Diabetic Ketoacidosis in Type 1 and Type 2 Diabetes Mellitus

Clinical and Biochemical Differences

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Background: Diabetic ketoacidosis (DKA), once thought to typify type 1 diabetes mellitus, has been reported to affect individuals with type 2 diabetes mellitus. An analysis and overview of the different clinical and biochemical characteristics of DKA that might be predicted between patients with type 1 and type 2 diabetes is needed.

Methods: We reviewed 176 admissions of patients with moderate-to-severe DKA. Patients were classified as having type 1 or type 2 diabetes based on treatment history and/or autoantibody status. Groups were compared for differences in symptoms, precipitants, vital statistics, biochemical profiles at presentation, and response to therapy.

Results: Of 138 patients admitted for moderate-to-severe DKA, 30 had type 2 diabetes. A greater proportion of the type 2 diabetes group was Latino American or African American (P < .001). Thirty-five admissions (19.9%) were for newly diagnosed diabetes. A total of 85% of all admissions involved discontinuation of medication use, 69.2% in the type 2 group. Infections were present in 21.6% of the type 1 and 48.4% of the type 2 diabetes admissions. A total of 21% of patients with type 1 diabetes and 70% with type 2 diabetes had a body mass index greater than 27. Although the type 1 diabetes group was more acidic (arterial pH, 7.21 ± 0.12 vs 7.27 ± 0.08; P < .001), type 2 diabetes patients required longer treatment periods (36.0 ± 11.6 vs 28.9 ± 8.9 hours, P = .01) to achieve ketone-free urine. Complications from therapy were uncommon.

Conclusions: A significant proportion of DKA occurs in patients with type 2 diabetes. The time-tested therapy for DKA of intravenous insulin with concomitant glucose as the plasma level decreases, sufficient fluid and electrolyte replacement, and attention to associated problems remains the standard of care, irrespective of the type of diabetes.

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pressed as mean±SD. Patients with type 2 diabetes were com-
appropriate. Unless otherwise indicated, all data are ex-

made in the emergency department by the presence of 3 labo-

healthy DKA. The diagnosis of moderate-to-severe DKA was

ated, duration of insulin infusion, time from presentation to

for the management of diabetic ketoacidosis. To convert blood glucose to millimoles per liter, multiply by

Based on the hourly blood glucose determination, change each of the 2

and 80% (63) were white, 54% (42) were Latino (mostly Mexican or Mexican Ameri-

Although 42% of the patients admitted to weight loss, only 78% of these patients were able
to quantify the amount of loss, which was reported to average 13.0 kg over 3 months.

A plausible explanation for the development of DKA was identified in 90.3% of admissions. Thirty-six pa-

RESULTS

A total of 138 patients accounted for the 176 admissions to Parkland Memorial Hospital’s University Dia-

Bettses Treatment Center for moderate-to-severe DKA. Eighty (58%) of the patients were male, 24 (17%) of the patients were white, 65 (47%) were African American, 48 (35%) were Latino (mostly Mexican or Mexican Ameri-

can), and 1 patient (1%) was Native American. The pa-
tients were between the ages of 15 and 66 years (mean age, 35.0±12.1 years). A total of 18.2% of the patients had a history of polysubstance abuse. A summary of the patient demographics for the subgroups analyzed is pre-
sented in Table 1. Differences between groups are noted for age and diabetes duration only.

Symptoms documented to be present at the time of presentation are summarized in Table 2. The duration of the symptoms, when they were reported to be present, is also shown. Although 42% of the patients admitted to weight loss, only 78% of these patients were able to quantify the amount of loss, which was reported to average 13.0 kg over 3 months.

