CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187

Available online at: http://www.iajps.com *A Case Report*

A SURVEY ON THE INCIDENCE AND SEVERITY OF HYPOGLYCEMIA IN TYPE II DIABETIC PATIENTS USING ORAL ANTI DIABETIC MEDICATIONS

Ananth Lakshmi G[1], Afifa khan[2], Srija B[3], Niharika T,[4] Pragathi Reddy D[5], Deepika A[6]

[1]Anantha Lakshmi G, Professor & Head, Department of Pharmacy Practice, Sri Venkateshwara College of Pharmacy, Hyderabad, India.

[2] Assistant professor, Department of Pharmacy Practice, Sri Venkateshwara College of Pharmacy, Hyderabad, India.

[3,4,5,6] Pharm.D Interns, Sri Venkateshwara College of Pharmacy, Hyderabad, India.

Abstract:

Hypoglycemia is a condition caused by very low level of sugar (glucose) which is the main energy source of the body. Hypoglycemia is often related to treatment of diabetes. However, a variety of conditions may cause low blood sugar level in people without diabetes like fever, Hypoglycemia is not a disease itself, it's an indicator of health problem. A survey on incidence and severity of hypoglycemia in a tertiary care Centre with administration of a questionnaire a prospective study was conducted in Apollo Hospitals, Jubilee Hills, Hyderabad. Outpatients enrolled in the study were fully informed and gave their consent. Information was gathered regarding patient demographics, location, risk factors, co-morbid conditions, treatment, ADR, episodes of hypoglycemia. A total of 270 patients were enrolled for the study among which 55% were males and 45% were females. Hypoglycemia was seen in (6%) of the study population. The study results suggested that hypoglycemic incidence was higher in the age groups of 42-67 years (38%). Co-morbid conditions were seen in (52.9%) of the study population which included, HTN, CKD, Thyroid (6.7%), and renal failure (3.3%). The study concludes that the most common reasons of hypoglycemia were altered food habits and the drugs. Sulphonylureas are the drugs involved majorly in the hypoglycemic episodes.

Key words: *Hypoglycaemia, Incidence, Tertiary care*

Corresponding author:

Anantha Lakshmi G,

Professor & Head, Department of Pharmacy Practice,
Sri Venkateshwara College of Pharmacy, Hyderabad, India.
anu_manas0108@yahoo.com

QR code

Please cite this article in press Anantha Lakshmi G et al., ***A Survey On The Incidence And Severity Of Hypoglycemia In Type Ii Diabetic Patients Using Oral Anti Diabetic Medications.,*** *Indo Am. J. P. Sci, 2024; 11 (01).*

INTRODUCTION:

