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ABSTRACT... Hypoglycemic symptoms are a very common experience for diabetics ranging from an innocent increased appetite to dreadful unconsciousness. This study was designed to assess the patient's awareness about the symptoms, experience of individual symptoms and their ability to recognize and to respond accordingly. **Materials and Methods:** All diabetic patients were assessed for the awareness of different symptoms of hypoglycemia, their experience of individual symptoms in last six months and ability of the patient and family members to recognize and to respond accordingly to these symptoms on a prescribed proforma with the help of trained staff. **Results:** We had 1260 new cases of DM during the study period with valid diagnosis and taking either sulphonylurea or Insulin who were enrolled in the study. 280 patients had no idea of the symptoms. 564 patients knew no more than three symptoms. Palpitation and sweating were the most commonly known 80% and experienced 65% symptoms. Hunger and epigastric discomfort were the next best known 73% and experienced 58% symptoms. Loss of consciousness was the next in the list in terms of knowledge 52% and experience 23%. Coldness of body 28%, severe weakness 24%, blurred vision 12%, abnormal behavior 12% and altered consciousness 6% were the next in the list of experience. Early morning headache, night terror and frequent awakening were the least known 3% and recognized 1% symptoms. Abnormal behavior and altered consciousness were not known to any patient as a symptom. Of those who knew or experienced the symptoms, eating anything available was the most common response, only 35% responded by eating rapidly available food items like sugar, honey, candies, beverages, fruit juice or jams. 3% of patients even resorted to taking diet colas initially and only later took other food after waiting for some time. In the event of patient getting unconscious, 80% of the times attendants did not consider hypoglycemia initially at home at first such experience. **Discussion:** Patient must be properly educated about these symptoms before prescribing these agents and shall be repeatedly evaluated at each visit. Failing to recognize early and mild symptoms may lead to a terrifying experience.

Key words: Hypoglycemia, Diabetes

INTRODUCTION

Diabetes Mellitus (DM) is a hyperglycemic state. The blood sugar level is determined through a fluctuating balance between the caloric load, physical activity and endogenous insulin. In diabetic who are being treated by sulphonylurea drugs or exogenous Insulin, this fine balance may tip to reduce the blood sugar below certain desirable levels resulting in a specific set of symptoms called Hypoglycemia Syndrome. The symptoms may range from a benign increased appetite or feeling hungry before the meal times to severe symptoms like drenching sweating, blurred vision, abnormal behavior, convulsions and unconsciousness. Recovery after appropriate measures to restore blood sugar level is quiet fast. It can

sometimes be difficult to determine whether a person's symptoms are due to hypoglycemia. Endocrinologists typically consider the criteria referred to as Whipple's triad as conclusive evidence that an individual's symptoms can be attributed to hypoglycemia instead of to some other cause¹.

- Symptoms known to be caused by hypoglycemia
- Low glucose at the time the symptoms occur
- Reversal or improvement of symptoms or problems when the glucose is restored to normal

Research in healthy adults shows that mental efficiency

declines slightly but measurably as blood glucose falls below 65mg/dL (3.6 mM) in many people. Hormonal defense mechanisms (adrenaline and glucagon) are normally activated as it drops below a threshold level (about 55mg/dL (3.0 mM) for most people), producing the typical hypoglycemic symptoms of shakiness and dysphoria². Obvious impairment may not occur until the glucose falls below 40mg/dL (2.2 mM), and many healthy people may occasionally have glucose levels below 65 in the morning without apparent effects. Since the brain effects of hypoglycemia, termed neuroglycopenia, determine whether a given low glucose is a "problem" for that person, most doctors use the term hypoglycemia only when a moderately low glucose level is accompanied by symptoms or brain effects.

Diabetic hypoglycemia represents a special case with respect to the relationship of measured glucose and hypoglycemic symptoms for several reasons. First, although home glucose meter readings are often misleading, the probability that a low reading, whether accompanied by symptoms or not, represents real hypoglycemia is much higher in a person who takes insulin than in someone who does not because injected insulin cannot be "turned off", diabetic hypoglycemia has a greater chance of progressing to serious impairment if not treated, compared to most other forms of hypoglycemia. Third, because glucose levels are often above normal for long periods of time (hours, days, or months) in persons with diabetes, hypoglycemic symptoms may sometimes occur at higher thresholds than in people whose blood sugar is usually normal. For all of these reasons, higher meter glucose thresholds are often considered "hypoglycemic" in people with diabetes. In both young and old patients, the brain may habituate to low glucose levels, with a reduction of noticeable symptoms despite neuroglycopenic impairment.

