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SCIENTIFIC LETTER

Clinical outcomes and biochemical characteristics of a Hispanic cohort of patients with diabetic ketoacidosis: 10-Year experience in an emergency department

Resultados clínicos y características bioquímicas en una cohorte hispana de pacientes con cetoacidosis diabética: experiencia de una década en el departamento de emergencias

Diabetic ketoacidosis (DKA) is a potentially life-threatening complication of diabetes mellitus characterized by hyperglycemia, high-anion anion gap metabolic acidosis, and the presence of ketone bodies. The most common causes are non-adherence to treatment and infections.[1] Hospital admissions have increased over the last decades with a mortality of 1% in developed countries[2] to 30% in low-income countries.[3,4] Complications include hypoglycemia and serum electrolyte disturbances, with potassium being the most commonly affected.[5]We report our ten-year experience of patients with DKA at an academic center in northeast Mexico.

This retrospective study includes 329 subjects diagnosed with DKA from January 2009 to March 2019 at the ''Dr. José E. González'' University Hospital of the School of Medicine of the Universidad Autónoma de Nuevo León in Monterrey, México. All subjects who presented to the emergency room and fulfilled the diagnostic criteria of DKA[6] were included. Treatment strategies and resolution criteria were selected by each treating physician according to The American Diabetes Association guidelines.[6] Mild DKA was categorized by a ph level of 7.25–7.30 and serum bicarbonate between 15 and 18 mEq/l, moderate DKA was categorized by a pH level between 7.0 and 7.24 and serum bicarbonate between 10 and 14 mEq/l; and severe DKA as patients with pH lower than 7.0 and a serum bicarbonate lower than 10 mEq/l. For this analysis, the resolution criteria were guided by current recommendations.[6] Hyperkalemia was defined as a potassium level > 5 mmol/L and clinically relevant hyperkalemia as > 6 mmol/L. Hypokalemia was defined as a potassium level < 3.5 mmol/L and relevant hypokalemia as <3.3 mEq/L.

The protocol was reviewed and approved by our local IRB, and the need for informed consent was waived. All relevant information was obtained from clinical records. Descriptive analyses were done using frequencies (%) and medians (q25–q75) or means ± SD, accordingly. Comparisons of quantitative variables were done using ANOVA. All statistical analysis was done using SPSS version 22.0 (IBM SPSS Statistics for Windows, IBM Corp., Armonk, NY), considering a p-value < 0.05 significant.

A total of 329 subjects with DKA were included in our analysis. Subjects had a median age of 32 years (range: 18–90) and 169 (51.4%) were women. Regarding initial biochemical characteristics, blood glucose was 475.6 ± 202.4 mg/dL, pH was 7.08 ± 0.15, serum bicarbonate was 7.7 ± 4.4 mmol/L and the anion gap was 23.8 ± 6.7 mmol/L. No significant difference was found between genders in clinical or biochemical features.

Regarding DKA severity, 236 (71.7%) cases were classified as severe, 73 (22.2%), as moderate and 20 (6.1%) as mild. Of the entire group, 10 (3%) subjects presented hypokalemia, 36 (10.9%) significant hypokalemia, and 6 (1.9%) severe hypokalemia. Hyperkalemia was found in 67 (20.40%) patients, severe hyperkalemia in 28 (8.51%), and the rest had normal potassium levels. Mean serum glucose was 550.5 ± 224.2 mg/dL in subjects with hyperkalemia, 454.5 ± 177.9 mg/dL in those with normal potassium, and 410.2 ± 205.3 mg/dL in subjects with hypokalemia (p < 0.001).

Hypoglycemia occurred in 27 (8.2%) patients during treatment. There were no cases of brain edema in our group. Of the whole cohort, time to resolution of DKA was 26 h and 22 min with a standard deviation of ±18 h and 10 min. A total of 8 (2.4%) deaths were documented; all of these associated with septic shock.

Clinical and laboratory features between mild, moderate and severe DKA were compared. As expected, statistically significant differences were found in pH, serum bicarbonate, and anion gap (p < 0.05). Significant differences were also found in hemoglobin, white blood cells, platelets, PCO_2, heart rate, respiratory rate, and blood urea nitrogen. Complete data are shown in Table 1.

