

Full Length Research Paper

Etiologies of patients admitted to emergency department with hypoglycemia

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Hypoglycemia is the most common endocrinologic problem seen in emergency departments. To explore its causes in patients who admitted to the emergency department with symptoms resembling hypoglycemia, 225 hypoglycemia cases were evaluated from January 2000 to May 2008. Of 225 hypoglycemia cases, 158 (70.2%) were receiving treatment for diabetes mellitus, which was the most common group (94 patients were using insulin, 55 were receiving oral anti-diabetics (OAD) and 9 patients both OAD and insulin). The other causes for hypoglycemia were as follows: reactive hypoglycemia cases (11.6%), insulinoma (2.7%), malignancies (2.2%), Sheehan syndrome (0.9%), chronic liver disease (0.9%), gestational diabetes mellitus (0.4%), OAD use by mistake (3.6%), and use of OAD for suicidal purposes (13%). In eight of the cases, the reason could not be identified. The study revealed that diabetes mellitus constitute the most common reason for hypoglycemia among the patients seen in emergency departments. Efforts should be made to prevent hypoglycemia by giving the patients better education.

Key words: Emergency department, hypoglycemia, endocrine emergency.

INTRODUCTION

Hypoglycemia is one of the most commonly seen endocrinologic problem in emergency departments and is defined as blood glucose level less than 50 mg/dL with hypoglycemic symptoms or blood glucose level less than 40 mg/dL (Boaz et al., 2001).

Although the most common causes are diabetes mellitus (DM) and antidiabetic drugs, patients may be referred to emergency departments for rare reasons such as insulinoma, cancers, chronic liver failure, and endocrinologic disorders (Güven et al., 2000). Checking blood glucose level in patients having blackout as a result of consciousness, convulsion, confusion or abnormal behaviors should be one of the priorities for physicians in the emergency department and it should be kept in mind

that there may be other reasons for hypoglycemia other than DM. We have examined the underlying causes and incidence rates of patients admitted to hospital for hypoglycemia.

PATIENTS AND METHODS

In our study, we evaluated the patients referred to our emergency department of Cumhuriyet University Hospital. The patients who were hospitalized for other reasons and developed hypoglycemia during their hospitalization time were not included in the study. Cases above 15 years old were included in our study. Hypoglycemia was defined as blood glucose beneath 50 mg/dL (2.8 mmol/L) with neuroglycopenic symptoms or less than 40 mg/dL (2.2 mmol/L) without the necessity of neuroglycopenic symptoms. DM was defined as fasting plasma glucose (FPG) ≥ 126 mg/dL or as postprandial plasma glucose ≥ 200 mg/dL. Reactive hypoglycemia was diagnosed through extended glucose tolerance test. In order to determine endocrine-based hypoglycemic disease, basal and dynamic tests were applied. Malignancies were diagnosed through

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Table 1. Etiological causes.

Causes	Male		Female		Total	
	n	(%)	n	(%)	n	(%)
Type 2 DM	60	43.2	79	56.8	139	100
Type 1 DM	13	68.4	6	31.6	19	100
Reactive hypoglycemia	5	19.2	21	80.8	26	100
OAD used due to ignorance	7	87.5	1	12.5	8	100
Insulinoma	2	33.3	4	66.7	6	100
Other malignancies	4	80.0	1	20	5	100
OAD use for suicidal purposes	0	0	3	100	3	100
Sheehan syndrome	0	0	2	100	2	100
Chronic liver disease	2	100	0	0	2	100
Pregnancy	0	0	1	100	1	100
Adrenal insufficiency	0	0	1	100	1	100
Other rare	1	20	4	80	5	100
Unknown reasons	4	50	4	50	8	100
Total	98	43.6	127	56.4	225	100

bone marrow aspiration and biopsy. Chronic liver disease was diagnosed through biopsy or clinical, serologic, and biochemical tests and extended prothrombin time. Diagnosis of renal failure was defined as receiving dialysis or creatine clearance below 60 mL/min.

The clinical data of study population were evaluated in terms of age, gender, blood glucose levels, renal and liver functions, diagnosis, symptoms, treatments, complications and outcomes. Data were analyzed using Statistical Package for Social Science (SPSS) 10.0 for windows. Statistical analyses were performed using Chi-square test. Institutional ethics committee approval is obtained for the study.

