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## **Treating Hyperkalemia: Avoid Additional Harm When Using Insulin and Dextrose**

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### **Abstract**

Hyperkalemia is a fairly common, potentially life-threatening electrolyte disturbance encountered in hospitalized patients. Treatment of hyperkalemia with insulin and dextrose, without implementing clear protocols and error-reduction strategies, can lead to hypoglycemia and other patient harm. A total of 198 events involving insulin and dextrose for treating hyperkalemia were identified by analysts in reports submitted to the Pennsylvania Patient Safety Authority between January 1, 2005, and December 31, 2016. The three most commonly reported types of events were delayed dose (n = 42), wrong route (n = 41), and wrong dose/over dosage (n = 15). Hypoglycemic episodes were reported in 57 of 198 patients. Standardized treatment protocols, including proper monitoring, can help prevent and detect errors with insulin administration for this indication.

### **Introduction**

Hyperkalemia can be a serious, sometimes life-threatening condition that is defined as a serum potassium level greater than 5 mEq/L.<sup>1</sup> Most (about 98%) of the body's potassium is located inside cells.<sup>1</sup> Potassium, which is a positively charged ion, plays a role in maintaining the cell's resting membrane potential; therefore, disturbances in the gradient (e.g., extracellular hyperkalemia) can negatively impact neuromuscular and cardiac excitability.<sup>2</sup> The effects of hyperkalemia on cardiac contractility can be detected on an electrocardiogram as peaked T-waves, a prolonged PR-interval, and a widened QRS-interval. In severe cases, this can lead to bradyarrhythmias, ventricular fibrillation, and asystole.<sup>1,2</sup>

About 80% of potassium is excreted renally, making patients with chronic kidney disease most at risk for developing hyperkalemia.<sup>1,2</sup> Although decreased elimination is one factor, other causes for the development of hyperkalemia include increased potassium ingestion, iatrogenic causes, and the shifting of potassium from the intracellular to the extracellular space.<sup>1</sup> Elevated potassium levels should be evaluated for accuracy because pseudohyperkalemia can result when a blood sample is hemolyzed, such as from a traumatic blood draw; when the leukocyte or platelet count is extremely elevated; or when the specimen is drawn above the site where a potassium-containing fluid is infusing.<sup>1,3,4</sup>

Goals for treating hyperkalemia include stabilizing cardiac membranes with intravenous calcium, shifting potassium back into the cell, and enhancing potassium elimination.<sup>2,5</sup> Short-acting insulin, usually given with dextrose to prevent hypoglycemia, rapidly redistributes potassium into the cells and is considered first-line treatment for severe hyperkalemia.<sup>1,5</sup> However, this redistribution is temporary, so other therapies that enhance the elimination of potassium from the body should also be used.<sup>1,2</sup>

Guidelines from the American Heart Association recommend treating adults who have severe cardiotoxicity or cardiac arrest due to hyperkalemia with an infusion of 25 grams of 50% dextrose mixed with 10 units of regular insulin infused intravenously over 15 to 30 minutes.<sup>6</sup> However, in the literature there is extensive variability in the type of insulin that should be used, the dose, and the time over which it should be administered. The two types of insulins used for treating hyperkalemia include rapid-acting insulin analogs (i.e., insulin aspart and insulin lispro) and regular insulin.<sup>4,7</sup> Doses between 5 and 20 units of insulin administered intravenously as a bolus or up to a 60-minute infusion have been reported in the literature.<sup>1,2,5</sup> There is also inconsistency in the amount of dextrose that should be given with insulin, with doses ranging from 25 to 100 grams.<sup>1,5</sup> Despite the use of dextrose, hypoglycemia is still a relatively common occurrence.<sup>5</sup> The potential for error and patient harm is considerable because of the severity of the condition, urgency of the situation, the variability in dosing regimens described in the literature, and the use of insulin, which is included on the "ISMP List of High-Alert Medications in Acute Care Settings."<sup>8</sup>

The purpose of this article is to identify the types of events, both harmful and harmless, that occur when insulin is ordered to treat hyperkalemia, to prevent harm by encouraging the use of best practices when using insulin to treat hyperkalemia, and to propose possible risk reduction strategies.

