PREVELANCE, RISK FACTORS AND OUTCOMES OF HYPOGLYCEMIA IN ELDERLY DIABETIC PATIENTS

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ABSTRACT

Objective: *To estimate the clinical outcomes of hypoglycemia in elderly diabetic patients, its associations with the different antidiabetic drugs and some predisposing factors or comorbid conditions.*

Methodology: *Both type 1 and type 2 diabetic patients with age 60 years or above fulfilling Whiple's criteria for hypoglycemia were included in this study. They were collected from the medical unit Hayatabad Medical Complex Peshawar from November 2010 to July 2011. The patient's history, clinical examination and investigations were recorded on a proforma. Patients with abnormal CNS findings on CT or MRI scan and those who didn't give any partial or complete response to the IV glucose, were excluded from the study.*

Results: *Eighty five patients with mean age of 75±6 years were included in this study. The average hospital stay was 10 days. Sixty-five percent (n=55) of these patients were using sulfonylureas, 20% (n=17) were using metformin alone and in combination, while 25% (n=21) were using insulin (combination of regular & intermediate acting). Impaired renal function in 40% (n=34), impaired liver functions in 20% (n=17) and neglected elderly in 30.6% (n=26) were the most common predisposing factors.*

Conclusion: *Diabetic treatment related hypoglycemia is more severe in the elderly population with a poor prognosis. Sulfonylureas are the most frequently associated drugs with poorer outcomes. Predisposing factors like impaired renal functions, liver functions and neglected elderly increase the frequency of hypoglycemia. HbA1c is not a good predictor of hypoglycemia in elderly population.*

Key Words: *Hypoglycemia, Sulfonylurea, Diabetic nephropathy, Insulin.*

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INTRODUCTION

Hypoglycemia is one of the most significant management related complication of diabetes mellitus in the elderly population[1]. Management of diabetes mellitus in elderly population needs more careful monitoring because of increased chances of hypoglycemia and its adverse health consequences like coronary ischemia, serious cardiac arrhythmias, irreversible brain damage and sudden death[2]. Hypoglycemia is more serious in elderly population than in young population[3]. The signs and symptoms of hypoglycemia in elderly population are more neurological like dizziness, weakness, delirium, and confusion as opposed to that in the younger population with prominent autonomic features like palpitation, and sweating[4]. Since the clinical features of hypoglycemia in elderly patients may be mild and non specific, therefore it may be easily missed by the relatives causing delay in seeking medical help. Hypoglycemia may also go unrecognized in the elderly population because of restricted communication, cognitive impairment, and possibly fewer adrenergic symptoms[5].

There are multiple factors which predispose the patients for hypoglycemia like impaired renal functions[6], impaired liver functions, imbalance intake of food and inappropriate timings of exercise with the insulin or oral drugs (sulfonylureas) intake[7], polypharmacy, drug–drug interactions, co morbidities and old age (decreased reserve of liver and kidneys)[1,8]. Impaired renal functions interfere with the elimination of those drugs which eliminate through the kidneys. So these drugs (glibenclamide) are responsible for

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prolonged hypoglycemia[8]. Concomitant use of certain other drugs like ACE inhibitors and beta blockers may also predispose to hypoglycemia[9].

Sulfonylureas are commonly prescribed drugs in the elderly population. Approximately 70% of the prescriptions for sulfonylureas are for individuals over the age of 60 years[10]. Up to 20% of patients taking sulfonylureas experience symptoms of hypoglycemia over a six-month period[10].

It is difficult to predict hypoglycemia in elderly patients because of their high susceptibility to hypoglycemia and poor glucostatic functions of the liver and kidneys[11]. Even an HbA1c level can not precisely predict the susceptibility of elderly patients to hypoglycemia[14].

The aims of this study was to estimate the clinical outcomes of hypoglycemia in elderly diabetic patients, its associations with the different antidiabetic drugs and some predisposing factors or comorbid conditions.

METHODOLOGY

This descriptive study was conducted at medical unit of Hayatabad Medical Complex Peshawar from November 2010 to July 2011. Eighty five elderly patients age 60 or above were enrolled for the study. Thirty seven were female and 48 were male. Some were admitted to the medical unit through emergency while others were already in the unit for some other illnesses and developed hypoglycemia.

Those patients having creatinine level of 1.5mg% or above were labeled as having impaired renal function. While the patients having bilirubin level of 2mg% or above with ALT two times or more of the upper limit of normal or chronic liver disease/ cirrhosis liver on ultrasound, were labeled as impaired liver functions.