A plausible explanation for the development of DKA was identified in 90.3% of admissions. Thirty-six pa-

tients were newly diagnosed as having diabetes. Eighty-five percent of the admissions by patients with a known history of diabetes followed a period of discontinuation of medical therapies during the days preceding presentation. Discontinuation of medication use, mostly insul-
in, was implicated in 90.2% of the admissions by the 16 patients with more than 1 admission during the year. Five of these patients had a history of polysubstance abuse. Infections were identified in 38% of all the patients and included urinary tract infections, upper respiratory tract infections, pneumonia, cellulitis, and cutaneous abscesses. These infections were present in 22% of the pa-
tients with type 1 diabetes and 48% of patients with type 2 diabetes. Pancreatitis was also present in 10% of the admissions. Since patients with an acute myocardial infarction were admitted to the cardiac care service rather than the University Diabetes Treatment Center, none of the patients in this study had a myocardial infarction as

Blood Glucose, Insulin Infusion, DS5%W,  

mg/dL  U/L  mL/h  mL/h  

<70  0.5  1.0  250  

71-100  1.0  2.0  225  

101-150  2.0  4.0  200  

151-200  3.0  6.0  175  

201-250  4.0  8.0  150  

251-300  6.0  12.0  100  

301-350  8.0  16.0  50  

351-400  10.0  20.0  0  

401-450  12.0  24.0  0  

451-500  15.0  30.0  0  

>500  20.0  40.0  0  

*Give 20 mL of D50%W IVP and repeat CBG in 15 minutes.

The methods described in the experiment:  

Of the 679 admissions to the Parkland Memorial Hospital Uni-

versity Diabetes Treatment Center between January and De-
cember 2001, 176 admissions by 138 patients were for moderate-
to-severe DKA. The diagnosis of moderate-to-severe DKA was

made in the emergency department by the presence of 3 labo-

ratory findings: a plasma glucose level of 250 mg/dL or higher

(<13.9 mmol/L); a serum bicarbonate level of 15 mEq/L or

lower, an arterial blood pH of 7.30 or lower, or a venous blood

pH of 7.25 or lower; and moderate or large urinary ketones.14

Patients were treated by residents of the University of Texas

Southwestern Medical Center under the supervision of an en-
docrinology fellow and an attending from the Division of En-
docrinology. Intravenous insulin was administered according

to the treatment algorithm shown in the Figure. This proto-
col was begun as soon as possible after initial evaluation in the

emergency department. Additional hydration and electrolyte

replacement were left to the discretion of the treating physi-
cians, although following the American Diabetes Association

practice guidelines was encouraged.13 The insulin infusion was

discontinued 2 hours after the administration of subcutane-

ous insulin once patients had resolution of their metabolic sta-

tus, including ketone-free urine sample, and were able to tol-
erate oral feedings.

These DKA admissions were reviewed retrospectively and
data collected on patient demographics, presenting symp-
toms, precipitating causes of DKA, vital signs, biochemical pro-
files at presentation to the emergency department, amount of

intravenous fluid administered, amount of insulin adminis-
tered, duration of insulin infusion, time from presentation to

resolution of urine ketones, insulin dose at discharge, and length of hospitalization.

Comparisons between the groups were performed using
the t test, Mann-Whitney rank sums tests, and the χ2 test as
appropriate. Unless otherwise indicated, all data are ex-
pressed as mean±SD. Patients with type 2 diabetes were com-
pared to the subgroup of patients with type 1 diabetes. Pa-

tients were assigned to the type 2 diabetes group if they were previously diagnosed as having diabetes and at some time in their disease, other than a time consistent with the "honey-
moon period," were managed with diet and exercise alone or

with oral hypoglycemic agents or were noncompliant with their

insulin regimen for more than 3 weeks preceding admission. Patients with newly diagnosed diabetes were assigned to the type 2 group if they tested negative for autoimmune antibody or if they had phenotypic features of type 2 diabetes (such as obesity, acanthosis nigricans, or a family history of type 2 dia-
betes) and were noted to have a stressful event (eg, infection) that precipitated the episode of DKA. Based on recent evi-
dence that indicates similar biochemical profiles and physical characteristics, patients with idiopathic type 1 diabetes (type

1B) were included in the type 2 diabetes subgroup for pur-

poses of analysis.13 Further analyses were performed compar-

ing patients diagnosed as having diabetes on admission for DKA

with those with a known history of diabetes. Additionally, pa-

tients with multiple admissions were compared with the group of patients with only 1 admission during the year.
a precipitant for the development of DKA. Similarly, surgical stress was not an observed cause for the development of DKA, since all of the patients in this study presented to the emergency department presumably from home.

