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Hypoglycemia in Emergency Department

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ABSTRACT

Objective: To study the epidemiology, etiologies and prognostic factors of hypoglycemia.
Methods: A retrospective chart review of hypoglycemic cases from December, 2009 to February, 2012 was conducted to gather the following patient data: age, gender, vital signs at triage, white blood cell count, serum glucose, C-reactive protein, glutamic oxaloacetic transaminase, creatinine, sodium, potassium, past history of liver cirrhosis, uremia, concomitant infection, concomitant cancer/malignancy, length of stay, lack of recent meal, status of acute renal failure and concomitant stroke. A total of 186 cases were enrolled in our study. We analyzed the data using commercial statistics software (SPSS for Windows, version 11.0, SPSS Inc., Chicago, IL). We used the Student´s t-test and χ^2 test for the statistical analyses, and significance was set at a P value less than 0.05.
Results: Hypoglycemia is related to several co-morbidities. In total, 10.2% of the patients had liver cirrhosis and 7.0% had uremia. More than half (55.4%) were bacterial infection during hospitalization. Acute renal failure accounted for 26.3% of the hypoglycemic episodes. In addition to the etiology of infection, the lack of a recent meal accounted for 44.6% hypoglycemic episodes. A total of 2.2% of the cases resulted from an acute cerebrovascular accident. Approximately 8.6% were concomitant with malignancy.
Conclusions: When hypoglycemic patients present in the emergency department, physicians should pay attention to the presence of infection, malignancy, liver diseases (liver cirrhosis and biliary tract infection), and acute renal failure.

1. Introduction

Hypoglycemia is an endocrine emergency that can alter the patient's mental status, resulting in lethargy, confusion and organ dysfunction. Common causes are a lack of adequate intake of food, chronic alcohol abuse, interactions among medications, increased physical exertion and overdose of medications (insulin/oral hypoglycemic agent). It presents with a variety of symptoms, ranging from impaired cognitive function to convulsions, coma and death. In the past, there have been many articles describing the etiologies of hypoglycemia, including old age, lack of a recent meal, infection, chronic renal insufficiency, liver diseases, and recurrent hypoglycemic episodes[1-3]. However, physicians have seldom mentioned or studied the prognostic factors of hypoglycemia. We studied hypoglycemia through a retrospective review of records from December, 2009 to February, 2012 at a tertiary teaching medical center in Northern Taiwan. The epidemiology, etiologies and prognostic factors for hypoglycemia are discussed in our report.

2. Materials and methods

A retrospective chart review of hypoglycemic cases (serum glucose less than 60 mg/dL) from December, 2009 to February, 2012 was conducted to gather data on patient age,

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gender, heart rate, systolic blood pressure, diastolic blood pressure at triage, white blood cell count (WBC), serum glucose, C-reactive protein (CRP), glutamic oxaloacetic transaminase (GOT), creatinine, sodium, potassium, past history of liver cirrhosis, uremia, concomitant infection [urinary tract infection (UTI) or pneumonia or biliary tract infection], concomitant cancer/malignancy, length of stay, lack of a recent meal, status of acute renal failure (ARF), and concomitant stroke. A total of 186 cases were enrolled in to our study, and we divided the patients into survival and mortality groups to compare the differences affecting the prognosis of hypoglycemia. The survival group was defined as the patients who survived until discharge. Concomitant stroke indicates newly-onset stroke with hypoglycemic episode in this emergency department (ED) visit. All charts reviewed with a paper-based manner. Data missed of 49 patients' CRP values and 4 patients' GOT levels were found. Only one case of 79 year-old female is out-of-hospital cardiac arrest case. All values were recorded on patients' arrivals of ED.

Patients with serum glucose levels less than 60 mg/dL were defined as hypoglycemic. Elderly age was defined as an age above 65 years old. Leukocytosis was defined as a WBC count above 10000/μL. Elevated CRP was defined as a level above 0.8 mg/dL. Elevated GOT was defined as a level above 41 U/L. Elevated creatinine was defined as a level above 1.3 mg/dL. ARF was defined as a doubling of level of creatinine within one month. Neonatal and pediatric patients (age less than 18 year-old) were excluded. We analyzed the data using commercial statistical software (SPSS for Windows, version 11.0, SPSS Inc., Chicago, IL). We used the Student's t-test and χ^2 test for statistical analyses, and significance was set at a P value less than 0.05.

3. Results

A total of 186 cases of hypoglycemia aged from 26 to 98 years old with an average age of 70.5±15.3 were encolled. Among these patients, 70.4% were elderly (131/186). Approximately 45.2% (84/186) had leukocytosis, which indicated that a possible inflammatory process was involved in the hypoglycemia. High CRP levels were noted in 82.8% (154/186) of the cases. About 62.4% (116/186) had impaired

Table 1

Basic information of patients with hypoglycemic cases conducted from December, 2009 to February, 2012 in Northern Taiwan.