In insulin-dependent diabetic patients this phenomenon is termed hypoglycemia unawareness and is a significant clinical problem when improved glycemic control is attempted. Another aspect of this phenomenon occurs when chronic hypoglycemia before diagnosis may be better tolerated than acute hypoglycemia after treatment is underway. A prolonged severe hypoglycemic event may lead to permanent neurological deficit. Similarly a

severe hypoglycemic event may precipitate angina or even myocardial infarction. For these reasons it becomes very important that every diabetic patient, the family members, work associates and close friends must be properly educated for the recognition of both early and severe symptoms and the appropriate response. All patients on sulfonylureas or Insulin must be assessed for these symptoms at each visit for reinforcement of education^{3,4}.

MATERIALS AND METHODS

This multicenter study was carried out at respective consultancies of the contributors, from January 2005 to December 2008, on diabetics presenting for routine consultancy. On the first visit diagnosis of diabetes was confirmed through available record and random blood sugar was checked by glucometer. Diabetes was defined as a fasting glucose level of ≥ 126 mg/dl or a 2-hour post-prandial glucose level of >200 mg/dl. Patients were asked to fill up the following proforma by the help of specially trained educator nurses.

**Do you know the symptoms of Hypoglycemia?
Which of the symptoms you have experienced? Tick if yes.**

How frequently you experience these symptoms in last 6 month?

**What actions do you take for these symptoms?
Verbatim**

Hunger	Palpitation	Sweating	Weakness
Coldness	Pallor	Epigastric pain	Blurred vision
Disorientation	Drowsiness	Unconscious	
Morning Headache	Night Terror		Night Awakening

If the patient claimed to know the symptoms of hypoglycemia, they were requested to name them. Then individual symptoms were told and asked about the recognition and then experience. The frequency of experience in last six months was asked for each symptom. Responses were recorded in verbatim.

INCLUSION CRITERIA

Any patient presenting with valid diagnosis of Diabetes Mellitus and using sulfonylurea group of oral hypoglycemics or Insulin.

EXCLUSION CRITERIA

Diabetic Patients unable to speak or having altered conscious level for whatsoever reason.

STUDY DESIGN

Observational multicentral study.

RESULTS

We had 1260 new cases of DM during the study period with valid diagnosis and taking either sulphonylurea or Insulin who were enrolled in the study. 840 were females and 420 were male. 760 were on oral Sulphonylurea alone or in combination with other oral hypoglycemic agents, 148 on a combination of Sulphonylurea and Insulin and rest on Insulin alone. 280 patients had no idea of the symptoms. 564 patients knew no more than three symptoms. Palpitation and sweating were the most commonly known 80% and experienced 65% symptoms. Hunger and epigastric discomfort were the next best known 73% and experienced 58% symptoms. Loss of consciousness was the next in the list in terms of knowledge 52% and experience 23%.

Coldness of body 28%, severe weakness 24%, blurred vision 12%, abnormal behavior 12% and altered consciousness 6% were the next in the list of experience. Early morning headache, night terror and frequent awakening were the least known 3% and recognized 1% symptoms. Abnormal behavior and altered consciousness were not known to any patient as a symptom. Of those who knew or experienced the symptoms, eating anything available was the most common response, only 35% responded by eating rapidly available food items like sugar, honey, candies, beverages, fruit juice or jams. 3% of patients even resorted to taking diet colas initially and only later took other food after waiting for some time. In the event of patient getting unconscious, 80% of the times attendants did not consider hypoglycemia initially at home at first such experience.

DISCUSSION

Like all other homeostatic systems, maintaining blood glucose levels is a fine balancing act. After food intake, depending upon the nature of the caloric load, glycemic index, speed of the digestion and absorption process, there is an increase in blood glucose level. This is balanced by calibrated release of endogenous insulin. During post-prandial period fall in blood glucose level is prevented by release of glucose from liver either from stored glycogen or through gluconeogenesis. Diabetes Mellitus is characterized by hyperglycemia. When lifestyle modification and dietary restriction fails to control hyperglycemia, hypoglycemic drugs are added. Insulin Sensitizers, Metformin and Acarbose are not associated with hypoglycemia when used alone or in combination with each other. Sulfonylureas and Insulins are associated with hypoglycemia.

The prevention or correction of hypoglycemia is the result of both dissipation of insulin and activation of counter-regulatory systems. Glucagon and epinephrine have been shown to be the key counter-regulatory factors. Deficient glucagon responses to decrements in plasma glucose, which are common in patients with IDDM and occur in some patients with NIDDM, result in altered counterregulation. But counterregulation is generally adequate, because epinephrine compensates for it⁵.

These symptoms come at variable blood sugar level and vary from person to person; severity depends upon the blood sugar level and intactness of autonomic responses. Some person may not show any early symptoms and get unconscious. Frequent attacks of hypoglycemia may in itself lead to hypoglycemic unawareness^{6,7,8}.

