Treatment of Diabetic Ketoacidosis With Subcutaneous Insulin Aspart

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OBJECTIVE — In this prospective, randomized, open trial, we compared the efficacy and safety of aspart insulin given subcutaneously at different time intervals to a standard low-dose intravenous (IV) infusion protocol of regular insulin in patients with uncomplicated diabetic ketoacidosis (DKA).

RESEARCH DESIGN AND METHODS — A total of 45 consecutive patients admitted with DKA were randomly assigned to receive subcutaneous (SC) aspart insulin every hour (SC-1h, $n = 15$) or every 2 h (SC-2h, $n = 15$) or to receive IV infusion of regular insulin ($n = 15$). Response to medical therapy was evaluated by assessing the duration of treatment until resolution of hyperglycemia and ketoacidosis. Additional end points included total length of hospitalization, amount of insulin administration until resolution of hyperglycemia and ketoacidosis, and number of hypoglycemic events.

RESULTS — Admission biochemical parameters in patients treated with SC-1h (glucose: 44 ± 21 mmol/l [means ± SD], bicarbonate: 7.1 ± 3 mmol/l, pH: 7.14 ± 0.09) were similar to those treated with SC-2h (glucose: 42 ± 21 mmol/l, bicarbonate: 7.6 ± 4 mmol/l, pH: 7.15 ± 0.12) and IV regular insulin (glucose: 40 ± 13 mmol/l, bicarbonate 7.1 ± 4 mmol/l, pH: 7.11 ± 0.17). There were no statistical differences in the mean duration of treatment until correction of hyperglycemia (6.9 ± 4, 6.1 ± 4, and 7.1 ± 5 h) or until resolution of ketoacidosis (10 ± 3, 10.7 ± 3, and 11 ± 3 h) among patients treated with SC-1h and SC-2h or with IV insulin, respectively (NS). There was no mortality and no differences in the length of hospital stay, total amount of insulin administration until resolution of hyperglycemia or ketoacidosis, or the number of hypoglycemic events among treatment groups.

CONCLUSIONS — Our results indicate that the use of subcutaneous insulin aspart every 1 or 2 h represents a safe and effective alternative to the use of intravenous regular insulin in the management of patients with uncomplicated DKA.

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Diabetic ketoacidosis (DKA) is the most common hyperglycemic emergency in patients with diabetes. DKA is the leading cause of death in children with type 1 diabetes (1,2) and accounts for a significant proportion of admissions in adult patients with type 1 or type 2 diabetes (1,3). The mainstay in the treatment of DKA involves the administration of regular insulin via continuous intravenous (IV) infusion or by frequent subcutaneous (SC) or intramuscular (IM) injections (3–5). Although several controlled studies in patients with DKA have shown that low-dose insulin therapy is effective regardless of the route of administration (4,6–8), the ideal route of insulin therapy is still a matter of debate. For most experts in the field, the administration of IV regular insulin is the preferred route because of the delayed onset of action and prolonged half-life of SC regular insulin. Fisher et al. (6) and Menzel and Jutzi (9) reported that patients with DKA treated with IV regular insulin experienced a more rapid fall in plasma glucose and ketone levels than patients treated with IM or SC insulin and that 30–40% of patients treated with IM or SC insulin did not lower their plasma glucose by 10% in the first hour of insulin therapy. Yet the cost of treating DKA with IV insulin may be higher, because in many institutions, patients are required to be admitted to an intensive care unit (ICU) or to a specialized diabetes care unit to receive IV insulin infusion (10–12).

Recently, new analogs of human insulin with a rapid onset of action—aspart insulin (Novolog; Novo Nordisk, Princeton, NJ) or lispro insulin (Humalog; Eli Lilly, Indianapolis, IN)—have become available and may represent alternatives to the use of regular insulin in the treatment of DKA. In a recent preliminary study, we reported that treatment of mild and moderate DKA with hourly injections of SC lispro insulin was as effective as the use of a standard IV regular insulin protocol (13). The mean time of treatment to correct hyperglycemia and ketoacidosis was similar between SC lispro and IV infusion of regular insulin. Treatment with SC insulin injections on an hourly schedule, however, may be difficult in most institutions because of the intensity of treatment and the shortage of nursing staff on regular wards. Therefore, we expanded our investigation on the use of SC insulin analogs by comparing the use of aspart insulin, given at different time intervals (1 and 2 h), with a standard IV low-dose insulin protocol.

