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Clinical and Biochemical Characteristics of Elderly Patients With Hyperglycemic Emergency State at a Single Institution

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Background: Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are two of the most serious acute complications of diabetes mellitus. In this study, we investigated the clinical characteristics of elderly diabetic patients in a hyperglycemic emergency state. **Methods:** We reviewed the medical records of elderly patients admitted with a diagnosis of DKA and HHS over the past 5 years at the National Medical Center in Korea. Patients were divided into 3 groups: those with only DKA, those with only HHS, and those with both DKA and HHS. We assessed the clinical characteristics, economic vulnerability, precipitating factors, and hospital mortality. **Results:** Twenty-seven patients (31 episodes) fulfilled the inclusion criteria. Nineteen episodes occurred in male patients. The mean age, blood glucose, and glycosylated hemoglobin (HbA1c) were 78.9 years, 700.7 mg/dL, and 10.6%, respectively. The mean mortality rate was 22.5%; the mortality rates of the DKA only group, the HHS only group, and the group with both DKA and HHS were 10%, 23%, and 37.5%, respectively. DKA was diagnosed in 10 patients (32%), HHS was diagnosed in 13 patients (42%), and both DKA and HHS were diagnosed in 8 patients (26%). There was no relationship between age, sex, economic vulnerability, HbA1c, insulin use, and mortality rate. However, the mortality rate was higher than that of a previous report. Self-discontinuation of diabetes medication and infections are the most common precipitating factors. **Conclusion:** Elderly patients with diabetes are prone to experience hyperglycemic emergency and have a high mortality rate. Therefore, more focused education and a social medical service system for those with diabetes should be instituted.

Key Words: Elderly, Hyperglycemic emergency state, Diabetic ketoacidosis, Hyperosmolar hyperglycemic state

INTRODUCTION

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are high-risk, acute complications of diabetes and have a high mortality rate. The common mechanism in both diseases includes insulin deficiency and an increase in counterregulatory hormones such as glucagon, catecholamines, cortisol, and growth hormone[1-7]. It is commonly known that DKA often occurs in young patients with type 1 diabetes, whereas the HHS mainly occurs in older patients with type 2 diabetes. In actual clinical cases, however, these patients' age varies, and there have been reported clinical cases in which ketoacidosis and hyperosmolar state existed together in 33% of the patients who presented to the hospital in a hyperglycemic emergency state[4,8,9].

Identifying clinical cases helps us diagnose appropriately and treat the diseases in elderly diabetic patients. There are a few recent studies on the clinical differences, disease progression, or socioeconomic characteristics of patients diagnosed with DKA, HHS, or both DKA and HHS among those aged 65 and older who present to the hospital in a hyperglycemic emergency state; therefore, this study analyzed the epide miological and clinical characteristics of these diabetic diseases in the elderly over the past 5 years in a single institution.

MATERIALS AND METHODS

1. Subjects

Among diabetic patients admitted to the National Medical Center from January 1, 2011 to January 31, 2016, this study

selected 31 cases in 27 elderly patients diagnosed with DKA, HHS, or both DKA and HHS. The data of these patients were retrospectively analyzed through medical records. During the study period, 2 of the 27 patients presented to the hospital in a hyperglycemic emergency state twice, and 1 patient presented thrice. The patients were categorized into 3 groups: the group with DKA, the group with HHS, and the group with both DKA and HHS.

A diagnosis of DKA was defined as having a serum glucose level of 250 mg/dL (13.9 mmol/L) or higher, an arterial blood pH of less than 7.30, a bicarbonate level of less than 18 mEq/L, and a positive test for ketones in the serum and urine at the time of presentation. A diagnosis of HHS was defined as having a serum glucose level of 600 mg/dL or higher, a serum osmotic pressure of 320 mOsm/kg or higher, an arterial blood pH of 7.30 or higher, and a bicarbonate level of 18 mEq/L or higher at the time when the patients presented to the hospital. When a patient had an arterial blood pH of less than 7.30 or a bicarbonate level of less than 18 mEq/L and a serum osmotic pressure of 320 mOsm/kg or higher, he or she was defined as having both DKA and HHS[2].

2. Methods

1) Study Methods

We retrospectively examined a total of 31 cases of 27 patients through medical records. In order to identify the patients' socioeconomic characteristics, sex, age, economic vulnerability, existence of an immediate family caregiver, duration of diabetes, and insulin treatment history were assessed. To assess economic vulnerability, the presence of insurance (health insurance or medical benefits) was examined.

To identify the patients' clinical characteristics, we examined the serum glucose level, osmotic pressure, glycated hemoglobin, C-peptide, blood urea nitrogen, creatinine, arterial blood pH and bicarbonate, existence of ketone bodies in the blood or urine, serum sodium level, and serum potassium level at the time of presentation to the hospital. In addition, we evaluated whether they would survive up to 6 months after admission.

