Iontophoresis Basics
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A product that is certain to change the way medications are delivered to animals was introduced at the recent American Association of Equine Practitioners meeting. Iontophoresis, also called ion transfer, makes use of direct current to drive water soluble medications into subcutaneous tissue. Iontophoresis is an attractive mode of drug delivery for the equine practitioner because of the minimal ionic concentrations required for its effectiveness, and because of its non-invasive nature.

Historical Background of Iontophoresis.
Athough it is new to the equine industry marketplace, iontophoresis is not a new modality. Drugs have been successfully introduced into the tissues below the skin surface by means of electric current since Fabre-Palaprat recovered iodide in the urine following its electrical transfer in 1833. The safety and comfort of this method of drug transfer is pointed out in the use of zinc ion transfer for corneal ulcers in 1929, and in calcium ion transfer through the eye for the treatment of diseases of the eye in 1932. Bee venom was used in therapeutic iontophoresis in 1938. In 1940, epinephrine was administered to asthmatic patients by electricity. It was observed that when the drug was deposited in the skin in this manner, it was absorbed gradually and the supply was available for a period of time. Histamine ion transfer was advocated in 1944, for the treatment of subacromial bursitis. The versatility of this procedure is indicated in the broad spectrum of ions used in the early days. Because current levels are low, indications and contraindications of iontophoresis pertain to the ion selected and its physiological action in the tissues, rather than to the use of electricity. The electrical current merely repels the drug ion through the skin pores and the hair follicles.

Iontophoresis was approved by the FDA in the 1970's. The use of this modality is increasing in human physical therapy and orthopedic medicine for the treatment of injury, arthritis, and over-use syndromes. Each year over 4 million people successfully receive drugs delivered by iontophoresis.

Theoretical Basis of Iontophoresis:
The Greek ion or iontos refers to an atom having a negative or a positive charge as a result of the loss or gain of one or more electrons. Phoresis refers to being carried. A direct electric current provides the electromotive force to move the ionized particle of the drug past the barrier of the skin and into the deeper tissues. The route of entry is through the pores, the sweat glands, and the hair follicles. Additionally, the overall resistance of the skin will decrease somewhat under the influence of electricity, allowing further passive passage of the drug into the dermal layers. The skin acts as a reservoir of the drug, extending its release into the deeper layers after the iontophoresis device is removed.

An iontophoresis device consists of:
1. A low voltage direct current generator, the power source. Modern units are the size of the palm of the hand and are powered by a 9-volt alkaline battery.

2. Lead wires consisting of a positive lead and a negative lead. One unit has dual channel capability, enabling treatment of two different sites at once.
3. Electrodes, consisting of a buffered drug containment electrode for delivery of the drug, and the grounding electrode, also called the dispersive or return electrode.

The central process of iontophoresis is the movement of ions. The basis of ion transfer lies in the principle that like poles repel and unlike poles attract. Ions, being particles with a positive or a negative charge are repelled in to the skin by an identical charge the electrode places over it. When a direct electric current activates the electrodes, anions in the solution, ions with a negative charge, move toward the positive electrode. Positively charged ions (cations) move toward the negative electrode. The electrical current will drive ions through the skin that would not be absorbed passively. The quantity of ions that are made to cross the skin barrier is directly proportional to the current density and to the amount of time the current flows through the solution. Current density is determined by the strength of electric field and electrode size. Most units use a current strength of 0.4mA, or 1mA per square inch of electrode surface. This current strength is just below sensory perception. Smaller electrodes concentrate the current, making it more readily felt by the patient.

Another factor that determines ion flow is the weight of the ion molecules. Examining the delivery efficiency of three differently weighted drugs, Phipps et al. found that sodium, the lowest weighted ion of a group that also included magnesium, potassium, and calcium, had the highest delivery efficiency. Elements of low atomic weight, less than 8,000 daltons, migrate much faster than those of high atomic weight. Such drugs include:

1. local anesthetics such as lidocaine
2. antibiotics such as gentamicin and ceftiofur
3. corticosteroids such as dexamethasone
4. NSAIDS such as phenylbutazone and funixin meglumine

A solution with a high concentration of ions will not increase the number of ions transferred. Indeed, a solution with a high concentration of ions may have a low delivery efficiency. Several investigators have demonstrated that medication at concentrations of between 1 and 5 percent are optimal for ion transfer. An analogy could be made to a doorway through which a finite number of people can pass at any given time. Because of competition for space at the doorway, one way to allow more people to pass through would be to keep it open longer. Increasing the number of people at the door would only create congestion. Optimal dosages for most drugs are achieved in treatment times of 10 to 20 minutes.