On presentation to the emergency department, patients were tachycardic, with an average heart rate of 117±19/min and had a slightly elevated systolic/diastolic blood pressure of 135±23/85±15 mm Hg. By the time of discharge from the hospital, the patients had normalization of the heart rate to 83±9/min and normalization of systolic/diastolic blood pressure to 113±16/73±10 mm Hg. Patients weighed 69.6±18.3 kg (range, 43.1-147.2 kg; median, 65.3 kg) at the time of admission to the hospital, having received an average of 3.7±1.5 L of intravenous fluid in the emergency department. Their weight increased by an additional 2.7±3.2 kg during the hospitalization. Patients newly diagnosed as having diabetes weighed more than those with a known history of diabetes (81.4±22.7 kg vs 67.3±16.5 kg, \( P = .02 \)). Based on weight at the time of discharge from the hospital, 25% of the patients had a body mass index (a measure of weight in kilograms divided by the square of height in meters) greater than 27. Using their admission weights and reported amount of weight lost, 21% of patients with type 1 diabetes and 70% of patients with type 2 diabetes had a body mass index greater than 27 before the onset of symptoms of uncontrolled diabetes.

Table 3 provides a summary of the distribution of laboratory values for the patients at the time of presentation with DKA. Patients had a hemoglobin A1c level of 13.0%±2.5%. Patients with a clinical diagnosis of pancreatitis at the time of admission accounted for 57% of the patients with elevated amylase levels and 42% of the patients with elevated lipase levels. Compared with those patients with normal or low potassium levels, the patients with hyperkalemia at the time of presentation had correspondingly more severe acidosis. They also had higher plasma glucose levels, lower serum sodium levels, lower chloride levels, and higher calcium, magnesium, and phosphate levels. Their blood urea nitrogen

<p>| Table 1. Demographics for Subgroups of Patients Classified by Type and Previous Diagnosis of Diabetes |</p>
<table>
<thead>
<tr>
<th>Variable</th>
<th>Previously Diagnosed Type 1 DM</th>
<th>Previously Diagnosed Type 2 DM</th>
<th>Newly Diagnosed Type 1 DM</th>
<th>Newly Diagnosed Type 2 DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>78</td>
<td>25</td>
<td>30</td>
<td>5</td>
</tr>
<tr>
<td>Age, mean ± SD, y</td>
<td>32.5 ± 11.2</td>
<td>41.0 ± 12.5*</td>
<td>38.2 ± 13.3*</td>
<td>42.5 ± 3.3</td>
</tr>
<tr>
<td>Sex, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>44 (56)</td>
<td>15 (60)</td>
<td>18 (60)</td>
<td>3 (60)</td>
</tr>
<tr>
<td>Female</td>
<td>34 (44)</td>
<td>10 (40)</td>
<td>12 (40)</td>
<td>2 (40)</td>
</tr>
<tr>
<td>Ethnicity, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>18 (23.1)</td>
<td>3 (12)</td>
<td>3 (10)</td>
<td>0</td>
</tr>
<tr>
<td>African American</td>
<td>36 (46.1)</td>
<td>12 (48)</td>
<td>12 (40)</td>
<td>5 (100)</td>
</tr>
<tr>
<td>Latino American</td>
<td>24 (30.8)</td>
<td>9 (36)</td>
<td>15 (50)</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>1 (4)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Duration of diabetes, mean ± SD, y</td>
<td>12.7 ± 10.0</td>
<td>5.6 ± 4.4†</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: DM, diabetes mellitus; NA, not applicable.
* \( P < .05 \) for comparison vs previously diagnosed type 1 DM group.
† \( P < .001 \) for comparison vs previously diagnosed type 1 DM group.

<p>| Table 2. Frequency and Duration of Symptoms Reported by Patients Admitted With Moderate-to-Severe Diabetic Ketoacidosis |</p>
<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency, Percentage of Admissions</th>
<th>Symptom Duration, Mean ± SD, d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyuria</td>
<td>75.2</td>
<td>22.3 ± 33.6</td>
</tr>
<tr>
<td>Polydipsia</td>
<td>74.4</td>
<td>23.1 ± 33.9</td>
</tr>
<tr>
<td>Polyphagia</td>
<td>33.1</td>
<td>26.3 ± 34.2</td>
</tr>
<tr>
<td>Weight loss</td>
<td>42.1</td>
<td>89.9 ± 97.7</td>
</tr>
<tr>
<td>Nausea</td>
<td>83.4</td>
<td>3.2 ± 3.1</td>
</tr>
<tr>
<td>Vomiting</td>
<td>78.5</td>
<td>3.1 ± 3.1</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>51.2</td>
<td>3.4 ± 3.3</td>
</tr>
</tbody>
</table>

