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Iontophoresis in Physical Therapy: A Review of the Literature

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IONTOPHORESIS IN PHYSICAL THERAPY: A REVIEW OF THE LITERATURE

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This Independent Study, submitted by Kurt D. Olson in partial fulfillment of the requirements for the Degree of Master of Physical Therapy from the University of North Dakota, has been read by the Faculty Preceptor, Advisor, and Chairperson of Physical Therapy under whom the work has been done and is hereby approved.

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Signature Kurt Olson

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ABSTRACT

Currently iontophoresis is used by many physical therapists on a variety of pathological conditions. Therefore, therapists must have a thorough understanding of this modality as to provide the best, most efficient care possible to our patients.

The purpose of this study is to provide clinicians with a review of the available literature on iontophoresis in physical therapy. The history and principles of iontophoresis are briefly discussed, followed by a review of the clinically performed studies. This section includes studies related to pain and range of motion, tissue repair, movement of fluids, and other diagnoses. Animal and in vitro experimental studies will accompany many of the clinical studies.

Many of the studies reviewed demonstrated relatively favorable results, but some of these were conducted in a non scientific manner. The decision to use iontophoresis must be made on an individual basis, and the therapist should make this decision only after reviewing the available literature on the specific case.

CHAPTER 1

INTRODUCTION

HISTORY

Iontophoresis has had many names throughout history, including; iontransfer,[1] iontherapy, ion medication, galvanoionization, and medical ionization.[2] These similar terms all have a common meaning being the propulsion of ions through a membrane with the use of electricity.

In 1747, Veratti used iontophoresis to drive ions into tissue, and this may be the first documented use of iontophoresis as we know it today.[2,3] The inception of iontophoresis for medical purposes came about with the work of Leduc in the early 1900's.[4,5] This involved the iontophoresis of strychnine into rabbits ears causing them to die a few minutes after the current was initiate.

The equipment used for iontophoresis has changed throughout history. In 1939, a study on the iontophoresis of copper into the hands and feet of subjects, utilized four pans of water and copper electrodes.[6] The original power source in this study was a battery to which a rheostat was connected. The authors indicated that there was potential for shocking the subject based on the make-break phenomenon. Eventually they constructed a device in which 110 volt

current was rectified to direct current. A similar battery power source was used by Rapperport et al[7] in 1965. The electrodes in this study were assembled using gauze saturated with aqueous solution of the chosen drug, lead electrodes, and connection alligator clips.

Today the power sources range from the typical line-operated DC generator to a battery powered, computerized, programmable device.[1,2] Depending on the physiological effects desired and drug chosen, some electrode configurations continue to use the gauze and tin foil electrodes[8] similar to that used by Rapperport.[7] Many of the current systems and common drugs can be applied utilizing patch electrodes with a self-containing pouch for the drug.[9]

PRINCIPLES OF IONTOPHORESIS

In the most simple terms, iontophoresis is defined as driving specifically charged ions through the skin by the use of a specific electrical charge.[5,10] Ions are charged particles and like charges repel.[1] Therefore if a drug is placed between the skin and the active electrode of the same charge, using DC galvanic current, the ions will be driven into the tissue below. The attraction of the ions towards the dispersive electrode (opposite charge) is insignificant in the iontophoresis process according to Barry.[10]

Studies show evidence that the most probable avenue for ion transfer is by way of the sweat glands.[2,11,12] However, the specific mechanism of transfer for some drugs has not

been established.[13]

Historically, continuous galvanic current has been the current of choice in iontophoresis.[1,8,14] Bagniefski and Burnette[15] compared pulsed and continuous currents in the iontophoresis of Na ions on excised mouse skin. They observed no significant difference in the ion transfer between pulsed or continuous galvanic current. Pikal and Shah[14] found similar results showing a slight decrease in ion transfer with pulsed current. An in vitro study by Thysman et al[15] concluded that continuous DC current was more efficient than pulsed. As the duty-cycle or pulsed current was decreased, the ion transfer also decreased.