## Methods

Analysts queried the Pennsylvania Patient Safety Reporting System (PA-PSRS) database for events in which insulin was used to treat hyperkalemia. PA-PSRS reporters can choose from ten different categories of event types to select the one they feel is most appropriate for a given Incident or Serious Event. For this reason, the query searched free-text data fields of the event description of all event types using variations of and wildcards for the following keywords: hyperkalemia, potassium, elevated potassium, high potassium, and critical potassium. The query also searched the drug-name fields of medication errors and adverse drug reactions (the two event categories that have discrete medication name fields) and the event descriptions of all events using variations of and wildcards for currently available insulin products (e.g., humul%, novol%), Kayexalate®, and polystyrene. One hundred ninety-eight events met the inclusion criteria and were included in the final analysis. Event reports were included if insulin was used for treating hyperkalemia and an error or adverse drug event occurred with insulin and/or dextrose. The initial search returned 1,565 events that occurred between January 1, 2005, and December 31, 2016, but 1,367 events were eliminated because they did not meet inclusion criteria. An example of an excluded event follows.\*

*An order received in pharmacy at 2000 read "If K+ [potassium] 3.5 [lower limit of normal range] then give K-Lyte [potassium bicarbonate and potassium chloride; to treat low potassium levels] 50 mEq via peg tube BID x 1 day." Order was entered and dispensed by the pharmacy as Kayexalate® [sodium polystyrene sulfonate to treat high potassium levels] 30 g PO BID. No potassium level was returned on the patient until 0600 [the next day]. The floor contacted the pharmacy to report the dispensing error. The Kayexalate was retrieved.*

Reporters assigned harm scores, which are adapted from the National Coordinating Council for Medication Error Reporting and Prevention harm index,<sup>9</sup> and categorized events based on the event type. Events classified as dose omission, wrong time, and prescription/refill delayed were combined and included in the analysis as "dose delayed" because reporters reported similar events using these three event types. An example of a dose delayed event follows:

*The physician order was entered at 0600; [made] frequent phone calls to pharmacy requesting drug; K+ level 5.9; Kayexalate was [ordered to be given] now; did not arrive until 1000; insulin did not arrive until 0850; confusion about insulin in [the automated dispensing cabinet (ADC)] when it was not there.*

The frequency of hypoglycemic episodes associated with insulin administration for treating hyperkalemia was studied in this analysis. Based on guidelines from the American Diabetes Association (ADA), blood glucose values less than 54 mg/dL are considered clinically significant.<sup>10</sup> Results were stratified using 54 mg/dL as a marker for morbidity.

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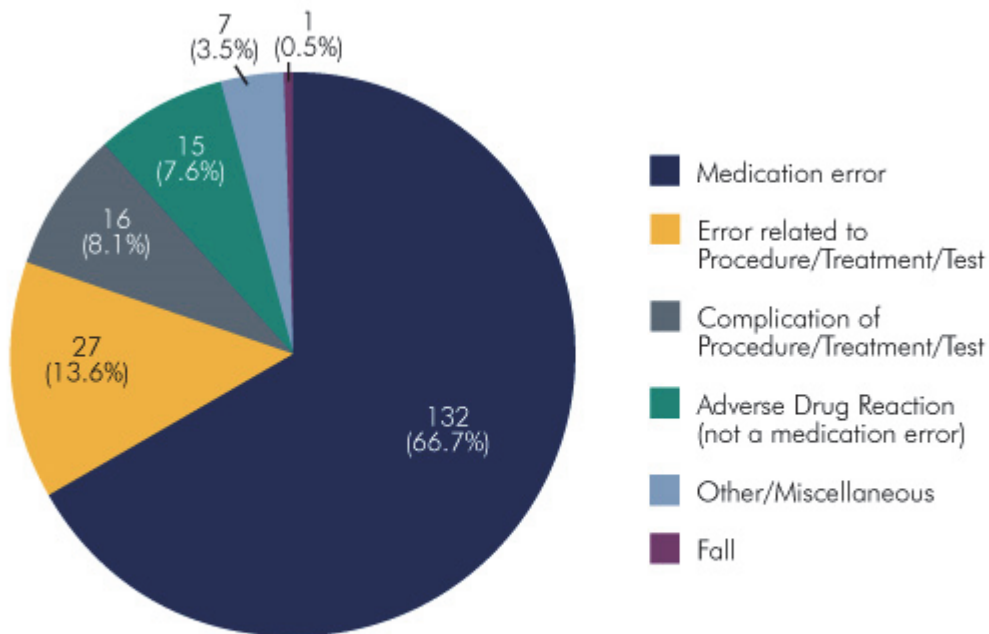
\* The details of the PA-PSRS event narratives in this article have been modified to preserve confidentiality.