Hypoglycaemia is a condition caused by very low level of sugar (glucose) which is the main energy source of the body. Hypoglycaemia is often related to treatment of diabetes. However, a variety of conditions may cause low blood sugar level in people without diabetes like fever, Hypoglycaemia is not a disease itself, it's an indicator of health problem. Immediate treatment of hypoglycemia is necessary when blood sugar levels are 70mg/dl or 3.9 mmol/lit or below. Hypoglycemia is a common complication in patients with diabetes, mainly in those treated with insulin, sulfonylurea, or glinide. Impairments in counterregulatory responses and hypoglycemia unawareness constitute the main risk factors for severe hypoglycemia. Episodes of hypoglycemia are associated with physical and psychological morbidity. The fear of hypoglycemia constitutes a barrier that impairs the patient's ability to reach good glycemic control. To prevent hypoglycemia, much effort must be invested in patient education regarding risk factors, warning signs, and treatment of hypoglycemia at an early stage, together with setting personalized goals for glycemic control. In this review, we present a comprehensive update on the treatment and prevention of hypoglycemia in type 1 and type 2 diabetic patients. Hypoglycemia causes physical and psychological morbidity in diabetic patients. Symptomatic hypoglycemia constitutes a concern and a distraction. It can impair judgment, performance of simple daily activities such as driving, and behavior. In more severe cases, hypoglycemia may result in convulsions and loss of consciousness. Sometimes transient neurological deficits may appear, and rarely, there may be permanent neurological damage. The symptoms of Whipple's triad have been used to describe hypoglycemia since 1938. For Whipple's triad, the practitioner must first recognize symptoms of hypoglycemia, then obtain low blood glucose, and finally, demonstrate immediate relief of symptoms by the correction of the low blood glucose with glucose treatment. Glucose is the primary metabolic fuel for the brain under physiologic conditions. Unlike other tissues of the body, the brain is very limited in supplying its glucose. Expectedly, the brain requires a steady supply of arterial glucose for adequate metabolic function. Potential complications can arise from an interruption in the glucose supply. As such, protective mechanisms to guard against low serum blood glucose (hypoglycemia) have evolved in the body. During fasting states, serum glucose levels are maintained via gluconeogenesis and glycogenolysis in the liver. Gluconeogenesis is the pathway in which glucose is generated from non-carbohydrate sources. These non-carbohydrate sources could be protein, lipids, pyruvate, or lactate. In contrast, glycogenolysis is the breakdown of glycogen stored into glucose products. Much of glycogenolysis occurs in hepatocytes (liver) and myocytes (muscle). Hypoglycemia is most often seen in patients who have diabetes that undergoing pharmacologic intervention. Among this group, patients with type 1 diabetes are three times as likely to experience hypoglycemia than patients with type 2 diabetes when receiving treatment. In patients who do not have diabetes, hypoglycemia is uncommon, but when it occurs, there are a few major causes of hypoglycemia: pharmacologic, alcohol, critical illness, counter-regulatory hormone deficiencies, and non-islet cell tumors Most hypoglycemia cases occur in patients with diabetes who are undergoing therapeutic intervention with meglitinides, sulfonylureas, or insulin. Drugs are the most common cause of hypoglycemia. Metformin, glucagon-like peptide-1 (GLP-1) receptor agonists, sodium-glucose co-transporter 2 inhibitors (SGLT-2), and dipeptidyl peptidase-4 (DPP-4) inhibitor use very infrequently will lead to hypoglycemia. Non-diabetic patients with intact hepatic function will rarely experience fasting hypoglycemia because of preventative counter-regulatory measures. An episode of true hypoglycemia in a non-diabetic patient might be due to iatrogenic causes such as surreptitious insulin use. Other potential causes of hypoglycemia are critical illness, alcohol, cortisol deficiency, or malnourishment. Alcohol inhibits gluconeogenesis in the body but does not affect glycogenolysis. Thus, hypoglycemia occurs after several days of alcohol consumption, and after glycogen stores are depleted. For example, in critical illness states, end-stage liver disease, sepsis, starvation, or renal failure, glucose utilization exceeds glucose intake, glycogenolysis, and/or gluconeogenesis. The result of this imbalance is potentially the reason why hypoglycemia may occur. Counter-regulatory hormone deficiencies can occur as in states of adrenal insufficiency. Hypoglycemia associated with such deficiencies is rare. Non-islet cell tumors may also cause hypoglycemia through increased secretion of insulin-like growth factor 2 (IGF-2). IGF-2 increases glucose utilization, which can lead to hypoglycemia.

Treatment involves quick steps to get your blood sugar level back into a normal range either with high sugar foods or drinks or with medications. Long term treatment requires identifying and treating the underlying cause of hypoglycemia. Over time, repeated episodes of hypoglycemia can lead to hypoglycemic unawareness. The body and brain no longer produce signs and symptoms that warn of low blood sugar such as shakiness or irregular heartbeats.

When this happens the risk of severe life-threatening hypoglycemia is increased. To find the incidence and severity of both mild and severe hypoglycemic episodes in type II diabetic patients using oral anti-diabetic agents in a tertiary care Centre with administration of a questionnaire. From the literature survey we have observed that there is scarce published literature in India regarding the hypoglycemic episodes associated with specific oral anti-diabetic agents. Hypoglycemic events occurred less frequently in patients using oral anti-diabetic medications when compared to patients on the insulin therapy. Highest incidence of hypoglycemia is seen in older patients with the use of anti-diabetic agents with long duration of diabetes along with other comorbid conditions. Sulphonylureas were responsible for causing most of the hypoglycemic episodes.

