Hypodermoclysis is the subcutaneous administration of isotonic infusates to correct short-term fluid and electrolyte imbalances. It has recently begun to regain recognition as a safe and effective alternative to intravenous fluid hydration in the mild to moderately dehydrated patient, particularly in the areas of palliative care and long-term care. Hypodermoclysis is easy to establish and maintain and has fewer complications than intravenous hydration. The medication hyaluronidase can be injected as a spreading agent to facilitate subcutaneous fluid absorption. Hypodermoclysis has the potential to help reduce the $1 billion annual US cost of avoidable hospitalizations for dehydration.

WHAT IS HYPODERMOCLYSIS?

Hypodermoclysis (HDC) is the subcutaneous administration of isotonic infusates to correct short-term fluid and electrolyte imbalances. Hypodermoclysis is also known by the term clysis or subcutaneous hydration. The term hypodermoclysis literally means a washing out beneath the skin. It is related to the more commonly heard term hypodermic, as in hypodermic needle.

MODE OF ACTION

Fluid is infused into subcutaneous tissue via a short 24- to 27-gauge needle or plastic catheter, using either a dedicated subcutaneous infusion set or an intravenous (IV) administration set adapted for subcutaneous use. The fluid infused absorbs into the intravascular compartment (IVC) by a combination of perfusion, diffusion, hydrostatic pressure, and osmotic pressure. Perfusion is the delivery of arterial blood to a capillary bed in the tissue. Diffusion is the spontaneous net movement of particles from an area of high concentration to an area of low concentration in a given volume of fluid. The pressure at any given point of a nonmoving (static) fluid is called the hydrostatic pressure. Osmotic pressure is the hydrostatic pressure produced by a solution in a space divided by a semipermeable membrane. It is caused by a differential in the concentrations of solute on either side of the membrane. These factors allow the absorption of infusate into the IVC, provided the infusate composition does not draw sodium and water out of the IVC (ie, an isotonic infusate) and the infusion rate is no greater than the limits of tissue perfusion.

The absorption of infused subcutaneous fluids (SCFs) has been found to be complete and comparable with the absorption of intravenous fluids (IVFs) when administered within the parameters of appropriate rate, amount, and fluid type for SCFs. In a study by Lipschitz et al, 500 mL of normal saline, containing radioactive markers, was infused subcutaneously over a period of 3 hours into an infraclavicular site of each human subject. The results showed complete absorption of the SCF 1 hour after the completion of the infusion. Chaliner et al reported that 34 older adults requiring parenteral fluids post-cerebral vascular accident were randomly assigned to a group to receive either IVF or SCF hydration. At the conclusion of the study, there was no significant difference in plasma osmolality (a dehydration marker) between groups. Generally accepted, safe, and effective HDC infusion rate and volume limits are

- 1.5 L/d per injection site (1 mL/min),
- up to 3 L/d per 2 sites,
- 1 L/8 h during a nocturnal infusion, and
- no faster than 1 L/2 h.

HISTORICAL PERSPECTIVE

Hypodermoclysis was first used in the 1940s for pediatric dehydration and became a popular mode of
Hydration therapy. During the 1950s, HDC fell into disfavor due to a combination of factors. There were anecdotal reports in the literature of shock and death caused by severe osmotic shifts from HDC. Later studies and review showed these to be related to improper techniques of HDC: the use of inappropriate fluids (electrolyte-free and/or hypertonic), excessive fluid volumes, and rapid infusion rates. Concurrently, the availability of improved disposable needles and equipment, plastic containers, and plastic tubing contributed to the increased ease of use of IVF administration. However, HDC has remained an effective and useful therapy in veterinary medicine over the years.

In the past 1 to 2 decades, there has been a resurgence of interest in and use of HDC, especially in Canada and some Asian countries, but it remains relatively unused. Few clinicians know enough about HDC to feel confident in prescribing it. The cost of treating dehydration by this technique in a nursing home is lower than the cost of giving IVF in a hospital. However, HDC does not generate an increased acuity level for reimbursement in many states like IVF hydration does.5

**EFFICACY**

Compared with other therapies, there are relatively few studies concerning the efficacy and safety of HDC. In a 1997 review of 18 studies, Rochon et al6 concluded that HDC is safe as long as the hydrating fluids contain electrolytes; potassium chloride may, with caution, safely be added to HDC infusions; the desirability of using hyaluronidase as an aid to absorption in HDC is unresolved; and there is a need for better-quality studies of HDC.

In a 2001 review in *American Family Physician*, Sasson and Shvartzman7 state that HDC is mainly used in geriatric and palliative medicine; is suitable for use in many hospital and homecare situations, regardless of the patient's age; can be administered by family members or by a nurse at home; is technically easier to administer than IVF administration; and is less objectionable than IVFs for hydration of terminally ill patients. The initiation of HDC for acute palliative care as an inpatient can ease the transition to home hospice care. It can help improve the quality of life for the terminally ill patient and is especially effective for hospice patients unable to tolerate the oral, nasogastric, or rectal routes of fluid and medication administration.7,8

In 2007, Remington and Hultman5 reviewed 8 studies of HDC from the years 1996 to 2006. They summarized: if HDC is administered properly, it is as safe and effective as IVF hydration for mild to moderate dehydration; it is potentially less expensive than IVFs; the annual cost in the United States of possibly avoidable hospitalizations for dehydration is $1 billion; there is a need for standardized HDC protocols such as those in the Infusion Nurses Society's *Policies and Procedures for Infusion Nursing of the Older Adult*; there is a need for better HDC studies using randomized controlled trials; and US healthcare finance policy regarding HDC versus IVF administration should be reexamined.