<p>| Table 3. Frequency of Laboratory Data Findings at the Time of Presentation |</p>
<table>
<thead>
<tr>
<th>Component</th>
<th>Reference Range</th>
<th>Low</th>
<th>Normal</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>65-110 mg/dL (3.6-6.1 mmol/L)</td>
<td>0</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.35-7.45</td>
<td>100.0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>22-31 mEq/L</td>
<td>100.0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sodium</td>
<td>135-145 mEq/L</td>
<td>77.0</td>
<td>21.8</td>
<td>1.2</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.6-5.0 mEq/L</td>
<td>4.6</td>
<td>58.6</td>
<td>36.8</td>
</tr>
<tr>
<td>Chloride</td>
<td>98-109 mEq/L</td>
<td>66.1</td>
<td>31.0</td>
<td>2.9</td>
</tr>
<tr>
<td>Blood urea nitrogen</td>
<td>7-21 mg/dL (2.5-7.5 mmol/L)</td>
<td>3.5</td>
<td>60.2</td>
<td>36.3</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.6-1.2 mg/dL (53.0-106.1 µmol/L)</td>
<td>1.2</td>
<td>57.3</td>
<td>41.5</td>
</tr>
<tr>
<td>Calcium</td>
<td>8.4-10.2 mg/dL (2.1-2.5 mmol/L)</td>
<td>12.4</td>
<td>68.2</td>
<td>19.4</td>
</tr>
<tr>
<td>Magnesium</td>
<td>1.4-1.8 mEq/L (0.7-0.9 mmol/L)</td>
<td>10.0</td>
<td>67.5</td>
<td>22.5</td>
</tr>
<tr>
<td>Phosphate</td>
<td>2.4-4.5 mg/dL (0.8-1.5 mmol/L)</td>
<td>8.8</td>
<td>54.1</td>
<td>37.1</td>
</tr>
<tr>
<td>Amylase</td>
<td>29-108 U/L</td>
<td>23.6</td>
<td>59.9</td>
<td>16.5</td>
</tr>
<tr>
<td>Lipase</td>
<td>7-59 U/L</td>
<td>11.6</td>
<td>58.9</td>
<td>29.5</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>4.1-10.9 × 10⁹/µL</td>
<td>0</td>
<td>44.3</td>
<td>55.7</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>45%-74%</td>
<td>0.6</td>
<td>35.1</td>
<td>64.3</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>16%-45%</td>
<td>64.9</td>
<td>34.5</td>
<td>0.6</td>
</tr>
<tr>
<td>Monocytes</td>
<td>4%-10%</td>
<td>22.8</td>
<td>69.0</td>
<td>8.2</td>
</tr>
</tbody>
</table>
Table 4. Laboratory Findings in Patients Grouped According to Type of Diabetes and Whether Admission Was for Newly Diagnosed Diabetes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Previously Diagnosed Type 1 DM</th>
<th>Previously Diagnosed Type 2 DM</th>
<th>Newly Diagnosed Type 1 DM</th>
<th>Newly Diagnosed Type 2 DM</th>
<th>Foster and McGarry†</th>
<th>Umpierrez et al§</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of admissions</td>
<td>115</td>
<td>26</td>
<td>30</td>
<td>5</td>
<td>88</td>
<td>126</td>
</tr>
<tr>
<td>Glucose, mg/dL (mmol/L)</td>
<td>529.2 ± 212.4 (29.4 ± 11.8)</td>
<td>480.3 ± 159.8 (26.7 ± 8.9)</td>
<td>461.4 ± 192.3 (25.6 ± 10.7)</td>
<td>396.6 ± 191.1 (22.0 ± 10.6)</td>