RESULTS

Mean age of the 225 patients was 59.1±18.6 (17 - 89). Of the study population, 98 (43.6%) were males and 127 (56.4%) were females. The lowest blood glucose level was 10 mg/dl, the highest blood glucose level was 49 mg/dl and the average glucose value was 34.0±10.4 mg/dL. Seven patients died and in 8 patients there were different degrees of neurological sequelae. Etiological causes are shown in Table 1. Among the diagnoses of 225 cases included in our study, hypoglycemia occurrence during DM treatment ranked the first place with the number of 158 (70.2%) cases. Of these cases, 103 were using insulin. The 61.8% of the hypoglycemia cases were Type II DM and 8.4% Type I DM. Hypoglycemia was diagnosed in 8 cases (3.6%) because of wrong OAD drug use and in 3 cases use of OAD for suicidal purposes. Twenty six cases (11.6%) had hypoglycemia because of reactive hypoglycemia, this was the second highest incidence. Of the 225 cases, other causes for hypoglycemia were insulinoma in 6

(2.7%) patients, malignancy in 5 (2.2%), Sheehan syndrome in 2 (0.9%), chronic liver disease in 2 (0.9%), and adrenal failure in 1 (0.4%). Several rare diseases seen were; anorexia (1 patient), ischemic hepatitis (1 patient) as a result of type II respiratory failure, multiple organ failure (1 patient) due to Crimean-Congo hemorrhagic fever sepsis and chronic liver disease (2 patients) as a result of amyloidosis. In 8 of the cases, the results of the tests were normal and the reason of hypoglycemia could not be explained.

Out of 158 DM patients who took part in our study, 64 (40.50%) were using OAD and 94 (59.50%) were not using OAD. Forty-three cases were using sulfonylurea among 64 patients who were using OAD. Rates of hypoglycemia due to sulfonylurea drug use are shown in Table 2. Hypoglycemia due to insulin use for their treatment was mostly seen in the first three months and between 1 - 5 years (Table 3). In 17 cases, there were repeating episodes of hypoglycemia and one of the patients had been applied to emergency department 10 times due to hypoglycemic coma. In this specific case, there were psychiatric findings and after 6 suicidal attempts, the patient died. Two hundred and ten (93.3%) patients were discharged in healthy condition. Mortality occurred in 7 cases (3.1%) and there were different levels of neurological sequelae in 8 cases (3.6%). Two patients did not gain their consciousness and one of these patients was a female who took OAD for suicidal purposes (Table 4). All the 7 patients died in the first 24 h. Two of the patients had sepsis and multiple organ failure, 2 had cancer and were in terminal period. The other 2 patients died from chronic renal failure. One of them had uremic coma and hyperpotassemia, and the other gastrointestinal bleeding occurred. One patient who did not have an additional disease died because of hypoglycemic coma.

DISCUSSION

Hypoglycemia is one of the most common and important endocrinologic causes for referral to emergency departments in the whole world (Comi, 1993). Even though it is a rare reason of emergency department applications, early diagnosis and immediate treatment are required when the adverse outcomes are taken into account. The most common reason for ambulance calls and emergency department applications is hypoglycemia (Goyder et al., 1997; Holmwood et al., 1992) for diabetic patients. Among the etiologies of hypoglycemia, there are antidiabetic drugs, increase in physical activity, fasting and alcohol intake (Hanley, 1990). As it is known that most of the hypoglycemia cases are treated by patients, their friends and relatives (Leese et al., 2003), the rate of applications to emergency department for hypoglycemia does not reflect the hypoglycemia incidence in diabetic patients. Even though a small portion of patients with

Table 2. Sulfonylurea types in hypoglycemia cases.

Sulfonylurea types	n	(%)
Glipizide	1	2.3
Gliclazide	15	34.9
Glimepride	25	58.1
Glibornuride	2	4.7
Total	43	100.0

Table 3. Insulin use rates among the hypoglycemic DM patients.

Insulin use	n	(%)
Does not use	55	34.8
Using for 3 months	28	17.7
Using for 3 -12 months	19	12.0
Using for 12 months - 5 years	31	19.6
Using for 5 -10 years	13	8.2
Using for 10 years and more	12	7.6
Total	158	100.0

($\chi^2 = 48.3$, $p = 0.001$, $p < 0.05$)

Table 4. The results of hypoglycemia cases.

