Case Report

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Be Aware of Critical Drugs in Emergency Departments: An Extreme Iatrogenic Insulin Overdose via Subcutaneous and Intramuscular Routes

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Abstract

Introduction: Insulin is a highly used parenteral medication in emergency departments. Although most severe insulin overdoses occur as suicide attempts, medication errors can be the reason. We aimed to highlight the potential medication errors in emergency departments due to the poor control of critical drugs like insulin and the similarities between the brand names of drugs, as we experienced during this case.

Case Report: We present a 75-year-old diabetic woman with an extreme insulin overdose. A total of 3000 UI of insulin was administered by subcutaneous and intramuscular routes. She developed typical and atypical episodes of hypoglycemia requiring intravenous dextrose, a high-calorie diet, and glucagon administration. Almost all of the classic side effects of glucagon occurred during her intensive care unit follow-up. She recovered without any sequela or recurrence of hypoglycemia at the end of 5 days of admission.

Conclusion: Insulin overdose can be a life-threatening condition by causing hypoglycemia. Albeit rare, insulin overdose can occur as a medication error in hospitals. To prevent such incidents for emergency departments, the medication errors should be objectively laid out, and proactive strategies should be integrated without adversely affecting acute care.

Keywords: insulin, overdose, misadministration, critical drugs, emergency department, medication error

Introduction

The term "medication error" can be described as any preventable event that may cause or lead to inappropriate medication use or patient harm based on The National Coordinating Council for Medication Error Reporting and Prevention. Healthcare professionals, patients, and consumers are potential culprits for this error. Medication errors can occur at any step of the medication-use process, including dosing, dispensing, administrating, and preparation for health care professionals[1]. The most common medication errors are associated with inappropriate usage and dosage of drugs and inappropriate indication selection[2]. Being medical hotpoints where various critical drugs are used frequently in the hustle and bustle, emergency departments (EDs) are very susceptible to these incidents[3]. Safe medication applications can only be achieved in the presence of well-planned management and attentive staff.

The investigations on medication errors have discovered some critical topics like awareness of confused drugs and control of high-risk drugs. The confused drugs, including look-alike, sound-alike (LASA) name pairs, are a critical group for medication errors[4]. LASA covers medications with visual similarities in physical appearance, packaging, and/or name (in the form of spelling and/or phonetics). One of the best examples is the drugs named Losec® (omeprazole) and Lasix® (furosemide), widely used in many countries. Potentially severe results are not surprising when these two are mixed[5]. Another aspect of medication errors is associated with high-risk drugs. The list of high-alert medications in acute care settings of The Institute for Safe Medication Practices (ISMP) covers the drugs bearing a heightened risk of causing significant patient harm. ISMP underlines the importance of and warns about all forms of insulin in their 2018 list.

A problem can only be solved after it is defined and understood comprehensively. It is only possible with the systematic reporting of medication errors in healthcare settings with a nonpunitive approach. The concept of "medication error" has been covered in the literature with an increasing trend since the 1970s[6]. Since then, some strategies were suggested to prevent iatrogenic medication errors, includ-

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ing medication error analysis, computerized provider-order entry systems, automated dispensing cabinets, bar-coding systems, medication reconciliation, standardizing medication-use processes, education, and emergency-medicine clinical pharmacists[7].

Herein, we present a massive iatrogenic insulin overdose case. We believe that this case we witnessed is a vivid example of medication errors and shows the medication error susceptibility of emergency departments.

Case Report

A 75-year-old diabetic woman was admitted to the ED because of a dog bite on the dorsal side of her right wrist. Post-exposure prophylaxis (PEP) regimen for Rabies (administration of immune globulin (Ig), given only once, and a series of five dose rabies vaccinations) was planned. A junior resident took out the Ig vials from the vaccine refrigerator. The half dose of PEP Ig (calculated totally as 3000 UI; 40 IU/kg, body weight: 75 kg) was injected into and around the wound. The remaining dose was administered intramuscularly into the deltoid muscle. The administrations were done by an intern. It was noticed immediately after the standard control procedure of matching vial labels to the patient's file that regular insulin (Humulin R®) was used accidentally instead of Rabies Ig.