<td>475 (26.4)</td>
<td>628 (34.9)</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.21 ± 0.12</td>
<td>7.27 ± 0.08*</td>
<td>7.19 ± 0.14</td>
<td>7.28 ± 0.03†</td>
<td>NA</td>
<td>7.16</td>
</tr>
<tr>
<td>Bicarbonate, mEq/L</td>
<td>10.1 ± 5.1</td>
<td>10.2 ± 4.1</td>
<td>9.8 ± 5.0</td>
<td>12.0 ± 4.6</td>
<td>&lt;10</td>
<td>9</td>
</tr>
<tr>
<td>Sodium, mEq/L</td>
<td>131.6 ± 5.0</td>
<td>129.5 ± 5.4</td>
<td>132.5 ± 5.8</td>
<td>130.6 ± 4.6</td>
<td>132</td>
<td>133</td>
</tr>
<tr>
<td>Potassium, mEq/L</td>
<td>5.1 ± 0.9</td>
<td>4.5 ± 0.9*</td>
<td>4.4 ± 0.8*</td>
<td>4.8 ± 0.5</td>
<td>4.8</td>
<td>5.3</td>
</tr>
<tr>
<td>Chloride, mEq/L</td>
<td>94.4 ± 8.1</td>
<td>93.1 ± 8.0</td>
<td>97.9 ± 6.3‡</td>
<td>94.4 ± 6.9</td>
<td>NA</td>
<td>92</td>
</tr>
<tr>
<td>Blood urea nitrogen, mg/dL (mmol/L)</td>
<td>22.8 ± 13.3 (6.1 ± 4.7)</td>
<td>19.7 ± 12.5 (7.0 ± 4.5)</td>
<td>17.6 ± 12.3‡ (6.3 ± 4.4)</td>
<td>13.8 ± 4.8 (4.9 ± 1.7)</td>
<td>25 (8.9)</td>
<td>27 (9.6)</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>1.5 ± 0.9 (132.6 ± 79.6)</td>
<td>1.2 ± 0.7 (106.1 ± 61.9)</td>
<td>1.2 ± 0.5‡ (106.1 ± 44.2)</td>
<td>1.2 ± 0.3 (106.1 ± 26.5)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Calcium, mg/dL (mmol/L)</td>
<td>9.5 ± 0.9 (2.4 ± 0.2)</td>
<td>9.4 ± 0.9 (2.3 ± 0.2)</td>
<td>9.2 ± 1.0 (2.3 ± 0.2)</td>
<td>8.9 ± 0.7 (2.2 ± 0.2)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Magnesium, mEq/L</td>
<td>1.7 ± 0.3 (0.9 ± 0.1)</td>
<td>1.7 ± 0.3 (0.8 ± 0.2)</td>
<td>1.7 ± 0.3 (0.8 ± 0.2)</td>
<td>1.5 ± 0.4 (0.7 ± 0.2)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Phosphate, mg/dL (mmol/L)</td>
<td>5.0 ± 2.3 (1.6 ± 0.7)</td>
<td>4.0 ± 2.7 (1.3 ± 0.9)</td>
<td>3.9 ± 2.0‡ (1.3 ± 0.6)</td>
<td>2.9 ± 1.3 (0.9 ± 0.4)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>White blood cells, ×10^9/L</td>
<td>13.0 ± 6.3</td>
<td>13.3 ± 6.8</td>
<td>14.1 ± 7.3</td>
<td>10.0 ± 1.3§</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Neutrophils, %</td>
<td>77.6 ± 10.7</td>
<td>73.2 ± 10.8</td>
<td>74.0 ± 13.5</td>
<td>71.3 ± 12.9</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Lymphocytes, %</td>
<td>14.9 ± 9.3</td>
<td>14.9 ± 10.1</td>
<td>14.9 ± 11.4</td>
<td>21.5 ± 10.8</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Monocytes, %</td>
<td>6.0 ± 3.1</td>
<td>6.7 ± 2.9</td>
<td>6.7 ± 2.7</td>
<td>6.0 ± 3.4</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: DM, diabetes mellitus; NA, not applicable.  
*P<.01 vs previously diagnosed type 1 DM.  
†P<.01 vs newly diagnosed type 1 DM.  
‡P<.05 vs previously diagnosed type 1 DM.  
§P<.05 vs previously diagnosed type 2 DM.