RESEARCH DESIGN AND METHODS

— A total of 45 consecutive patients with DKA admitted to the University of Tennessee Regional Medical

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Abbreviations: DKA, diabetic ketoacidosis; ICU, intensive care unit; IM, intramuscular; IV, intravenous; SC, subcutaneous; SC-1h, subcutaneous aspart insulin every hour; SC-2h, subcutaneous aspart insulin every 2 h.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Treatment protocol*

IV fluids
1. 0.9% saline at 500–1,000 ml/h for 2 h
2. 0.45% saline at 250–500 ml/h until blood glucose <13.8 mmol/l (250 mg/dl)
3. Dextrose 5% in 0.45% saline at 150–250 ml/h until resolution of DKA

Potassium replacement
1. If serum K^+ >5.5 mmol/l, do not give K^+, but check serum K^+ every 2 h
2. K^+ = 4–5.5 mmol/l, add 20 mmol of KCl to each liter of IV fluid
3. K^+ = 3–4 mmol/l, add 40 mmol of KCl to each liter of IV fluid
4. K^+ = <3 mmol/l, give 10–20 mmol of KCl per hour until serum K^+ >3 mmol/l, then add 40 mmol of KCl to each liter of IV fluid

Insulin therapy
1. SC-1h
   a) Initial dose SC: 0.3 units/kg body wt, followed by
   b) SC aspart insulin at 0.1 units/kg every hour
   c) When blood glucose <13.8 mmol/l (250 mg/dl), change IV fluids to D5% 0.45% saline and reduce SC aspart insulin to 0.05 units · kg^{-1} · h^{-1} to keep glucose at ~11.1 mmol/l until resolution of DKA.
2. SC-2h
   a) Initial dose SC: 0.3 units/kg body wt, followed by
   b) SC aspart insulin at 0.2 units 1 h later and every 2 h
   c) When blood glucose <13.8 mmol/l (250 mg/dl), change IV fluids to D5% 0.45% saline and reduce SC aspart to 0.1 units/kg every 2 h to keep glucose at ~11.1 mmol/l (200 mg/dl) until resolution of DKA
3. IV regular insulin
   a) Initial IV bolus: 0.1 units/kg body wt, followed by
   b) Continuous insulin infusion at 0.1 units · kg^{-1} · h^{-1}
   c) When blood glucose <13.8 mmol/l (250 mg/dl), change IV fluids to D5% 0.45% saline and reduce insulin infusion rate to 0.05 units · kg^{-1} · h^{-1} to keep glucose at ~11.1 mmol/l until resolution of DKA
4. Laboratory
   a) *Admission*: Cell blood count with differential complete metabolic profile, venous pH, and serum β-hydroxybutyrate
   b) *During treatment*: Basic metabolic profile (glucose, bicarbonate, sodium, potassium, chloride, urea, and creatinine), venous pH, phosphorus, and β-hydroxybutyrate at 2 h, 4 h, and every 4 h until resolution of DKA
   c) *Glucose by fingerstick*: Check glucose every hour in patients receiving SC-1 h and every 2 h in patients receiving IV insulin or SC-2h

Center, Memphis, served as the study population. The diagnosis of DKA was established in the emergency department by a plasma glucose level >13.8 mmol/l (250 mg/dl), a serum bicarbonate level <15 mmol/l, a venous pH <7.30, and a positive serum ketone level at a dilution ≥1:4 by the nitroprusside reaction, and/or a serum β-hydroxybutyrate level >3.0 mmol/l. We excluded patients with persistent hypotension (systolic blood pressure <80 mmHg) after the administration of 1 liter of normal saline and patients with acute myocardial ischemia, end-stage renal or hepatic failure, anasarca, dementia, or pregnancy. The institutional review board at the University of Tennessee Health Sciences Center approved the study protocol.