DOSAGE

The quantity of ions delivered to the tissue for therapeutic purposes will depend on three factors:[8] 1) Current density under the active electrode where higher density increases ion transport, 2) Time which current is allowed to flow,[2] and 3) Concentration of ions in the solution. A low concentration of ions is recommended for iontophoresis.[1,16] A formula using the specific electro-chemical equivalency (ECE) is used to determine amounts of ion transfer.[1] Intensity (amperes) X Time (hours) X ECE = grams of ion transferred.

PURPOSE

Currently iontophoresis is used by many physical therapists on a variety of pathological conditions. Third-

party payers, physicians, and patients are beginning to demand proof that treatments are effective and efficient. Therefore, therapists must have a thorough understanding of this modality and which treatments are or are not supported by research. The purpose of this study is to provide clinicians with a review of the available literature on iontophoresis used in physical therapy.

CHAPTER 2

CLINICAL STUDIES: LITERATURE REVIEW

PAIN AND RANGE OF MOTION

Many disorders have pain, inflammation, and/or muscle spasms as signs and symptoms. A complex cycle can form among the symptoms with pain causing inflammation and/or muscle spasms. Each of these can cause an increase in symptoms and ultimately a spiraling cycle is formed.[17] As the cycle continues, function in the involved area diminishes.

Range of motion (ROM) is one of the early functions to be limited. Although ROM is not directly affected by the iontophoretic delivery of specific substances, it can be altered through reductions in pain. The goal of iontophoresis is to utilize a specific drug, depending on its pharmacological effect, to break the pain cycle and restore the patient to the highest level of function possible.

Dexamethasone sodium phosphate (DSP) is a commonly utilized analgesic drug used in iontophoresis.[18] A study by Glass et al[19] found measurable amounts of DSP could transfer down to and including tendinous and cartilaginous tissue though the use of iontophoresis. DSP and lidocaine

hydrochloride are two substances frequently used in combination during iontophoresis.[20] The lidocaine has an analgesic effect, while DSP is used in many inflammatory conditions.

Petelenz and associates[21] researched the delivery of DSP combined with lidocaine in in vivo and in vitro studies. The in vitro studies demonstrated that significant amounts of DSP were delivered when the two drugs were combined, but the amount delivered nearly doubled when DSP was phoresed as an isolated substance. In vivo studies provided no significant differences, between positive versus negative electrode, in the amount of DSP delivered. A study by Chantraine et al[22] is not in support of this research, and failed to provide evidence of the delivery of various steroids including DSP.

Bertolucci[23] implemented a study to determine the effects of DSP on pain and range-of-motion (ROM). Fifty-three subjects were utilize. Diagnoses included: infraspinatus and supraspinatus tendinitis; adhesive capsulitis of the shoulder; bicipital tendinitis; lateral epicondylitis; and sacroiliiitis. Subjects were randomly assigned to a experimental group or a control group. The experimental group received four treatments of 4 mg/ml DSP combined with 2 cubic cm of lidocaine hydrochloride at 65 mA-min each. Pain levels were assessed on day 1 and 3. The age group which indicated the highest incidence of excellent

benefits was the 18 to 34 year old group. The thirty-five to 44 year old group indicated significant pain reduction while only 41% of the subjects in the >45 age group received any relief from treatment. As the subjects pain decreased their ROM increased.

Weinstein and Gordon[24] studied the effects of iontophoresis on subdeltoid bursitis based on a chart review of 50 randomly selected patients. Treatment involved iontophoresis of a 2% solution of magnesium sulphate at 10-20 mA-min. This was the only treatment administered. In 68% of these cases all signs and symptoms were alleviated and full ROM was recovered.

Treatment of trigger areas in shoulder girdle myofascial syndrome was studied by Delacerda.[25] The study compared the treatment of DSP iontophoresis with a group that received muscle relaxants and pain medication and one that received hot packs and ultrasound. Although all subjects experienced some pain relief, the iontophoresis group experienced complete pain relief after day nine.

