ORIGINAL RESEARCH PAPER

General Medicine

CLINICAL PROFILE OF PATIENTS PRESENTING WITH HYPOGLYCAEMIA IN A TERTIARY CARE HOSPITAL

KEY WORDS: Hypoglycemia, Iatrogenic, Sulfonylureas, Elderly.

Satish Kumar Assistant Professor Department Of Medicine, IGMC Shimla H.P.

Balbir Singh Verma* Professor Department Of Medicine, IGMC Shimla H.P. *Corresponding Author

Dinesh Kumar Senior Resident, Department Of Medicine, IGMC Shimla H.P.

ABSTRACT

INTRODUCTION: Hypoglycemia remains a significant barrier to optimizing glucose control with some co-morbidities and glucose-lowering medications1. Iatrogenic hypoglycemia is more frequent in patients with profound endogenous insulin deficiency. We did this study to find out the clinical profile and risk factors associated with hypoglycaemia in our population.

MATERIAL AND METHODS: This retrospective study was conducted in the department of medicine, IGMC Shimla. The indoor data of the patients admitted with hypoglycaemia as per the inclusion criteria from August 1st 2017 to July 31st 2019 (2 years) was retrieved from the record section of IGMC Shimla. The detailed history and investigations were recorded. The data thus obtained was analyzed.

RESULTS: One hundred patients of hypoglycaemia were included in the study. Most of the patients (68%) belonged to rural background. Type 2 Diabetes was present in 92% of patients. Overall a total of 36% patients were receiving insulin. Glimepiride was the most commonly used sulfonylurea. Mean random blood sugar on admission was 37.12mg/dl. Altered consciousness was the most common presentation in our study (90%). Most of the patients improved with treatment (98%).

CONCLUSION: Elderly diabetics are more prone to the development of hypoglycaemia, especially those on insulin and sulfonylureas. Care should be taken while prescribing these drugs to the elderly and frequent self monitoring of blood glucose should be advised.

INTRODUCTION

The clinical management of type 2 diabetes emphasizes the importance of glycemic control to reduce the risk of diabetes-related complications[1]. However, hypoglycemia remains a significant barrier to optimizing glucose control with some co-morbidities and glucose-lowering medications[1].The International Hypoglycaemia Study Group recommends a glucose concentration <3.0 mmol/L (<54 mg/dL), considered to be clinically significant biochemical hypoglycaemia[2]. Iatrogenic hypoglycemia is more frequent in patients with profound endogenous insulin deficiency—type 1 diabetes and advanced type 2 diabetes—and its incidence increases with the duration of diabetes. It is caused by treatment with a sulfonylurea, glinide, or insulin and occurs about two to three times more frequently in type 1 diabetes than in type 2 diabetes[3,4]. Older adults with diabetes are at much higher risk for falls, incontinence, frailty, cognitive impairment, and depressive symptoms[5]. The cognitive and executive dysfunction in the elderly interferes with the patient's ability to perform self-care activities appropriately and follow the treatment regimen[6].

Our institute is a tertiary care hospital catering to a large population, a majority from rural areas with limited access to healthcare facilities. Moreover, owing to poor economic condition, most of these patients are taking sulphonylureas which are less costly and even available in the government supplies. We planned this study to find out the clinical profile and risk factors associated with hypoglycaemia in our population so that we can adopt certain measures to prevent this potentially fatal complication of diabetes mellitus.

MATERIAL AND METHODS

This retrospective study was conducted in the department of medicine, IGMC Shimla. The indoor data of the patients admitted with hypoglycaemia as per the inclusion criteria from August 1st 2017 to July 31st 2019 (2 years) was retrieved from the record section. Patients with blood glucose less than 70 mg/dl with or without symptoms of hypoglycaemia were included in the study and those patients with blood glucose more than 70 mg/dl even with symptoms of hypoglycaemia were excluded from the study. The detailed history including demographic profile, drug intake both prescription and otherwise and presenting symptoms with duration were recorded in the predesigned performa. Details of investi gations, management and outcome were also recorded. The data thus obtained was analyzed to see different demographic profiles, duration and type of diabetes, presenting symptoms, findings of investigations and outcome.