All patients with insulin dependent and non insulin dependent diabetes mellitus with the age 60 or above fulfilling the Whipple criteria for hypoglycemia: which means, signs and symptoms of hypoglycemia, low serum glucose level (<50mg/dl in this study) and improvement (partial or complete) in the signs and symptoms with the oral or IV glucose. were included in the study.

Patients having altered neurological symptoms because of primary nervous system lesions, as evident on CT or MRI were excluded from the study, as well as patients who didn't respond to IV glucose at all. Patients who were already having neuropsychiatric symptoms as evident by the past history, which can not be differentiated from hypoglycemia, were also excluded from the study.

Social history of the patients was also noted. Those patients who were living alone and unattended by their relatives, arranging their drugs, meals and other life necessities themselves were labeled as neglected. Those bedridden patients who were not receiving drugs on proper times were also labeled as neglected patients.

The bio-data, clinical history, examination and investigations were recorded in a pre formed pro-forma. The data recorded include age, sex, duration of diabetes mellitus, drugs history, co morbidities, duration of current symptoms, conscious level, neurological signs, blood glucose at the time of presentation, and HbA1c level. All the patients were given glucose orally or IV depending on the conscious level. The response as complete or partial recovery was noted. To quantify the response, Glasgow coma score before and after glucose infusion was noted. Those patients, who partially responded and remained with neurologic signs and symptoms for one or more than one week, were diagnosed as having hypoglycemic brain damage.

RESULTS

We included 85 consecutive patients (37 male and 48 female) in this study. 8.5% (n=10) patients were already in the unit for other illnesses and the rest were admitted to the unit with hypoglycemia. They were in the age range of 60 to 85 years (mean age 75$\pm$5 years). Their average hospital stay was 10 (5 to 16) days.

They were using various antidiabetic drugs. Some were using single drug while others were using combinations of antidiabetic drugs (Table 1). The most frequently associated drugs with hypoglycemia were sulfonylureas (65%) (n=55). Other drugs like metformin alone and in combination (20%) (n=17) and combination of intermediate and regular insulin (25%) (n=20) were also in use. All the 10 (8.5%) in hospital patients were using the above mentioned insulin preparation.

Important predisposing factors like impaired renal functions in 40% (n=34), impaired liver functions in 20% (n=17) and unfriendly social and environmental conditions collectively termed as neglected elderly in 30.6% (n=26), were also found to be associated with hypoglycemia.

Sixty percent (n=51) of the patients presented in complete or semi-conscious state with the Glasgow coma score of 4 to 8. Others presented with various clinical features (Table 2).

Only in 9.8% (n=8) of patients the HbA1c level was less than 7% showing that it is not a

good predictor of hypoglycemia in the elderly population.

We treated these patients with oral glucose or IV hypertonic glucose solutions depending on the conscious level of the patients. We divided them in three groups according to the response:

1. Sixty percent (n=51) patients responded and fully recovered. Only 10% of this group was having impaired renal functions.
2. Twenty five percent (n=21) patients partially responded with improvement of the Glasgow coma score but not up to the normal and remained in low conscious level up to the hospital stay. They were labeled as having irreversible brain damage. Most of them remained with the signs and symptoms of hypoglycemia for more than 48 hours before admission to the hospital.
3. 15% (n=13) of the patients deteriorated again because of the intercurrent complications and co-morbidities. 10.5% (n=9) (70% of the group) expired during the hospital stay all were having impaired renal functions. Most of the patients of this group were using sulfonylureas for diabetic control.

Table 1: Anti Diabetic Medications, Patients were using and their association with Hypoglycemia and its outcomes

Drug	Frequency	Outcome		
		Improved	IRBD*	Expired
Glibenclamide.	36.5% (n=31)	18.8% (n=16)	10.6% (n=9)	5.95% (n=5)
Glimeperide.	15.3% (n=13)	10.6% (n=9)	3.5% (n=3)	1.2% (n=1)
Gliclazide.	13% (n=11)	9.4% (n=8)	2.4% (n=2)	1.2% (n=1)
Metformin (total).	20% (n=17)	17.6% (n=15)	2.4% (n=2)	-
Metformin alone	9.4% (n=8)	8.5% (n=7)	1.2% (n=1)	-
Insulin preparations	25% (n=21)	16.5% (n=14)	5.9% (n=5)	1.2% (n=2)
Combination.	10.6% (n=9)	8.3% (n=7)	2.4% (n=2)	1.2% (n=1)
(sulfonylurea+metformin)	7.05% (n=6)	3.55% (n=3)	2.4% (n=2)	1.2% (n=1)
(insulin+metformin)	3.55% (n=3)	4.75% (n=4)	-	-

The total numbers and % age is more than the total sample size probably because of double counting due to combination therapy.
*IRBD-irreversible brain damage; patient not improved completely during hospital stay.