A subgroup of 52 patients with significant hypokalemia during treatment was studied; after a median of 6 units per hour of continuous insulin infusion, and a potassium replacement of 10 mEq per hour, only 5 (9.6%) did not improve to >3.3 mEq/L of potassium in the next measurement of serum electrolytes.

Even though DKA is a well-known complication of diabetes mellitus, data on clinical and biochemical features are scarce. Similar to a previous study from Canadian institutions,[7] severe DKA was frequent, but a lower mean pH was found in our group. This could be due to the greater number of uninsured patients in our population, who commonly delay seeking medical attention.

Table 1 Comparison of mean values of clinical and laboratory in mild, moderate and severe diabetic ketoacidosis (DKA) at diagnosis. ANOVA test.

	Mild DKA Mean (±SD)	Moderate DKA Mean (±SD)	Severe DKA Mean (±SD)	*P* value
Blood glucose, mg/dL	396.20 (196.19)	448.07 (152.81)	490.86 (214.28)	0.056
pH	7.28 (0.04)	7.21 (0.06)	7.03 (0.15)	<0.001
Bicarbonate	17.0 (1.98)	12.79 (2.0)	5.44 (2.37)	<0.001
ANION GAP	14.95 (1.92)	20.56 (6.27)	25.83 (6.20)	<0.001
Serum osmolality	291.40 (5.32)	300.45 (10.69)	297.96 (12.06)	0.278
Lactate	1.97 (0.99)	2.59 (2.39)	2.59 (2.29)	0.536
White blood cells $\times 10^9$/L	13.47 (6.21)	14.75 (7.08)	19.73 (14.61)	0.008
Hemoglobin, g/dL	12.95 (3.03)	16.03 (1.98)	15.58 (3.22)	0.047
Platelet count $\times 10^9$/L	270.54 (89.84)	299.18 (125.81)	326.18 (118.36)	0.048
PCO_2	35.09 (4.52)	32.02 (7.22)	20.94 (12.93)	<0.001
Systolic pressure	120.00 (27.77)	116.74 (23.39)	115.68 (23.06)	0.712
Diastolic pressure	71.35 (12.55)	75.07 (15.18)	74.60 (16.18)	0.638
Cardiac frequency	102.55 (22.81)	105.42 (24.02)	114.27 (23.56)	0.005
Respiratory frequency	19.25 (5.24)	23.72 (11.73)	27.51 (11.34)	0.001
Creatinine	1.46 (1.05)	1.56 (1.17)	1.85 (1.32)	0.821
Blood urea nitrogen	24.35 (16.51)	27.32 (22.44)	21.35 (16.38)	0.045
Sodium	132.76 (5.29)	133.14 (6.20)	132.63 (6.12)	0.822
Potassium	4.36 (0.65)	4.44 (0.84)	4.55 (1.09)	0.559
Chloride	100.73 (6.42)	100.55 (7.21)	101.85 (10.71)	0.578

Hypoglycemia during treatment is a known and frequent concern. In a study from the UK more than 25% of patients[8,9] had a serum glucose level below 70 mg/dL. This event was only present in 8.2% of our patients. The mortality rate in our group was 2.4%, slightly higher than that reported in high-income countries[6] but significantly lower than others.[3,4]

Interestingly, almost half of the patients in our cohort presented at the emergency department with serum potassium abnormalities. In this respect, insulin plays a determinant role for cellular potassium regulation, promoting its influx from the extracellular compartment. Hypokalemia is also worsened by increased diuresis after aggressive IV hydration, vital in the management of DKA. Furthermore, in subjects with DKA, sodium is retained at the expense of augmented potassium excretion, and renal loss of potassium is also magnified by the accompanying acidosis.[1] Hypokalemia on admission was traditionally documented as an uncommon event[10]; however, this affirmation was completely different in our population. Mortality attributable to this electrolyte disturbance is infrequent, and in this respect, none of the deaths in our cohort were associated with this complication. We documented this and other problems in our Mexican cohort where diabetes mellitus is a current health problem. Nevertheless, complications during treatment of DKA need to be further evaluated in a prospective manner. Some limitations in our study are its single center and retrospective design and the absence of follow-up after discharge. Some of the strengths are the considerable number of patients included and strict adherence to the American Diabetes Association guidelines.

