Original Article

Hypoglycaemic Effect of Drugs

To Compare the Hypoglycaemic Effect of Sitagliptin/ Metformin Combination VS Glimiperide in Type II Diabetes Patients during Ramadan

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ABSTRACT

Background. Different drugs have been used in the past during Ramazan Sharif with none of them shown to be Gold standard. Recent data has shown DPP-IV inhibitor, sitagliptin/ metformin combination leads to less hypoglycaemic episodes when compared to sulphonylurea drug glimipride. Data is lacking from Azad Kashmir about the efficacy of these drugs during Ramazan sharif.

Study Design: Randomized controlled study

Place and Duration of Study: This study was conducted at Cardiac Outdoor, at District Head Quarters Hospital Teaching Hospital Mirpur Azad Kashmir in Ramazan Sharif the holy month of Islamic calendar during August 2011.

Materials and Methods: Those patients included in this study who were well controlled on diet and oral drugs, no acute illness, adults more than 30 years, Type II diabetes, Both Genders those who gave consent and Baseline HBA 1c <10.

Results: Patients using sitagliptin/ metformin combination had less episodes of hypoglycaemia than glemipiride.

Conclusion: DPP-Iv inhibitors sitaglipitin/ metformin combination is better tolerated than glemipiride during Ramazan Sharif.

Key Words: Hypoglycaemic, Sitagliptin/Metformin, Glimiperide

INTRODUCTION

Ramadan is the ninth month in the Islamic calendar and considered as one of five pillars of Islam. All diabetic patients who want to fast during Ramadan should receive detailed counseling 1–2 months before the onset of Ramadan. Assessment should include a full annual review, detection of complications along with measurements of HbA1c, blood pressure and lipids, as risks of fasting. This is an ideal time to suggest changes regarding diet as well as medications for treatment of diabetes. Educational counseling should include patient and family members about the awareness of symptoms of hypo- and hyperglycaemia, planning of meals, blood glucose monitoring, administration of medicines, physical activity as well as management of acute complications [7].Different oral hypoglycemic agents have been used during Ramadan and few of them have been found to cause less hypoglycemia as compared to other agents[1]. Similarly an other large multi centered study conducted was suggestive less hypoglycemic episodes when patients receiving sulfonylurea drugs were switched over sitagliptin [2]. Still an other study also proved less hypoglycemic episodes when sitagliptin was used in diabetic patients during Ramadan Sharif. [3] yet another study conducted in five countriesRevealed that amongst fasting individuals, highest incidence of hypoglycaemia was found to be In Glibenclamide group [4]. "DPP-IV inhibitors The DPP-IV inhibitors sitagliptin and vildagliptin are new oral hypoglycemic agents. In a 24-week study, sitagliptin as monotherapy reduced HbA1c by 0.6% to 0.8%. It reduced HbA1c by up to 1.8% when used in combination with metformin, while vildagliptin monotherapy lowered HbA1c by 1.0% to 1.4% after 24 weeks." [5]. Hypoglycaemia may cause cardiac events which can be life threatining[6,7] .NICE guidelines also recommend alternative therapies inpatients with risk of hypoglycaemia[8].

One more study clearly showed low risk of hypoglycaemia with sitagliptin as compared to glipizide[9]. (DPP-4) inhibitors effectively lower blood glucose levels in a glucose-dependent manner, which results in a low incidence of hypoglycemia Reduction of glycosylated hemoglobin is with DPP-4 inhibitors (up to 0.9%), asis reduction of postprandial glucose (PPG). Hypoglycemia has often been described as mild, moderate, or severe based on the individual's ability to treat him/ her hypoglycaemia.

Was defined as blood sugar levels less than 70mg/dl.varying dose of glimeperide from 1-4mg was used in our study. However, there are no clinically important reasons to distinguish between mild and moderate hypoglycemia, and younger children will almostalways need to be treated by a parent or caregiver. Therefore, mild and moderate hypoglycemia

are considered together.hypoglycaemia remains one of the most important concerns during Ramzan fasting.[1011121314]

Another way to define hypoglycaemia is to divide into asymptomatic and symptomatic hypoglycaemia requiring assistance and this method was adopted in our study.

