A FATAL CASE OF METFORMIN INDUCED SEVERE ACUTE PANCREATITIS PRECIPITATED BY ACUTE RENAL FAILURE

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Abstract

Metformin is a biguanide, and it is one common type of oral anti-diabetic drugs for type 2 diabetic patients. Its most common complication is gastrointestinal discomfort. Lactic acidosis is a rare but fatal complication when metformin is prescribed to the patient with impaired renal function. Acute pancreatitis may be caused by some drugs, but it is seldom reported to be induced by metformin therapy. We report a 63-year-old female who suffered from acute pancreatitis, lactic acidosis and acute renal failure. We excluded particular causes of pancreatitis, such as biliary stones or sludge, alcohol use, hypertriglyceridemia, or hypercalcemia. Metformin induced acute pancreatitis precipitated by acute renal failure was confirmed.

Key words: Metformin, Acute pancreatitis, Acute renal failure, Lactic acidosis

Introduction

A conservative estimate of the incidence of drug induced pancreatitis ranges from 2% of acute pancreatitis in general population to as high as 40% in HIV patients.¹ Biguanides are one type of oral anti-diabetic drugs, and phenformin, buformin and metformin are three anti-diabetic drugs from the biguanide class. No buformin induced pancreatitis was reported on English literature. There were few reported cases of acute pancreatitis associated with phenformin.²⁻⁴ Only four cases of pancreatitis have been linked with metformin.⁵⁻⁸ We report one case with metformin-induced acute pancreatitis and lactic acidosis that resulted in fatal outcome.

Case Report

A 63-year-old female received oral medicines for diabetes and hypertension for more than 12 years. She had been told to have diabetic nephropathy, and her renal function and lipid profile on April 7, 2003 were creatinine of 1.7 mg/dl and triglyceride of 147 mg/dl. Her medication in recent one year included losartan (25 mg per day), dipyridamole (25 mg three times per day), isosorbide-5-mononitrate (20 mg two times per day), acarbose (50 mg three times per day), and metformin (500 mg three times per day). She was taken to the emergency department on May 4, 2006 with a history of vomiting for five days and abdominal pain for two days,
followed by oliguria and dyspnea for one day. The therapy of metformin was continued in spite of persistent symptoms. She did not report any history of acute or chronic pancreatic disease, and she also denied alcohol consumption, toxic habits or taking any other medications including over-the-counter medications or herbal remedies. On physical examination, her consciousness was alert. Initial blood pressure was 112/72 mm Hg, her pulse rate was 82 beats/min and the respiratory rate was 25/min with an oxygen saturation of 96% on room air. Abdominal examination revealed epigastric tenderness without muscle guarding or rigidity. Laboratory investigations showed white cell count of 3460/mm^3, urea of 96 mg/dl, creatinine of 11.6 mg/dl, sodium of 136 mmol/l, potassium of 5.84 mmol/l, calcium 8.1 mg/dl, chloride of 97 mmol/l, blood glucose 261 mg/dl, and lactate of 11 mmol/l (0.5-2.2). Arterial blood gases showed a pH of 6.95 and an anion gap of 43 mmol/l. Urine study by urine strip revealed ketone of more than 3+ and protein of more than 3+, and neither pyuria nor hematuria was noted. Liver function tests were normal. Amylase was raised at 4830 IU/l (25-125), and lipase was of 1064 IU/l (23-300). Sonography of the abdomen was suggestive of pancreatitis but did not disclose any gall stone or hepatic abnormality. She never had history of hypertriglyceridemia before. Furthermore, the patient was not taking recreational drugs, over-the-counter medications, herbal remedies, or any other drugs (such as azathioprine, estrogen, furosemide, hydrochlorothiazide, triamterene, prednisolone, acetaminophen, and sulfonamides, etc) potentially able to trigger the onset of acute pancreatitis. Although there are a few reported cases of phenformin induced pancreatitis, but acute pancreatitis due to metformin is a distinctly rare complication. A computer-based search (MEDLINE; years, 1966 - July 2008) of the English-language literature identified 4 additional previously reported cases of metformin induced acute pancreatitis. The first patient had a metformin overdose, and the others had acute renal failure at the onset of pancreatitis. In contrast to the above survival cases, our patient presented with high APACH II scores, which predicted the high mortality. She expired in spite of aggressive hydration, and continuous renal replacement therapy.

Without doubt, metformin remains the drug of choice for most type 2 diabetes patients with normal renal function. Careful and thoughtful use of this drug, especially in patient on other nephrotoxic drug, has the potential to avoid life-threatening adverse events. In patients with acute renal failure, metformin may cause severe acute pancreatitis arising with lactic acidosis and lead
REFERENCES

Metformin 引發急性胰臟炎導致死亡病例報告

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摘要

Metformin 是雙胍類的降血糖藥物，它被普遍用於第2型糖尿病患，最常見的副作用是腸胃不適。急性胰臟炎曾經被報告果可能被某些藥物引發，但是很少被報導和metformin有關。我們提出一個死亡病例，此病患為63歲女性，罹患糖尿病十二年，最近2至3年腎功能開始變差，仍然持續服用metformin，突然發生急性胰臟炎、乳酸血症和急性腎衰竭，我們排除常見急性胰臟炎的原因，例如：膽道結石、酗酒、高三酸甘油酯血症、高血鈣，所以推測此病患可能是遭遇少見的metformin引發急性胰臟炎導致死亡病例。

關鍵詞：Metformin，急性胰臟炎，急性腎功能衰竭，乳酸血症

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