

A STUDY ON PATIENTS' AWARENESS, RECOGNITION MANAGEMENT AND PREVALENCE OF HYPOGLYCEMIC EPISODES IN TYPE 2 DIABETES MELLITUS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: To assess patients' awareness on management of hypoglycemic episodes and analyzing the prevalence of hypoglycemic episodes in patients with Type 2 diabetes mellitus.

Methods: A prospective-observational comparative study was carried out for a period of 6 months in the outpatient unit of endocrinology and general medicine department. Patients who had hypoglycemic episodes were classified into mild, moderate and severe hypoglycemia with respective to age, anti-diabetic therapy and co-morbidities. Prevalence of hypoglycemia was calculated using prevalence formula; hypoglycemic episodes for anti-diabetic therapy were compared using ANOVA and independent t-test.

Results: Of 200 patients, (43%) were male and (57%) were female patients. Patients with systemic hypertension (30%) were more predominant than other co-morbid conditions. According to anti-diabetic therapy (49.5%) patients were on oral hypoglycemic agents (OHA's), (16.5%) on insulin and (34.5%) on both insulin and OHA's. The calculated value of t (2.831) was greater than table value (2.45) and mean of OHA (24.75) was greater than the mean of insulin (8.25). Prevalence of hypoglycemia was (51%).

Conclusion: The results from this study showed that more number of patients taking OHAs was found to experience hypoglycemia and patients with SHT as co-morbid condition were found to experience hypoglycemia than other co-morbid conditions. Prevalence of hypoglycemia was found to be more in females and elderly population.

Keywords: Hypoglycemic episodes, Prevalence, Insulin, Oral hypoglycemic agents, Co-morbid condition.

INTRODUCTION

Hypoglycemia is a lower than normal level of blood glucose. It can be defined as "mild" if episode is self-treated; "moderate" if assisted and "severe" if hospitalized and assisted by a physician (DCCT 1993) [1].

Hypoglycemia is a true medical emergency, which requires prompt recognition and treatment to prevent organ and brain damage. The spectrum of symptoms depended on duration and severity of hypoglycemia and varied from autonomic activation to behavioral changes to altered cognitive function to seizures or coma. The short and long-term complications include neurologic damage, trauma, cardiovascular events and death. Severe untreated hypoglycemia can cause a significant economic and personal burden. Therefore identification and prevention of hypoglycemia can reduce diabetes burden by prevention of hypoglycemia complications [2].

METHODS

Study design

A prospective observational comparative study was conducted at a 900 bedded multispecialty tertiary care teaching hospital in the south region of Tamil Nadu. Study approval with the proposal number of 13/048 was obtained from the Institutional Human Ethics Committee. Data sources for the study were patient history, treatment charts, physician guidance and hospital information systems.

Patients were selected according to the inclusion and exclusion criteria. Patients of age >18 years, patients treated with oral hypoglycemic agents (OHAs) and insulin, Type 2 diabetic patients for more than 2-3 years, patients with other co-morbid conditions were included in the study. Pregnancy and lactating women, psychosis and mental retardation, active substance abuse, significant depression and Type 1 diabetes mellitus (DM) were excluded.

The study was commenced in March 2013, in the outpatient unit of endocrinology and general medicine department. A data collection form was used to document patients' demographics, clinical laboratory data, past and present medications, diabetic history and co-morbid conditions.

Patients were categorized according to the anti-diabetic medications they were receiving as subcutaneous insulin either once or twice a day as prescribed; patients treated with OHAs; patients treated with both insulin and OHAs.

Patients were assessed about their awareness, recognition and management of hypoglycemic episodes as well as their awareness of hypoglycemic episodes and management during driving using a standard questionnaire.

Statistical analysis was performed using ANOVA and Student's unpaired t-tests (independent t-tests) at the 0.05 significance level, and prevalence was calculated using period prevalence formula, episodes from the past 6 months were calculated.

$$\text{Prevalence} = \frac{\text{Number of cases that occurred in a given period}}{\text{Number of people in the population during this period}}$$

RESULTS

Patient demographics

Calculated value of F (5.095) was greater than table value (4.26) showed difference between three groups. Since calculated value of t (2.831) is greater than table value (2.45) showed difference between OHA and insulin and the mean of OHA (24.75) is greater than mean of insulin (8.25) more hypoglycemic episodes were observed with OHAs.

