The Professional Medical Journal
www.theprofesional.com

DOI: 10.17957/TPMJ/17.4022

ORIGINAL PROF-4022

ACUTE PANCREATITIS;

FREQUENCY IN DIABETIC PATIENTS TAKING COMBINATION OF SITAGLIPTIN AND METFORMIN.

Hafiz Bilal Bashir[1], Zonaira Zubair[2]

1. B.Sc, MBBS
Medical Officer
Independent University Hospital, Faisalabad.
2. MBBS
Medical Officer
BHU, Jaranwala

Correspondence Address:
Dr. Hafiz Bilal Bashir
Medical Officer
Independent University Hospital, Faisalabad.
bilal_bashir@hotmail.com

Article received on:
08/03/2017
Accepted for publication:
25/06/2017
Received after proof reading:
03/07/2017

ABSTRACT… Objectives: To determine the frequency of acute pancreatitis in patients taking sitagliptin and metformin. A study conducted on 100 type II diabetic patients. **Study design:** It is the descriptive case series study. **Setting:** It is a single center study conducted in the medicine department of Independent university hospital Faisalabad. **Duration of study:** From June 2015 to December 2015. **Material and methods:** 100 type II diabetic patients were taken and given combination of sitagliptin and metformin and observed for 6 months for signs and symptoms of acute pancreatitis. **Results:** out of 100 patients 39 (39%) were males, 61(61%) were females. Mean age of study population was 44.51±10.22. 13 (13%) were having diabetes of less than 3 years duration. 47 (47%) were having diabetes of 4 to 6 years duration, 17 (17%) were having diabetes of 7 to 9 years duration and 13 (13%) of the patients were having 13+ years duration. After 6 month of observation 79 (79%) of the patients appear to have symptom of all type of abdominal pain, 78 (78%) of the patients have had at least one episode of vomiting and 79 (79%) patient have had at least one episode of fever. These patient underwent serum amylase and serum lipase testing but none of them was found to have acute pancreatitis. **Conclusions:** Combination of sitagliptin and metformin causes gastrointestinal side effects but we found no case of acute pancreatitis associated with this medicine.

Key words: Acute Pancreatitis, Sitagliptin, Metformin.

Article Citation: Bashir HB, Zubair Z. Acute pancreatitis; Frequency in diabetic patients taking combination of sitagliptin and metformin. Professional Med J 2017;24(7):952-954. **DOI:** 10.17957/TPMJ/17.4022

INTRODUCTION

Diabetes mellitus is a common disease in Pakistan with 90% of the people having type II diabetes mellitus. Uncontrolled diabetes can cause cardiovascular, cerebrovascular, chronic kidney disease and retinopathy.[1] Metformin is the drug of first choice in type II diabetes.[2] Patient having poor glycemic control on metformin alone need add on therapy. Previously we have limited number of drugs to control diabetes but now we have a number of combination of oral hypoglycemic medications for glycemic control with promising results.[3]

DPP-IV inhibitors were introduced in 2006 for the treatment of type 2 diabetes mellitus.[4] sitagliptin first DPP-IV was launched in 2006, in 2007 vildagliptin, saxagliptin in 2009, linagliptin in 2011 gemipligtin in 2012, and anagliptin teneligliptin[5] in 2012, alogliptin in 2013, 2015 and trelagliptin and later generation include dutogliptin which is still in phase III. The latest omarigliptin which is approved in Japan in 2015, showed sustained control of blood sugar and can be used once a week. Metformin in combination with sitagliptin was found synergistic in action and is more effective than either drug alone.[6] DPP-IV inhibitors are considered weight neutral and decrease cardiovascular risk by reducing triglycerides, low density lipoprotein cholesterol, improve [7] high density lipoprotein. Despite the potential benefits of DPP- IV inhibitors, these drugs are thought to be associated with the grave complication of acute pancreatitis. Based on this observation a study was designed to look for incidence of acute pancreatitis in diabetic patients taking combination of sitagliptin and metformin.

MATERIAL AND METHODS

Study design

Descriptive case series

Place of study

Independent university hospital Faisalabad

Duration of study

From June 2015 to December 2015.

Sampling technique

Non-Probability Consecutive Sampling

Sample size

By using WHO sample size calculator with confidence interval 95%, 100 patients of type II diabetes were selected from both sexes, ages between 25 to 80 years who were having poor control of diabetes on single drug therapy either metformin or sulfonylurea. Before including patients into our study other risk factors for acute pancreatitis (gall stones, alcoholism and very high triglyceride level) were excluded by appropriate testing. Patients were given combination of sitagliptin and metformin 50/850 1xB.D and observed for 6 months for development of signs and symptoms of acute pancreatitis. Those who develop pain abdomen, vomiting or fever of any cause, acute pancreatitis was excluded by testing serum amylase and lipase.