2) Statistical Analysis

The variables are expressed as the mean±standard deviation. The mean for each variable was compared, and a one-way analysis of variance and the Scheffé *post hoc* test were used for comparison of the 3 groups. Cross tabulation was used to compare categorical variables. When the p-value was less than 0.05, it was considered to indicate statistical significance. All statistical analyses used IBM SPSS Statistics ver. 20.0 (IBM Co., Armonk, NY, USA). This study was approved by the Clinical Examination Committee of the National Medical Center (No. H-1601-062-003).

RESULTS

1. Clinical Symptoms and Signs

Among the elderly patients who came to the National Medical Center for hyperglycemic emergency state, we examined a total of 31 cases, including 19 male and 12 female patients. The average age was 78.9, and the average duration of diabetes was 12 years. The mean laboratory values on admission were as follows: glucose, 700.7 mg/dL; glycated hemoglobin, 10.6%; serum osmotic pressure, 437.23 mOsm/kg; aerial blood, pH 7.28; bicarbonate, 16.38 mmol/L; blood urea nitrogen, 68.26 mg/dL; serum creatinine, 2.6 mg/dL; serum sodium, 135.77 mEq/L; serum potassium, 5.26 mEq/L; fasting C-peptide, 1.67 ng/mL; and 2-hour postprandial C-peptide, 3.28 ng/mL (it was changed to C-peptide). No patient had recently received steroid treatment or surgery within a month before hospital admission.

The patients were divided into 3 groups — the DKA group, the DKA and HHS group, and the HHS group — comprising 10 cases, 8 cases, and 13 cases, respectively. Table 1 describes each group's sex, age, existence of a caregiver, duration of diabetes, insulin treatment history, and economic vulnerability (presence of health insurance). The DKA group, the DKA and HHS group, and the HHS group had an average age of 75.2, 81.0, and 80.5, respectively, and there was no significant difference among those groups. The duration of diabetes was 13.3 years, 3.7 years, and 14.6 years, respectively, and although the duration of diabetes in the DKA group and the HHS group was longer, there was no significant difference. Two patients in the DKA and HHS group were newly diagnosed with diabetes when they presented to the hospital; thus the diabetes duration in this group was significantly shorter than in the group with only HHS (p=0.047).

In 13 of the 31 cases (41.9%), the patients had medical benefits, showing that there were many economically vulnerable patients. The most frequent cause for hyperglycemic emergency state was discontinuation or irregular administration of insulin and hypoglycemic agents due to improper education and a lack of understanding about diabetes, which was observed in 13 of 31 cases (41.9%). The second most frequent cause was infection such as pneumonia, which was observed in 11 of 31 cases (35.4%). However, of those patients, no case of infection involved sepsis or septic shock. We also examined the diabetes treatment methods before the hyperglycemic emergency state and found that among 30 patients, not including 1 patient whose drugs were not described, 14 patients (46.7%) were treated with insulin, and 16 patients (53.3%) were treated with oral hypoglycemic agents. The proportion

Table 1. Clinical characteristics of the study subjects at presentation

Characteristic	DKA (n=10)	DKA+HHS (n=8)	HHS (n=13)	p-value*
Sex, male:female	7:3	4:4	8:5	0.687
Age (yr), mean±SD	75.2±8.2	81.0±9.1	80.5±6.2	0.196
Disease duration (yr)				0.047†
Mean±SD	13.3±12.2	3.7±3.6	14.6±9.8	
95% CI	(4.5-22.0)	(0.7-6.7)	(8.6-20.5)	
Insurance	6 (60)	2 (25)	5 (38.4)	0.309
Infection	3 (30)	4 (50)	4 (30.7)	0.608
No caregiver	2 (20)	0 (0)	1 (7.7)	0.336
Alcoholics	4 (40)	1 (12.5)	1 (7.7)	0.128
Prior insulin treatment	6 (60)	4 (50)	6 (46.1)	0.875
Self-discontinuation of diabetes medication	5 (50)	3 (37.5)	5 (38.4)	0.820
Death	1 (10)	3 (37.5)	3 (23.0)	0.382

Values are presented as number (%) unless otherwise indicated.
DKA, diabetic ketoacidosis; HHS, hyperosmolar hyperglycemic state; SD, standard deviation; CI, confidence interval.
*p-values obtained by chi-square test, one-way analysis of variance with Scheffé *post hoc* test. †p<0.05, HHS alone group versus combined DKA and HHS group.