and creatinine levels were both elevated, but the ratio was similar between the 2 groups.

Patients were classified as having type 2 diabetes, either type 2 diabetes or idiopathic type 1 diabetes, in 17.6% of the admissions. A greater percentage of these patients were of African American or Latino American ethnicity than the group of patients with type 1 diabetes (P<.001 by χ² test). Infections accounted for 15 of the 31 admissions for the 30 patients in this group. Patients previously diagnosed as having type 2 diabetes were found to be noncompliant with their diabetes therapy in 69.2% of the admissions. No significant differences were observed in the frequency of symptom complaints in this group compared with the type 1 diabetes group. This group of patients weighed more than the patients with type 1 diabetes (85.4±25.2 kg vs 66.1±14.4 kg, P=.002). Other vital signs were not significantly different between the groups.

Laboratory data for the various subgroups analyzed are shown in Table 4. The laboratory data from 2 other reviews are also included in Table 4 for comparison. The cholesterol levels were similar in all groups except for the high-density lipoprotein cholesterol levels, which was lower in patients with a history of type 2 diabetes than in those with type 1 diabetes (34.3±13.6 mg/dL [0.9±0.4 mmol/L] vs 46.4±14.2 mg/dL [1.2±0.4 mmol/L], respectively, P<.001) and in those who were newly diagnosed as having classic type 1 diabetes (34.2±10.7 mg/dL [0.9±0.3 mmol/L], P<.001). No differences were observed in liver function test results.

The insulin-glucose infusion algorithm shown in the Figure was used in most admissions. Overall, patients had cleared their urine ketones at an average of 31.7±11.1 hours after presenting to the emergency department and 21.5±10.5 hours after being initiated on an insulin infusion protocol. They received 9.5±3.5 L of intravenous fluid during that time. Patients continued with the intravenous insulin infusions for a total of 36.3±28.4 hours and received a total of 200.3±130.1 U of insulin from this infusion and a total of 13.8±7.9 L of fluid. Compared with patients with a known history of type 1 diabetes, who required 28.9±8.9 hours from the time of presentation to the emergency department and 152±47 U of insulin to achieve a negative urine ketone status, patients with newly diagnosed type 1 diabetes and those with type 2 diabetes required both longer periods
charge dose (62±23 U vs 72±28 U, respectively) and more insulin (283±156 U, P=.01; and 175±69 U, P=.23; respectively) to achieve a negative urine ketone status. The patients with a known history of type 1 diabetes and those with type 2 diabetes achieved a negative urine ketone status at similar times following initiation of the intravenous insulin infusion protocol (19.1±8.4 and 23.1±11.6 hours, respectively, P=.22). Patients newly diagnosed as having type 1 diabetes required 31.7±13.3 hours (P=.005) to achieve negative urine ketones after initiating the intravenous insulin protocol.

With regard to complications associated with treatment of DKA, 4 patients had a blood glucose level of less than 70 mg/dL (<3.9 mmol/L) at some point during the insulin infusion. Three of these episodes occurred after the patient received a subcutaneous injection of insulin in anticipation of discontinuing the intravenous insulin infusion but failed to tolerate the associated meal, attesting to the adequacy of the insulin-glucose infusion. None of the episodes of hypoglycemia were reported to be clinically significant. Patients received an average of 235±213 mM of potassium during their hospitalization; however, since a specific protocol for potassium management was not provided to the treating physicians, the frequency of patients developing hypokalemia could not be appropriately assessed. Of note though, 8% of the patients did not receive any potassium supplementation. None of the patients developed cerebral edema, and there were no deaths. One patient developed a deep venous thrombosis during his hospitalization. Another patient was diagnosed as having adult respiratory distress syndrome within a few hours of presentation to the emergency department.

Patients remained hospitalized for an average of 4.5±3.3 days, consistent with the national average length of stay for DKA of 4.5 days.13 Patients with known type 1 diabetes were discharged home on an average daily insulin dose of 1.02±0.25 U/kg per day or 69±22 U/d of insulin. Patients with type 2 diabetes received 1.10±0.38 U/kg daily or 92±39 U/d (P=.03 vs group with type 1 diabetes). Patients with newly diagnosed type 1 diabetes were discharged on a protocol of 89±36 U/d or 1.02±0.25 U/kg per day or 92±39 U/d (P=.03 vs group with type 1 diabetes). Patients newly diagnosed as having type 1 diabetes required 31.7±13.3 hours (P=.005) to achieve negative urine ketones after initiating the intravenous insulin protocol.