	All	Survival	Mortality	P value
Age	70.5±15.3	70.5±15.1	70.3±17.2	0.1980
M: F	96:90	82:83	14:07	0.000*
BT ℏ	36.4±1.2	36.4±1.1	36.3±1.4	0.087
HR /min	86.5±18.1	85.3±15.9	95.7±29.5	0.001*
SBP mmHg	139.3±30.0	141.7±27.3	120.0±41.2	0.286
DBP mmHg	73.3±18.1	74.6±16.9	63.7±23.8	0.079
WBC (/μL)	11 223.0±7 198.0	10 969.0±6 438.0	13 219.0±11 608.0	0.008*
Glucose(mg/dL)	34.9±12.4	35.1±12.0	33.1±15.6	0.026*
CRP (mg/dL)	5.1±6.5	4.7±5.4	9.1±13.1	0.008*
GOT (U/L)	110.0±340.0	82.2±312	324.0±461.0	0.001*
Creatinine (mg/dL)	2.8±2.6	2.8±2.6	2.9±2.9	0.837
Na (meq/L)	134.5±11.1	134.8±11.1	131.8±11.2	0.274
K (meq/L)	4.1±1.0	4.0±1.0	4.7±1.2	0.185
LOS (days)	15.2±18.9	14.6±16.0	20.2±34.3	0.022*
Liver cirrhosis	19/186 (10.2%)	12/165 (7.3%)	7/21 (33.3%)	0.000*
Uremia	13/186 (7.0%)	11/165 (6.7%)	2/21 (9.5%)	0.348
With Infection	103/186 (55.4%)	89/165 (54.0%)	14/21 (66.7%)	0.001*
UTI	62/186 (33.3%)	54/165 (32.7%)	8/21 (38.1%)	0.394
Pneumonia	43/186 (23.1%)	36/165 (21.8%)	7/21 (33.3%)	0.051
BTI	5/186 (2.7%)	3/165 (1.8%)	2/21 (9.5%)	0.000*
Lack Ingestion	83/186 (44.6%)	71/165 (43.0%)	12/21 (57.0%)	0.976
ARF	49/186 (26.3%)	39/165 (23.6%)	10/21 (47.6%)	0.006*
With cancer	16/186 (8.6%)	11/165 (6.7%)	5/21 (23.8%)	0.000*
With CVA	4/186 (2.2%)	3/165 (1.8%)	1/21 (4.8%)	0.088

BT: Body temperature; HR: Heart rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; WBC: White blood cell count; CRP: C-reactive protein; GOT: Glutamic oxaloacetic transaminase; LOS: Length of stay; UTI: Urinary tract infection; BTI: Biliary tract infection; ARF: Acute renal failure; CVA: Cerebrovascular disease; *: $P<0.05$, significant difference.

renal function and 38.2% (71/186) had elevated GOT.

Hypoglycemia was associated with several comorbidities. About 10.2% (19/186) had liver cirrhosis, and 7.0% (13/186) of the patients had uremia. More than half of the patients (55.4%) were infected during hospitalization. About 33.3% (62/186) had UTIs and 23.1% (43/186) had pneumonia and 2.7% (5/186) had biliary tract infections. ARF accounted for 26.3% (49/186) of the hypoglycemic episodes.

In addition to the etiology of infection, the lack of recent meal accounted for 44.6% (83/186) of the hypoglycemic episodes. About 2.2% (4/186) of the cases resulted from an acute cerebrovascular accident (CVA). Approximately 8.6% (16/186) were concomitant with malignancy. Overall in-hospital mortality rate was 11.3% (21/186).

In the male patients, tachycardia, elevated WBC, low serum glucose, high CRP and GOT were associated with an increased risk of mortality. Hepatic problems [liver cirrhosis and biliary tract infection (BTI)] concomitant with malignancy, infection and ARF were also associated with higher mortality (Table 1). In the cases with concomitant malignancy, gastrointestinal tumors (5.4%) were the most commonly observed, and lung cancer (2.2%) was the second most common extraintestinal tumor in hypoglycemic patients (Table 2).

Table 2
Hypoglycemic patients with malignancy.