MATERIALS AND METHODS:

METHOD: This prospective study was conducted in tertiary care center for a period of 6 months (Jan – June 2018). The study protocol was approved by institutional ethics committee (SVCP/2017/48). All the patients participating in this study were fully informed and give their informed consent. Data was gathered as demographic details, co-morbidity, duration of disease, HbA1c. The report was analyzed by descriptive statistics.

RESULTS AND DISCUSSION:

A total of 270 patients enrolled during the study period. To survey incidence and prevalence of hypoglycemia assess the incidence in the study subjects regarding the hypoglycemia it is important to know the demographic characteristics **(Table 1).** medications used by the study population with DM and along with other comorbid conditions are compared **(Table 2).** Anti-diabetic treatment prescribed for the study population was also compared **(Table 3).** Study population using monotherapy **(Table 4),** dual therapy **(Table 5),** more than 2 oral diabetic medications were analysed **(Table 6),** hypoglycemic episodes in the study population **(Table7)** and details of the hypoglycemic episodes are analysed **(Table 8).**

Table 1: Demographic characteristics of study population

Characteristics	Total number (n=270) (%)
Gender	
Male	149(55%)
Female	121 (45%)
Age groups (years)	
18-25	0(0%)
25-45	64(24%)
46-65	169(63%)
>66	37(14%)
HbA1c (%)	
<6	22(8%)
6-7	80(30%)
7-8	73(27%)
8-9	43(16%)
9-10	22(8%)
>10	30(11%)
Duration of DM (years)	
<1	30(11%)
1-5	105(39%)
6- 10	70(26%)
11-15	38(14%)
16-20	20(7%)
>20	7(3%)
Serum creatinine (mg/dl)	
<0.6	23 (8%)
0.6-1.2	229 (85%)
>1.2	18 (7%)
Comorbidities	146 (54%)
Hypertension	17 (12%)
Dyslipidemia	26 (18%)
Obesity	14 (10%)
Thyroid	11 (9%)
HTN+Dyslipidemia	18 (12%)
HTN+Thyroid	3 (2%)
HTN+Dyslipidemia+obesity	2 (1%)
HTN+Dyslipidemia+thyroid	4 (3%)
Others	51 (35%)
None	143 (53%)

Table 2: Medication use in study population

Indication	No. of patients (n=270) (%)
DM+ other comorbid conditions	**143 (52.9%)**
DM only	**127 (47.03%)**

Table 3: Anti diabetic treatment prescribed for the study population

Therapy	No. of patients (n=270) (%)
Monotherapy	84 (31.11%)
Dual therapy	110 (40.74%)
More than 2 drugs	76 (28.14%)

Table 4: Details of monotherapy for DM used in study population

Drugs	Dose(mg)	Frequency	Route	No. of patients (n)	Percentage
Sulphonylureas					
Gliclazide	40	BID	PO	5	5.95%
	80	TID	PO	2	2.38%
Biguanides					
Metformin	1000	QD	PO	41	48.80%
	500	QD	PO	23	27.38%
DPP-4 inhibitors					
Sitagliptin	100	BID	PO	1	1.19%
Linagliptin	5mg	QD	PO	9	10.71%
Vildagliptin	500	QD	PO	1	1.19%
SGLTinhibitors					
Dapagliflozin	10mg	QD	PO	2	2.38%

Table 5: Details of dual therapy used in study population

Drug Combinations (mg)	No. of patients using (n)	Percentage
Metformin+Gliclazide	**80**	**90.90%**
500/40mg	23	20.90%
500/80mg	57	51.81%
Metformin+Glibenclamide	**1**	**0.90%**
500/5mg	1	0.90%
Metformin+ Glimepiride	**2**	**1.81%**
500/1mg	1	0.90%
1000/1mg	1	0.90%
Metformin+Linagliptin	**4**	**3.63%**
500/5mg	2	1.81%
1000/5mg	2	1.81%
Metformin+Linagliptin	**17**	**15.45%**
500/50mg	9	8.18%
1000/50mg	7	6.36%
1000/100mg	1	0.90%
Metformin+Voglibose	**1**	**0.90%**
500/0.2mg	1	0.90%
Metformin+ Dapagliflozin	**1**	**0.90%**
1000/10mg	1	0.90%
Gliclazide Linagliptin	**3**	**2.72%**
80/5mg	3	2.72%
Gliclazide Sitagliptin	**1**	**0.90%**
80/100mg	1	0.90%