Patients were randomly assigned in the emergency department to receive SC aspart insulin every hour (SC-1h, $n = 15$) or every 2 h (SC-2h, $n = 15$), or to receive IV regular insulin ($n = 15$). Because of hospital regulations that did not allow the use of IV insulin drips outside the ICU, patients treated with IV regular insulin were admitted to the ICU, whereas patients treated with SC aspart were managed in the general medicine floor or in a stepped-down unit. All patients were managed by members of the internal medicine residency program, who received a copy of the assigned treatment protocol (Table 1). Orders for IV fluids and potassium administration were similar in the three study groups (14). Initial fluid therapy with isotonic saline (500–1,000 ml/h) was directed toward expansion of intravascular volume and restoration of renal perfusion; subsequent fluid therapy was administered as 0.45% saline (200–500 ml/h) to replace approximately half of the estimated volume deficit during the first 12 h. Potassium chloride was added to the IV fluids when serum potassium levels were <5.5 mmol/l. No patients in this study received bicarbonate therapy.

Patients treated with SC-1h received an initial injection of 0.3 units/kg body wt, followed by 0.1 units · kg^{-1} · h^{-1} until blood glucose reached 13.8 mmol/l (250 mg/dl). At that time, insulin dose was reduced to 0.05 units · kg^{-1} · h^{-1}, and the IV fluids were changed to D5% 0.45 saline to maintain blood glucose at ~11.1 mmol/l (200 mg/dl) until resolution of DKA.

Patients treated with SC-2h received an initial dose of 0.3 units/kg followed by 0.2 units/kg 1 h later and every 2 h until blood glucose reached 13.8 mmol/l (250 mg/dl). At that time, insulin dose was reduced to 0.1 units/kg every 2 h, and the IV fluids were changed to D5% 0.45 saline to keep blood glucose at ~11.1 mmol/l (200 mg/dl) until resolution of DKA.

Patients treated with IV regular insulin received an initial bolus of 0.1 units/kg, followed by a continuous infusion of regular insulin calculated to deliver 0.1 units · kg^{-1} · h^{-1} until blood glucose levels were ≤13.8 mmol/l (250 mg/dl). At that time, insulin dose was reduced to 0.05 units · kg^{-1} · h^{-1}, and the IV fluids were changed to D5% 0.45 saline to maintain blood glucose at ~11.1 mmol/l (200 mg/dl) until resolution of DKA (14).

Ketoacidosis was considered resolved

Table 2—*Biochemical profile on admission*

	SC-1h	SC-2h	Regular IV insulin
n	15	15	15
Age (years)	36 ± 8	38 ± 12	40 ± 13
Sex (M/F)	11/4	10/5	10/5
BMI (kg/m^2)	27 ± 6	29 ± 7	27 ± 7
DKA precipitating cause			
Poor compliance	8 (53)	9 (60)	9 (60)
New-onset diabetes	3 (20)	3 (20)	2 (13)
Glucose (mmol/l)	44 ± 21	42 ± 21	40 ± 13
Bicarbonate (mmol/l)	7.1 ± 3	7.6 ± 4	7.1 ± 4
Venous pH	7.14 ± 0.09	7.15 ± 0.12	7.11 ± 0.17
Anion gap (mmol/l)	24 ± 5	24 ± 6	24 ± 7
Serum potassium (mmol/l)	5.3 ± 1.6	5.7 ± 1.1	4.9 ± 1.3
Serum osmolality (mmol/kg)	319 ± 30	312 ± 27	317 ± 20
β-Hydroxybutyrate (mmol/l)	9.8 ± 2	9.1 ± 3	8.8 ± 3
Free fatty acids (mmol/l)	1.4 ± 0.8	1.5 ± 0.6	1.4 ± 0.7
HbA_{1c} (%)	11.5 ± 1.6	11.4 ± 2	11.7 ± 2

Data are means ± SD or *n* (%).

when serum bicarbonate level was ≥18 mmol/l and venous pH was >7.30 (14). When these levels occurred, the IV infusion of regular insulin or SC aspart injections was discontinued 1 h after the administration of patients' preadmission dose of short- and intermediate-acting insulin. Patients with newly diagnosed diabetes received a split mixed insulin dose of 0.6 units · kg body wt^{-1} · day^{-1}, two-thirds as intermediate-acting (NPH) insulin and one-third as regular insulin. Two-thirds of this total daily dose was given in the morning and one-third in the evening.