## Results

Events involving insulin and/or dextrose to treat hyperkalemia were classified by reporters under several different event types (Figure 1). The majority of reports (66.7%; n = 132 of 198) were coded as medication errors. However, the event type selected by the reporter does not always match what is described in the event description. For example, the following report, which described a preventable event, was categorized as an unpreventable "adverse drug reaction (not a medication error):"

*Physician used hyperkalemia order set to order insulin for hyperkalemia; however, ordered dose that was 10-fold too high, so patient had hypoglycemia that required additional dextrose bolus.*

**Figure 1. Reported Event Types for Hyperkalemia Events Involving Errors with Insulin or Dextrose (N = 198)**



\* There were no reports submitted using the following event types: Equipment / Supplies / Devices; Transfusion; Skin Integrity; or Self-Harm.

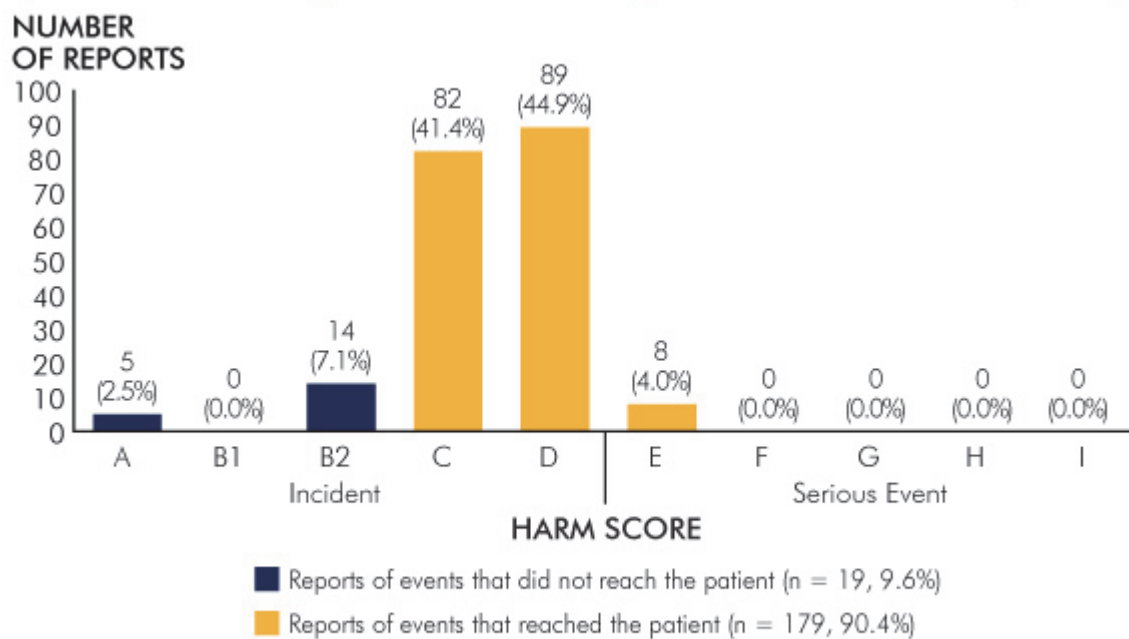
**Note:** Data reported through the Pennsylvania Patient Safety Reporting System, January 2005 through December 2016.

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According to the reporter-assigned harm score, 90.4% (n = 179) of errors reached the patient (harm scores C through I; Figure 2). Four percent (n = 8) of the events were reported as causing patient harm (harm scores E through I). In this analysis, the most harmful event was defined by the reporter as category E, "an event occurred that contributed to or resulted in temporary harm and required treatment or intervention." The following is an example of what reporters classified as a harm score E adverse event:

*The physician inadvertently ordered insulin 12 units/hr via IV [intravenous] infusion with dextrose to treat hyperkalemia when he meant to order insulin 12 units IV push times one dose. The patient received the insulin infusion over 1 hour and his blood glucose levels dropped to 32 [mg/dL]. At that time, the patient began to seize and went into cardiac arrest requiring resuscitation and intubation. The patient rapidly progressed and stabilized. The patient has since been discharged home in stable condition. Event recognized during review of code and disclosed to the patient.*

Figure 2. Harm Scores for Hyperkalemia Events Involving Errors with Insulin or Dextrose (N = 198)



Note: Data reported through the Pennsylvania Patient Safety Reporting System, January 2005 through December 2016.

