Incidence and Risk Factors for Hyperlactatemia in ED Patients with Acute Metformin Overdose

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Background: Metformin causes hyperlactatemia by inhibiting hepatic lactate uptake and the conversion of lactate to glucose. Lactic acidosis is a known complication, but clinical risk and prognosis remain unclear.

Research Question: To describe the incidence of hyperlactatemia and clinical risk factors for lactic acidosis in patients with acute metformin overdose.

Methods: This was a secondary data analysis of a prospective observational cohort of adult ED patients presenting with acute drug overdose at two urban tertiary care hospitals over 5 years. Chronic, pediatric, and non-drug overdoses were excluded as were those missing outcome information. We collected demographics, exposure details, laboratory information, initial serum lactate, and extracorporeal indications per EXTRIP guidelines. Missing lactate data were accounted for by multiple imputation using a derived bicarbonate correlation. The outcomes were hyperlactatemia (lactate ≥2mmol/L) and lactic acidosis (MALA, lactate ≥5mmol/L with pH<7.35). Assuming 20% outcome prevalence, we needed 50 patients to show two-fold increased risk with 80% power and 5% alpha. Clinical risk factors for MALA were derived using multivariable logistic regression in SPSSv22.

Results: We screened 3739 acute overdoses; 2872 met eligibility, and 56 self-reported metformin overdose (57% female, mean age 55.7, 0% end-stage renal disease). There was a high incidence of hyperlactatemia during hospital stay (53.6%); MALA was less frequent (30.4%); there were no inpatient deaths. Initial serum bicarbonate and lactate were highly correlated (r^2=0.63, p<0.01). Repeat serum lactate increased in only 3 patients (hyperlactatemia rose by 1.8%, MALA by 3.8%). EXTRIP guidelines indicated hemodialysis for 3, all of whom received it. Clinical risk factors for MALA were lower PCO_2 (p=0.02), older age (5% increased risk per year of age, p=0.078), and acetaminophen co-exposure (adjusted OR=15.6, p=0.07).

Discussion: These data suggest a good prognosis for ED patients with acute metformin overdose; hyperlactatemia occurred in over half, but MALA in less than one-third. Additionally, indications for hemodialysis were rare, and none died. There was minimal utility in trending lactate, as rising lactate was exceedingly rare.

Conclusion: Hyperlactatemia was common in ED patients with acute metformin overdose. Independent clinical risk factors for MALA were acetaminophen co-exposure, compensatory respiratory alkalosis, and older age.