During treatment, blood glucose was determined at bedside by a fingerstick every 2 h in patients treated with IV infusion of regular insulin or with SC-2h and every hour in those patients who received hourly injections of SC aspart. Levels of glucose, electrolytes, phosphorus, venous pH, β-hydroxybutyrate, free fatty acids, and insulin were measured on admission before the initiation of insulin and at 2, 4, 8, 12, 16, and 24 h of treatment. Medical care data included site of admission and treatment in the hospital, amount of fluid and insulin administration, and length of hospitalization. Response to medical therapy was evaluated by assessing the time and amount of insulin required for resolution of hyperglycemia and ketoacidosis and the number of hypoglycemic events during therapy. Hypoglycemia was defined as a blood glucose value ≤3.3 mmol/l (60 mg/dl).

Analytic methods

Plasma glucose was measured using the glucose oxidase method. Serum β-hydroxybutyrate was determined by a standard enzymatic method. Plasma free fatty acids were measured by a colorimetric method established in our laboratory by the previously described method (15).

Statistical analysis

All data in the text, tables, and figures are expressed as means ± SD. To compare baseline demographic and clinical characteristics between groups, ANOVA was used for continuous variables. For comparison of categorical variables, χ^2 analyses were performed. We arbitrarily estimated a difference between groups ≥4 h to resolve ketoacidosis as clinically significant. A sample size of 15 patients was needed in each group to provide a power of 0.81, given an α error of 0.05 and an SD of 3. StatView version 5.0 (SAS Institute, Cary, NC) and PS: Power and Sample Size version 2.1.23 (Vanderbilt Medical Center, Nashville, TN) were used for the statistical analysis and sample size calculations, respectively (16).

RESULTS — The study population included 15 patients treated with SC-1h and SC-2h and 15 patients treated with IV regular insulin. The clinical characteristics on admission are shown in Table 2. The mean age, duration of diabetes, and precipitating cause for DKA were similar among treatment groups. Poor compliance with insulin therapy was the most common precipitating cause of DKA and was recorded in more than half of patients treated with SC aspart and IV regular insulin. In the SC-1h group, poor compliance was the precipitating cause in eight patients (53%), four patients had an associated comorbid condition (leg abscess, pneumonia, urinary tract infection, pancreatitis), and three patients (20%) had newly diagnosed diabetes at presentation. In the SC-2h group, the precipitating cause of DKA was poor compliance with insulin in nine patients (60%), four patients (27%) had an associated medical illness (cellulitis, urinary tract infection, olanzapine [Zyprexa] overdose, failure to take oral antidiabetic agent), and three patients (20%) were newly diagnosed with diabetes at presentation. The precipitating cause for DKA in the IV insulin–treated group was poor compliance with

Table 3—*Response to medical treatment*

	SC-1h	SC-2h	Regular IV insulin
n	15	15	15
Length of hospital stay (days)	3.4 ± 3	3.9 ± 5	4.5 ± 3
Duration of therapy until glucose <13.8 mmol/l (h)	6.9 ± 4	6.1 ± 4	7.1 ± 5
Duration of therapy until resolution of DKA (h)	10 ± 3	10.7 ± 3	11 ± 3
Amount of insulin until glucose <13.8 mmol/l (units)	67 ± 37	65 ± 26	62 ± 28
Amount of insulin until resolution of DKA (units)	85 ± 33	94 ± 32	82 ± 28
Episodes of hypoglycemia	1	1	1

Data are means ± SD.