Rational of our study was Different studies and guidelines have been adapted, but due to marked variation. In duration and cultural practices, local guidelines need to address this problem more effectively. These general guidelines have not taken into consideration, different time zones simultaneously and after every, 28 to 30 years the holy month of Ramzan cycles from winter to summer and time difference changes to many hours, with chances of dehydration and hypoglycemia. Becoming less during winter. There was need to see pattern and practices of Ramzan Sharif in Azad Kashmir. Similarly eating and drinking practices vary in different parts of the world. Similarly in cities like skardu and interior Sindh there is little variation in temperature in whole year. Overall according to world fact book even one country like china have different time zones making uniform applications of guidelines very difficult[14,15,16,17].

MATERIALS AND METHODS

This was a randomized controlled, prospective study District Head Quarter Hospital Mirpur. (Cardiology Outdoor) Initial two weeks during Ramadan Sharif during august 2011. Well controlled with diet alone, sulphonylureas metformin, or thiazolidinediones, and otherwise healthy. Following patients were included:

Well controlled on diet and oral drugs, No acute illness, Adults more than 30 years, Type II diabetes, Both Genders those who gave consent and Baseline HBA 1c <10.

Following patients were excluded:

Severe hypoglycemia within the last 3 months prior to Ramadan, History of recurrent hypoglycemia, Sustained poor glycemic control, Diabetic keto-acidosis within the previous 3 months, Acute illnesses, Hyperosmolar-hyperglycemic-state within the previous 3 month, Performing intense physical labor, Pregnant ladies, On chronic dialysis

Who sample size calculator was used to calculate Sample size estimation was done using results of previous vector study and our sample size was comparable to vector study. There were 64patients enrolled initially, 10of them did not turn up.

Ethical approval was taken from ethical committee DHQ teaching hospital Mirpur Azad Kashmir.

Data was taken one month prior and three months after Ramadan. A Performa was distributed in the patients and collected after Ramazan.

Data analysis was done using SPSS version 16. Means and standard deviations were calculated for quantitative variables and frequencies and chi square tests for qualitative variables. P value was considered significant when <0.05.

RESULTS

64 patients according to WHO sample size calculator based on hypoglycaemic out comes in previous studies.[4] 10 patients were lost in the followup and did not turn up. Mean age range was 36 to 71 years. mean age was 52+_8.85 standard deviation.

Table No.1: hypoglycemia * drug Crosstabulation

Count		drug		Total
		sitagliptin metformin	glemipiride	
hypogly-cemia	hypoglycemia absent	20	11	31
	Asymptomatic	5	8	13
	symptomatic hypoglycemia	1	7	8
Total		26	26	52

Table No.2: BMI

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	normal	14	26.9	26.9	26.9
	overweight	31	59.6	59.6	86.5
	obese	7	13.5	13.5	100.0
	Total	52	100.0	100.0	

Table No.3: Statistics

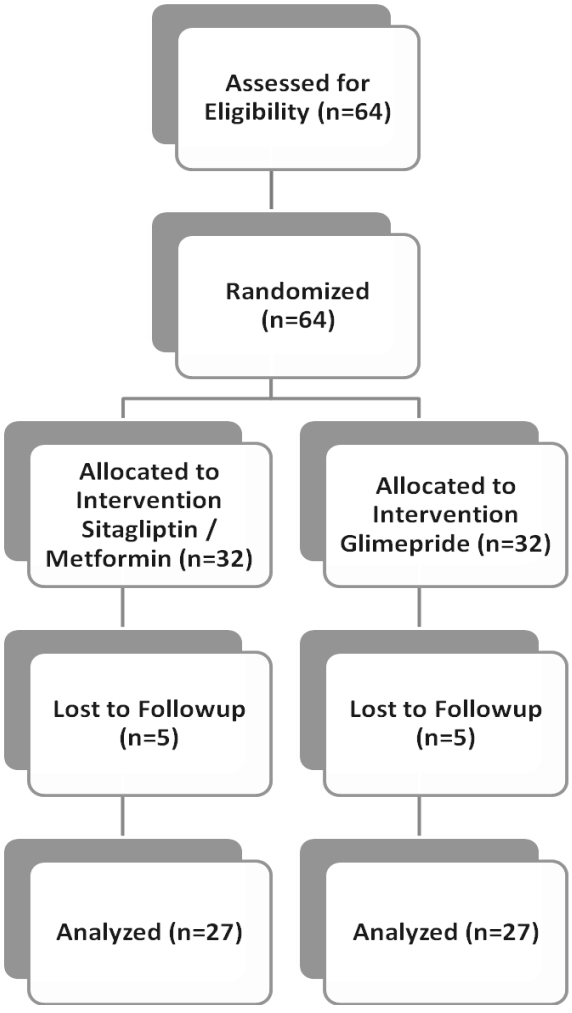
		hba1cA	hba1cB
N	Valid	52	52
	Missing	0	0
Mean		9.0769	8.5096
Median		9.0000	8.0000
Mode		9.00	7.00
Std. Deviation		2.58272	2.01341
Range		16.00	10.00
Sum		472.00	442.50

