Iontophoresis, or ion transfer, is a form of electrotherapy used to deliver drug molecules across intact skin. Specific drugs that ionize in solution can be driven into the skin and underlying tissue by applying a direct current through surface electrodes. Because an electrode will repel similarly charged ions, positively charged ions can be introduced into tissue by the positive electrode (anode); ions with a negative charge can be introduced by the negative electrode (cathode).

Effective skin penetration of various drugs has been documented in humans and laboratory animals. It should, therefore, be reasonable to expect that this therapeutic technique can be applied in clinical veterinary medicine. Potential uses for iontophoresis include local anesthesia and treatment of musculoskeletal conditions in performance animals. The information in this column was derived from literature on basic research and the treatment of humans, primarily athletes.

Equipment and Technique

The procedure and instrumentation for iontophoresis are relatively straightforward. Direct current is required to ensure the unidirectional flow of ions during the procedure. A typical battery-operated unit incorporates a control for adjusting the current output, an ammeter to measure the current, a voltage control knob and meter, and a timer (Figure 1). In the United States, at least three companies market iontophoresis units that are small and portable. The prices vary from approximately $500 to $1000.

Factors that can determine the amount of medicine introduced into tissue include polarity, intensity, and duration of the current; electrode size; skin resistance; ionization potential; and nature of the solvents used. Typical current intensity is in the range of 3 to 5 milliamps (mA), with a treatment duration of 10 to 20 minutes. For humans, the stimulation sensation can be used to gauge the intensity of the current. When initiating treatment, the intensity of the current is usually increased slowly until the person reports feeling a tingling sensation. A guideline that could be followed in treating animals would be to set the amplitude to deliver a current density of 0.1 to 0.5 mA/cm² of the active electrode surface. Opinions differ on the effect of the stimulus intensity. Many authors, however, state that low-intensity currents appear to be more effective as a driving force than are currents with higher intensities. Therefore, iontophoresis in animals could likely be effective at intensities that would not cause pain or discomfort.

The two electrodes, termed active and dispersive, are applied to the skin surface. Electrode systems range from simple electrodes fabricated in a clinical to commercial electrodes specifically made for iontophoresis units. Commercially available disposable iontophoresis electrodes have a well (filled with medication) that contacts the skin with a semipermeable membrane. Electrode size and shape alter current density and affect the size of the area being treated. As a rule, the smaller the electrode, the larger the current density is. The selection of

*KEY POINTS*

- By applying a direct current through surface electrodes, iontophoresis can be used to deliver drug molecules across intact skin.

- Iontophoresis is used by physical therapists primarily for the treatment of musculoskeletal inflammatory conditions such as bursitis and tendinitis.

- In addition to physical therapy–related uses, iontophoresis can potentially be applied in other areas such as veterinary ophthalmology, anesthesiology, and dermatology.
electrode size depends on the lesion. When a large or poorly localized area is to be treated, larger electrodes are indicated.

Does Haircoat Affect Technique?

An intact haircoat impedes the penetration of ultrasound waves into tissue. Whether iontophoresis can be delivered efficiently through an intact haircoat remains undetermined. For humans, authors typically caution that the skin should be shaved and cleaned to ensure maximum electrode contact. In published animal experiments, the haircoat has been removed and the skin cleaned. There is, however, reason to expect that iontophoresis could be performed on animals with an intact haircoat. Proper electrical conductivity has been established for other techniques involving electrical stimulation, despite the presence of an intact haircoat. Proper electrical conductivity has been established for other techniques involving electrical stimulation, despite the presence of an intact haircoat. For instance, the haircoat of domestic animals can be parted but does not need to be clipped when applying surface-stimulating electrodes for sensory nerve conduction velocity studies. Furthermore, electrical impedance is low enough that electroencephalograms have been recorded with surface recording electrodes in horses and companion animals without clipping the haircoat.