Cases	n	(%)
Recovery	210	93.3
Sequelae	8	3.6
Death	7	3.1
Total	225	100.0

diabetic hypoglycemia admit to emergency departments, these patients constituted the major group of our study. In our study, 103 out of 158 patients with diabetic hypoglycemia, 103 were using insulin. In the first three months DM treatment period hypoglycemia was common (28 patients out of 103). We suggest that better training is required for patients in order to be protected from hypoglycemia when insulin is chosen for DM treatment. Sulfonylureas were the most common hypoglycemia causes among the patients who were using OAD drugs. When the sulfonylureas are examined within their group in our hypoglycemic patients, it was observed that glimepiride and gliclazide were seen more. The probable cause for this is the fact that the both groups of drugs are commonly used in the study area for OAD drug treatment. The other reason for this is that our study group is old and sulfonylurea drug group cause hypoglycemia more often in this age group.

Reactive (postprandial) hypoglycemia is that which occurs due to delayed insulin decrease in the blood when blood glucose levels start to drop (Virally and Guillausseau,

1999). Out of 26 reactive hypoglycemia cases in our series, dumping syndrome was the cause in 3 cases. High rate of reactive hypoglycemia in our study may have resulted from obesity causing insulin resistance.

Malignancies are one of the other causes of hypoglycemia. Increase in glucose uptake by the tumor tissue or decrease in the production of hepatic glucose can cause hypoglycemia (Marks and Teale, 1996). Furthermore, IGF-II, which is secreted by the tumor tissue, causes reduction in glucagons and growth hormone levels, leading to hypoglycemia (Phillips and Robertson, 1993). We identified malignancy with hypoglycemia in 12 of our cases; however, as DM was present in 7 of these cases, we included them in the diabetic hypoglycemia group. We determined gastrointestinal malignancy in 8 cases, bladder tumor in 2 cases, lung cancer in 1 case and leukemia in 1 case.

Insulinomas are the endocrine tumors that cause hypoglycemia. Six of our cases that applied to emergency department with hypoglycemia had insulinoma. Interestingly, we found that 2 of them were receiving psychiatric treatment. After surgical treatment, complete recovery was established. Piccillo et al. (2005) reported that 2 similar cases were receiving treatment for anxiety and epilepsy and after surgical treatment for insulinoma the psychiatric symptoms disappeared and psychiatric treatments had been stopped.

Hypoglycemia was defined in 11 cases as a result of OAD intake without diabetes. While 8 of these patients had taken the drugs by mistake, 3 of them used it for suicidal purposes. We found that there was secretagogue intake in 3 cases and in 8 cases sulfonylurea use was present. Hypoglycemia development due to sulfonylurea use by mistake or for suicidal purposes was reported (Klonoff et al., 1995). Whereas hypoglycemia development due to secretagogue use was reported more rarely (Boaz et al., 2001). In our study, hypoglycemia due to ignorant use of drug was seen especially among the elderly (more than 70 years of age), drug use for suicidal purposes was seen more often in younger age group. Hypoglycemia is rarely seen due endocrine reasons. Hypophyseal, adrenal or primary thyroid gland failure is among the endocrinologic disorders causing hypoglycemia (Samaan, 1989). In our series, there were only 3 cases due to endocrinologic disorders. Sheehan syndrome was present in 2 cases and primary adrenal failure in 1 case. As glucocorticoids are increasing blood glucose by antagonizing the effect of insulin on muscles and liver, and stimulating hepatic gluconeogenesis hypoglycemia can be seen in the diseases in which this hormone is insufficient (Pilkis and Granner, 1992; Ruzzin et al., 2005). Liver and kidney are important in regulating blood glucose. Decrease in glucose output in these organs may cause hypoglycemia (Sumida et al., 2007). In our study, we discovered 2 cases due to chronic liver failure and 1 case due to ischemic hepatitis.

In our cases, one of the rare causes of hypoglycemia

was secondarily due to Crimean-Congo hemorrhagic fever. In this case, liver enzymes and kidney functions were normal. We suggest that hypoglycemia might be due to hypocortisolemia. As Crimean-Congo hemorrhagic fever disease is common in our region, further studies are needed to define the incidence rate of hypocortisolemia in these patients.

In conclusion, the most common reason for hypoglycemia is the diabetic patients receiving treatment. Therefore, we concluded that these patients should be better trained about DM treatment which can protect them from hypoglycemia.

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