A study by Harris[9] examined the effects of iontophoresis on individuals with inflammatory conditions consisting of tendinitis, bursitis, ligamentous sprains, and epicondylitis. Fifty subjects received one to three treatments consisting of 80 mA-min. The utilized drug was 1 cc of 4 mg dexadron and 2 cc of 4% xylocaine. Evaluation of treatment effectiveness was based on active range-of-motion

(AROM), pain, edema, temperature, and function. The results indicated that: 75% of the patients had good to excellent results; 14% had significant decreased pain and increased strength and ROM; and 11% had little to no decreased pain. Delacerda[26] found immediate but short-term pain relief from 2.5% xylocaine iontophoresis. Although the focus of a study by Psaki and Carroll[27] was on calcium absorption, they found favorable results in pain reduction and increased ROM.

Individuals with temporomandibular joint (TMJ) disorders can have secondary symptoms including pain, inflammation, muscle spasms, and decreased ROM.[17,28] Lark and Gangarosa[29] describe a protocol for the iontophoresis of DSP in the treatment of individuals with TMJ disorders. Braun[28] describes the use and results of the iontophoretic delivery of 1 cc DSP and 2 cc lidocaine hydrochloride (4%) in the treatment of TMJ pathology. In this case study, the patient received two 80 mA-min treatments with one day separating the treatments. The patient also performed a home exercise program consisting of AROM, stretching, and rhythmic stabilization exercises. Decreases in pain along with increases in ROM were reported after the initial treatment and continued this progression throughout treatment. Results similar to these were reported by Lark and Gangarosa[29] in several case studies.

A case study by Kahn[30] focused on pain and decreased ROM of the TMJ in a subject following minor surgery for

infected maxillary sinuses. The subject reported complete TMJ pain relief after the second treatment of 100 mA-min iontophoresis of hydrocortisone ointment followed by three minutes of ultrasound. ROM was also increased throughout treatment. Similar relief in pain with hydrocortisone iontophoresis was reported by Paski et al.[31] but findings by other researchers were not as supporting.[19,22]

The purpose of a study by Paski et al[31] was to determine the effectiveness of hydrocortisone iontophoresis on subjects with rheumatoid arthritis (RA) and osteoarthritis (OA). One-hundred white males between the ages of 25 and 65 years old were selected as subjects. Thirty subjects were diagnosed with RA and the remainder had OA. Pain and ROM were assessed at the onset of the study then weekly for three months. Skin condition and x-ray results were assessed where applicable. Treatment areas included the hand, wrists, elbows, shoulders, knees, ankle, foot, toes, and back. Chronic cases received treatment biweekly for at least six weeks and acute cases three times per week for at least six weeks. Each area in question received infrared heat prior to and during treatment. Hydrocortisone ointment was massaged into the effected area and current was applied. Subjects with back involvement received 300 mA-min of iontophoresis while the remainder of the subjects received 60-150 mA-min depending on current tolerated by each subject.

Of the subjects with RA, 90% had pain relief and ROM was restored fully in 50%, but some subjects experienced increased pain initially followed by decreased pain. In 50% of the subjects with OA, pain relented entirely and the remaining cases demonstrated pain reduction. ROM was also fully recovered in 50% of the subjects.

In a study utilizing citrate iontophoresis, Coyer[32] demonstrated only temporary pain relief. Thirty-five subjects with the diagnosis of and acute exacerbation of RA were assigned to three groups. Group 1 received 200-300 mA-min of iontophoresis in a bath containing 2% solution of potassium citrate and distilled water. Group 2 and 3 were both control groups, and received tap water iontophoresis with either negative or positive charge at an average of 20 mA. The treatment time was not indicated for group 2 or 3. Treatment was administered every other day for four weeks.

