



Case Report

Identification of highly concentrated dextrose solution (50% dextrose) extravasation and treatment—a clinical report

Abstract

Treatment for significant hypoglycemia includes administration of dextrose containing agents, including 50% dextrose (D50%W) intravenously. Significant extravasation of D50%W can lead to complications, including skin and soft tissue injury, loss of limb, or death. The aim of this case report, using an interdisciplinary team approach, explores extravasation protocols as well as literature review, is to provide information about the proper use of hyaluronidase in patients with D50%W extravasations. A 46-year-old African American man presented to the emergency department (ED) after blood glucose level was initially 13 mg/dL. Emergency medical service established a large bore intravenous (IV) line in the right antecubital vein and administered a total of 50 g of D50%W. Upon arrival to the ED, the patient's level of consciousness had significantly improved. After arrival to the ED, the patient started complaining of pain in his right arm, near the site of the IV line insertion. On inspection, the IV site was grossly infiltrated. Hospital protocols for hyperosmolar infiltration were used. Extravasation is a common medical complication of infused medications and needs to be properly identified and treated. The multitude of skills from nursing, medicine, and pharmacy ensures that extravasation is managed appropriately and effectively to ensure safety to patients. Recognition, communication, and awareness of the institutional guidelines on how to treat infiltration and extravasation should be encouraged in all ED and intensive care unit medical personnel who deal with a variety of infusions and IV medications that have serious implications if not treated correctly.

It is a universal practice to administer intravenous (IV) fluids and medications to patients who are admitted as inpatients, commonly through a peripheral IV line access. Most medications used are safe for peripheral line administration; however, with few select medications, there is an increased risk of infiltrations and/or extravasations. As these adverse infusion reactions occur infrequently, the available evidence-based interventions are minimal and are mostly based on empirical knowledge from small uncontrolled trials, case studies, or animal studies.

In most cases, there are no alternatives to the use of IV medications, especially in well-established high-risk medications such as vasopressors and chemotherapy agents, and in these cases, an infiltration or extravasation has a higher rate of occurrence and may result in unfavorable patient outcomes. The spectrum of adverse effects ranges from local infusion site irritation to death depending on the anatomical site, class and quantity of medication, and the patient overall medical condition.

A commonly overlooked irritable medication is IV dextrose. It is commonly used to treat severe hypoglycemia in diabetic patients. Dextrose concentrations range from 5% to 50% wt/vol, with the most common concentration of dextrose given in a severely hypoglycemic patient is the 50% wt/vol in 50 mL given as a slow IV push. Dextrose is considered a vesicant drug if the concentration is 10% or greater, and because it is a key medication in reversing dangerously hypoglycemic patients, extra care has to be taken during administering this medication. If extravasation does occur, it is important to have established protocols established and available to clinicians to reduce complications.

A 46-year-old African American man presented to the emergency department (ED) after a reported hypoglycemic episode. According to the prehospital report, the patient was found by his wife at 5 AM unresponsive to commands. The wife called 911 and upon emergency medical services personnel arrival, the blood glucose level was initially found to be at 13 mg/dL. Emergency medical services established a large bore IV line in the right antecubital vein and administered a total of 2 ampules of 50 mL (25 g) for a total of 100 mL of 50% dextrose (D50%W), which corrected the hypoglycemia to a level of 46 mg/dL. Concerned that the correction of the hypoglycemia was not adequate, the patient was also given 1 mg of glucagon, which corrected the hypoglycemia to a blood glucose level of 126 mg/dL. The patient slowly regained consciousness and was transported to the ED for further evaluation and management of the hypoglycemic episode.

Upon arrival to the ED, the patient's mental status had significantly improved, with an appropriate affect; he was alert and oriented to person, place, and time. A repeat blood sugar at the ED revealed a level of 138 mg/dL. Evaluation of the patient revealed a medical history that was significant for type 1 diabetes (poorly controlled), diabetic retinopathy, peripheral neuropathy, depression, hypertension, hypovitaminosis D, and gastroesophageal reflux disease. The patient also has a history of several hypoglycemic episodes in the past. His medications upon ED admission were aspirin 81 mg daily, carvedilol 12.5 mg twice daily, escitalopram 10 mg daily, esomeprazole 20 mg daily, hydrochlorothiazide 25 mg daily, insulin glargine 25 units subcutaneously daily, insulin lispro 3 units three times daily before meals, insulin lispro sliding scale, and lisinopril 40 mg tablet daily.