- Table value was obtained from standard tables in textbook of statistics
- It can be obtained by calculating the degrees of freedom using the formula: $n_1 + n_2 - 2$
- For larger samples, degrees of freedom can be calculated by: $n_1 + n_2$
- The obtained degrees of freedom correlated with the table value.

Prevalence of hypoglycemia in patients with Type 2 diabetes

Number of hypoglycemic cases in the given period = 102

Number of people in the population during the given period = 200

Period prevalence = $102/200 = 51\%$

DISCUSSION

Anti-diabetic therapy-induced hypoglycemia is the limiting factor in the glycemic management of diabetes. It precludes maintenance of euglycemia over a lifetime of diabetes and thus full realization of the established microvascular and potential macrovascular and other benefits of long-term glycemic control. It compromises physiological and behavioral defenses against subsequent falling plasma glucose concentrations and thus causes a vicious cycle of recurrent hypoglycemia [3,4]. Because of steady improvements in the glycemic management of diabetes, it is possible both to improve glycemic control and to minimize the risk of hypoglycemia in many patients [5,6].

Patients with mild hypoglycemia were defined as being with or without specific symptoms but manageable without help. Patients with moderate hypoglycemia experienced symptoms of hypoglycemia and required assistance from a second person (e.g. a relative or friend), but no attention of a medical professional was necessary. Patients with severe hypoglycemia were seeking medical attention or were admitted to hospital because of hypoglycemia [7,8].

According to age and gender

Hypoglycemia was more common in the elderly population. Among the 200 patients 60-70 years age group experienced frequent symptoms and episodes of hypoglycemia as shown in Tables 1 and 2. Older adults with diabetes have a greater risk of hypoglycemia associated with the physiological decline of ageing, and the extended duration of diabetes and insulin treatment [9,10]. The elderly are also more prone to the effects of hypoglycemia such as the increased risk of accidents, falls and fractures, hospitalizations, in-hospital mortality, and long-term impairment of cognition [11,12].

Table 1: According to age and gender

Age in years	Number of patients
31-40	1
41-50	45
51-60	59
61-70	56
71-80	34
81-90	4
91-100	1
Total male	86
Total female	114

Table 2: Hypoglycemic episodes according to age wise

Age	Mild	Moderate	Severe	No episodes
31-40	-	-	-	1
41-50	13	2	2	28
51-60	10	12	11	26
61-70	8	11	17	20
71-80	4	8	12	10
81-90	-	1	3	-
91-100	-	-	1	-

Of 200 patients (43%) were male and (57%) were female patients hypoglycemia was more common among female patients than male patients. Female patients had lower counterregulatory responses to hypoglycemia than male patients [13].

According to co-morbidities

Systemic hypertension was the common co-morbid condition among patients with Type 2 diabetes. About 30% of the patients as shown in Table 3 were having hypertension as co-morbidity. According to statistical analysis, the calculated value of t (2.467) was greater than table value that showed a difference between systemic hypertension and other co-morbid conditions. The mean of systemic hypertension was greater, and hence it was more prevalent than other diseases. DM and hypertension are interrelated diseases that strongly predispose an individual to atherosclerotic cardiovascular disease. Indeed, an estimated 35-75% of diabetic cardiovascular and renal complications can be attributed to hypertension because populations are aging, and both hypertension and non-insulin-dependent diabetes mellitus incidence increases with age [14]. About 15% of the patients had renal failure as co-morbidity as shown in Table 3. The increased risk of hypoglycemia in patients with declining renal function is attributed largely to decreased renal clearance of insulin and accumulation of insulin [15,16]. It seems likely that loss of endogenous glucose production with decline renal function contributes to risk of hypoglycemia [17,18].

According to anti-diabetic therapy

According to Table 4 and statistical analysis (unpaired Student's t -test) calculated value of t (2.831) was greater than table value (2.45), which showed a difference between OHA and Insulin. Since mean of OHA (24.75) was greater than mean of insulin (8.25) more hypoglycemic episodes were observed with OHAs. The coefficient of variance of OHAs was found to be 45.25%, which was significant than insulin (45.12%) and also both insulin and OHAs (28.82%) as in Table 5. Patients receiving sulfonylureas with biguanides and insulin with biguanide experienced more number of hypoglycemic episodes than those taking biguanide alone as in Table 6. The risk of hypoglycemia was almost 3 times greater in patients receiving sulfonylurea than those receiving metformin [19].