Table 6: Details of >2 oral anti-diabetic agents used in study population

Drugs	No. of patients using (n)	Percentage
Metformin+Gliclazide,Sitagliptin	**14**	**18.42%**
500/50,100mg	1	1.31%
80/500,100mg	13	17.10%
Metformin+Gliclazide,Linagliptin	**6**	**7.89%**
500/80,5mg	6	7.89%
Metformin+Gliclazide,empagliflozin	**3**	**3.94%**
500/80,10mg	3	3.94%
Metformin+Gliclazide,Dapagliflozin	**9**	**11.84%**
500/40,10mg	1	1.31%
500/80,10mg	8	10.52%
Metformin+Sitagliptin,Dapagliflozin	**7**	**9.21%**
1000/50,10mg	4	5.26%
1000/100,10mg	3	3.94%
Metformin+Sitagliptin,Glimepiride	**1**	**1.31%**
1000/50/2mg	1	1.31%
Metformin+Gliclazide, Metformin+Sitagliptin	**26**	**34.21%**
500/50mg, 500/80mg	26	34.21%
Metformin+Gliclazide, Sitagliptin, Dapagliflozin	**2**	**2.63%**
500/80mg, 100mg,10mg	2	2.63%
Metformin+Gliclazide, Metformin+Voglibose	**1**	**1.31%**
500/80mg,500/0.2mg	1	1.31%
Metformin+Gliclazide, Metformin+Glimepiride	**1**	**1.31%**
500/80mg, 500/2mg	1	1.31%
Metformin+Gliclazide, Sitagliptin,Pioglitazone	**2**	**2.63%**
500/80,100,7.5mg	1	1.31%
500/80,100,10mg	1	1.31%
Metformin+Gliclazide, Linagliptin, Dapagliflozin	**1**	**1.31%**
500/50mg,10mg, 10mg	1	1.31%

Metformin+Gliclazide, Metformin+Sitagliptin, Dapagliflozin 500/50mg, 500/80mg, 10mg	**1** 1	**1.31%** 1.31%
Metformin+Gliclazide, Metformin+Sitagliptin, Empagliflozin 500/50mg, 500/80mg, 10mg	**1** 1	**1.31%** 1.31%
Metformin+Gliclazide, Metformin+Sitagliptin, Tenegliptin 500/80mg, 500/50mg, 20mg	**1** 1	**1.31%** 1.31%

Table 7: Hypoglycemic episodes in study population

Total no.of patients	Patients with hypoglycemic episodes(n)	Percentage
270	6	2.22%

Table 8: Details of patients with hypoglycemic episodes

Case no.	7	10	101	126	245	270	Avg
Age (years)	54	63	42	53	64	57	55.5
Gender	Male	Male	Female	Male	Male	Female	
Duration of DM (years)	4	8	8	8	16	10	9
HbA1c (%)	7.20	7.70	8	6.50%	5.80	6.9%	7.01
Drugs	G+M	G+M , E	G+M	S+M , D	G+M , S+M	G+M , S+M	

Dose	80/500mg	80/500mg, 10mg	40/500mg	50/1000mg, 10mg	50/500mg, 40/500mg	80/500mg, 50/500mg	
Frequency	TID	TID,QD	BID	BID, QD	BID, TID	TID,BID	
No. of episodes of hypoglycemia	1	1	10	1	4	1	3
No. of mild episodes	1	1	6	1	0	1	1.66
No. of moderate episodes	0	0	3	0	0	0	0.5
No. of severe episodes	0	0	1	0	4	0	0.83

In our study titled "a survey on the incidence and severity of hypoglycemia in type ii diabetic patients using oral anti-diabetic medications in tertiary diabetes center" a total of 270 patients both males and females were enrolled for the study, Pediatric population and pregnant women were excluded.