Precautions

The most severe complications associated with iontophoresis in humans are adverse drug reactions and skin burns under the cathode as well as skin irritation possibly associated with changes in skin pH. The incidence of adverse drug reactions can be reduced by carefully selecting the drugs to be used in patients with known allergies. The incidence of skin burns has decreased as current-regulated generators have become available. Safety features are available to automatically terminate treatment if impedance increases too quickly or reaches an unacceptable level. Caution should be used if the skin is already injured. Because damaged skin has a lower-than-normal resistance to the current, a burn may occur more easily.

Iontophoresis at incision sites could likely be performed if investigators determined which intensities and treatment times could be used without producing skin irritation. Some reports advise that skin blemishes in humans should be protected with petroleum jelly to avoid skin injury. Care should also be taken when there is a sensory deficit. A recent study on the use of iontophoresis to treat carpal tunnel syndrome reported that this method of delivering dexamethasone has an excellent complication and side-effect profile compared with other methods. This study also reported that no complications occurred, including no significant increase of serum glucose in insulin-dependent diabetics.

Clinical Indications

Currently, iontophoresis is used by physical therapists primarily to treat musculoskeletal inflammatory conditions (e.g., bursitis, tendinitis). Most of the published clinical information on iontophoresis involves the treatment of inflammatory conditions (see Indications for the Use of Iontophoresis in Humans). Iontophoresis concentrates the drug directly into the problem area to achieve more rapid recovery. Lidocaine iontophoresis can produce local anesthesia that has a more prolonged duration than can be obtained with topical application of the drug but a shorter duration than with local infiltration. The degree of anesthesia provided with lidocaine iontophoresis is sufficient to enable suture placement. Lidocaine iontophoresis has also been used to perform myringotomies in which anesthesia of the ear canal and eardrum were obtained.

Administering Drugs by Iontophoresis

The drug administered must be both water and lipid soluble. The agent must be water soluble to remain ionized in solution, and it must be lipid soluble to permeate cell
**Indications for the Use of Iontophoresis in Humans**

- Allergic rhinitis
- Analgesia
- Burns
- Calcium deposits
- Edema
- Fungal infection
- Gout
- Herpes infection
- Hyperhidrosis
- Inflammation
- Ischemia
- Muscle spasm
- Open skin lesions
- Reflex sympathetic dystrophy
- Scar tissue
- Tumors

The report also described a preliminary study on iontophoresis, and local drug delivery has been available for musculoskeletal tissue in horses. Betamethasone was found in serum 7 hours, but not 24 hours, after the last treatment.

To determine the role of iontophoresis in both human and veterinary medicine, outcome assessments comparing iontophoresis with parenteral, oral, and topical routes of administration are needed. Unfortunately, many published clinical trials on the use of iontophoresis to treat human conditions have not had optimal experimental design. Clinical trials have tended to lack adequate controls and random assignment to treatment groups, or relevant treatment parameters have not been reported. In some studies, patients received additional modalities (e.g., therapeutic exercise, heat, electrotherapy, ultrasonography) or had various musculoskeletal conditions and did not represent a uniform population.

In a study by Glass and colleagues, iontophoresis was performed (4 to 5 mA for 20 minutes) on two Rhesus monkeys. Significant penetration of dexamethasone (but not hydrocortisone) occurred compared with controls. Local tissue concentrations of dexamethasone were higher than would be obtained by systemic therapy but lower than would be obtained by local injection. The authors concluded that the concentrations of steroid recovered in various tissue were sufficient to produce clinical antiinflammatory effects. In sites treated with dexamethasone and lidocaine hydrochloride, the depth of penetration was approximately 1.7 cm. The authors reported that iontophoresis was concentration independent because electrodes containing 8 mg of drug delivered the same amount as did electrodes containing 4 mg of drug.