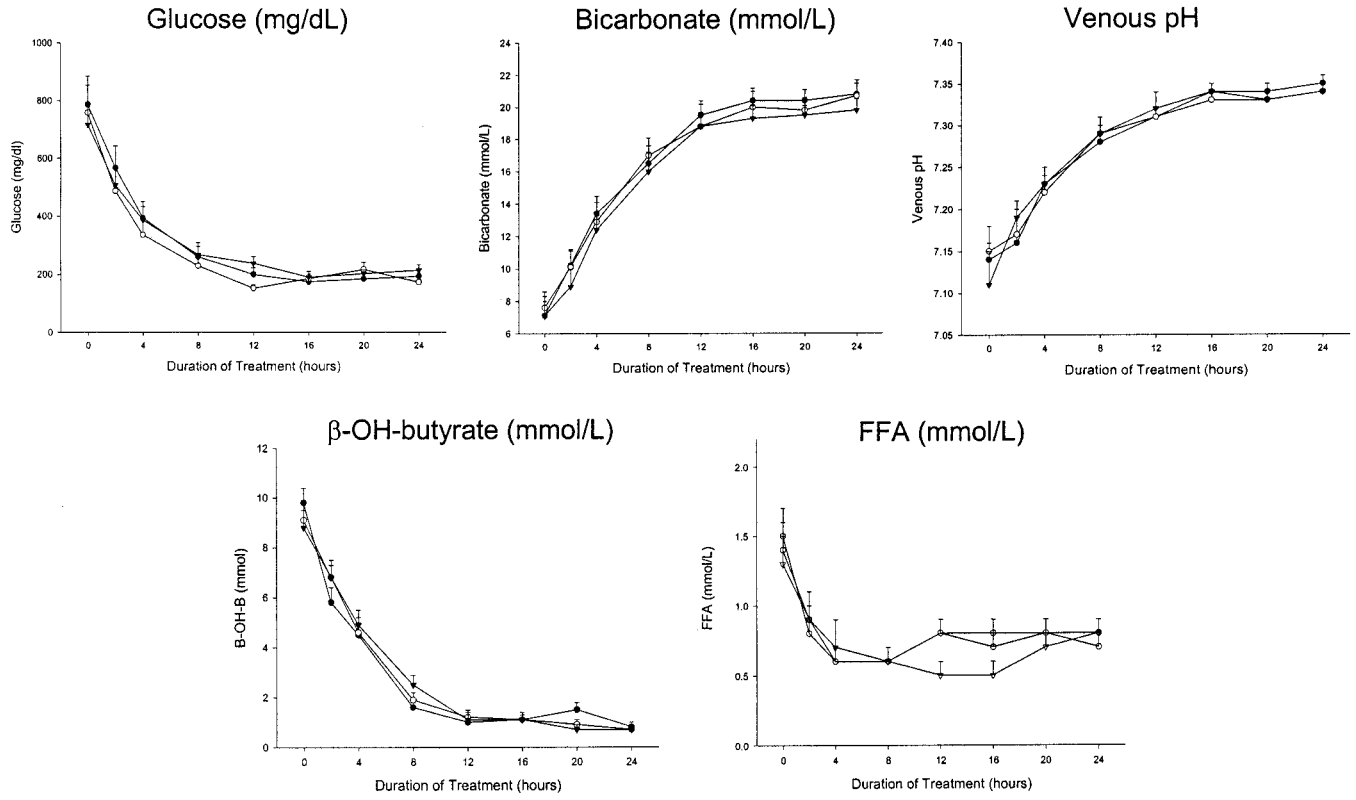

Figure 1—*Changes in metabolic profile in patients with DKA treated with SC-1h (●) and SC-2h (○) and with IV regular insulin (▲, △). B-OH-B/β-OH-butyrate, β-hydroxybutyrate; FFA, free fatty acid.*

insulin in nine patients (60%) and infection in four patients (pneumonia, cellulites, urinary tract infection, and tooth abscess), and two patients were newly diagnosed with diabetes on admission.

The admission biochemical parameters were not significantly different among treatment groups. In patients treated with SC-1h, the mean admission serum glucose was 44 ± 21 mmol/l (787 ± 378 mg/dl, range 337–1,569), serum bicarbonate 7.1 ± 3 mmol/l (4–13), pH 7.14 ± 0.09 (6.93–7.29), and β-hydroxybutyrate 9.8 ± 2 mmol/l (6.51–14.7). In patients treated with SC-2h, the mean admission serum glucose was 42 ± 21 mmol/l (758 ± 373 mg/dl, range 348–1,782), bicarbonate 7.6 ± 4 mmol/l (2.0–15), pH 7.15 ± 0.12 (6.99–7.27), and β-hydroxybutyrate 9.1 ± 3 mmol/l (5.95–13.7). These values were not statistically different from the mean admission values in patients treated with IV regular insulin (glucose 40 ± 13 [717 ± 239 mg/dl, range 323–1,110], bicarbonate 7.1 ± 4 mmol/l [4–14], pH 7.11 ± 0.17 [5.7–15.5], and β-hydroxybutyrate 8.8 ± 3 mmol/l [5.65–15.5]). The admission free fatty acid levels were similarly elevated in the three treatment groups and returned to normal values after resolution of ketoacidosis.