Continuous direct current is the current of choice for iontophoresis, since this mode ensures the maximum ion transfer per unit of applied current. It provides a constant, unidirectional electrostatic field between the electrodes to allow continuous transmission of drug. Other forms of current, such as high-voltage galvanic, sine wave, interferential, and microcurrent are not effective in iontophoresis.

Applications of Iontophoresis:
In the past, human patients faced a risk of mild burning or a prickling sensation under

iontophoresis electrodes. For this reason, lidocaine hydrochloride was added to the delivery electrode, along with the desired drug. Recent advances in electrode technology as well as in current modulation have eliminated the need for lidocaine to reduce sensation from the electrodes. These advances have also made it possible to deliver more drug in less time. Skin pH at the electrode can affect ion transfer so buffered electrodes provide the most efficient delivery. As with any other approach to drug delivery, iontophoresis must follow a complete veterinary evaluation and diagnosis to determine the nature of the injury, its location and extent.

In iontophoretic drug delivery, it is critically important that the drug is applied through the electrode with the appropriate polarity, that is, a drug with a negative charge is applied with the negative electrode. If the polarity is reversed, there will be no drug delivery.

Before applying the electrodes, inspect the area of skin to be treated, looking for abrasions, lacerations, scar tissue, or inflammation. Damaged skin is more sensitive to electrical current and may make the application uncomfortable or cause irritation at the delivery site. Clean the area thoroughly to remove oils, dirt, sweat, or other medications. Treatments should take place in a clean, well lighted area where the horse can relax. Iontophoresis is well tolerated by the horse.

Prepare the delivery electrode by attaching the appropriate lead wire and filling the drug reservoir pad with at least 6cc of solution. Place it over the treatment site and apply a wrap to secure it in place. To prepare the ground, or return electrode, attach the wire of the opposite polarity and apply a dab of transmission gel on the karyra gum pad or wet it with water to increase its conductivity. This electrode is placed on the same side of the body, about four inches away from the delivery electrode and wrapped in place. The electrodes have an adhesive backing to hold them in place, but additional wraps are recommended to ensure good contact and maintain electrode placement. Maintaining contact between the skin surface and the electrode is essential to obtain optimal current flow and to avoid uneven current density. Generally, shaving the hair coat is unnecessary, although a very thick coat may inhibit good contact between the electrode and the skin.

One device on the market today has a built in ramping mode to slowly increase the current to delivery level. At the end of treatment, the current is automatically ramped down to 0. This ramping procedure allows a more gradual increase or decrease in current resulting in a comfortable treatment without the sensation of being shocked. The delivery electrode can be left in place for additional time to allow for any passive absorption of the medication that may occur. Treatments are usually given every other day for one to eight weeks. Generally, results are seen within the first few treatments.

Iontophoresis can be used along with, and in many cases may enhance, other forms of physical therapy. Stretching exercises are used to increase range of motion and are useful in reducing muscle spasm or in elongating scars or adhesions. Electrical stimulation, low level light, or magnetic fields can be used to maintain pain relief and edema reduction. Therapeutic ultrasound reduces muscle spasm, increases membrane permeability, and increases absorption of the ions.

Pointing out the compatibility of iontophoresis and other physical therapy modalities, iodine was used for its sclerolytic effects in addition to ultrasound and stretching. The results of this case

study of post-surgical scarring in a tendon were complete pain relief and normal range of movement in five treatments.