Several studies have been conducted on cases of tendinitis in humans, with varying results. In 30 patients with infrapatellar tendinitis, iontophoresis (dexamethasone and lidocaine) was compared with an established protocol consisting of modalities and transverse friction massage. Patients were assessed with a visual analog pain scale, a functional index questionnaire, rating of tenderness on palpation, and number of step-ups needed to elicit pain. The authors concluded that iontophoresis may be more effective in decreasing pain, reducing inflammation, and promoting healing than was the established protocol. In a subsequent randomized, controlled trial, acetic acid iontophoresis and ultrasonography were compared for treatment of calcifying tendinitis of the shoulder. Patients were stratified according to the type of lesions evident on radio-

**Agents Administered by Iontophoresis**

Positive ions:
- 5-Fluorouracil
- Acyclovir
- Ara-AMP
- Cefazolin
- Copper (copper sulfate as source)
- Dexamethasone
- Hyaluronidase
- Idoxuridine
- Lidocaine
- Magnesium (magnesium sulfate as source)
- Ticarcillin
- Zinc (zinc oxide as source)

Negative ions:
- 6-Hydroxydopamine
- Acetate (acetic acid as source)
- α-Methylparatyrosine
- Chloride (sodium chloride as source)
- Ciprofloxacin
- Epinephrine
- Gentamicin
- Iodine
- Ketoconazole
- Salicylate
- Tobramycin
- Vancomycin
graphs. No significant difference was identified between the two treatment groups, suggesting that this condition may be amenable to treatment with either modality. In a randomized, double-blind, placebo-controlled study of patients with plantar fasciitis, Gudeman and colleagues investigated whether iontophoresis (dexamethasone) in conjunction with other traditional modalities provided more rapid pain relief than did traditional modalities alone. In this study, treatments were given six times over 2 weeks. Iontophoresis combined with traditional modalities led to greater improvement than did traditional methods alone at the end of the treatment period. However, there was no significant difference between the groups at 1-month follow-up. These results suggest that when used in conjunction with traditional modalities, iontophoresis provides immediate reduction in symptoms and should be considered when prompt results are needed (e.g., treating athletes).

Potential Applications in Ophthalmology

The defense mechanisms of the eye make it difficult to achieve effective drug concentrations within the eye. Drugs given systemically have poor access to the inside of the eye because of the blood–aqueous and blood–retinal barriers. Topically applied drugs are rapidly eliminated from the precorneal area. In addition, the corneal epithelium has anular tight junctions that completely surround and seal the superficial epithelial cells.

One treatment approach is to modify the integrity of the corneal epithelium transiently using techniques such as iontophoresis. The role of iontophoresis in clinical ophthalmology remains undetermined. Ocular iontophoresis, however, offers a fast, painless, and safe drug delivery system and can deliver high concentrations to a specific site. Transcorneal iontophoresis of an antibiotic resulted in high and sustained drug concentrations in the cornea and aqueous humor with potential for treating bacterial keratitis and anterior segment infections. With an intact lens, almost no drug reaches the vitreous via this route.

Transcorneal iontophoresis can bypass the lens and deliver drug to the vitreous for treatment of posterior segment infections (e.g., endophthalmitis). In a recent study, iontophoresis was evaluated as a method of delivering dexamethasone for the treatment of endotoxin-induced uveitis in rats. Using a 1-ml reservoir electrode covering the cornea, limbus, and first millimeter of the sclera and a treatment duration of 4 minutes, the authors reported that iontophoresis inhibited anterior and posterior signs of intraocular inflammation as effectively as did systemic administration of dexamethasone. No clinical or histologic damage resulted from the iontophoresis. The lack of adverse reactions has been confirmed by other sources. The investigators concluded that iontophoretic administration of dexamethasone could facilitate treatment of the posterior as well as the anterior segment of the eye and may provide an alternative to systemic administration of glucocorticoids in severe ocular inflammation.

Conclusion

Claims for medication transfer by electricity were made as early as the 1700s, with the first scientific studies pertaining to iontophoresis conducted by Le Duc in 1908. As commercial equipment becomes safer and more portable and with rehabilitation of equine athletes receiving increased attention, treatment via iontophoresis will likely find a role in veterinary medicine. In addition to physical therapy–related indications (e.g., treating tendinitis), this method may potentially be applied in other areas such as veterinary ophthalmology, anesthesiology, and dermatology. In the future, miniaturized iontophoresis systems may become available for long-term administration of certain drugs to animals in which sustained, low plasma drug concentrations are desired.

References

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