Subjective reports of significant pain relief were conveyed by 86% of the experimental group, but this effect wore off throughout the immediate day. Of the control groups, 90% experienced no pain reduction, while 30% indicated increased pain and swelling. On the average, grip strength improved in the citrate iontophoresis group but not in either control group.

Kahn[33] used iontophoresis of lithium in a subject with gouty arthritis. He demonstrated immediate short term relief of pain and long term relief after four weekly treatments.

The lithium was transferred at a dosage of 100 mA-min.

Salicylate iontophoresis was found to be effective in eliminating prolonged muscle pain post-surgery.[34] Nearly two months post total hip replacement, the subject developed pain in her rectus femoris. Numerous treatments, including chloride iontophoresis and mecholyl iontophoresis, were attempted with minimal success. After three treatments of salicylate iontophoresis, at 80 mA-min, the subject reported significant pain relief. Two months later, thigh pain returned, but it was eradicated following one salicylate iontophoreses treatment. A one year follow up on this subject indicate no return of thigh pain.

Singh and Roberts[35] have demonstrated the depth of penetration of salicylic acid to be only 3-4 mm. The concentration of salicylic acid at depths >3-4 mm is not significantly greater with iontophoresis than with passive transportation.

Delacerda[26] utilized 12 subjects with shinsplints, six of which had bilateral cases, for a total of 18 cases of shinsplints. The subjects rated their pain as mild, moderate, or severe. During each treatment the subject received 100 mA-min of iontophoresis at 48 hour intervals. A limit was set at a maximum of ten treatments. Complete pain relief was experienced by a group that initially received xylocaine iontophoresis (2.5%). Since pain returned prior to subsequent treatment, the xylocaine treatment was

discontinued after the third treatment and replaced with hydrocortisone (0.5%) for the remainder of the study. One to six (average 3.05) treatments were required to eliminate pain in all of the cases of shinsplints.

Although acute pain may be beneficial, chronic pain linked to neuralgic and neuralgiform pain syndromes appears to serve no real purpose.[36] This type of pain is connected with diagnoses such as: post-discotomie syndrome[37] which can occur following surgical procedures involving the intervertebral disk; post-herpetic neuralgia;[38] terminal pain,[39] metabolic polyneuropathy, and trigeminal neuralgia.

The remainder of this section on pain will focus on the use of vinca alkaloid iontophoresis treatment of subjects with various types of chronic pain secondary to peripheral nerve lesions. The premise behind this treatment is that the vinca alkaloids possess the ability to block the retrograde transmission within the peripheral nervous system.[37,39] Research by Knyihar-Csillik et al[40] supports the physiological and ionic transport mechanisms of these procedures.

Csillik and associates[39] studied the effects of vinca alkaloids on subjects with chronic pain secondary to various diagnoses ranging from intercostal neuralgia to terminal pain (11 different diagnoses). Fifty-one subjects received daily vinblastine (0.01%) or vincristine (0.001%) iontophoresis for eight to 24 days. Subjects each initially

received placebo treatment for seven to 14 days followed by vinca alkaloid iontophoresis. Diagnoses of the limbs and trunk received 600-1800 mA-min of treatment while areas involving the head received 120-300 mA-min. Subjects rated their pain on a scale of <0-0-100 with 100 being total elimination of pain, 0 being no change in pain, and a negative number indicating increased pain. The subjects received no pain relief from placebo treatment. At a one year follow-up, 78% of the subjects had experienced no return of pain, 16% had partial or temporary alleviation of pain, while 6% had felt no decrease in pain.

Long term pain relief was demonstrated by Knyihar-Csillik and colleagues.[40] Subjects (n=48) with approximately 20 different diagnoses and resulting chronic pain were treated with vinca alkaloid iontophoresis. At a one year follow up, continuance of pain relief ranged from 0-100% (mode 100%; mean 91%) with 17% of the subjects experiencing some type of relapse during that one year period. The poorest results and highest rate of relapse were experienced by subjects with trigeminal neuralgia (n=15).