**INDICATIONS**

Hypodermoclysis is indicated for the prevention or treatment of mild to moderate dehydration in patients with 1 or more of the following conditions: inability to take adequate fluids orally; fluid loss due to vomiting, diarrhea, diuretics, etc; difficult or impractical IV access; drowsiness; confusion; hyperthermia; and difficulty in administering enteral or parenteral nutrition. In addition, HDC is indicated during the terminal phase of life for the concomitant infusion of opioid analgesics and anxiolytics with fluids; for the prevention of dry mouth, constipation, and confusion; and at the request of the patient or relatives of the patient. Clys can also be used for the infusion of amino acid solution to limit malnutrition.4,7

**CONTRAINDICATIONS**

Hypodermoclysis is contraindicated in emergency situations such as circulatory failure, severe electrolyte imbalance, and severe dehydration. It is not indicated for patients with the following critical laboratory values: serum Na > 150 mEq/L; serum osmolality > 300 mOsm/kg; and a blood urea nitrate/serum creatinine ratio > 25.4,9,10

Hypodermoclysis is also contraindicated in patients with obvious coagulopathy; fluid volume excess; fluid requirements greater than 3 L per 24 hours; no available intact skin sites; or who have hypoalbuminemia with gross edema.4,9,10

**ADVERSE EFFECTS**

The possible adverse effects of HDC are rare and usually avoidable. A patient might experience a sensitivity reaction to the absorption adjunct hyaluronidase if used. An intradermal test dose of hyaluronidase is recommended before using it with clysis. It is possible to inadvertently puncture a blood vessel when inserting the subcutaneous access set. The clinician should always attempt to aspirate blood after inserting the device. If blood is noted upon aspiration, the device should be removed and a new one inserted at an alternative site. Pulmonary edema, circulatory overload, and electrolyte imbalances have less frequent incidences with HDC than with IVF hydration. The patient should be monitored for signs and symptoms of these adverse effects and, if noted, the infusion should be stopped and the physician notified.10
COMPLICATIONS

Localized complications are reported in 11% to 16% of patients undergoing HDC. These may include warmth or redness at the site or edema in surrounding tissue. Edema can be managed by massaging the site, reducing the rate of infusion, and using hyaluronidase to aid in absorption. Pain at the insertion site can be a symptom of inadvertent placement of the access device in muscle tissue instead of subcutaneous tissue. If pain occurs, the device should be removed and replaced in an alternative location. Other possible complications include bleeding at the insertion site, abscess formation at the insertion site, or cellulitis.

ADVANTAGES

The advantages of HDC, as an alternative to IVF hydration, in the mildly to moderately dehydrated patient are numerous. It is a safer route and a less-complicated and easier-to-maintain procedure than IVF hydration. There are no inherent complications of thrombophlebitis, thrombosed catheters or veins, air or catheter emboli, or septicemia with HDC. Insertion and maintenance of the access device cause less discomfort, which results in reduced distress for patients, particularly those who are cognitively impaired. Either an RN or a licensed practical/licensed vocational nurse can initiate and monitor clysis because it is not an IV procedure. Placement in the subscapular area renders the device difficult to dislodge by the confused patient, and inadvertent dislodgment does not cause serious problems. Hypodermoclysis does not require routine flushing regimens, use of an electronic infusion device, or limb immobilization with the risk of subsequent pressure sores. The use of a nighttime infusion allows for daytime mobility of the patient. Hypodermoclysis can result in fewer hospital admissions with a potential for cost savings. Finally, the use of clysis may enable a terminal patient to remain at home with family.

DISADVANTAGES

Hypodermoclysis is not appropriate for emergency situations in which the patient may need large fluid volumes, electrolyte-free solutions, or hypertonic solutions. It has a rare potential for cardiac failure and hypotension. It also has the potential for hyaluronidase sensitivity reactions and site abscess formation.

EQUIPMENT

Equipment choices and usage for HDC are in part governed by Standard 64 of the Infusion Nurses Society’s Infusion Nursing Standards of Practice. Practice Criteria D states: “hydration fluids (hypodermoclysis) should be administered via a manual flow control device or an electronic infusion device.” Practice Criteria G states: “The selected continuous subcutaneous access device should be of the smallest gauge and shortest length necessary to establish subcutaneous access.”