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The top three patient care areas identified in events were emergency departments (31.3%, n = 62 of 198), medical/surgical units (15.2%, n = 30), and telemetry units (5.6%, n = 11).

### Medication Errors

The most frequent event type category reported was medication error (66.7%, n = 132 of 198). The most common types of errors reported as medication errors were dose delayed (31.8%, n = 42 of 132); wrong route (31.1%, n = 41); and wrong dose/over dosage (11.4%, n = 15).

The primary reason for delayed doses was that insulin was ordered but not given prior to transferring the patient to another unit (35.7%, n = 15 of 42), most notably from the emergency department to another unit (73.3%, n = 11 of 15). Another reason for delayed doses was the ordering of IV insulin for patients on certain units where IV insulin is not permitted (4.8%, n = 2 of 42), so patients had to be transferred to receive IV insulin. A third reason for delayed doses was unavailability of the medication (4.8%, n = 2 of 42). An example of a delayed dose due to the patient being located on a patient care unit that prohibited IV administration of insulin follows:

*Critical potassium level 7.2 non-hemolyzed called to attending. Order received. EKG [electrocardiogram] obtained. Attending spoke to nephrology; more orders received. Physician ordered IV insulin, unable to safely give on general medical floor. Spoke to pharmacist and supervisor; told the patient needs to be transferred to cardiac floor.*

There were 41 reports of insulin given via the incorrect route. Wrong-route errors were seen at both the prescribing (29.3%, n = 12 of 41) and administration nodes (58.5%, n = 24) of the medication-use process. Reports of wrong-route errors included orders for intravenous insulin given subcutaneously (n = 25), orders entered in the computerized prescriber order entry (CPOE) system for subcutaneous insulin when the IV route was intended (n = 10), and orders for subcutaneous insulin administered intravenously (n = 2).

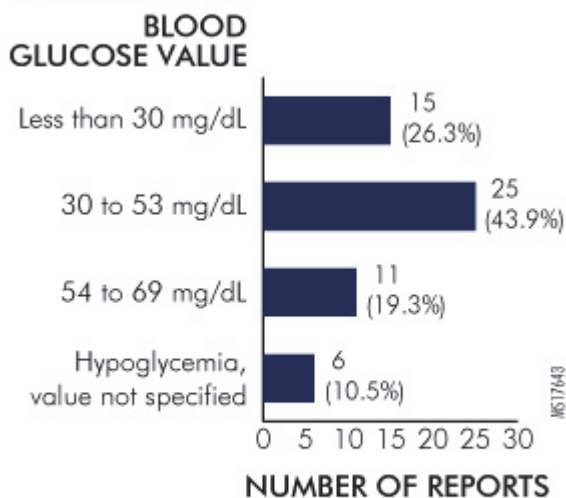
Wrong dose/over dosage errors occurred during administration (33.3%, n = 5 of 15), preparation of the medication (26.7%, n = 4), and at the prescribing phase (26.7%, n = 4). An example follows.

A patient with potassium of 6.9, orders received for albuterol 0.5% inhalation x2, IV regular insulin 8 units, dextrose 50% 25 g IV, sodium bicarb 1 ampule IV. The nurse told the charge nurse he was unfamiliar with giving these medications. Another nurse assisted him with administration of medications and verified them in the MAR [medication administration record]. The insulin was not drawn up in an insulin syringe—it was drawn up in a 1 mL syringe. The insulin syringes used in this facility are not compatible with IV push. At 1600, the patient's family member requested help from the nurse when checking on the patient. The patient was diaphoretic, shaky, and had a decreased level of consciousness. Blood sugar was checked and was 20.

### Cases of Hypoglycemia

More than a quarter (28.8%, n = 57 of 198) of event descriptions mentioned an episode of hypoglycemia or blood glucose less than 70 mg/dL, with 70.2% (n = 40 of 57) of patients experiencing a blood glucose value less than 54 mg/dL, and more than a quarter (26.3%, n = 15 of 57) of patients having a blood glucose result less than 30 mg/dL (Figure 3). Of 198 reports, 9 (4.5%) mentioned errors with dextrose. In all but one case, dextrose administration was delayed or omitted. One of the reasons for delayed doses was the way dextrose was ordered in the electronic health record. Rather than being ordered as a one-time stat dose with a scheduled time populated on the MAR, 50% dextrose was ordered "as needed" for hypoglycemia. Overall, the most common medication errors contributing to hypoglycemia included delayed dose of dextrose (10.5%, n = 6 of 57), wrong dose/over dosage of insulin (10.5%, n = 6), and wrong route insulin errors (8.8%, n = 5).