Metformin plays a pivotal role in the treatment of patients with Type 2 diabetes. Metformin decreases basal glucose output by suppressing gluconeogenesis and glycogenolysis in the liver and increasing glucose disposal in muscle tissue [20]. Since metformin does not directly stimulate insulin secretion, hypoglycemia risk may be lower than for that of other oral anti-diabetic drugs. However, hypoglycemia in patients using metformin may occur in association with strenuous physical activity or fasting [21,22]. Long-acting sulfonylureas were associated with a higher risk of hypoglycemic episodes than short-acting sulfonylureas [23]. The risk for moderate to severe hypoglycemia was approximately threefold for users of sulfonylureas, particularly in the early phase of therapy, compared with metformin users [24,25].

Table 3: According to co-morbid conditions

Co-morbidity	Number of patients
Systemic hypertension	60
Renal failure	30
Other cardiovascular diseases	31
Others	23

Table 4: According to anti-diabetic therapy

Medication	Number of patients
OHA's	99
Insulin	33
Both (insulin and OHA)	68
Hypoglycemic episode (male)	39
Hypoglycemic episode (female)	63

OHA: Oral hypoglycemic agents

Patients' awareness and management of hypoglycemic episodes

Of 200 patients, 130 patients were aware about the symptoms of hypoglycemia. The patients who were aware about the symptoms of hypoglycemia managed by reducing dose of insulin (63%), reducing the dose of tablets (31%), eating more carbohydrate rich food (6%) as in Fig. 1.

Impaired awareness of hypoglycemia is a potentially serious complication of insulin therapy that is more likely to occur the longer a patient suffers from insulin-treated diabetes, and can also develop in association with strict glycaemic control. It is thought to result from recurrent exposure to hypoglycemia, with a resultant reduction in counterregulatory hormonal responses, and attenuation of the symptomatic response to hypoglycemia [26]. The glycaemic thresholds for initiation of these responses become re-set at lower blood glucose levels [2].

Diminished symptomatic awareness of hypoglycemia in patients with diabetes is more than just a lack of knowledge. Many biochemical

responses to hypoglycemia are known to be attenuated in those with impaired awareness of hypoglycemia, and recent research suggests reduced behavioral responses in the amygdala and orbitofrontal cortex regions of the brain. Thus, individuals who are unaware of an individual episode of hypoglycemia may have a failure in primary glucose sensing and a failure in generating higher cerebral responses (and behavioral responses) [27]. Fear of hypoglycemia in patients with diabetes is often greater than the patient's concern about the long-term consequences of hyperglycemia and can, therefore, act as a barrier to their medication-use and glycaemic control [28,29].

Patients' awareness and management of hypoglycemia during driving

Out 200 patients, 64 patients drive frequently. 16 patients had hypoglycemic episodes during driving. 11 patients were aware of management of hypoglycemia during driving and 53 patients were not aware of management of hypoglycemia during driving as shown in Table 7. Hypoglycemia also associated with increased accident risks while driving in people with Type 2 diabetes receiving anti-diabetic drugs without insulin [30]. It is important that physicians are aware of this association and educate people with diabetes about the warning symptoms of hypoglycemia and the precautions that can be taken to avoid motor vehicle accidents and falls. Sulfonylureas significantly increase hypoglycemia risk, and this increased risk is augmented when thiazolidinediones are added to sulfonylurea therapy [31].

CONCLUSION

Hypoglycemia has serious clinical outcome and its occurrence in Type 2 diabetes is likely to escalate along with the increase in disease prevalence. According to this study prevalence of hypoglycemic episodes were more, female patients have experienced more hypoglycemic episodes than male patients. The incidence of hypoglycemic episodes was more significant in patients taking OHA's. Hypoglycemia is not just the result of insulin use; in fact, most hypoglycemia is seen in patients using OHAs. This study provides strong evidence that treatment with sulfonylureas increases the risk of hypoglycemia in patients with Type 2 diabetes. The incidence of hypoglycemia was more in patients with systemic hypertension and renal impairment as co-morbid conditions.

