Metformin in type 2 diabetes

TO THE EDITOR:

A POEM published in the April 2004 issue of the journal ("Metformin-induced lactic acidosis extremely rare," *J Fam Pract* 2004; 53:261) based on Salpeter et al's[1] meta-analysis of metformin use in patients with type 2 diabetes deserves additional comment. Specifically, unwary readers may interpret this analysis to suggest the usual precautions that have become customary with this drug are unnecessary. Many entities—such as congenital varicella syndrome and, at least initially, Reye syndrome—exist in our lexicon mostly because of case reports.

Report of a case. A 48-year-old woman with type 2 diabetes mellitus presented to the emergency department in extremis. She had a 4-day history of abdominal pain, and a several hour history of near-continuous vomiting. She had a prior history of hypertension, myocardial infarction, coronary artery bypass grafting, osteoarthritis and, presumably, diabetic neuropathy. She had never experienced diabetic ketoacidosis and renal function had previously been normal as best we could ascertain. (We were covering for another practice.) Her medications prior to admission were metformin, omeprazole, amitriptyline, and metoprolol, to which rofecoxib had recently been added. On examination, the patient appeared hypovolemic with a blood pressure of 136/78 mm Hg and pulse of 136 beats per minute. She was afebrile, tachypneic, and hyperpneic with a respiratory rate of 28. Otherwise, examination revealed only the stigmata of her known chronic illnesses. Urine ketones and serum acetone were negative. The patient had a serum bicarbonate of 9, and a lactic acid level of 12 (ULN 2.1). White blood cell count was normal and there was no evidence for sepsis or ingestion of methanol, ethylene glycol, salicylates, or other toxin. Creatinine on admission was 2.1 and BUN 27 which, after administration of IV fluids and discontinuation of the metformin and rofecoxib, normalized to 1.2 and 12 by 48 hours after admission.

The patient was discharged on glyburide, with instructions never to take metformin containing products again. She was also instructed that her renal function needed to be monitored closely with any drug that could reduce renal blood flow including nonsteroidal anti-inflammatory drugs and beta-blockers.

In this patient, we surmise the addition of rofecoxib reduced renal blood flow and caused sufficient renal dysfunction to allow the development of metformin-induced lactic acidosis, despite a "normal" baseline creatinine. It is also possible that vomiting caused a prerenal azotemia, leading to the development of the sufficient renal dysfunction to precipitate the metformin-induced lactic acidosis. However, we surmise the vomiting was the result of the acidosis.

Metformin lactic acidosis is a real phenomenon from which patients can die. Prescribers should stick within the "creatinine" (creatinine 1.5 or less for men, 1.4 or less for women) and "creatinine clearance" (greater than 60 mL/min) guidelines when prescribing metformin to reduce risk to their patients.

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REFERENCES

1. Salpeter SR, Greyber E, Pasternak GA, Salpeter EE. Risk of fatal and nonfatal lactic acidosis with metformin use in type 2 diabetes mellitus. *Arch Intern Med* 2003; 163:2594–2602.

Editorial

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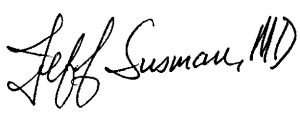
to tackle these issues in an all-embracing manner.

There is no doubt in my mind that we are both in "the best of times, and the worst of times." I simply hope, whoever has assumed the Presidency begins to seriously address this issue facing all Americans. Or I may once again become a drug "smuggler."



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