RESULTS

One hundred patients of hypoglycaemia were found to be eligible for inclusion in the study. Out of them, 56(56%) patients were males and 46(46%) were females. Age of the patients ranged from 25-88 years with mean age of 61.64 years. 32 patients were more than 70 years of age (Figure 1). Most of the patients (68%) belonged to rural background. Type 2 Diabetes was present in 92% of patients, 6% patients had Type 1 Diabetes and 2% patients had gestational diabetes. Mean duration of Diabetes was 10.2 years. Hypertension was the most common co-morbid condition associated with diabetes in 58% patients followed by CAD (12%), Chronic kidney disease (10%), hypothyroidism (6%) and cerebrovascular disease, obesity and malignant disease in 4% each. 22% of the patients were receiving only insulin, 14 % patients were receiving insulin with oral drugs and 64% patients were receiving only oral drugs. Overall a total of 36% patients were receiving insulin. Among oral drugs, the most common was metformin (64%) followed by sulphonylureas (60%). Glimeperide was the most commonly used sulphonylurea whereas only 4 patients received gliclazide. Other oral drugs used in decreasing order of frequency were DPP4 inhibitors (28%), glitazones (10%), SGLT2 inhibitors (4%). Mean random blood sugar on admission was 37. 12mg/dl. Number of patients with different range of blood sug ar at admission is given in figure 2. Altered consciousness ra nging from mild confusion to comatose state was the most co mmon presentation in our study (90%). 30% patients gave hi story of sweating as the initial symptom. Tremors and pa lpitations were present in 12% patients each. 8% patient had a generalised tonic clonic seizure at presentation and 2%

patients had a focal neurological deficit (Figure 3). Missed meal due to multiple reasons was the most common identified precipitating factor for hypoglycaemia in our patients (76%). Infection was present at admission in 16% patients. Only 6% patients reported increased dose of oral drugs or insulin as the precipitating factor (Table 1). 8% patients reported a documented previous episode of hypoglycaemia. Mean glycosylated haemoglobin was 7.55% with minimum of 4.4% and maximum of 14.1%. 40 % patients had a good control of diabetes with glycosylated haemoglobin level less than 7%. Only 6 patients presented within 1 hour of symptom onset. Most (68%) presented between 1-6 hours. 2 patients presented after 24 hours (Table 2). Most of the patients improved with treatment (98%) and only two patients died during treatment.

DISCUSSION

Iatrogenic hypoglycaemia is the limiting factor in the glycemic management of diabetes mellitus[7]. It causes recurrent symptomatic and sometimes disabling episodes in most patients with type 1 diabetes as well as in those with advanced type 2 diabetes, and it sometimes may be fatal[8]. The present study included patients from mainly rural with a mean age of 61.4 years and many patients (32%) were more than 70 years of age which makes them more susceptible to hypoglycaemia. The risk is further increased in this population with presence of multiple co-morbidities. Most of the patients had type 2 diabetes. We could not find any non-diabetic patient in our study. This is in contrast to the findings of Brijesh Mukherjee et al[9] where they showed that 69% hypoglycaemic patients had Type 2 diabetes as compared to 31% patients with type 1 diabetes. In contrast to our findings, Heller[10] has reported that risks of hypoglycemia are less in type 2 diabetes mellitus patients, but are higher during insulin treatment. Hepburn et al[11] in their study found that when matched for duration of insulin therapy (mean duration 12 years) and HbA1C, the frequency of severe hypoglycaemia is similar in type 1 and type 2 diabetes mellitus patients. Because most of the patients were elderly, the presence of multiple co-morbidities was expected in these patients. The presence of CKD in 10% of patients made them prone to the development of hypoglycaemia. Because of the long duration of diabetes in most of the patients, a large number of them (36%) were using insulin. Common oral drugs incriminated for hypoglycaemia, sulfonylureas were used in a large number of patients, mainly glimepiride which has a long duration of action. Glimepiride when used with insulin, especially in elderly patients poses a high risk of hypoglycaemia. Brijesh Mukherjee et al[9] showed that insulin therapy was the most common cause of hypoglycemia accounting for 79% (either alone or in combination with OAD) of diabetic patients. Carroll et al[12] also found that insulin treatment of diabetes is the most common cause of severe hypoglycemia in adults. Insulin use in our patients was less as compared to their study. The reason may be less acceptance of insulin in rural people. United Kingdom Prospective Diabetes Study (UKPDS)[13] reported severe hypoglycaemia in 11.2% of patients treated with insulin[14]United Kingdom Prospective Diabetes Study (UKPDS)[13] has reported severe hypoglycemia due to sulfonylureas in 3.3% of patients and 2.4% of those treated with biguanides. Jennings et al[15] have found, that hypoglycemia in patients receiving sulfonylurea treatment vary widely but were reported to be as high as 20% over a 6 month treatment period. Shorre al[16] described a crude rate of serious hypoglycaemia of 1.23 per 100 person-years in users of sulfonylureas aged 65 years or older. Though 64% of our patients were receiving metformin, and many patients were also receiving other drugs like DPP4 inhibitors, glitazones, SGLT2 inhibitors and acarbose but all these were in combination with either insulin or sulphonyureas. No patient was on glinides. Therefore risk of hypoglycaemia with drugs other than insulin and sulphonylureas cannot be ascertained.