In our study population, the average age of patients experiencing hypoglycaemia was 55. when compared with other study the elderly patients were having incidence of hypoglycaemia. The average number of mild hypoglycemic episodes observed in the study population were higher when compared to severe hypoglycemic episodes. As per drug monograph the incidence of hypoglycaemia with Metformin 0-2%, Gliclazide 3.4%, Sitagliptin is 1.6%, Sitagliptin + Metformin is 3.9%. Except one all the patients with hypoglycemic episodes were on the combination of Gliclazide + Metformin.

Out of 270, 80 patients were on the combination of Gliclazide + Metformin of which 2 experienced hypoglycemic episodes which accounts for 2.5%. 40 patients were on the combination of Gliclazide + Metformin, Sitagliptin + Metformin of which 2 patients experienced hypoglycaemia that is 5%. When two agents were used incidence of hypoglycaemia was 2.5% when add on therapy is used the incidence was increased to 5% from the limited data of study population. In concordance to literature there will be substantial reduction in risk of hypoglycaemia with DPP-4 inhibitors compared to Sulphonylureas when added to Metformin.

Incidence of hypoglycemic episodes were higher with Sulphonylureas as per drug monograph and literature. From our study we observed the similar results, that the incidence of hypoglycaemia was higher with Sulphonylureas.

Limitation

- To know the incidence of hypoglycemia, we need a large population but the sample size is limited.
- It was an interim study with limited duration.

CONCLUSION:

Hypoglycemia is a lower level of normal blood glucose, which requires prompt recognition and treatment to avoid the serious effects. Hypoglycemia incidence and prevalence in clinical trials may be lower when compared to clinical practice. Knowing the incidence of hypoglycaemia is important to provide insight into its impact both clinically and from a patient level. As clinical pharmacists, we can counsel the patients regarding the hypoglycaemia condition and the symptoms during hypoglycaemia and immediate steps to resolve the condition. Especially in the diabetic population with multiple oral agents also with varying diets and lifestyle, it is difficult to pinpoint any class of oral anti-diabetic agents for the cause of hypoglycaemia. But all the patients with episodes had Sulphonylureas in common. We can conclude that Sulphonylureas are responsible for causing most of the hypoglycemic episodes.

REFERENCES:

1. Holstein A, Plaschke A. and Egberts, E. (2001), Lower incidence of severe hypoglycemia in patients with type 2 diabetes treated with glimepiride versus glibenclamide. Diabetes Metab Res Rev. 2001 Nov-Dec;17(6):467-73.
2. Suellen M. Curkendall, Bin Zhang, Kelly S. Oh, Setareh A. Williams, Michael and John Graham,et al. study on Incidence and Cost of Hypoglycemia Among Patients with Type II Diabetes in the United States: Analysis of a Health Insurance Database Vol. 18, No. 10 October 2011 pg no. 455- 462.
3. Masato Odawara, Takashi Kadowaki and Yusuke Naito Incidence and predictors of hypoglycemia in Japanese patients with type II diabetes treated by insulin glargine and oral antidiabetic drugs in real-life: ALOHA post-marketing surveillance study sub-analysis. Diabetol Metabolic Syndrome. 2014; 6: 20.
4. Krobot KJ, Ferrante SA, Davies MJ and Seck T, et al.Lower risk of hypoglycemia with sitagliptin compared to glipizide when either is added to metformin therapy: a pre-specified analysis adjusting for the most recently measured HbA(1c) value. Curr Med Res Opin. 2012 August;28(8):1281-1287.
5. Shorr RI, Ray WA, Daugherty JR, Griffin MR. Individual sulfonylureas and serious hypoglycemia in older people. Journal of American Geriatric Society.1996 July; 44(7):751-755.
6. Edridge CL, Dunkley AJ, Bodicoat DH, and Rose TC, et al. Prevalence and Incidence of Hypoglycaemia in 532,542 People with Type 2 Diabetes on Oral Therapies and Insulin: A Systematic Review and Meta-Analysis of Population Based Studies. PLoS One. 2015 June 10;10(6):e0126427.
7. Asplund K, Wiholm BE, Lithner F. Glibenclamide-associated hypoglycaemia: a report on 57 cases. Diabetologia. 1983 June;24(6):412-417.