The close monitoring of the patient was started instantly. Her GCS was 15, with finger-stick glucose of 116 mg/dl. A central venous catheter was placed, and 10% dextrose infusion with a rate of 250 cc/h and 20 mEq/L/h KCl were initiated. Baseline blood samples and electrocardiogram were in the normal range. The patient was admitted to the intensive care unit (ICU). The first measured blood glucose and potassium levels were 207 mg/dl and 4.2 mEq/L, respectively. The blood insulin level was measured 1000 uU/ml at 2nd hour after the insulin injection. An individualized oral diet program (1600 kcal/day) containing high levels of glucose, potassium, magnesium, and phosphate was initiated and given hourly manner. Due to a sudden drop of her blood glucose to 79 mg/dl approximately at the 4th hour, glucagon 1 mg was applied subcutaneously, and 30% dextrose infusion was given. During the 7th minute of glucagon injection, the patient had nausea and vomiting episodes. No significant heart rate or blood pressure changes were noted. The glucose level increased within 15 minutes. An additional 1 mg iv glucagon administration with 30% dextrose was required due to the second drop of glucose (70 mg/dl) at the 7th hour after the first glucagon injection. No additional side effects were noted during glucose monitoring (**Table 1**). No additional medical treatment like steroids was needed. A stable blood glucose level was achieved following the end of the first 24 hours.

The patient was fully conscious and able to take oral diet during the whole ICU follow-up. The patient was discharged to home after 5 days of hospitalization (2 days in ICU and 3 days in the ward) with full recovery.

Discussion

Accidental and suicidal intakes are the most common causes of fatal insulin overdoses[8]. Insulin is a high-risk drug with its narrow therapeutic index for accidental or intentional overdoses. Johansen and colleagues found that 95% of insulin overdose cases were intentional among 45 case reports and the median total insulin dose was 900 IU (range 26–4800 IU)[9]. Another interesting point of insulin overdose is that it is commonly used by medical staff for suicidal attempts[10]. Our literature search shows several examples of massive insulin overdose. However, our case is one of the highest doses by receiving 3000 IU.

Humulin R® U-100 is human insulin that acts within a short duration. It is expected to affect approximately in 30-

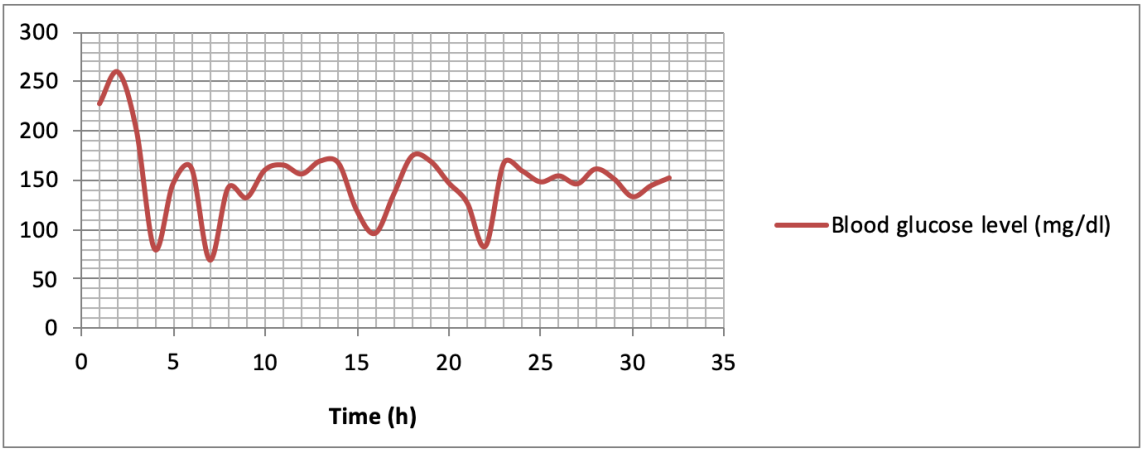

Table 1. The blood glucose levels of the patient by time.

60 minutes following subcutaneous administration. The peak effect starts approximately at 2.5 hours and terminates in 5-8 hours after the incident. However, the half-life of insulin is elongated after massive overdosing, necessitating more prolonged close monitoring of glucose levels[11]. Our patient stayed in ICU for two days in total. While blood glucose levels were irregular on the first day, a stable interval was achieved on the 2nd day. She could only be transferred to the ward on the 3rd day. In our case, dextrose had been started immediately after the misadministration of insulin was noticed. However, mild hypoglycemia (Glucose: 79 mg/dl) was observed with the expected insulin peak time at the 4th hour. Another hypoglycemic episode (Glucose: 70mg/dl) was observed approximately 7 hours after the injection. This unexpected hypoglycemic peak could be attributed to intramuscular administration of 1500 IU insulin. In a report describing the case of an 80-year-old non-diabetic male patient who used 10,000 IU Humulin R® and 6000 IU of Humulin N® subcutaneously for a suicide attempt, intravenous dextrose infusion was needed for 13 days in order to stabilize blood glucose between 100-180 mg/dl. Hyponatremia, hypokalemia, hypophosphatemia, and elevated liver enzymes were also detected during the follow-up[8]. The regarding electrolyte disorders or other possible complications were not seen in our patient. We believe that it might result from variables such as a relatively lower dose of insulin, immediate recognition and management of the medical error, and use of intravenous dextrose infusion and potassium replacement.

