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### **87. 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 antidiabetic 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  $\geq 20$ . 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  $\leq 7.2$ ). 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.