Our results help illustrate the variability of clinical characteristics of patients who present with DKA and point out the fact that patients with type 2 diabetes also develop ketoacidosis. Even when restricting the population to those patients with moderate or severe DKA, the patients have a variety of clinical and biochemical findings as shown in Table 3. We found that some of the variability relates to the precipitating factors for DKA in that patients with newly diagnosed diabetes have different biochemical findings compared with patients with a known history of diabetes as shown in Table 4. Additionally, we found that patients with type 2 diabetes have a different biochemical presentation of DKA, with less severe acidosi...
terregulatory hormones contribute to the hyperglycemia through glycolysis, gluconeogenesis, and decreased peripheral use of glucose. Volume depletion is probably the principal factor that results in the marked hyperglycemia seen in DKA. The metabolic acidosis that develops in DKA is primarily the result of accumulation of the metabolic acids, acetooacetic acid and β-hydroxybutyric acid, in the plasma. These ketoacids develop as a consequence of the lipolysis and proteolysis that occur when elevated glucagon-insulin ratios cause increased hepatic levels of carnitine and decreased malonylcoenzyme A concentrations.

Other electrolyte abnormalities seem to develop as a secondary effect of the hyperglycemia and metabolic acidosis. The glycosuria that is present leads to at least mild dehydratation and an associated increase in blood urea nitrogen levels, as well as a mild increase in serum creatinine levels. Although serum sodium levels might be expected to be increased in a dehydrated state, the osmotic effect of glucose draws water into the extracellular space and tends to reduce the sodium concentration. Potassium levels will tend to be high because of the physiologic compensation of the metabolic acidosis and the hyperosmolarity and insulin deficiency present, although it is known that total body stores of potassium are depleted in DKA. It is therefore surprising to find that nearly 8% of the patients in this review did not require potassium supplementation during treatment of their DKA. Although phosphate is severely depleted because of glycosuria, the plasma values will vary because of transmembrane shifts in the ion distribution caused by metabolic acidosis and insulin deficiency. A stress-induced leukemoid response is responsible for elevated leukocyte counts.

A little more than one fourth of the patients had newly diagnosed diabetes, accounting for approximately 20% of the admissions. Consistent with other reports, newly diagnosed diabetes presenting with DKA was diagnosed in a substantial number of overweight patients, a condition frequently associated with type 2 diabetes. Our results suggest that patients with newly diagnosed type 1 diabetes have a more normal electrolyte profile than patients who have a known history of diabetes despite similar degrees of acidosis. This is a bit surprising, since they had similar glucose levels, pH levels, apparent ketonuria, and duration of symptoms. It is known that the severity of ketoacidosis is decreased when counterregulatory hormone levels are low. Furthermore, it would be expected that patients with newly diagnosed diabetes would have a more intact counterregulatory hormone system than patients with a prolonged duration of diabetes. As such, we might predict that the newly diagnosed diabetes would be associated with higher glucagon and epinephrine levels, which would ultimately induce a greater degree of ketogenesis and a more severe picture of DKA. Hyperkalemia would be expected in both groups of individuals, since the insulin deficiency is present in both, but would be predicted to be greater in the more acidic group. Since the groups had similar pH levels, the potassium and phosphate levels would be predicted to be similar if this were a major contributing factor. Therefore, the normokalemia in the newly diagnosed group suggests that another process, possibly related to the osmolarity, may be involved.

The newly diagnosed group did not have markedly increased blood urea nitrogen levels and only very mildly increased creatinine levels, possibly explained by the known interference of acetooacetate with the assay, which might suggest that they are not as dehydrated as the patients with a known history of diabetes. The new diagnosis group required more than 4 L of additional fluid and more than 12 additional hours of treatment with the insulin-glucose infusion to achieve a ketone-negative status, as well as 10 L of additional fluid during the hospitalization compared with the previously diagnosed group. However, the patients who also had pancreatitis accounted for most of this increased fluid requirement. A trend toward increased fluid requirements remained when the patients with pancreatitis were excluded from the analysis (data not shown). Some of the normalcy of the laboratory results in the new diagnosis group could be related to fluid intake and maintenance of urine output before presentation to the emergency department; however, this cannot be verified given the retrospective nature of our study. The status of the counterregulatory hormones may or may not be useful in understanding the observed differences between these groups; however, since these hormones are generally not of practical value in the clinical management of DKA, this study cannot address this possibility.