Table 2. Biochemical characteristics of the study subjects at presentation

Characteristic	DKA (n=10)	DKA+HHS (n=8)	HHS (n=13)	p-value*
HbA1c (%)	11.1±1.7	11.7±1.6	9.6±2.2	0.065
Glucose (mg/dL)				0.080
Mean±SD	570.7±163.9	772.7±240.0	756.5±227.0	
95% CI	(453.4-687.9)	(572.0-973.4)	(618.9-894.0)	
Serum osmolarity (mOsm/kg)	298.8±40.2	349.2±43.0	335.1±33.0	0.051
pH	7.14±0.12	7.24±0.15	7.40±0.05	<0.001†
HCO_3 (mmol/L)	10.9±4.0	12.2±3.0	23.1±3.5	<0.001†
BUN (mg/dL)				0.066
Mean±SD	46.0±42.4	92.1±46.4	70.6±33.3	
95% CI	(15.61-76.38)	(53.28-130.96)	(50.54-90.84)	
Creatinine (mg/dL)	1.6±0.5	3.5±1.2	2.7±2.0	0.045§
Na (mEq/L)				0.021‖
Mean±SD	118.7±33.5	146.5±17.1	142.3±11.7	
95% CI	(94.6-142.7)	(132.1-160.8)	(135.23-149.3)	
K (mEq/L)	4.8±0.7	5.3±1.	5.5±0.8	0.194
Fasting C-peptide (ng/mL)				0.433
Mean±SD	0.90±0.59	2.18±2.28	1.97±1.74	
95% CI	(0.16-1.65)	(0.65-5.02)	(0.72-3.22)	
PP2 C-peptide (ng/mL)				0.114
Mean±SD	2.03±2.05	5.58±5.13	2.65±1.61	
95% CI	(0.12-4.18)	(0.19-10.96)	(1.50-3.80)	

Values are presented as number (%) unless otherwise indicated.
DKA, diabetic ketoacidosis; HHS, hyperosmolar hyperglycemic state; HbA1c, glycosylated hemoglobin; SD, standard deviation; CI, confidence interval; BUN, blood urea nitrogen; PP2, 2-hour postprandial blood glucose.
*p-values obtained by one-way analysis of variance followed by Scheffé *post hoc* test. †p<0.05, DKA alone group versus combined DKA and HHS group and HHS alone group versus combined DKA and HHS group; Scheffé *post hoc* test. ‡p<0.05, DKA alone group versus HHS alone group; Scheffé *post hoc* test. §p<0.05, DKA alone group versus combined DKA and HHS group; Scheffé *post hoc* test. ‖p<0.05, DKA alone group versus combined DKA and HHS group and DKA alone group versus HHS group; Scheffé *post hoc* test.

of patients who did not have the caregiver was relatively small, 3 of 31 cases (9.6%), but we could not confirm with medical records alone whether the caregivers lived together with and supported the patients even if there were family to care for them. In 6 of 31 cases (19.3%), the patients were drunken at the time of their presentation to the hospital or they had been drinking instead of having a meal.

2. Laboratory Results

The patients' laboratory results are recorded in Table 2. The mean glycated hemoglobin was 11.1% for the DKA group, 9.6% for the HHS group, and 11.7% for the DKA and HHS group. For all 3 groups, these were high levels, indicating that the blood glucose level was not very well controlled in their daily lives. Although the HHS group and the DKA and HHS group had a higher glucose level than did the DKA group, the difference was not significant. The arterial blood pH of the DKA group and the DKA and HHS group was significantly lower than that of the HHS group ($p<0.001$). The bicarbonate level in the DKA group was significantly lower than in the HHS group ($p<0.001$). The serum creatinine level in the DKA and HHS group was significantly higher than in the DKA group ($p=0.045$). The serum sodium level in the DKA group was significantly lower than in the DKA and HHS group and the HHS group ($p=0.021$). Although there was no significant difference in serum C-peptide among the 3 groups, the fasting C-peptide tested at the time of admission in the DKA group was 0.90 ng/mL, and 2-hour postprandial C-peptide level was 2.03 ng/mL, which were lower than the normal level of 4–10 ng/mL.

3. Treatment and Clinical Course

The patients were divided into the group of patients who died within 60 days and the group who survived. The number of patients who died in the DKA group, the DKA and HHS group, and the HHS group was 1, 3, and 3, respectively. Although there was no significant difference among those groups, 7 of 31 cases iwas dead, resulting in a high mortality rate of 22.5%. Three of the 7 patients died of metabolic acidosis or dehydration within 48 hours after entering the hospital. In addition, 6 of the 7 deceased patients had pneumonia at the time of their hospital admission. Two of the patients who presented to the hospital with pneumonia were admitted to the intensive care unit and treated with a ventilator but did not survive, and 3 patients died because either their guardian or they refused ventilator treatment or cardiopulmonary resuscitation. One patient had acute kidney failure and was referred to this hospital for hemodialysis but died during treatment due to cardiac arrest. For 1 patient, although his metabolic acidosis and blood sugar were corrected, general weakness was aggravated and developed a ileus. During conservative treatment, this patient was not able to recover and died.