Table 2: Different clinical features & their association with the outcomes of Hypoglycemia

Clinical feature	Frequency	Duration of symptoms	Outcome		
			Improved	IRBD*	Expired
Episodic dizziness	17.7% (n=15)	3 days(2-4)	17.7% (n=15)	-	-
Hallucinations & irrelevant talk	15% (n=13)	4 days(2-6)	10.6% (n=9)	3.55% (n=3)	1.2% (n=1)
hemi paresis	6% (n=5)	3 days(1-5)	3.55% (n=3)	2.4% (n=2)	-
Slurred speech.	10.6% (n=9)	2 days(1-3)	10.6% (n=9)	-	-
Fits. (No History of epilepsy)	3.55% (n=3)	1 day	1.2% (n=1)	-	2.4% (n=2)
Night sweats	8.3% (n=7)	3 days(1-5)	-	-	-
Unconscious.	60% (n=51)	3 days(2-4)	24.7% (n=21)	23.5% (n=20)	7.05% (n=6)

*IRBD-irreversible brain damage; patient not improved completely during hospital stay.

Out of 34 patients with impaired renal functions 9 (26.5%) expired. Mortality was largely dependent on the severity at presentation and co-morbidities. Nine percent (n=8) of the patients were using only metformin. All were having the strong predisposing factor of renal impairement.

DISCUSSION

Since this study was performed on those patients who presented to the hospital for admission or patients already in the hospital for other diseases, therefore the clinical features may not be representative of all the elderly diabetic patients with hypoglycemia. In this study almost all the patients presented with neurological features which is comparable with the other literature [4]. Renal impairment was found to be the strong predictor of hypoglycemia and its mortality in this study. Other studies also showed increased frequency of hypoglycemia and mortality associated with renal impairment[6].

Although overall hypoglycemia is more frequent in insulin treated patients, in this study oral hypoglycemic drugs having long half life (e.g. glibenclamide) were associated with hypoglycemia in greater number of patients (36.5%) with higher mortality (5.95%) than insulin. Other study performed in Malaysia on fasting diabetic Muslims also showed higher frequency of hypoglycemia with glibenclamide (7.9%) as compared to repagenide (2.8%)[12]. Nicola N at al reported higher frequency of hypoglycemia with oral hypoglycemic drugs having longer half life (glibenclamide) than those of shorter half life[7].

This study showed that about 30.6% of the patients were having unfriendly environmental and social factors which may contribute to hypoglycemia in elderly population. These factors were collectively termed as neglect on the part of caring relatives. Though other local or international literature is lacking on how much these factors can contribute to hypoglycemia in the elderly diabetic population, there are a lot of work on neglect of elderly diabetic people leading to increased complications of diabetes mellitus[13].

Strict blood glucose control in the elderly diabetic patients as indicated by the normal or below normal HbA1c level is an isolated risk factor for hypoglycemia. This has been reported by many authers.[14] In this study only 9.4% (n=8) of the patients were having the HbA1c level of less then 7% indicating that even poorly controlled elderly diabetic patients may have increased susceptibility to hypoglycemia. Other literature also states that a high level of HbA1c may not decrease the susceptibility to hypoglycemia in elderly population[15].

The total mortality in this study was 10.5% while it was 26.5% in patients with impaired renal functions. Other literature mentioned 3% mortality in all hypoglycemic patients with diabetes mellitus[16] and 22-48% in critically ill hospitalized patients[17].

Though it is generally considered that hypoglycemia donot occur with metformin if used alone for diabetes mellitus. This study shows hypoglycemia in 9.4% of the elderly patients associated with use of metformin alone. All these patients were having renal failure. This issue is not extensively mentioned in other literature, though few authors mentioned about hypoglycemia with metformin alone if other predisposing conditions are present[18].

CONCLUSIONS

Diabetic treatment related hypoglycemia is more severe in the elderly population with a poor prognosis. Some antidiabetic drugs like Sulfonylureas are the most frequently associated drugs with co morbid conditions like renal impairment increase its duration and mortality even metformin can cause hypoglycemia if other predisposing facters like renal failure and cirrhosis liver, are present. Predisposing factors like impaired renal functions, liver functions and neglected elderly increase the frequency of hypoglycemia. HbA1c is not a good predictor of hypoglycemia in elderly.

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CONTRIBUTORS

NS conceived the idea and planned the study. A, MHA , SJ & MAM did the data collection and helped in the write-up of manuscript. All the authors contributed significantly to the research that resulted in the submitted manuscript.