Defective glucose counterregulation due to combined deficiencies of glucagon and epinephrine secretory responses occurs in many patients, typically those with longstanding diabetes, and must be added to the list of factors known to increase the risk of hypoglycemia, at least during intensive therapy⁹.

The symptoms may be as benign as just feeling hungry

before the routine dietary schedule, to epigastric and abdominal cramps. Palpitation, pallor, coldness of the skin, generalized weakness and sweating, which may be profuse, are other common symptoms. Blurred vision, altered behavior, drowsiness, convulsions and unconsciousness are the common neurological symptoms. Hypoglycemia during sleep manifests as frequent awakening, night terror, unpleasant dreams, early morning headache and feeling hungry on waking up. Apart from being unpleasant to alarming emergency requiring frequent emergency visits, prolonged severe hypoglycemia may result into permanent neurological damage. According to a 12-month prospective study there were 125 visits to the Harlem Hospital Emergency Room for symptomatic hypoglycemia. Sixty-five patients had obtundation, stupor, or coma; 38 had confusion or bizarre behavior; 10 were dizzy or tremulous; 9 had had seizures; and 3 had suffered sudden hemiparesis. Diabetes mellitus, alcoholism, and sepsis, alone or in combination, accounted for 90% of predisposing conditions; others included fasting, terminal cancer, gastroenteritis, insulin abuse, and myxedema. Average blood glucose level were lower among comatose than among obtunded patients, but overlap was considerable, and overall there was little correlation among cause, blood glucose levels, and symptoms. Although mortality was 11%, only one death was attributable to hypoglycemia per se, and only four survivors had focal neurological residua^{10,11}.

Severe hypoglycemia may precipitate myocardial angina or even infarction or precipitate cardiac decompensation and atrial fibrillation.

Frequency of hypoglycemic events varies with different sulfonylureas and insulins^{12,13}.

The prevalence of symptoms decreases with increasing duration of sulfonylurea administration. Mean glycosylated hemoglobin and postprandial plasma glucose were significantly lower in patients reporting hypoglycemic symptoms than in those without symptoms. The prevalence of hypoglycemic symptoms was significantly higher in patients treated with glyburide than in patients treated with gliclazide or chlorpropamide. The prevalence of symptoms was higher in patients

taking metformin, acarbose and insulin sensitizers additionally¹⁴.

For all these reasons it is especially advised that every diabetic patient must be properly educated about these symptoms. All the family members, work associates and friends must also be educated to recognize and respond accordingly. Physician must ask about these symptoms at each visit. A patient who never had experienced hypoglycemia probably never had a good glycemic control. Eating some quickly digestible carbohydrate may bring the sugar level up in the normal range. If symptoms are severe then white sugar, honey, jam and candies, fruit juices, soft colas are a handy replacement. If the patients get very drowsy then one must apply honey or jam inside the cheeks to improve the neurological status where oral intake is feasible. If all this is not applicable then intravenous glucose replacement is the only answer. Intramuscular glucagon is a very useful home emergency measure but is not commonly available¹⁵.

It is very important to recognize that palpitation, cold sweating, epigastric pain and severe weakness may very well be symptoms of myocardial infarction. If adequate glucose replacement fails to correct these symptoms then a proper detailed cardiac assessment is warranted. This is especially important since NIDM is a cardiovascular disease right from the time of diagnosis and with passing years it is a common complication¹⁶.

Renal failure is again a common complication of long term DM. As renal failure sets in chances of hypoglycemic events become more frequent due to deranged mechanism of insulin clearance. Frequent hypoglycemic events without a change in dose, diet or activity must lead to assessment of renal and hepatic status. Chronic Liver Disease due to Hepatitis C Virus, a very common accompaniment of DM, leads to decreased ability of liver to generate glucose in postprandial state.

Symptoms of anxiety and panic attack resemble very closely to hypoglycemic symptoms. Palpitation, agitation, cold sweating, abdominal cramps finger

tremors and severe weakness mimic hypoglycemic symptoms and in most likelihood respond to eating. Spot glucose testing is the only way to differentiate. But this consideration must not deter the patient from taking readily absorbable sugars in case of doubt because hypoglycemia is dangerous in immediate cardiovascular and neurological consequences¹⁷.

SUMMARY

Hypoglycemia is very common in diabetics taking Sulphonylurea or Insulin. Knowledge of symptoms and their recognition is quite poor especially in newly diagnosed patients. Proper education about the symptoms at the time of initiation of treatment and reinforcement at follow-ups is mandatory.

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PREVIOUS RELATED STUDIES

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**Small minds are concerned
with the extraordinary, great
minds with the ordinary.**

Blaise Pascal