In conclusion, DKA is a serious but preventable complication of diabetes mellitus; similarities to other groups regarding mortality, clinical, and biochemical features were found. Nevertheless, a higher than expected prevalence of severe DKA was found. In addition, potassium disturbances tend to be more frequent but none of them were directly associated with mortality.

Conflict of interest

The authors declare no conflict of interest.

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Raúl Alberto Jiménez-Castillo*,
Edgar Francisco Carrizales-Sepúlveda,
Marco Antonio Román-Montalvo,
Daniel Eduardo Benavides-Salgado, Raymundo Vera-Pineda,
Jorge Rafael Violante-Cumpa, José Luis Herrera-Elizondo,
Giselle Rivas-Wong, Dulce Georgina Corpus-Ruiz,
Homero Náñez-Terreros

Internal Medicine Department, Hospital Universitario, Universidad Autónoma de Nuevo León, Monterrey, Nuevo León, Mexico

* Corresponding author.
E-mail address: raulalbertojc10@gmail.com
(R.A. Jiménez-Castillo).

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Bruns-Garland syndrome (diabetic amyotrophy) is associated with a rapid improvement in metabolic control☆

Amiotrofia diabética síndrome de Bruns-Garland asociado a rápida mejoría en el control metabólico

Diabetic amyotrophy or Bruns-Garland syndrome is a rare disorder affecting less than 1% of all diabetic patients. It manifests as unilateral or bilateral muscle pain, weakness and atrophy in the proximal region of the lower limbs. It is more common in the fifth decade of life among patients who have suffered type 2 diabetes for several years. However, the condition is not directly related to the severity of diabetes, and may even precede its diagnosis.[1] The underlying etiopathogenesis is multifactorial and little known, and the diagnosis is based on the clinical findings and the exclusion of other possible causes. The present case is of interest in that it suggests a new mechanism that may influence the course of the disease.

A 53-year-old woman presented with reactive depression following the death of a relative and the onset of type 2 diabetes three months before admission, with glycemia 224 mg/dl and HbA1c: 10.9%. Weight: 56 kg, height: 1.5 m; the body mass index (BMI): 24.9 kg/m^2. Treatment was started with the prescription of a 1200 kcal diet and metformin 850 mg/12 h, with good patient adherence. Concomitant to the diagnosis of type 2 diabetes, she developed right lumbosciatalgia, which subsequently became bilateral, with very poor pain control despite the treatment prescribed (Table 1). The patient was admitted to Neurology for the evaluation of bilateral subacute lumbosacral radiculoplexus neuropathy, exhibiting gradual worsened gait, with falls and the need for crutches over the previous few weeks. She was seen to have lost weight (10 kg) from the time of her diabetes diagnosis, this being largely attributable to the prescribed diet. The neurological examination revealed predominantly proximal paraparesis in addition to quadriceps atrophy and areflexia of the lower extremities, with no sphincter involvement. The electromyogram showed bilateral spontaneous activity at L2-S2 level, consistent with lumbosacral radiculoplexus neuropathy, with motor axonal degeneration and abundant signs of acute and active denervation. Lumbar and pelvic magnetic resonance imaging and thoracoabdominal computed tomography ruled out compressive and infiltrative causes. Lumbar puncture showed slightly elevated proteins in the cerebrospinal fluid (0.57 g/l), while the remaining parameters proved normal, including histopathology and the microbiological data. The laboratory test results only showed a decrease in HbA1c concentration (6.6%). The liver function and lipid profile, albumin, sideremia, the transferrin saturation index, ferritin, ionogram, calcemia, vitamin D, vitamin B12, and folic acid were all normal. No anti-GAD or anti-ganglioside antibodies were detected, and cytomegalovirus (CMV) and HIV testing proved negative. The funduscopy findings and the absence of microalbuminuria allowed us to discard the possibility of microangiopathic complications.

Having discarded compressive/infiltrative causes, and based on the suggestive clinical findings, Bruns-Garland syndrome was diagnosed. Treatment was started with intravenous boluses of methylprednisolone, opiates for pain control, and rehabilitation. After 5 months, there was less pain and improved motor balance, and part of the medication could be suspended. Table 1 details the clinical characteristics and the electromyographic findings.

In Bruns-Garland syndrome, immune-mediated inflammation is central to the physiopathology of the disorder, causing microvasculitis with the presence of mono- and polymorphonuclear cells and immune complexes and complement

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