Although healthcare providers aim for patients' good under the motto of "*primum non nocere*," they can be the origin of harm. Our main intention was to apply Rabies Ig (Equirab®) prophylaxis to our patient who was bitten by a stray dog. However, regular insulin (Humulin R®), stored in the same fridge in a similar bottle, was applied. Although these drugs seem to have no name similarity, at first sight, Human-Immunoglobulin and Humulin R may cause confusion. The "R" could also be perceived as Rabies. Larger font sizes for brand names and smaller font sizes for nonproprietary names and doses in labels may result in such mistakes (**Figure 1**).

Another possible cause of the error would be the similarity of the containers of the drugs. Containers of both drugs were in the form of flacon bottles. The spelling and the physical form similarities suggest a LASA-like situation in this incident like Losec-Lasix[5]. However, we assumed that the medication error in our case was not limited to LASA for two reasons: First, both drugs were stored in the same refrigerator section. Second, the area where drugs were stored was accessible for all healthcare providers. The management of critical drugs, authority protocols for the accessibility of such drugs, and emergency staff training could prevent these medication errors in future applications. Real-time and post-application controls, recording and reviewing, and implementing technology strategies are as critical as pre-application controls, as Monroe and colleagues suggested[12].

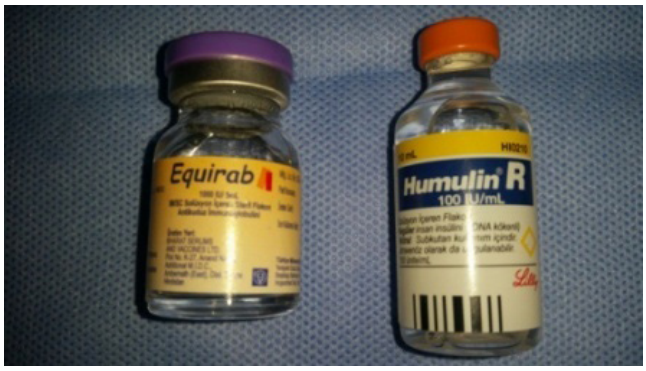

Figure 1. The vials of Rabies Ig (Equirab®) and Regular insulin (Humulin R®).

Medicine should not consider medication errors as random accidental misfortune. They should be treated as a disease, its pathophysiology should be revealed, controlling risk factors should be provided, and preventive medicine approaches should be developed[1]. Voluntary reporting of medication errors should be promoted so that problems could be identified[3]. The voluntary reporting system cannot be expected to be successful if the evaluation system focuses on punishment and affects providers' lives irreparably. The aim should not be to blame the person but to obtain data and develop systemic adjustment strategies[6]. It should also be kept in mind that some medication errors may not be easily noticed. Checklists during the application and verification procedures held by more than one person after the application are useful approaches, as our case exemplifies.

The significant risk factors include special populations exposed to medical harm and the high-risk areas for patient care. The vulnerability of the population to harm and the nature of the provided health care may cause the distributional variation in medication errors. The well-known vulnerable groups include geriatric, pediatric, pregnant groups, and patients with communication problems. Goal-oriented software and warning systems are among the options for drug applications to these particular groups. They are also crucial in terms of drug interactions. The high-risk zones are ICU, oncology units, units with thrombolytic therapy (coronary or stroke units), pre-hospital settings, and emergency departments. Computerized provider-order entry systems, automated dispensing cabinets, bar-coding systems, medication reconciliation, standardizing medication-use processes, education, and emergency-medicine clinical pharmacists are suitable for the aforementioned selected zones[1,7,12]. The integration of these systematic changes is likely to be considered unnecessary, tiring, time-consuming, or even prolonging the treatment process for providers and patients. Therefore, it is essential that existing and future systems focus not solely on safety but also to be more user-friendly, practical, and faster.

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Conclusion

The potential medication errors due to the poor control of critical drugs and the similarities between the brand names of drugs used in EDs should be prevented by well-designed medication-use process strategies.

Conflict of interest statement

None of the authors have any conflict to disclose.

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Statement on informed consent

Verbal consent to use this case for publication was obtained from the patient during a routine clinical care encounter, documented in the medical records. This case report was deemed as being appropriate by the IRB for publication purposes as no patient-specific identifiable health information was disclosed.

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