DISCUSSION

Among elderly patients who presented to the hospital in a hyperglycemic emergency state, 32.2% (10 cases) had DKA, 25.8% (8 cases) had both DKA and HHS, and 42% (13 cases) had HHS. In the past, DKA and HHS were categorized as different diseases. Recently, however, some patients with acute hyperglycemic complications were observed to have the characteristics of both DKA and HHS. Therefore, these two diseases are now considered as belonging to the same disease group, not different ones[3,4,9-11].

Kim et al.[6] reported that when 102 patients with hyperglycemic emergency state were divided into a DKA group, a DKA and HHS group, and a HHS group, the average age for each group was 45.6, 50.7, and 61.7. The study by Maclsaac et al.[8] observed the average age for each group as 33, 44, and 69 and reported that the HHS group was significantly older than the DKA group. In this study on elderly patients aged 65 or older, the average age for each group was 75, 81, and 80, and although the HHS group was older than the DKA group, this was not significantly different. In their study on the causes of DKA, Hartalkar et al.[12] reported that 47 of 53 patients (94%) belonged to the middle or low socioeconomic group. In addition, Randall et al.[11] reported that in approximately one-third of patients who voluntarily stopped taking insulin, the treatment was discontinued due to economic reasons including the cost to purchase insulin, and based on this finding, argued that a patient's socioeconomic status affected treatment compliance. To identify the patients' economic vulnerability, this study investigated the presence of health insurance. The results showed that patients had medical benefits in 13 of 31 cases (41.9%), which was higher than the percentage of patients aged 65 or older with medical benefits in 2014 (7.6%)[13]. It can be inferred that patients who visited the hospital for hyperglycemic emergency state were economically more vulnerable than the typical patient aged 65 or older.

Previous studies reported that the causes of DKA and HHS included infections, side effects of medications such as diuretics and antihypertensive drugs, low treatment compliance, undiagnosed diabetes, drug abuse, and accompanying disease, and infection was the most frequently reported cause[10,11,14,15]. Regarding the cause of the diabetes complications, this study observed patients' or their caregivers' discontinuation of insulin or antidiabetic drugs due to a lack of understanding about diabetes (13 cases). Infection was another leading cause and was observed in 11 patients, 10 of whom had pneumonia. In addition, there were cases related to daily alcohol consumption (6 cases), and 2 patients had undiagnosed diabetes.

Trachtenbarg[3] stated that although DKA occurs in patients

with type 1 diabetes, who are mostly young, it could also occur in patients with type 2 diabetes. In this study, all the patients had type 2 diabetes. MacIsaac et al.[8] examined the mortality rate depending on the age and disease status of 312 patients with hyperglycemic emergency state (the DKA group, the DKA and HHS group, and the HHS group); they observed that the mortality rate of those aged 55 or older with DKA was 6.3% (1 person), the mortality rate for the DKA and HHS group was 14.3% (5 people), and that of the HHS group was 19% (8 people), and they reported that as age and serum osmotic pressure increased, so did the mortality rate. In the present study, the mortality rate for the DKA group was 10% (1 person), that of the group with both DKA and HHS was 37.5% (3 people), and that of the HHS group was 23% (3 people). The average age of the DKA group was lower than that of the HHS group, and so were the serum osmotic pressure and mortality rate.

This study has the following limitations: some items were not assessed in some patients because this study was conducted retrospectively; although patients had their caregivers, it was not confirmed whether they lived together with the patients; and this study could not obtain detailed information about the specific drugs that the patients voluntarily chose to discontinue.

This study confirmed that for patients who presented to the hospital in a hyperglycemic emergency state, the disease causes included the patient's voluntary discontinuation of antidiabetic medicine due to a lack of understanding about diabetes, new diabetes diagnosis, and infectious causes such as pneumonia. This study also determined that 41.9% of the patients were economically vulnerable, and their mortality rate was high at 22.5%. In addition, their clinical and biochemical characteristics were identified. People aged 65 or older accounted for 12.7% of the Korean population in 2014, and diabetes was surveyed as the fifth leading cause of death among the elderly, following cancer, cerebrovascular disease, cardiovascular disease, and pneumonia[16]. As the elderly population grows, more attention is focused on having a healthy lifestyle rather than longevity. In the future, there needs to be more focus on continuous diabetes management, regular screening, and treatment of diabetes in the elderly, and education to improve the understanding of diabetes. Furthermore, education on glucose control and diabetic complications should be initiated in the early stages of diabetes, and detailed and various strategies should be established to treat elderly people who are isolated socioeconomically.

Conflicts of Interest Disclosures: The researchers claim no conflicts of interest.

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