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Risk of Fluid Overload From Failure to Concentrate High-Dose Insulin as an Intravenous Antidote

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Standard-concentration regular insulin for intravenous (IV) infusion is potentially dangerous when used as therapy for overdose. High-dose insulin is generally accepted as beneficial for severe β -blocker or calcium channel blocker toxicity.¹ Regular insulin is typically administered for diabetic ketoacidosis at 0.1 U/kg/h, whereas as an antidote, it is dosed at 1 to 10 U/kg/h or higher. The use of unconcentrated insulin can result in fluid overload, further complicating overdose-induced reduction in cardiac contractility. This adverse event occurred in a patient we recently cared for.

The patient was a 44-year-old woman with an 8.4-g verapamil extended-release overdose. She was on the medication for migraine prophylaxis and had no cardiovascular or renal history. Her vasodilatory and cardiogenic shock was treated with IV fluid initially, then multiple vasopressors and other medications. She was responsive to high-dose regular insulin at 10 U/kg/h, with a concentration of 1 U/mL. The patient received 1 L every 80 minutes solely from insulin and was net positive 15 L of fluid in 24 hours. She was intubated and developed difficulty with oxygenation because of pulmonary edema. Although some case reports describe noncardiogenic pulmonary edema from calcium channel blocker overdose, fluid overload in this case was likely the primary etiology.²

Regular insulin is typically added to normal saline, to a final concentration of 1 U/mL; however, it is stable at 16 U/mL with normal saline for 2 weeks at room temperature in a polyvinyl chloride IV bag.³ Laskey et al³ chose to examine the stability of 16 U/mL instead of 10 U/mL to mitigate 10-fold dosing errors. We advise concentrating insulin when used as an antidote to minimize volume overload. Additional risks of high-dose insulin include hypokalemia in 29% of patients and hypoglycemia in 32%.¹ Dextrose infusions to prevent hypoglycemia, in addition to vasopressors, should likewise be concentrated to reduce fluid overload.

The above patient ultimately recovered. A root cause analysis was performed after submission to the hospital's adverse event reporting system. Standard insulin concentration was administered because, given the lack of barcode scanning recognition and pump safeguards for a more concentrated solution, there were concerns that the risk of medication

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error outweighed benefits. We present this case to clarify the risk of fluid overload and emphasize the importance of concentrating high-dose insulin as an antidote. Our institution has subsequently standardized high-dose insulin at 16 U/mL in our electronic order and IV pumps; a carrier fluid will be used if the rate falls below 10 mL/h. Regional Poison Control Centers can assist in management of this complex antidote. Pharmacists and clinicians should recognize the importance of concentrating high-dose insulin as an antidote to reduce fluid overload, and hospitals should use modern safeguards to reduce medication errors with concentrated insulin.

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