Data collection and Analysis

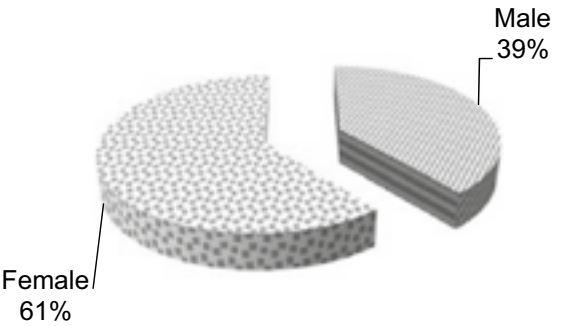
All the data was analyzed by using SPSS 17. Effect modifiers like age, gender and duration of diabetes was controlled by stratification. P value ≤0.05 was considered significant.

RESULTS

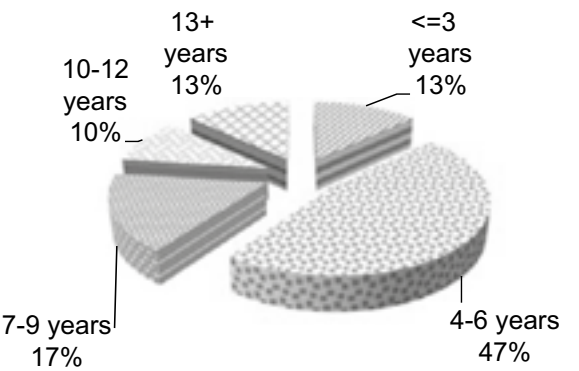
100 patients were included in the study. 39 (39%) were males and 61 (61%) were females. Mean age of study population was 44.51±10.22. 13 (13%) were having diabetes of less than 3 years duration, 47(47%) patients were having diabetes of 4-6 years duration,17 (17%) of patients were having diabetes of 7-9 years duration,10(10%) of the patients were having diabetes of 10-12 years duration, and 13(13%) of the patients were having diabetes of 13+ years duration.

Regarding the symptoms of pancreatitis over the observation period of six 6 months total of 79 (79%) of patient appear to have symptom of all type of abdominal pain, 78 (78%) of patient have had at least one episode of vomiting, and 79 (79%) patient have had at least one episode of fever, Those patient who develop vomiting, fever, or pain abdomen underwent serum amylase and lipase testing, but none of them was found to have acute pancreatitis.

Genderwise distribution of respondents



Distribution of respondents regarding duration of DM



	N	Min.	Max.	Mean	SD
Age (years)	100	26	80	44.51	10.22
Duration (years)	100	1	30	7.74	6.17
FBS Fasting Blood Sugar	100	127.00	304.00	215.47	38.86
RBS Random Blood Sugar	100	191.00	470.00	313.61	50.63
HbA1c	100	6.70	11.50	8.63	0.946
Serum Amylase (U/L)	88	20.00	135.00	79.08	25.94
Serum Lipase (U/L)	88	14.00	130.00	67.75	27.64

Table-I. Descriptive statistics of quantitative variables
N = number of respondents
SD = Standard deviation

DISCUSSION

Diabetes mellitus is a rapidly growing epidemic of modern times and it has been estimated that the burden of diabetes will double after 15 to 20 years. DPP-IV inhibitors are a new class of drugs and sitagliptin is most often used in this group. It can be used in combination with metformin safely. It has the advantage of neutrality weight and less chance of hypoglycemia compared to sulfonylureas.

Despite having several potential benefits, FDA issued warning in 2008 that incretin based drugs may be associated with acute pancreatitis, and warned the doctors all over the world to be vigilant while prescribing this medicine.[8]

This study was conducted to look for safety of sitagliptin and metformin in the treatment of diabetes mellitus type II patients and frequency of acute pancreatitis associated with the use of this medicine.

While gastro intestinal side effects were reported by most of the patients included in our study but these effects were not of any serious consequences.

A trial was conducted and published in 2014 in BMJ, looking for incidence of pancreatitis in patients taking sitagliptin or exanatide. This study also concluded that there is no increased risk of pancreatitis with the use of this medicine.[9]

CONCLUSIONS

It has been concluded from this study that combination of sitagliptin and metformin is associated with gastrointestinal side effects but and we found no case of acute pancreatitis associated with this medicine.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Hafiz Bilal Bashir	Data collection	
2	Zonaira Zubair	Data collection, Proof reading