Gastrointestinal 10/186 (5.4%)	Hypopharyngeal	1
	Esophagus	1
	Stomach	4
	Hepatocellular	2
	Cholangiocarcinoma	1
	Rectum	1
Lung	4/186 (2.2%)	
Breast	1/186 (0.5%)	
Bladder	1/186 (0.5%)	

4. Discussion

Hypoglycemia is a life-threatening emergency. It can lead to various forms of cognitive dysfunction and death. Hypoglycemia occurs most frequently in the elderly. In our study, 70.4% of the cases were over 65 years old[4,5]. In a Korean report conducted in 2012, the mean age of hypoglycemic patients was 69.5 years old, similar to our study (70.5 years old)[1]. With respect to gender, there was no significant difference in the case distribution. Some hypoglycemic patients exhibited cold sweating and hypothermia when hypoglycemia occurred. Approximately 11.3% (21/186) of the hypoglycemic patients were hypothermic in our study.

There were several precipitating factors contributing to hypoglycemia, including the lack of a recent meal (44.6%-52.0%), alcohol consumption (21.0%), the presence of coronary artery disease, concomitant infection, CVA, or ARF, malignancy and recent hospital discharge[2,5-8]. In our study, concomitant infection (55.4%) was more commonly observed than the lack of a recent meal (44.6%). UTI (33.3%) was more commonly observed than pneumonia (23.1%) and BTI (2.7%). In 1980, Dr. Miller described hypoglycemia as a warning sign of bacterial sepsis, and the mechanisms included depleted glycogen stores, impaired gluconeogenesis, and increased glucose utilization by the infecting pathogens[9]. Clinically, we observed several indicators, such as tachycardia, elevated CRP, and elevated WBC, which implyed inflammatory processes in the patients. For hypoglycemic patients with tachycardia, high CRP, and elevated WBC, the mortality rate increased by 4-, 2- and 1.1-fold compared with normal cardiac patients and those with normal CRP and WBC levels. Higher CRP levels were found in the mortality group of hypoglycemic patients than in the survivor group (9.1 vs. 4.7, P=0.008<0.05). Up to 82.8% of hypoglycemic patients had elevated CRP levels, indicating concomitant infection or other tissue damage when the hypoglycemia occurred. These hypoglycemic patients with concomitant infection were recommended for hospitalization.

The diagnosis of hypoglycemia relies on blood tests. If the patient is critically ill, a rapid glucose test is a good way to know whether hypoglycemia is present. To collect data on liver and renal function, CRP, WBC, urine analysis, and chest X-ray are all necessary to exclude infection and determine the severity and prognosis. If there is a neurologic deficit a few hours after intravenous dextrose administration, a neurologist should be consulted to exclude stroke.

Although there was a small fraction (8.6%) of hypoglycemic with patients with concomitant malignancy, more than half of the malignancies originated from the gastrointestinal tract. Others sites of origin included the lungs, breast and bladder. The general status of a reduced appetite in patients with cancer involving the gastrointestinal system led to hypoglycemia.

Comorbidities related to hypoglycemia are impaired renal function and hepatic diseases[1,3]. In our study, 62.4% of the hypoglycemic patients had impaired renal function

and 26.3% of patients had ARF at the time of the hypoglycemic episode. A German report in 2003 reported that 54.0% of the hypoglycemic patients had renal impairment. Another report from Southern Taiwan in 2006 reported that 5.7% hypoglycemic patients had extensive liver disease[3,10]. Hypoglycemic patients with liver cirrhosis and BTI had 9.6- and 3.2-fold higher mortality rates compared to those without liver problems in our study.

In the treatment of hypoglycemic patients, intravenous dextrose (1 gm/kg body weight) is rapidly effective within a few minutes after administration. If a patient presents with a serum glucose level less than 60 mg/dL and impaired mental status without alertness, the administration of dextrose water is necessary. Serial determination of serum glucose level is mandatory.

Hypoglycemia is related to several vascular diseases, such as coronary artery disease, stroke and peripheral arterial diseases[11]. In our study, 2.2% of hypoglycemic patients presented with CVA at the time of the hypoglycemic episodes. In such a situation, intravenous dextrose fluid could not alleviate the neurologic deficit due to the initial hypoglycemia. The overall mortality rate of hypoglycemic patients in our study was 11.3%.

When hypoglycemic patients are encountered in the ED, physicians should consider the presence of infection, malignancy, liver disease (liver cirrhosis, biliary tract infection) and ARF. It is important to further examine possible inflammatory processes and consider the possibility of deteriorated renal function in hypoglycemic patients.

We can not define ARF in patients who have no medical records in the same hospital before their ED visits in our study. This could be a bias in number of ARF patients. Data missed of 49 patients' CRP values and 4 patients' GOT levels were found. Only one case of 79 year-old female is out-of-hospital cardiac arrest case. This study is based on data of single center in Northern Taiwan. The conclusion might be different in national registry or including cases from Southern Taiwan. These are all influenced factors in data analyses.

Conflict of interest statement

The authors report no conflict of interest.

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