

ISMP Canada Safety Bulletin

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Wrong-Route Incident Involving Insulin and Dextrose Prescribed for Hyperkalemia

Medications are sometimes used off-label to treat conditions not covered by regulatory approvals. ISMP Canada recently received a report of a serious incident that involved the prescribing and administration of salbutamol, dextrose, and insulin to treat hyperkalemia (elevated serum potassium). The case is shared to help practitioners understand some of the underlying hazards associated with the use of common, high-alert medications (such as insulin) for off-label indications.

Medication Incident

A nondiabetic patient who was undergoing regular hemodialysis was admitted to a surgical unit for supportive management of a small bowel obstruction. Bloodwork performed on the unit the morning of the admission showed a high serum potassium level. To address the hyperkalemia, the physician wrote orders for salbutamol by inhalation, 1 ampoule of dextrose 50% in water (D50W; route not specified), and regular insulin (Humulin R) 10 units (route not specified). Treatment of hyperkalemia can include off-label use of both salbutamol and insulin.^{1,2} The patient received the salbutamol by nebulizer, the D50W intravenously (based on instructions the nurse obtained from the pharmacist), and the regular insulin by subcutaneous injection.

Later that evening, the patient was discovered unresponsive; the blood glucose level was measured and found to be undetectable. Intubation was

required, and the patient was subsequently transferred to the intensive care unit. The patient experienced an anoxic brain injury. It was later discovered that the patient's serum potassium level had been falsely elevated because of hemolysis of the blood sample provided for analysis.

Background

Potassium is the major intracellular cation in the human body.³ Hyperkalemia is defined as serum concentration of potassium greater than a specified level (usually 5 mmol/L, although the cut-off may vary between laboratories). It is associated with potentially fatal cardiac arrhythmias.³

Pharmacologic options for the acute treatment of hyperkalemia include calcium gluconate or calcium chloride (in the presence of electrocardiogram changes or cardiotoxicity), insulin, beta₂-adrenergic agonists (e.g., salbutamol), sodium bicarbonate, a cation-exchange resin (e.g., Kayexalate) or a combination of these agents.^{3,4} Regular insulin administered intravenously acts rapidly and is very effective in reducing serum potassium.^{3,4} For this off-label indication, the insulin is given intravenously in conjunction with intravenous dextrose, to prevent hypoglycemia.^{5,6}

Regular insulin is a short-acting insulin that may be administered by subcutaneous, intramuscular or intravenous injection.² When delivered intravenously,

the onset of its hypoglycemic action is immediate.³ However, when regular insulin is given by the subcutaneous route, the onset of hypoglycemic action is delayed and its duration more prolonged.⁵ In the case described here, administration of insulin by subcutaneous injection likely extended its duration of action beyond that of the intravenously-administered D50W. This error probably contributed to the ensuing hypoglycemia and associated complications.

Discussion

Analysis of the incident identified the following potential contributing factors:

- The prescriber's orders were handwritten; the facility had no standardized paper or electronic order set for the treatment of hyperkalemia.
- The route of administration was not stated for either dextrose or insulin, and these details of the order were not clarified with the prescriber.
- The medication orders were verified by a second nurse with the route specified on the transcription.
- There was no independent double check for the preparation of the insulin.
- At this institution, clinical pharmacy services were limited on the surgical floors. A nurse consulted a pharmacist about the route of administration for D50W; however, the full set of orders was not reviewed by a pharmacist before administration of the medications.
- Both insulin and D50W for injection were available in ward stock for immediate administration. Ward stock availability bypassed review of the orders by a pharmacist.
- Insulin is most commonly administered via the subcutaneous route, although the intravenous route was intended in this case. The nurse's familiarity with the subcutaneous route for insulin administration led to confirmation bias, the tendency to interpret information to confirm pre-existing beliefs.
- The medication order did not mention the need for blood glucose monitoring subsequent to insulin administration.
- Hemodialysis therapy added an element of complexity to the overall care of this patient. To facilitate the appropriate management of patients undergoing hemodialysis, the renal program in this

facility had created guidelines and instructions for blood work and interprofessional communication to be used by inpatient staff whenever a hemodialysis patient is admitted to hospital. In this case, however, unit staff members were unfamiliar with this information.

- The dialysis team was not contacted directly for guidance. Disturbances in electrolyte balance are often corrected during dialysis. This patient was scheduled for dialysis the next morning; communication with the dialysis team might have led to a different treatment plan, such as waiting for the scheduled dialysis.
- The design of the hospital's computer system may have been a factor in the misinterpretation of the laboratory results. To interpret test results, users must access a second screen of laboratory findings to determine whether a blood sample was hemolyzed (which would falsely elevate the serum potassium level). If the hemolysis had been recognized, the treatment plan could have been different.

The severity of the permanent disability in this case was mitigated by rapid identification of the underlying issue by the nurse taking over the care of the patient at shift change. She recognized that the patient had recently received insulin, which prompted her to check the patient's blood glucose level.

Safe Practice Recommendations

Review of this case identified several opportunities to reduce the likelihood of recurrence of a similar error. The following strategies are suggested for consideration.

Hospitals

- Consider developing order sets (paper or electronic) or protocols, including required monitoring parameters, to support standardized management of hyperkalemia. This approach could be applied to other off-label uses of medications. Standardized order sets or protocols help practitioners to identify appropriate medications, doses, routes of administration, and monitoring parameters.

- Establish laboratory guidelines requiring tests on hemolyzed blood samples to be repeated prior to reporting of results.
- Develop standardized processes to ensure that contact information for primary care and specialist providers is readily available in health records, particularly for complex patients.
- Remove insulin from ward stock and dispense this drug individually for patients when required, to support pharmacist review of all orders for this drug before administration of the first dose.
- Share collaborative patient care information, such as that provided by the hemodialysis unit, throughout care areas in the facility. Ensure this information is readily available to front-line staff.

Prescribers

- Confirm abnormal laboratory results by repeat testing, especially if the patient is asymptomatic.
- Develop a personal checklist to use with each order, to ensure that all handwritten medication orders include the drug name, dose, frequency, and route of administration. Include monitoring parameters in the orders, such as laboratory tests to be repeated, when required.
- Whenever possible, communicate directly with the responsible nurse to ensure that the treatment plan is clear to nursing staff, especially for uncommonly encountered situations such as acute electrolyte disturbances and use of medications for off-label indications.
- Whenever possible, consult the team of care providers for complex patients, such as those with renal failure necessitating dialysis.

Nursing and Pharmacy

- Ensure that appropriate information in support of treatment decisions (e.g., protocol for treatment of hyperkalemia) is readily accessible and available to staff members.
- Develop mechanisms for review of orders by a pharmacist prior to the first dose, including clarification with the prescriber if appropriate and a review of laboratory data.
- Use independent double checks in situations where high-alert medications, such as insulin, are being administered. In the case described here, an

independent check might have identified the absence of information about route of administration.

Vendors for Software-Based Hospital Laboratory Systems

- Eliminate requirements for clinicians to consult more than one page of information to accurately interpret the results of laboratory tests.

Conclusion

As demonstrated by the highlighted case, confirmation bias is one of several hazards associated with using a well-known medication for an off-label indication. A key safety strategy is ensuring that pertinent information and guidance are readily accessible, through development of protocols and standardized order sets for common off-label uses of high-alert medications. Several additional systems-based and discipline-specific strategies have been offered to improve communication and address other identified contributing factors.

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