**Figure 3. Incidence of Hypoglycemia in Hyperkalemia Events Involving Insulin or Dextrose (n = 57)**



**Note:** Data reported through the Pennsylvania Patient Safety Reporting System, January 2005 through December 2016.

### Incorrect Laboratory Values

Incorrect laboratory values contributed to 9.1% (n = 18 of 198) of errors. The use of an incorrect potassium value to determine treatment accounted for most of these reports (55.6%, n = 10 of 18). Causes for treating an incorrect potassium level or failing to treat a critical potassium value included: the wrong patient's critical potassium result was verbally communicated by the laboratory to the practitioner; results were incorrectly reported as hemolyzed; and an elevated creatinine value was confused for the patient's potassium level. The second most common (22.2%, n = 4 of 18) error involving laboratory values involved improper blood collection technique, which occurred when a blood specimen was obtained above the site where fluids with potassium were infusing or the sample was collected using the wrong collection tube. Examples of errors involving laboratory values follow.

50 y.o. [year old] female on hemodialysis, presented to the ED [emergency department] with abdominal pain. On routine labs, patient had potassium of 6.9. Per interdisciplinary narrative, the nurse notified the physician of the critical result, but stated the potassium was hemolyzed. However, no visible hemolysis was seen. EKG was obtained which showed peaked T-waves. Calcium, insulin, and Kayexalate were not administered until 2300 when the overnight attending saw the patient and admitted her to Internal Medicine.

Patient received in PPN [peripheral parenteral nutrition]: Na [sodium] 80 mEq, K [potassium] 50 mEq, Ca [calcium] 5 mEq, Mg [magnesium] 12 mEq, and Phos [phosphorous] 15 mmol. The patient's labs today were: Na = 137, K = 6.2, Ca = 1.15, Mg = 3.0, Phos = 5.8, and glucose = 322. A repeat lab was ordered per pharmacy at 8 am. Results were within normal limits. Therefore, appears the lab drew the [first set of] levels from the PPN line. However, patient did receive corrective action for high K level with Kayexalate and insulin, treatment that was not required.

## Discussion

Hyperkalemia severe enough to cause disturbances in cardiac conduction is considered a medical emergency.<sup>3</sup> The most common event type reported in cases of hyperkalemia was a delayed dose of insulin. Treatment was often postponed until the patient was transferred to another unit, which frequently led to delays of an hour or more. Treatment should not be delayed, because even benign changes on electrocardiogram can quickly progress to lethal arrhythmias, and potassium levels greater than 7 mEq/L are associated with increased risk of cardiac arrest.<sup>3</sup>

The second most frequently identified event type was insulin given via the wrong route. This type of error was seen during both the prescribing and administration nodes of the medication-use process. Insulin should be given via the intravenous route for treating hyperkalemia to ensure instant and consistent bioavailability.<sup>3</sup>

Wrong dose/over dosage events were the third most common event type. The exact mechanism behind these errors was not clearly described in the event descriptions, but most mentioned measuring the insulin in "cc" or "mL" instead of units. A previous article by Grissinger about the misadministration of insulin for hyperkalemia treatment stated one of the reasons for wrong-dose insulin errors was a lack of understanding the difference between insulin syringes and other parenteral syringes.<sup>11</sup> One consideration is that insulin for hyperkalemia must be administered with a syringe (e.g., one with a Luer Lock tip) capable of connecting to needleless access devices and lines in order to be given intravenously. However, most insulin syringes available in hospitals have an attached needle appropriate for subcutaneous administration. This needle and syringe does not connect to a needleless system. Also, some hospitals may use insulin pens for subcutaneous insulin delivery, so newer nurses may be unfamiliar with drawing up insulin from a vial with an insulin syringe.