Most of our patients (90%) presented with altered consci ousness of varying severity and classical symptoms like sweating, tremors and palpitations were present in lesser number of patients. In contrast to our findings Brijest Mukherjee et al[9] and McAulay et al[17] found almost similar symptoms in their patients. Sweating was the most common autonomic symptom followed by palpitation, in-coordination, altered sensorium, tremors and other symptoms. As most of our patients presented late to the hospital with an average duration of 7.61 hours and most of them being elderly, altered consciousness is the most common presentation. Pennebakeretal[18] has found that no single symptom correlate significantly with a specific blood glucose concentration in humans. Hence, it is important that diabetic patient on treatment should be familiar with their own symptom profile, so that they can perceive the early onset of hypoglycemia and know what appropriate action has to be taken.

Missing of a meal due to multiple reasons was the commonest precipitating factor identified in our patients. Findings similar to our study were noted by Shriraam V et al[19] for most of the patients (87%), the precipitating factor was missing meals followed by exertion (33%). Most of our patients were admitted with first episode of hypoglycaemia and only 8 patients reported previous documented admission with hypoglycaemia. Majority of the patients had good glycemic control (average HbA1C 7.7%) and most were on multiple drugs targeted to achieve strict glycemic control. The fact that most of our patients recovered with treatment underlies the importance of early recognition of hypoglycaemia symptoms and appropriate and timely treatment and preventive measures.

CONCLUSION

Hypoglycemia is more common in patients taking insulin and sulfonylureas especially glimeperide. Elderly patients are more prone to hypoglycaemia due to multiple co-morbidities and impaired metabolism of drugs. Education of the patient and caregivers about symptoms of hypoglycaemia and its management should be a part of every hospital visit in these patients.

LIMITATIONS OF THE STUDY

Since this was a small retrospective study, only limited information was available from hospital records. A large prospective study is required to study the detailed clinical and etiological profile of hypoglycaemia.

CONFLICT OF INTEREST:None

TABLES AND FIGURES

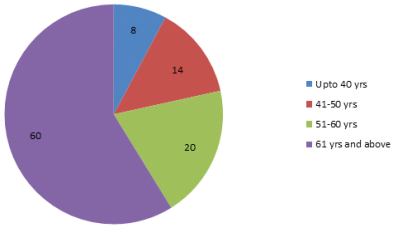

Figure 1 : Age distribution of the patients

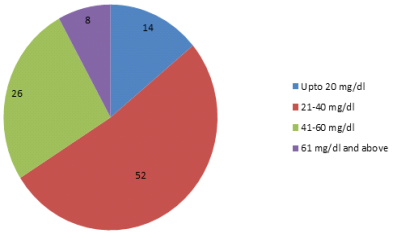

Figure 2 : Number of patients in different glycemic range

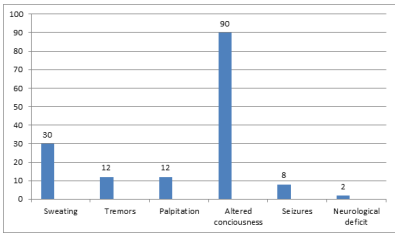

Figure 3 : Symptoms in patients with hypoglycaemia

Table 1: Precipitating causes of hypoglycaemia

Precipitating cause	Percentage of patients
Missed meal	76
Infection	16
Increased drug dose	6

Table 2: Duration of symptoms at presentation.