There are a variety of subcutaneous access devices available on the market. Some are needle sets and some are over-the-needle catheter sets. Previously, it was nearly impossible to find a safety-engineered subcutaneous access device suitable for HDC, but they are now starting to become available. An access set is typically used in conjunction with an insertion set containing an appropriate skin cleanser, such as chlorhexidine or povidone-iodine, and a transparent semipermeable membrane dressing. An administration set with manual flow control is also necessary. An IV administration set works well for this purpose (Figure 1).

HYDRATION SOLUTIONS

Most isotonic fluids used for IVF hydration are acceptable for HDC. Those fluids containing sodium chloride, with or without glucose, are most commonly used. In addition, lactated or nonlactated electrolyte solutions may be used. Potassium chloride, 20 to 40 mmol/L, can be added to these solutions. Dextrose 5% and 10% solutions are not used.

MEDICATIONS

Hyaluronidase is an enzyme that, when added to the SCF infusion, acts as a physical adjunct to increase absorption and dispersion of the fluid. The agent modifies the permeability of connective tissue through the hydrolysis of...
hyaluronic acid. This causes rapid spreading of subcutaneously injected material, provided the local interstitial pressure gives an adequate mechanical impulse. The rate of perfusion is proportional to the amount of hyaluronidase present, and the extent of diffusion is proportional to the volume of solution present.\textsuperscript{12-14}

Hyaluronidase is an antigen to humans and can cause hypersensitivity reactions. The Infusion Nurses Society recommends the use of an intradermal test dose before starting the clysis to test for hypersensitivity to the drug. This is typically 0.02 mL (3 U) of a 150 U/mL solution. A positive reaction consists of a wheal appearing within 5 minutes and persisting for 20 to 30 minutes, accompanied by localized itching. Erythema by itself is not a positive reaction. A positive test reaction is a contraindication to use of the drug.\textsuperscript{12-15}

The usual dosage of hyaluronidase is 150 U in a liter or more of fluid. Alternatively, 150 to 200 U injected subcutaneously at the site prior to initiation of HDC will facilitate the absorption of 1000 mL or more of fluid. Hyaluronidase should not be used in or around any area of infection or inflammation. It should not be used if cloudy or discolored, or if it contains particulate matter. The fluid-spreading effect of the drug is completely eliminated by 48 hours postinjection. Adverse drug reactions can include injection site reactions, anaphylaxis, angioedema, urticaria, and edema.\textsuperscript{13}

The brand of hyaluronidase previously used extensively for HDC, Wydase\textsuperscript{®} (Wyeth Pharmaceuticals, Madison, NJ), has not been manufactured since 2001. Amphadase\textsuperscript{®} (Amphastar Pharmaceuticals, Cucamonga, California) comes from a bovine source, and Vitrase\textsuperscript{®} (ISTA Pharmaceuticals, Irvine, California) is from an ovine source. Hylenex recombinant\textsuperscript{®} (Baxter Healthcare Corporation, Deerfield, Illinois), a recombinant human hyaluronidase injection, is said to have less risk of hypersensitivity reaction than do products with an animal source.\textsuperscript{16,17}

## SITE SELECTION

Any area with a relatively large area of subcutaneous tissue is an appropriate site for the infusion. The lateral abdominal wall is the most common site. Other common sites include the anterior of lateral thighs and subclavicular region. The interscapular or subscapular region can be useful for confused patients who attempt to dislodge the device. It is common practice to infuse at 2 sites simultaneously by using a dedicated access device with 2 separated needles or 2 access devices connected to the administration set with a Y-connector (Figure 2).\textsuperscript{4}

## PROCEDURE

INS Standard 64, Practice Criteria C, E, and F, respectively, states: “Aspirate device prior to fluid administration for absence of blood”; “Access site should have intact skin and be away from the umbilicus and bony prominences”; and “Subcutaneous sites used for hypodermoclysis should be monitored frequently and the site rotated based upon volume of fluid given, patient comfort, and appearance of infusion site.”\textsuperscript{11(pS68-S69)}

Aseptic technique and standard precautions should be used in accessing, maintaining, and removing the device. The site should have adequate subcutaneous tissue—a fat fold of at least 1 in or 2.5 cm between thumb and forefinger. The site should be prepared with a single-dose skin antiseptic solution, such as chlorhexidine, 10% povidone-iodine, alcohol, or 2% tincture of iodine. The site and device shield should be covered with a transparent semipermeable membrane dressing. The site should be changed every 72 hours or sooner if complications occur. It should be relocated at least 2 to 3 in from the previous site. Documentation of the procedure should include the size and the length of the device, site location, type of dressing, type of infusate and rate of administration, complications noted with
interventions taken, and patient assessment and response to the therapy (Figure 3).12

CONCLUSION

Hypodermoclysis is a misunderstood and underused hydration therapy that offers many advantages and few disadvantages to the patient who is mildly to moderately dehydrated, particularly the older adult patient. It is easier to establish and maintain, with fewer complications, than IVF hydration. It can be less expensive than IVF hydration and has the potential to be even more cost-effective if current reimbursement policies are revised to include HDC as an acceptable alternative to IVF hydration when appropriate. The more clinicians learn about HDC and observe its safety and effectiveness, the more likely HDC will regain the position it once held as a useful and widely used therapy.

REFERENCES