Patients with type 2 diabetes can develop more than mild ketosis and may experience moderate-to-severe DKA. It has been said that these patients require a precipitating stressor; however, consistent with other reports, we found that 29% of the patients did not have a precipitating other than noncompliance with their medical therapy. The tendency for the patients with type 2 diabetes who develop DKA being Latino or African American compared with white may only be a reflection of the demographics of the overall patient population at Parkland Memorial Hospital. However, the possibility of a true ethnic variation in patients with type 2 diabetes who are prone to develop DKA, possibly from a genetic predisposition, cannot be excluded. In contrast to other reports that compared DKA in type 1 and type 2 diabetes, we found a difference in the serum electrolyte concentrations and other biochemical levels of these 2 groups. Some of the differences we observed may be secondary to differences in counterregulation and basal insulin levels in these groups. Our patients with type 1 diabetes had had their disease for a duration of 12.7 years, which is likely long enough to place the patients at a time long after the “honey-moon period” and at a time when they are likely to have absolute insulin deficiency. The patients with type 2 diabetes had a disease duration of 5.6 years and thus would be expected to still have residual β-cell activity. Although the type 2 diabetes group had insufficient insulin to prevent DKA, it is theoretically possible that they had enough insulin to modulate the disease process. In support of this idea is the finding of lower potassium levels in this group, which as noted herein are dependent on insulin presence or absence. The less severe acidosis suggests a lower level of ketoacids; however, this was not detected in this study. Although we did not observe dif-
ferences in the degree of ketonuria between the subgroups studied, we acknowledge that our method of measuring ketoacids by semiquantitative urine testing fails to identify the ketoacid that is most prevalent in DKA and that a difference in β-hydroxybutyric acid levels could exist, although this has not been studied.

The importance of recognizing DKA in a patient with type 2 diabetes is illustrated by the time it took for these patients to achieve a negative urine ketone status. Once patients with either type 1 or type 2 diabetes were treated by the intravenous insulin infusion protocol, the duration of treatment required to achieve a negative urine ketone status was similar between the 2 groups. Patients with type 2 diabetes, however, required more time from initial presentation to the emergency department to achieve negative urine ketones. Some of this delay may be the result of a failure to suspect DKA in the “atypical patient.”

Our results also show that the insulin-glucose infusion algorithm outlined in the Figure can be used safely in the management of patients who present with DKA irrespective of the type of diabetes. Complications that have been reported with management of DKA were infrequent in our population in part because of the age of our patients but also because of the inclusion of a variable glucose infusion algorithm in the treatment protocol. Resolution of the acidosis caused by the presence of ketoacids is often used as a marker of resolution of DKA. Reports that serum 3-β-hydroxybutyric acid levels are elevated in patients with type 2 diabetes who have normal fasting blood glucose levels raise concerns about their utility in DKA management in patients with type 2 diabetes. Our use of urine ketone testing does not provide direct evidence of β-hydroxybutyric acid levels, but since acetocetotic acid levels remain elevated longer and since urine levels may be positive even after resolution of serum levels of acetocetate, the resolution of ketonuria would imply adequate resolution of ketonemia. Through our continuation of the insulin-glucose infusion protocol until the urine was ketone free, we have shown successful use of ketonuria as a marker of resolution of DKA in both type 1 and type 2 diabetes. Finally, given our results of the successful, almost uneventful management of DKA, we have shown that in adults the modern management of DKA with essentially no complications of treatment consists of effective intravenous insulin therapy with concomitant glucose administration when plasma glucose levels decrease below 300 mg/dL (16.7 mmol/L), sufficient volume and electrolyte replacement, and careful attention to identification and management of associated problems, such as acute pancreatitis and infection.

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REFERENCES


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