There were 17 male and36 female patients. baseline bmi in 16 was normal,32 were overweight and 7 patients were obese.mean hbaic was8.5with1.995+_standard deviation ranging from 6 to 16. 32 patients did not develop hypoglycaemia,13 patients had mild and8 of them moderate hypoglycaemia.out of 26 patients in sitagliptin metformin group,20 remained normal, 5 had episode of asymptomatic hypoglycaemia, 1had symptomatic hypoglycaemia. out of 26 patients in Glemipiride group, 11 had no hypoglycaemia,8 patients had asymptomatic and 7 patients had symptomatic hypoglycaemia. Chi square test was significant for less episodes of hypo glycaemia with sitagliptin metformin

group than glemipiride group. HbA1c reduction was 1% in sitagliptin metformin group as compared to 1.5% to 1.8% in glemipride group. One major finding in our study was all the patients included in the study tolerated both drugs very well, no case of pancreatitis was reported in sitagliptin / metformin group. Overall hba1c reduction was also similar in both groups of about 1 to 1.5 reduction in hba1c.

Table No.4: Statistics

		age	sex
N	Valid	52	52
	Missing	0	0
Mean		52.4615	1.6731
Std. Deviation		8.85717	.47367
Range		35.00	1.00
Minimum		36.00	1.00
Maximum		71.00	2.00



DISCUSSION

Recently there has been renewed interest and lot of new studies has been published addressing challenges faced by diabetic patients who keep Ramadan fasting and data favours new agents like sitagliptin. Our findings are consistent with other studies as few episodes of hypoglycaemia were reported in sitagliptin/ metformin group as compared to glemipiride. At the same time we should not forget that due to religious factor, it's very difficult to follow contra indications as specified by guidelines. Recent

Guidelines for Ramzan fasting recommend dpp1v inhibitors as safe drugs during

Ramzan Shareef.[18-24].

Treatment of diabetes mellitus includes life style modification, behavior therapy and detailed counseling before keeping fast. Our study is first ever study conducted in Azad Kashmir which clearly shows the trends of diabetes management in Azad Kashmir and Ramadan practices. Although this was very difficult to strictly follow guidelines. Two times or three times monitoring of Blood glucose levels at home particularly before sehar, two hours before after and after was told to the patients. our study clearly proved that sitagliptin when used in combination with metformin is better tolerated and causes less episodes of Hypoglycaemia and improving patients compliance who even in some cases either gave up the drugs or gave up fasting creating glycaemic control problems and getting deprived of metabolic benefits of Ramzan Shareef.

CONCLUSION

Lot of studies has been done for best drug for Ramadan fasting and recent data has favoured DPP-IV inhibitors. Because of strict religious beliefs and at the other hand to become more sick if one fast is the crux of the problem. For Example a person with contra indications may be willing to keep Ramadan fast and another person with no contra indication may not be willing due to fear of hypoglycaemia.

There for e all the patients who want to keep Ramadan fast should be counselled before Holy month of Ramadan about various measures to be taken particularly if the patient is receiving oral hypoglycaemiac agents. Our study concludes that DPP-IV inhibitors like sitagliptin/metformin combination have few episodes of hypoglycaemia.

Study limitation: Our sample size was small and practically motivate a patient not able to keep Ramadan fast was a difficult job. Patients couldn't be blinded .similarly our patients could not follow instructions of making blood sugar chart due to different educational background, glucometer and glucometer strips issues .

Recommendations: Due to marked variations in timezones and different cultures and eating patterns. Across the globe, local studies and guidelines are

needed to identify best agents causing very few hypoglycaemic episodes during Ramzan Shareef.DPP1V inhibitors have promised to cause less hypoglycaemia as compared to Sulphonylureas are worth trying and studies with large sample size are further required.

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