Specific Uses of Iontophoresis:
Corticosteroids are the primary drugs used with iontophoresis in human physical therapy. Formulated as a water soluble salt, the corticosteroid molecule has a negative charge. Dexamethasone is often administered by iontophoresis in the treatment of joint or musculoskeletal disorders. In a comparative study of three different approaches to over-use injury of the shoulder, iontophoresis provided the most rapid resolution to muscular pain. Orally administered muscle relaxant and analgesic medications were given to one subject group, while another group received treatment with hot packs and ultrasound. The iontophoresis treated group received 1cc of 0.4% dexamethasone sodium phosphate and 2cc of 0.4% lidocaine hydrochloride. Although all three treatment procedures resulted in increased pain-free range of motion, the subjects receiving oral medication had the least increase and those receiving iontophoresis had the most. The investigators felt that this was because the iontophoresis administered the medication directly to the target tissues.

In another study, 50 patients with various musculoskeletal conditions including epicondylitis and tendonitis, were treated with dexamethasone sodium phosphate and xylocaine. All showed positive results within 24 hours after the first treatment. Cumulative effects of up to three treatments in a one week period resulted in permanent relief in some cases.

A case report of gouty tophi and osseous degeneration, which would be equivalent to degenerative joint disease in the horse, showed positive response to lithium iontophoresis. The patient reported immediate improvement following the first treatment. Subsequent treatments resulted in complete relief of edema and pain.

Calcific deposits are amenable to treatment with the acetate ion found in acetic acid. A reduction in the density of the deposit and in the size of the deposit was confirmed by x-ray. Two investigators reported the results of applying acetic acid solution to bursal calcification, tendon sites, and myositis ossificans. Radiographs three months after treatments showed complete absorption of the heavy calcific deposits seen before treatment.

An unpublished study examined the reproducibility of iontophoretic drug delivery to the hock joint of the horse. Using three horses, 6 hock joints were treated with betamethasone at three different concentrations and three different treatment durations. The data indicated a 2.4% solution of betamethasone administered in a 40-80mA/min dose was optimal. These parameters were found to deliver betamethasone concentrations considerably above estimated therapeutic concentrations as proposed by Lillich.

Copper sulfate has been used to treat fungal infections such as tinea pedia (athlete's foot) with marked improvement in 24 hours. Perhaps this could lead to investigations of iontophoresis treatments for white line disease or fungal skin diseases in horses.

Benefits of Iontophoresis:
Iontophoresis offers the benefits of being painless and non-invasive. In addition, there is no

danger of infection or damage due to needle insertion or to impact from a bolus of fluid. The local concentration of the drug is high, while the systemic concentration is minimal. Only minute amounts of the drug reach the systemic circulation, greatly reducing side effects. Drug dosage is accurately controlled by controlling the quantity of electrical current used to transfer the drug. For areas such as the distal tarsal joint or around the hoof, where injection is difficult, iontophoresis offers an alternative mode of drug delivery. As the medication passes through the tissues, the peri-articular tissues, as well as the articular surface, are bathed in the medication. Exposure to mild electrical current provides added therapeutic effects. Contraindications with this modality pertain to sensitivity to the drug rather than to the modality itself. The manufacturer suggests avoiding electrode placement so that the current pathway crosses the heart or the brain. Also the area of the eye should be avoided. Abraded skin or new scar tissue should be avoided as these areas are sensitive to electrical current, making the treatment uncomfortable.

The equipment available today is efficient and miniaturized. The possibility of shock or burns, a problem with iontophoresis in the past, are now eliminated by advanced electrode design and modulated current. Iontophoresis has the potential to provide substantial benefits when this mode of therapy is applied in the appropriate manner. There is little doubt that many substances can be introduced into the body by this method. Iontophoresis offers a means of introducing medications through the surface of the skin in a safe, easy and painless manner. As with many new modes of therapy, however, there is need for more studies that document the use and effects of iontophoresis in various clinical situations.

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Additional Reading & Links:
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Update: March, 2001

For last two years a few pioneering veterinarians have been experimenting with the following "cocktail" for conditions such
as ring bone, chronic wind puffs, suspensory problems and bow tendons.
The work using this "cocktail" is unpublished as of this date, but so far appears to be quite promising.

1.5 cc of Dexamethasone (Neg.)
.5 cc Depo Medrol (Neg.)
1.5 cc Sarapin (Pos.)
3.5 cc Total

Other: For calcium deposits:
1.5 cc Saline (Neg)
2.0 cc Apple Cider Vinegar (Pos.)
or
1.5 cc Saline Neg
1.0 Apple Cider Vinegar (Pos.)
1.0 cc Sarapin (Pos.)