Admission

	Hyperchloremic acidosis	Mixed acidosis	Normochloremic acidosis
$\Delta Gap/\Delta HCO_3$	<0.4 %	0.4 - 0.8 %	>0.8 %
Adrogue	11	43	46
INNSZ	8	25	67

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Patients in our institution are exclusively adults. This is why our series does not include diabetic patients younger than 15 years of age. The average age of our

group was 35 years which might explain why the frequency of DKA as the initial presentation of diabetes mellitus is not as high (15%) as in those series which include pediatric subjects (20 - 25%) (10).

We found six patients with four or more episodes of DKA during the study period. These episodes of recurrent ketoacidosis have been attributed to various causes, such as inadequate metabolic control, inappropriate patient education, inability to prevent or identify acute or chronic complications of diabetes at early stages, or a certain predisposition to develop recurrent bouts of DKA (11,12).

Regarding the frequency of DKA, it is interesting that the majority of episodes (56.5%) occurred in 26 patients whose diabetes began between 20 and 40 years of age. In this group, eight patients (30.7%) had more than three episodes of DKA. Different terms have been used to identify this group of patients, such as type 1½ diabetes, intermediate diabetes, and autoimmune latent diabetes of the adult. Clinically, they are patients who share characteristics from type I and type II diabetes. This intermediate behavior may complicate both their classification and the choice of treatment (13-15). We believe these patients should be put early on insulin therapy in order to avoid recurrent DKA and late stage complications. In one prospective study performed at our institute to identify non-classifiable patients (as being type I or type II), we found that 72% corresponded to an intermediate type of diabetes and 12% had an episode of DKA during the study period. This figure emphasizes the need of early treatment with insulin to obtain a good metabolic control in this group of diabetics (16). From the other groups, 35% of the classical IDDM had an episode of DKA while in the group with NIDDM there were four episodes (8.7%). It is clear from the above data that DKA is not an exclusive complication of type I diabetes.

As in other series reported in the literature (10,17-19), the most frequent precipitating factor found in our group was infection, specifically UTI being the most prevalent. The second most frequent cause of DKA was lack of adherence to insulin treatment and dietary transgressions, two elements traditionally associated with the apearance of both acute (20) and chronic (21) complications of diabetes.

When comparing our data with those from Kitabchi and Foster (Table 2), we found no significant differences in the laboratory parameters analyzed. Although on admission, mean serum sodium and potassium levels were normal, they were low, high or normal in particular cases. This should be considered when decisions are made about the type of solution, electrolyte additions and insulin schedule.

The metabolic acidosis found in DKA is characterized by an increment in the anion gap. In our series, it was 30.4, which is similar to the observed reduction in bicarbonate level. However, many patients with DKA may deviate from this pattern and present varying degrees of anion-gap and hyperchloremic metabolic acidosis as coexistent medical problems. When we compare our series with Adrogue's (Table 3), we can see that 33% of our patients (54% in Adrogue's series) had hyperchloremic metabolic acidosis. This finding of hyperchloremic acidosis may reveal a more gradual installation of the initial metabolic derangement or other acid-base disturbances.

We had three deaths in our series, which represent a 7% mortality rate. This figure is lower than that reported by other series which include adults only. Two of the three patients who died were younger than 50 years. It has been previously established that age is the main risk factor for mortality in adult patients with DKA. In a review of various series, mortality in patients under 50 years was 2 to 7%, while it was 12 to 43% in patients over age 50 (1). Mortality rates, in adult patients, seems to reflect the presence of concomitant diseases (myocardial infarction, pancreatitis, etc.) rather than a different behavior of DKA itself. This may be the reason why death rates do not change significantly when compared with retrospective reviews or cohort-compared series (22).

In conclusion, characterizing the epidemiological features, clinical findings, and biochemical features of DKA provides us with useful elements for future therapeutic strategies planning. Future studies can be designed to evaluate the changes in morbidity and mortality obtained with prospective specifically implemented strategies. As more information is generated about the clinical characteristics of the Mexican diabetic population, it will be possible not to use information generated in other populations which, in the great majority of cases, have important differences with ours.

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