More than a quarter (28.8%) of reports mentioned hypoglycemia after treatment with insulin for hyperkalemia. The incidence of hypoglycemia associated with the treatment of hyperkalemia in the literature has been reported to be between 6.1% and 75%.<sup>7,12</sup> The wide range may be due to the variability in dosing of insulin and dextrose, the duration of infusions, the sequence in which dextrose and insulin are given, the type of insulin used, and patient-specific factors, such as chronic kidney disease.<sup>7,12</sup> The plasma insulin concentration that causes maximal effect on the redistribution of potassium is 500 microunits/mL, whereas the concentration that causes a maximal glycemic effect is only 100 microunits/mL.<sup>4</sup> Based on the pharmacokinetics of regular insulin, a bolus dose of 10 units results in insulin concentrations high enough to promote maximum potassium reuptake within 20 minutes after administration but also concentrations high enough to cause hypoglycemia for an extended period of time.<sup>7</sup> Other factors that have been linked to a high risk of hypoglycemia include a lower dose of dextrose (e.g., 25 grams), administering the dextrose after the bolus of insulin, and lower pretreatment glucose levels.<sup>12-14</sup> The use of a rapid-acting insulin instead of regular insulin may also decrease the incidence of hypoglycemia because it has a shorter half-life. In one study that used 10 units of a rapid-acting insulin and 50 grams of dextrose to treat hyperkalemia, only 6.1% of patients

experienced a blood glucose value less than 70 mg/dL.<sup>7</sup> Renal dysfunction may also predispose patients to hypoglycemia because of impaired insulin elimination and decreased renal gluconeogenesis.<sup>15</sup> Nonetheless, hypoglycemia is a serious complication and steps should be taken to avoid it.

## Limitations

In-depth analysis by the Authority of hyperkalemia events is limited by the information reported through PA-PSRS, including the event descriptions. As with all reporting systems, the type, quantity, and quality of reports depends on the reporter as well as the design and implementation of the reporting system. It is known that renal dysfunction and lower baseline glucose values contribute to hypoglycemia after insulin administration, but not all contributing factors, such as patient-specific information, were included in the event descriptions. Most reports also did not specify how much dextrose was given or the order of administration in relation to insulin.

## Strategies

Insulin is a high-alert medication<sup>8</sup> that is commonly involved in medication errors.<sup>16</sup> It should not be assumed that all healthcare practitioners are familiar with the dosing, route, preparation, and administration of insulin and dextrose to treat hyperkalemia. Consider the following recommendations, based on events reported to the Authority, current literature, and observations from the Institute for Safe Medication Practices (ISMP) to prevent errors.

- Establish standardized, facility-wide hyperkalemia treatment protocols that address the dosing of insulin, type of insulin, route of administration, dose of dextrose, sequence of dextrose and insulin administration, and monitoring parameters.
- Create standardized order sets, automatically populated with the correct dose and route of insulin, to facilitate the appropriate prescribing of insulin in patients with hyperkalemia.
- Dispense insulin preparations for treating hyperkalemia from the pharmacy in a ready-to-use form (e.g., in a syringe that can connect to a needleless system). This workflow ensures that an independent double-check takes place.<sup>11</sup> In organizations without 24-hour pharmacy services, pharmacy can create and provide hyperkalemia treatment kits that include a 3-mL vial of insulin, a Luer Lock insulin syringe, and directions for administration. The 3-mL vial of insulin is recommended, to reduce the potential amount of insulin a patient can receive if a dose of insulin is measured incorrectly.<sup>11,17</sup>
- Stock insulin syringes with a Luer Lock tip on patient care units, but be sure to store these separately from other parenteral syringes so they are not inadvertently mixed up.<sup>11,18</sup>
- Require an independent double check to evaluate the laboratory result, that the correct type of insulin is used, that the route is appropriate for the indication, and that the dose drawn up in the insulin syringe is correct.<sup>11,17</sup>
- Provide education to all healthcare practitioners who are involved in insulin administration about the differences between insulin syringes and other parenteral syringes, how to measure doses, and how to administer the medication.<sup>11</sup>
- Ensure adequate monitoring of glucose levels and for signs and symptoms of hypoglycemia for several hours after insulin administration.<sup>12</sup> Symptoms of hypoglycemia may be delayed by as much as six hours after insulin and dextrose administration, especially if the patient has renal impairment.<sup>14,19</sup>



## Conclusion

Hyperkalemia can be a serious, sometimes life-threatening condition; however, it is clear from the analysis of events with insulin and dextrose used in treating hyperkalemia that steps can be taken to enhance the safety of patients treated for this life-threatening condition. Errors with insulin prescribing, preparation, and administration can have severe consequences on patients' health. Effective strategies should be implemented to prevent unnecessary delays in treatment, wrong route errors, over dosages, and hypoglycemia.

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