Brief Communication

Mild acute pancreatitis with vildagliptin use

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Abstract

Vildagliptin has not been associated with the development of acute pancreatitis in postmarketing reports except one case report from Sydney, Australia. We present the case report of a 42-year-old male, diabetic, with no history of alcohol use, on vildagliptin 50 mg and metformin 500 mg daily since 6 months, who presented with severe abdominal pain radiating to back, nausea and fever. On evaluation, serum pancreatic enzymes were elevated, triglycerides were not raised and ultrasound showed swollen and echogenic pancreas, loss of peripancreatic fat plane and pancreatic duct was not dilated. Vildagliptin was stopped and the pancreatitis resolved. On follow-up, no secondary cause was not identified. This appears to be the first reported case of acute pancreatitis from India probably attributable to use of vildagliptin, thus raising the possibility that this rare reaction may be a class effect of the DPP-4 inhibitors.

Key words: Vildagliptin, pancreatitis, India

Introduction

The US Food and Drug Administration (FDA) received 88 reports of acute pancreatitis in persons taking dipeptidyl-peptidase 4 (DPP-4) inhibitor sitagliptin or sitagliptin plus metformin between October 2006 and February 2009. Unlike sitagliptin, vildagliptin has not been associated with the development of acute pancreatitis in post-marketing reports, except one case report from Sydney, Australia. Saxagliptin has had isolated, unconfirmed reports of pancreatitis, with two cases reported to a public Website in 2005-2007, but no published cases.

Case Report

A 42-year-old man presented with a 7-day history of severe abdominal pain radiating to back, nausea, and fever. Type 2 diabetes mellitus had been diagnosed 5 years earlier and was initially treated with metformin. Six months before presentation, he commenced therapy with vildagliptin 50 mg in combination with metformin 500 mg daily before dinner. His post-prandial sugar was below 160 mg/dl. His glycemic control was good (HBA1c, 7%). He was also taking rosuvastatin 5 mg, s-omeprazole, and domperidone.

Mild acute pancreatitis was diagnosed on the basis of findings on abdominal ultrasound done 3 days after the episode, which showed swollen and echogenic pancreas, loss of peripancreatic fat plane and pancreatic duct was not dilated; and elevated levels of serum pancreatic enzymes (amylase, 202 U/l [reference range, <110 U/l]; lipase, 669 U/l [reference range, <60 U/l]). Other tests: FPG-97 mg/dl, Triglyceride-143 mg/dl, LDL-65 mg/dl, LFT-normal. He stopped taking vildagliptin and metformin on doctor’s advice 3 days after the episode on the day of the test. Next day, there was a decrease in serum amylase to 118 U/l and lipase to 184 U/l. He was managed conservatively with liquid diet, pancreatic enzyme supplement, and antispasmodics as he refused admission in his local place and came to Kolkata for further evaluation and management. Blood tests were repeated on 6th day which showed the following results: TC-7800/cu mm, Hb%-15.9g%, ESR-3 mm/hr, CRP-4 mg/l, FPG-99 mg/dl, Calcium-9.4 mg/dl, urea-20 mg/dl, creatinine-1 mg/dl, amylase-75 U/l, lipase-130 U/l. His lipase was still elevated.

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CT scan upper abdomen (both oral and IV contrast) done on 6th day show mild diffuse swelling of pancreas with normal contour without any necrosis or collection [Figure 1].

A notable feature of this patient’s condition was the distinct absence of an identifiable cause for his pancreatitis. There was no radiographic evidence of cholelithiasis or biliary dilatation. He abstained from alcohol use and was not receiving any medication other than metformin and vildagliptin for control of diabetes. He was not obese (body mass index, 27 kg/m²). His triglyceride was not raised. In the absence of an obvious secondary cause for pancreatitis and considering the temporal sequence of events, this case suggests a causal link between the initiation of vildagliptin and the late development of pancreatitis. The patient's condition and biochemical parameters improved with the timely cessation of vildagliptin.

**DISCUSSION**

DPP-4 inhibitors effectively treat type 2 diabetes and achieve hemoglobin A1c reductions of approximately 0.7% over 12 weeks when compared with placebo. On the basis of numerous phase 2 and 3 studies, they are considered safe and well tolerated.[5]

The patient we describe appears to represent the first reported case of acute pancreatitis from India probably attributable to use of this agent, thus raising the possibility that this rare reaction may be a class effect of the DPP-4 inhibitors. We could not explain why pancreatitis did not develop initially while he was taking vildagliptin for 5-6 months.

In a similar case report by Christian M. Girgis, a 61-year-old diabetic woman presented with acute pancreatitis 5 weeks after the commencement of vildagliptin. Her pancreatic enzymes were elevated (amylase, 1205 U/l; lipase, 8846 U/l), and abdominal computed tomography demonstrated diffuse pancreatic swelling, cyst formation, and necrosis in the body of the pancreas. The patient recovered after vildagliptin therapy was ceased.[3]

The incidence of pancreatitis is generally 3 to 4 times higher in persons with type 2 diabetes mellitus (risk factors - obesity, gallstones, elevated TG) and a direct independent causative effect of DPP-4 inhibitors is therefore difficult to establish. Drugs cause pancreatitis either by a hypersensitivity reaction or by the generation of a toxic metabolite. Autodigestion is a currently accepted pathogenic theory; according to it, pancreatitis results when proteolytic enzymes are activated in the pancreas rather than in the intestinal lumen by exotoxins. Activated proteolytic enzymes, especially trypsin, not only digest pancreatic and peripancreatic tissues but also can activate other enzymes, such as elastase and phospholipase A2.

**CONCLUSION**

We report what appears to be the first case of acute pancreatitis in a patient receiving vildagliptin from India. Until we gain further experience, clinicians should apply the same caution to vildagliptin as to sitagliptin and carefully monitor patients taking these agents for the possible development of pancreatitis.

**DISCLOSURE**

Dr. Saraogi has received speaking honoraria from Merck-Sharpe-Dome and research honoraria from Novartis. Dr. Saraogi has no multiplicity of interest to report.

**REFERENCES**

1. US Food and Drug Administration. Medwatch 2009 safety alerts for
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1. Sitagliptin. Available from: http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm183800.htm. [Last accessed on 2011 May 31].

2. Ligueros-Saylan M, Foley JE, Schweizer A, Couturier W, Kothny W. An assessment of adverse effects of vildagliptin versus comparators on the liver, the pancreas, the immune system, the skin and in patients with impaired renal function from a large pooled database of phase II and III clinical trials. Diabetes Obes Metab 2010;12:495-509.

3. Girgis CM, Champion BL. Vildagliptin-induced acute pancreatitis. Endocr Pract 2011;17:e48-50.

4. PatientsVille.com. Saxagliptin side effects. Available from: http://www.patientsville.com/medication/saxagliptin_side_effects.htm.

5. Richter B, Bandeira-Echtler E, Bergerhoff K, Lerch C. Emerging role of dipeptidyl peptidase-4 inhibitors in the management of type 2 diabetes. Vasc Health and Risk Manag 2008;4:753-68.

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