Shortly after arrival to the ED, the patient started complaining of pain in his right arm, near the site of the IV line insertion. Inspection revealed that the IV site was grossly infiltrated. The patient's right forearm had swollen significantly compared with the left forearm and was painful to light palpation circumferentially from the mid forearm to mid arm. Otherwise, his physical examination was unremarkable.

Upon identifying the cause of infiltration, the institutional management of extravasation of nonchemotherapeutic vesicants and irritants protocol was initiated. Immediately, the **IV line was removed and the arm was elevated**, and the ED clinical pharmacist was consulted by the physician for guidance regarding the antidote options regarding medication extravasations. A review of the hospital-based protocol was performed between the physician and the **pharmacist**, discussing the appropriate course of therapy. It was decided that the use of hyaluronidase was indicated in this case of extensive extravasation. **Cold compresses were placed over the site of extravasation for 15 to 30 minutes and repeated every 4 hours** while elevating the arm. The hyaluronidase was injected subcutaneously into the outer edges of the extravasation site. The patient was monitored for an additional 5 hours for response to therapy. Swelling and redness markedly decreased before the discharge of the patient; the patient was instructed to return to the ED for a 24-hour follow-up visit and then at 48 hours with his primary care physician in the outpatient clinic. Within 24 hours, the arm had returned to its normal size, with no patient reports of pain or visible redness and full range of motion. Other than some degree of bruising around the site of injection, the patient had no complaints and was at his baseline health. The patient has done well with a normal arm examination at long-term follow-up.

Hypoglycemia defined as a blood glucose level 70 mg/dL or less is a medical emergency, which may be life threatening if not recognized and corrected promptly. Patients with hypoglycemia usually present with diaphoresis, tremors, difficulty with concentration, lightheadedness, lethargy, and, in extreme situations, unconscious. When a patient presents with signs and symptoms of hypoglycemia, he or she may not be alert; thus, oral glucose administration may not be an option. Thus, rapid management to correct the hypoglycemia must be undertaken, which includes obtaining IV access for the administration of IV dextrose. In the case that IV access cannot be obtained, glucagon can be given intramuscularly. The goal of therapy is to correct the blood glucose level such that the signs and symptoms of hypoglycemia resolve.

Dextrose 50% is often given to patients with an altered level of consciousness both in the field and in the hospital setting upon recognition of clinical hypoglycemia. Before dextrose administration, IV access must be obtained but may be difficult to establish when a patient's blood glucose levels are extremely low. Dextrose 50% is a hyperosmolar solution, and it is critical that IV access must occur in a larger vein. In addition, IV fluids are administered simultaneously with continuous monitoring of the IV site for extravasation. Failure to take the appropriate steps in insuring safe administration of D50%W, such as improperly placing the IV and or rapidly administering dextrose, has been associated with extravasation.

Dextrose 50% is a hyperosmolar solution at 2520 mOsm/kg, providing 500 g/L of glucose; noting that hyperosmolar solution is defined as an osmolality greater than 250 mOsm/kg [1]. The introduction of a hyperosmolar solution in the tissue surrounding the vein due to a misplaced IV or the leakage of the solution causes a **fluid shift into the tissue** space between adjacent cells, drawing fluid from the neighboring cells and blood vessels into the surrounding area [2]. Immediate signs and symptoms of extravasation include edema, subcutaneous **inflammation and pain, discomfort, and, in severe cases, compartment syndrome** [1]. Loss of limb function, significant tissue loss, and nerve damage are permanent complications of compartment syndrome resulting from improper timely management of extravasations [1]. Thus, it is important to ensure safe administration of D50%W to these patients.

Upon recognition of the signs and symptoms of an infiltrated vein, it is important to consider the type of solution infused and the indications of the available antidotes for timely and successful treatment [3]. Leakage of a nonvesicant solution is termed infiltration, and leakage of a vesicant solution is termed extravasation [3]. A

vesicant drug is capable of causing blisters or severe tissue destruction, which may be a lasting injury. Nonvesicant drugs are known as irritants, which present as local site irritation in the extravasated area, but there are no tissue necrosis and are self limiting [4]. The type of vesicant determines both the approach for the management and the type antidote used to counteract the extravasated fluid. The 2 classes of vesicants that cause extravasations are **hyperosmolar solutions and sympathomimetics**. Examples of **hyperosmolar solutions that may cause extravasations are penicillin, phenytoin, and dextrose (>5%)**, all can be **treated with hyaluronidase**.