The highest incidence of hypoglycemia is seen in older patients with poor glycaemic control and is associated with the use of anti-diabetic agents that increase blood insulin concentrations independently of blood glucose concentration (OHA's or exogenous insulin).

Using individualized treatment targets to base treatment strategies around individual circumstances may reduce the risk of hypoglycemia.

Impaired awareness of hypoglycemia and accompanying impaired counter - regulation continue to limit the ability of individuals with anti-diabetic therapy to achieve tight glycaemic control. Therefore, there is a need of continued vigilance and development of strategies to decrease potentially avoidable hypoglycemic episodes requiring medical intervention.

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Table 5a: T-test

Group OHA and insulin	N	Mean	Standard deviation	Standard error mean
1.00	4	24.7500	11.02648	5.51324
2.00	4	8.2500	3.77492	1.88746

OHA: Oral hypoglycemic agents

Table 5b: T-test

OHA and insulin	t-test for equality of means	
	95% Confidence interval of the difference	
	Lower	Upper
Equal variances assumed	2.24092	30.75908
Equal variances not assumed	-0.22253	33.22253

OHA: Oral hypoglycaemic agents

Table 6: Hypoglycemic episodes according to anti-diabetic therapy

Antidiabetica therapy	Mild	Moderate	Severe	No episodes
Sulfonylurea	3	2	4	-
Biguanide	5	2	-	14
Gliptins	2	2	-	4
Sulfonylurea+biguanide	19	13	9	20
Injection actrapid	3	3	3	2
Injection mixtard	8	5	8	1
Insulin+biguanide	13	13	8	6
Insulin+sulfonylureas	7	4	13	4

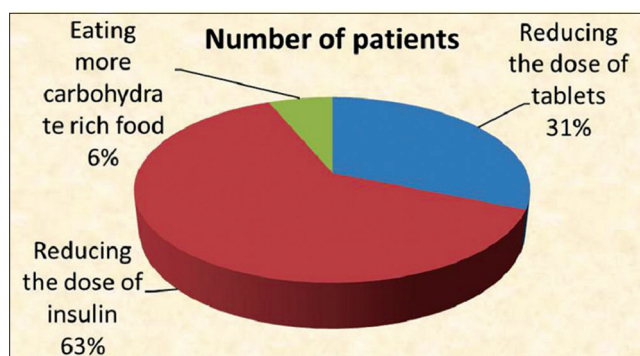


Fig. 1: Management of hypoglycemic episodes

Table 7: Awareness of hypoglycaemic episodes

	Number of patients
Awareness	130
Unawareness	70
Awareness during driving	11
Unawareness during driving	53

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HYPOGLYCEMIA QUESTIONNAIRE

1. Are you aware of the symptoms caused by low blood sugar? (Yes/No)
2. Have you experienced any of these symptoms?
 - (a) Frequent headaches (Yes/No)
 - (b) Feel shaky at time (Yes/No)
 - (c) Vomiting sensation (Yes/No)
 - (d) Sweating (Yes/No)
 - (e) Feel hungry frequently (Yes/No)
 - (f) Rapid heart beat (Yes/No)
 - (g) Drowsiness (Yes/No)
 - (h) Difficulty in talking (Yes/No)
 - (i) Blurred vision (Yes/No)
 - (j) Double vision (Yes/No)
 - (k) None of the above (Yes/No)
3. How often have you experienced hypoglycemic episodes in the past 6 months?
4. How do you manage your hypoglycemic episode?
 - (a) Did you take sugar or candy?
 - (b) Did someone assist you?
 - (c) Were you hospitalized?
5. What have you done to prevent further episodes of hypoglycaemia?
 - (a) Reducing the dose of Insulin
 - (b) Reducing the dose of tablets
 - (c) Eating more food (rich in carbohydrates)
6. Do you drive regularly? (Yes/No)
7. What precautions do you take to prevent or treat hypoglycaemic episode during driving?
 - (a) Keeping candy or chocolate in the vehicle
 - (b) Check your blood glucose before driving
 - (c) After a hypoglycaemic episode when do you start driving again?
 - Immediately after eating
 - After 10 minutes
 - After 20 minutes