Changes in plasma glucose, acid-based parameters, and free fatty acid levels during treatment of DKA are shown in Fig. 1. The rate of decline of blood glucose concentration and changes in acid-based parameters during treatment were not significantly different among treatment groups. The mean duration of treatment until glucose concentration was <13.8 mmol/l (<250 mg/dl) and was not statistically different between patients treated with SC-1h (6.9 ± 4 h) and SC-2h (6.1 ± 4 h) or with IV regular insulin (7.1 ± 5 h). Similarly, the mean duration of treatment until resolution of ketoacidosis was not different among treatment groups (10 ± 3, 10.7 ± 3, and 11 ± 3 h, respectively, NS).

There were no statistical differences in the length of hospital stay in patients treated with SC aspart insulin (SC-1h, 3.4 ± 3 days, and SC-Q2h, 3.9 ± 5 days) and those treated with IV regular insulin (4.5 ± 3 days, NS) (Table 3). The length of hospital stay was related more to the precipitating cause of DKA than the type of insulin treatment. Patients with poor compliance with insulin therapy treated with SC aspart insulin had a length of hospital stay of 2.4 ± 2 days compared with 3.1 ± 1.6 days in patients treated with IV insulin ($P < 0.05$), whereas the length of hospital stay was 6.4 ± 6 and 7.2 ± 3 days in subjects with associated medical illness treated with SC aspart or IV regular insulin, respectively (NS). Similarly, although we observed no differences in the mean admission serum glucose, the mean duration of treatment until correction of hyperglycemia was significantly shorter in patients with poor compliance (5.6 ± 4 h) compared with subjects with a comorbid condition (8.8 ± 1 h, $P < 0.01$). Interestingly, we observed no differences in the time to resolve DKA in patients with or without a precipitating comorbid condition (10.4 ± 2.5 and 10.7 ± 10 h, NS).

The amount of insulin administered until serum glucose decreased to a level <13.8 mmol/l (67 ± 37, 65 ± 26, and 62 ± 28 units) and the amount of insulin until resolution of DKA (85 ± 33, 94 ± 32, and 82 ± 28 units) were not signifi-

cantly different among patients treated with SC-1h and SC-2h or with IV regular insulin, respectively (NS). There was no need to increase or change the dose or route of insulin administration because of delayed or inadequate response in any of the treatment groups. In addition, there were no differences in the number of hypoglycemic events during therapy (one patient in each group) among the three study groups. There was no mortality, and none of the patients had recurrence of ketoacidosis during their hospital stay.

CONCLUSIONS — The mainstay in the treatment of DKA involves the administration of regular insulin via continuous IV infusion or by frequent SC or IM injections (3,4,6–8). Until 1972, because of fears of insulin resistance, large doses of insulin (≥100 units/h IV or SC) were thought to be necessary (17–19). In 1973, several reports demonstrated the effectiveness of small doses of insulin in patients with DKA (7,12,20,21). Although multiple controlled studies in patients with DKA have shown that low-dose insulin therapy is effective regardless of the route of administration (4,6,7,22,23), most medical centers and authorities recommend the administration of IV infusion because of the delayed onset of action and prolonged half-life of SC regular insulin (2,5,9,11,12,24,25). In a prospective randomized study in patients with DKA treated either with IM or SC injections or with continuous IV infusion of regular insulin, Fisher et al. (6) reported that 30–40% of patients in the IM and SC groups did not lower their plasma glucose by 10% in the first hour after insulin injection and that the concentration of ketone bodies was lowered at a significantly faster rate in the IV group than with IM or SC insulin. The delay in onset of action of regular insulin is substantiated by the report of Menzel and Jutzi (9), who treated patients with frequent small SC injections, but only 4 of 24 patients showed a fall in blood glucose concentration in the first 3 h of therapy. These differences in response can be explained by delays in reaching a maximal circulating insulin concentration. Maximal insulin peak is achieved within the first hour in patients treated with IV regular insulin, but not until the second or third hour of therapy in patients treated with IM or SC injections (26). New analogs of human insulin (aspart and lispro) with a rapid onset of action may represent a better alternative to the use of IV regular insulin in the treatment of DKA. The SC administration of these insulin analogs have an onset of action within 10–20 min, reach a peak insulin concentration within 30–90 min, and have a duration of action of ~3–4 h. These values are significantly shorter than with SC regular insulin, which has an onset of action of 1–2 h and a half-life of ~4 h (4,27).