When extravasation of D50%W into the surrounding tissues occurs, appropriate interventions are necessary to decrease complications. There are two components to proper management of extravasations, which include supportive care and medical intervention. Although supportive care is indicated in most cases, medical intervention is much less commonly needed.

Upon the recognition of an extravasated solution, the offending agent should be **immediately discontinued**. Following discontinuation, the clinician should **attempt to aspirate** as much as possible of the vesicant from the dysfunctional IV catheter [5]. The next step should be the **removal of the IV** catheter, while attempting to gently withdraw with a syringe to remove any solution remaining in the catheter and vein. Lastly, the infiltrated areas should be well marked to gauge the progress of the therapy. Other health care providers providing care to the patient should be informed of the incident to assist in the management and reporting it as a adverse drug event is strongly encouraged.

Therapeutic management of a D50%W extravasation consists of two parts, including non-medication (supportive) and medication aspects. Nonmedication therapy includes the **elevation** of the affected limb while applying cold compresses to the area of extravasation **every 15 to 30 minutes for 24 to 48 hours** to decrease swelling and limit the spreading of the medication. It is important to note the different between warm and cold compresses, as warm compresses are usually applied for infiltrated medications and not for extravasations [6].

Antidote management of extravasated hyperosmolar agents requires the use of **hyaluronidase**, such in the case of D50%W extravasations. Hyaluronidase is manufactured from bovine and ovine sources, with the trade names of Amphadase and Vitrase, respectively. In 2009, the Food and Drug Administration approved a new formulation called Hylenex, which is a human recombinant formulation of hyaluronidase [7,8]. Both Amphadase and Hylenex are supplied as 150 U/mL concentrations and Vitrase as 200 U/mL vial. It is important to note that hyaluronidase does not have a Food and Drug Administration indication for the use in dextrose extravasation; however, it has been used successfully in other hyperosmolar extravasations and in a recent dextrose extravasation case report [7,9,10]. The authors reported a 17-year-old adolescent girl with extravasation of the forearm after the administration of 50 g of D50%W secondary to a hypoglycemic episode and successfully treated with hyaluronidase [2]. This report was the only available documented case of D50%W treated with hyaluronidase, successfully.

The administration dose of hyaluronidase for extravasation ranges from **0.1 to 0.2 mL** (administered via a hypodermic needle) **subcutaneously 5 times** around the area of extravasation. It is recommended **not to reuse the same needle** for administration due to the risk of infection [7]. Hyaluronidase mechanism of action is that of an enzyme that promotes the hydrolysis of hyaluronic acid, which is responsible for cellular adhesion [11]. Hyaluronidase temporarily **decreases the viscosity** of the cellular connections, allowing for the **diffusion** of the extravasated fluid in between the cells to dissolve back **into the vasculature** [6,8]. Hyaluronidase does **not have any contraindications to its use, and the reported adverse effects are limited to injection site reactions, anaphylaxis, and edema. To avoid the risk of anaphylaxis, a test dose of hyaluronidase is always recommended**

before administering a full treatment dose. The package insert recommends a skin test dose of 3 units (0.02 mL) of a 150 units/mL and to observe from 5 to 20 minutes [8]. A study investigating the rates of allergy in patients having administered recombinant hyaluronidase have found no increased risk of allergic reactions; however, this could not be translated into animal-derived hyaluronidase [12].

Of course, the best management strategy starts with prevention of IV infiltration and, thus, extravasation. It is vital that the IV is placed in a large, straight vein, ideally not over a joint, if such is possible. Before administration, the IV site should be inspected for signs of infiltration and blood return. The IV site should be secured in a way that the site can be visualized and inspected. During the administration while IV fluids are infusing simultaneously, continuous monitoring of the IV site is essential. If there is any noticeable swelling at the site, increasing resistance, or complaints of pain, administration of the D50%W is stopped so that the site can be reassessed. If there are any doubts about cannulation or integrity of the vessel, the D50%W should not be given at this site and new IV access obtained.

Extravasation is a common medical complication of medication infusion, which must be properly identified and treated. The multitude of expertise from nursing, medicine, and pharmacy ensures that extravasation is managed appropriately and effectively to ensure safety to patients. Recognition, communication, and awareness of the institutional guidelines on how to treat infiltration and extravasation should be encouraged of all ED and intensive care unit nurses who deal with a variety of infusions and IV bolus medications that have serious implications if not treated correctly. This case report demonstrates that hyperosmolar dextrose extravasation when recognized promptly was effectively treated appropriately with hyaluronidase.

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