Metformin Intentional Overdose and its Association with Metabolic Acidosis and Elevated Lactate—As Reported by Toxicologists

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**Background:** Metformin is the most commonly prescribed antiglycemic agent in the USA. Some have suggested that the potential for metabolic acidosis and hyperlactatemia is spurious in patients taking this medication.

**Hypothesis:** We hypothesize that metabolic acidosis with hyperlactatemia occurs not infrequently in patients taking metformin.

**Methods:** We retrospectively analyzed Toxicology Investigators Consortium (ToxIC) registry data from January 1, 2010 to September 30, 2015. We searched for all patients with metformin toxicity, with emphasis on metabolic acidosis (pH < 7.2) and lactate concentrations. We reviewed demographics, laboratory analyses, co-exposures, treatments, and survival.

**Results:** Seventy-seven cases with metformin listed as “primary agent, most consequential” were available for analysis. Intent was reported as intentional overdose (n = 65), unintentional (n = 9), adverse drug reaction (n = 2), and drug abuse (n = 1). Of 65 intentional ingestions, all of which were acute, the dose was reported in 12 (range, 4–100 g). Co-exposures were present in 47 (72.3 %). Twelve (18.5 %) cases reported no sequelae. Ten (15 %) experienced a blood glucose 20. Lactate was reported in 17 cases of metformin exposure (mean, 3 mmol/L; range 0.17–27.99 mmol/L). In patients coded with metabolic acidosis (n = 7), the mean serum lactate was 4.91 mmol/L (range, 0.44–27.99 mmol/L). Nine patients (13.8 %) had acute kidney injury (creatinine >2.0 mg/dL). Four patients were decontaminated with activated charcoal; one received gastric lavage. Interventions included sodium bicarbonate (18.5 %), hemodialysis (12.3 %), and continuous renal replacement therapy (7.7 %). Hypoglycemic patients received glucose >5 %. No fatalities were reported.

**Discussion:** In ToxIC, the majority of metformin exposures were acute, intentional overdoses. Approximately 40 % of the patients with metformin overdoses in ToxIC had metabolic acidosis (pH 20). Our analysis of lactate was limited as it was not specifically included in ToxIC until 2015. Renal insufficiency occurred in 13.8 % of patients.

**Conclusion:** Metabolic acidosis was present in a significant number of patients with acute metformin exposures. Providers should be cognizant of this significant toxicity.