Hospital presentation (hrs)	Number of patients (%)
Upto 1 hour	6
1-6 hrs	68
Upto 24 hours	22
More than 24 hours	2

REFERENCES

1. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycaemia in type 2 diabetes, 2015: a patient-centered approach. Update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetologia 2015;58:429–442
2. Simon R. Heller(International Hypoglycaemia Study Group) Glucose Concentrations of Less Than 3.0 mmol/L (54 mg/dL) Should Be Reported in Clinical Trials: A Joint Position Statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2017 Jan; 40(1): 155-157.
3. Heller SR, Choudhary P, Davies C, et al. ; UK Hypoglycaemia Study Group Risk of hypoglycaemia in types 1 and 2 diabetes: effects of treatment modalities and their duration. Diabetologia 2007;50:1140–1147
4. Donnelly LA, Morris AD, Frier BM, et al. ; DARTS/MEMO Collaboration Frequency and predictors of hypoglycaemia in Type 1 and insulin-treated Type 2 diabetes: a population-based study. Diabet Med2005;22:749–755
5. Bruce DG, Casey GP, Grange V, et al. Cognitive impairment, physical disability and depressive symptoms in older diabetic patients: the Fremantle Cognition in Diabetes Study. Diabetes Res Clin Pract2003;61:59–67
6. Sinclair AJ, Conroy SP, Bayer AJ. Impact of diabetes on physical function in older people. Diabetes Care 2008; 31:233–235.
7. Cryer PE: Glucose homeostasis and hypoglycemia, in Williams Textbook of Endocrinology, 11th ed. Kronenberg HM et al (eds). Philadelphia, Saunders, an imprint of Elsevier, Inc 2008, pp 1503–1533 .
8. Cryer PE. Diverse causes of hypoglycemia associated autonomic failure in diabetes. N Engl J Med 2004; 350: 2272-9.
9. Brijesh Mukherjee and Subhradipta Bhattacharyya. CLINICAL PROFILE OF DIABETICS PRESENTING WITH HYPOGLYCEMIA AT THE EMERGENCY ROOM (ER) IN A TERTIARY CARE HOSPITAL: A PROSPECTIVE STUDY. Volume-8 | Issue-9 | September-2018.143-145.
10. Heller SR. Diabetic hypoglycemia. Bailliere'sClinEndocrinolMetabol 1999; 13:279-94
11. Hepburn DA, Macleod KM, Pell AC, ScougalIJ, Frier BM. Frequency and symptoms of hypoglycemia experienced by patients with type 2 diabetes treated. Diabet Med 1993; 10: 231-37.
12. Carrol MF, Burge MR, Schade DS. Severe hypoglycemia in adults. Rev EndocrMetabolDisord 2003; 4: 149-57[1].
13. The UKPDS Research Group: Overview of 6 years of therapy of type 2 diabetes: A progressive disease. Diabetes 1995; 44: 1249-58.
14. CryperPE. Hypoglycemia in Type 1 Diabetes Mellitus. EndocrinolMetabClin North Am 2010;Sep:39(3):641-54.
15. Jennings AM, Wilson RM, Ward JD. Symptomatic hypoglycemia in NIDDM patients treated with oral hypoglycemic agents. Diabetes Care 1989; 12: 203-08.
16. Shorr RI, Ray WA, Daugherty JR, Griffin MR. Antihypertensives and the risk of serious hypoglycemia in older persons using insulin or sulfonylureas. J Am Med Assoc 1997; 278: 40-43.
17. McAulay V, DearyIJ, Freir BM. Symptoms of hypoglycemia in people with diabetes. Diabet Med 2001; 18: 690-705.
18. PennebakerJW, Cox DJ, Gonder-Frederick L, Wunsch MG, Evans WS, Pohl S. Physical symptoms related to blood glucose in insulin-dependent diabetics. Psychosomatic Med 1981; 43: 489-500.
19. Shriraam V, Mahadevan S, Anitharani M, Jagadeesh NS, Kurup SB, Vidya TA, et al. Reported hypoglycemia in Type 2 diabetes mellitus patients: Prevalence and practices-a hospital-based study. Indian J Endocr Metab 2017;21:148-53.