We recently reported that treatment of patients with mild and moderate DKA with hourly injections of SC lispro insulin is as effective as treatment with low-dose IV regular insulin (13). The use of SC insulin injections on an hourly schedule, however, may be difficult to follow in many medical centers because of the intensity of treatment and shortage of nursing staff on general wards. Therefore, we expanded our investigation on the use of SC insulin analogs by comparing the use of aspart insulin, given at different time intervals (1 and 2 h), to a standard IV low-dose insulin protocol. Our results indicate that treatment of DKA with SC aspart insulin every 1 or 2 h is as safe and effective as the treatment with IV regular insulin. The rate of decline of blood glucose concentration and the mean duration of treatment until correction of ketoacidosis were similar among different treatment groups. In addition, we observed no significant differences in the length of hospital stay, total amount of insulin administration until resolution of hyperglycemia or ketoacidosis, or the number of hypoglycemic events among treatment groups.

DKA is the most common hyperglycemic emergency in patients with type 1 and type 2 diabetes. It is associated with significant morbidity and use of health care resources (10,28,29). In 1983, the annual cost of hospitalization for DKA in Rhode Island was estimated to be $225 million (30). More recently, it was projected that treatment of DKA episodes accounts for one out of every four health care dollars spent on direct medical care for adult patients with type 1 diabetes and for one of every two dollars in those patients experiencing multiple episodes of DKA (29). Based on recent estimates of mean cost per hospitalization of about $11,000 per patient experiencing a DKA episode (28), the annual hospital cost for patients with DKA in the U.S. may be greater than $1 billion.

In urban medically indigent populations, we and others have reported that poor compliance with insulin treatment is the most common precipitating cause, accounting for more than half of all DKA admissions (28,31–33). Most patients with poor compliance are younger, are less critically ill, have lower disease severity scores, and have a lower rate of complications and mortality than non-DKA patients admitted to the ICU (11,31,34). Although these patients should be candidates for early discharge, the length of hospitalization in mild DKA has been reported to be similar to patients admitted with moderate or severe DKA (10,34). In addition, although no clear benefits have been shown in treating DKA patients in the ICU compared with stepped-down units or general medicine wards (10,35), the majority of patients with DKA are admitted to the ICU (10–12). Our study indicates that patients with uncomplicated DKA could be safely treated with SC aspart insulin every 1 or 2 h in non-ICU settings.

We acknowledge several limitations in our study, including a relatively small number of patients and the fact that we excluded patients with hypovolemic shock, comatose state, acute myocardial ischemia, congestive heart failure, end-stage renal or hepatic failure, anasarca, and pregnancy. Although the administration of frequent insulin injections may be difficult in some institutions because of the shortage of nursing staff on regular wards, it is important to note that restrictions on the intensity of nursing care, our protocol was well accepted by the nursing staff. It is important to notice that restrictions on the intensity of nursing care in our institution are consistent with the nursing care available in general hospitals in the Southeast (31). Before the completion of this study, because of hospital regulations in our institution, patients with DKA were admitted to the ICU to receive treatment with IV insulin. The results of this study enabled us to revise our admission policy, allowing us to treat patients with uncomplicated DKA in general wards and intermediate care units.

Our results indicate that treatment of DKA with SC insulin analogs every 1 or 2 h represents a safe and effective alternative to treatment with IV regular insulin. In agreement with our previous reports (11,13,34), this study indicates that patients with uncomplicated DKA, under

appropriate supervision and nursing care, can be safely managed with rapid-acting insulin analogs in general medicine wards or in stepped-down units.

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