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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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References

1. Kitabchi AE, Nyenwe EA. Hyperglycemic crises in diabetes mellitus: diabetic ketoacidosis and hyperglycemic hyperosmolar state. Endocrinol Metab Clin North Am. 2006;35:725–51.
2. Guisado-Vasco P, Cano-Megías M, Carrasco-de la Fuente M, Corres-González J, Matei AM, González-Albarrán O. Clinical features, mortality, hospital admission, and length of stay of a cohort of adult patients with diabetic ketoacidosis attending the emergency room of a tertiary hospital in Spain. Endocrinol Nutr. 2015;62:277–84.
3. Otieno C, Kayima J, Omonge E, Oyoo G. Diabetic ketoacidosis: risk factors, mechanisms and management strategies in sub-Saharan Africa: a review. East Afr Med J. 2005;82.
4. Elmehdawi RR, Ehmida M, Elmagrehi H, Alaysh A. Incidence and mortality of diabetic ketoacidosis in Benghazi-Libya in 2007. Oman Med J. 2013;28:178.

5. Wong B, Cheng A, Yu C, Goguen J. Examining the ''Killer K'' of diabetic ketoacidosis at a tertiary care hospital: an exploratory study. Can J Diabetes. 2016;40:204–9.
6. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. Diabetes Care. 2009;32:1335–43.
7. Galm BP, Bagshaw SM, Senior PA. Acute management of diabetic ketoacidosis in adults at 3 teaching hospitals in Canada: a multicentre, retrospective cohort study. Can J Diabetes. 2019;43:309–15, e2.
8. Varadarajan M, Patel M, Kakkar N, Sin ELPW-P, Maxey D, Nunney I, et al. Are the results from the 2014 UK national survey on the management of diabetic ketoacidosis applicable to individual centres? Diabetes Res Clin Pract. 2017; 127.
9. Dhatariya K, Nunney I, Higgins K, Sampson M, Iceton G. National survey of the management of diabetic ketoacidosis (DKA) in the UK in 2014. Diabet Med. 2016;33:252–60.
10. Beigelman PM. Potassium in severe diabetic ketoacidosis. Am J Med. 1973;54:419–20.

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

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

La amiotrofia diabética o síndrome de Bruns-Garland es una entidad rara, que afecta a menos del 1% de los pacientes con diabetes. Se manifiesta con dolor, debilidad y atrofia muscular, uni- o bilateral en la región proximal de los miembros inferiores. Es más frecuente en la quinta década de vida en pacientes con varios años de evolución de diabetes tipo 2. Sin embargo, no guarda relación directa con la gravedad del curso de esta, pudiendo incluso preceder al diagnóstico[1]. La etiopatogenia es multifactorial y poco aclarada, siendo el diagnóstico clínico y de exclusión. El caso que presentamos tiene interés al sugerir un nuevo mecanismo que puede influir en la evolución de la enfermedad.

Mujer de 53 años con depresión reactiva al fallecimiento de un familiar y comienzo de diabetes tipo 2 tres meses previos al ingreso, con glucemia de 224 mg/dL y HbA1c: 10,9%. Peso: 56 kg, talla: 1,5 m; IMC: 24,9 kg/m^2. Se inició tratamiento con dieta de 1.200 Kcal y metformina 850 mg/12 h con buena adherencia por parte de la paciente. Concomitantemente al diagnóstico de diabetes tipo 2, inicia lumbociatalgia derecha, siendo posteriormente bilateral, con muy mal control del dolor a pesar del tratamiento prescrito (tabla 1). Ingresa en neurología para estudio de radiculoplexopatía bilateral lumbosacra subaguda, presentando empeoramiento progresivo de la marcha, con caídas y precisando muletas las últimas semanas. Se objetiva una pérdida de peso de 10 kg desde el diagnóstico de la diabetes en gran parte atribuible a la dieta seguida por la paciente. La exploración neurológica reveló la presencia de paraparesia de predominio proximal además de atrofia de cuádriceps y arreflexia en extremidades inferiores, sin afectación de esfínteres. El electromiograma mostró actividad espontánea a nivel L2-S2 bilateral, compatible con radiculoplexopatía lumbosacra, con degeneración axonal motora y abundantes signos de denervación aguda y activa. La resonancia magnética lumbar y de pelvis y la tomografía computarizada toracoabdominal descartaron causas compresivas e infiltrativas. La punción lumbar mostró ligera hiperproteinorraquia (0,57 g/L), siendo el resto de los parámetros normales, incluyendo la anatomía patológica y resultados microbiológicos. En la analítica únicamente destacaba un descenso de la HbA1c (6,6%). El perfil hepático y lipídico, la albúmina, sideremia, índice de saturación de la transferrina, ferritina, ionograma, calcemia, vitamina D, vitamina B12 y ácido fólico fueron normales. No se detectaron anticuerpos anti-GAD o antigangliósidos y el estudio de citomegalovirus y VIH resultó negativo. El examen fundoscópico y la ausencia de microalbuminuria descartaron la presencia de complicaciones microangiopáticas.

Descartadas causas compresivas/infiltrativas y siendo clínicamente indicativo, se orientó el caso como síndrome de Bruns-Garland. Se inició tratamiento con bolus intravenosos de metilprednisolona, derivados mórficos para control del dolor y rehabilitación. A los 5 meses la paciente presentó mejoría del dolor y del balance motor, pudiendo retirarse parte de medicación. En la tabla 1 se detallan las características semiológicas y los hallazgos del electromiograma.

En el síndrome de Bruns-Garland la inflamación inmunomediada constituye el eje de la explicación fisiopatológica, causando una microvasculitis con presencia de mono- y polimorfonucleares, complejos inmunes y complemento activado. El daño microvascular se traduce en isquemia de los *vasa nervorum* de los plexos y raíces nerviosas. Esto produce daños degenerativos axonales y desmielinización con consecuente atrofia focal de fibras musculares que alternan con fibras sanas. Aunque, el diagnóstico es clínico, se confirma con los estudios electrodiagnósticos que muestran daño axonal multifocal de raíces y plexos por desmielinización y denervación[2], como muestra nuestro caso. La