In the study by Csillik et al,[39] pain relief experienced by post-surgical subjects with discopathy was 100% one year post treatment. Penickova and associates[37] reported conflicting results. They[37] used 16 post-discectomy subjects with chronic (5-16 years) nerve root pain, and 20 subjects with chronic nerve root pain in the

dermatomal regions. Numerous conservative and pharmaceutical approaches had failed to provide any measure of long-term relief. Initially a 0.01% solution of vinblastine was used, but this was changed to a protective anode solution allowing for a maximum of 50 ml of 0.01% vinblastine solution. Subjects each received 150-450 mA-min of iontophoresis three to five times per week until a total of ten treatments had been administered.

The measures of treatment effect were based on a pain scale (0-5), a scale rating the effect of pain on ADL's (0-5), and a modified McGill Pain Questionnaire. These three categories were assessed to obtain overall treatment effectiveness (0-5). Mean results from Student's t-tests are as follows: no improvement 0%; negligible improvement < 9%; slight improvement 10%-24%; medium improvement 25%-45%; and considerable improvement > 50%. Although short-term relief was experienced, only one post-discectomy subject had continued relief lasting longer than six months in duration. Sixty-three percent of the subjects had relief for less than three months. The 150-450 mA-min treatment, used in this study compared to Csillik's[39] 600-1800 mA-min treatment, may have been the confounding variable which may explain the differences in long-term results.

A single blind study was carried out by Layman and copartners[41] using subjects diagnosed with post-herpetic neuralgia. The pain in all of the subjects (n=20) had

previously been unresponsive to treatments which included TEN's, opiate analgesics, antidepressants, and subcutaneous infiltration of lignocaine or hydrocortisone.

A solution containing 0.01% vincristine, 0.9% saline, and 5% dimethyl sulfoxide was delivered to the experimental group (n=10) while a control group received only saline iontophoresis. Subjects received treatment three times per week for a total of 12 treatments at 900-1800 mA-min (dependant on subject tolerance). Subjects completed a three-point ordinal pain scale and a visual analogue pain scale (VAS) prior to each treatment and at a six week follow up.

At the close of treatment, 80% of the experimental group showed improvements on the VAS (mean improvement 59%, $P<0.05$) compared to 10% showing improvement in the control group. At six weeks, 60% of the experimental group showed improvements on VAS (mean improvement 27%, $P<0.05$).

Comparable pain relief was demonstrated by Tajti et al[38] when they evaluated 35 cases of subjects who had been treated with iontophoresis for post-herpetic neuralgia. Percentage of pain relief ranged from 28% to 100% (mean 54%). Because these were case studies, treatment parameters varied and are as follows: 1% vincristine was combined with 1% hyaluronidase then mixed with distilled water (30ug vincristine per cm^2 of surface tissue); 60-300 mA-min treatments for areas of the head and neck; 600-1800 mA-min

treatments for the limbs and trunk; each subject receive ten to 30 treatments. These current-time parameters were very similar to those used by Csillik and associates.[39]

Delacerda[25] researched the use of iontophoresis for the treatment of myofascial syndrome. The subjects (n=23) job tasks required them to hold their arm abducted to at least 70° for approximately 15 seconds at a time. Each of the subjects developed what was diagnosed as shoulder girdle myofascial syndrome. Seven subjects received pharmaceutical treatment, eight received hot packs followed by ultrasound, and eight received iontophoresis of 1 cc DSP (0.4%) combined with 2 cc lidocaine hydrochloride. The iontophoresis was delivered at 85 mA-min for 10 days or to elimination of pain, which ever came first. The subjects who received medication continued to have ROM deficits on day 10 along with two from the ultrasound group. By day 9, all of the subjects from the iontophoresis group had full pain-free ROM.

Another potential cause of reduced ROM can be calcium deposits which may occur in untreated tendinitis or deposits which form within the muscle itself. If tendinitis is not treated, calcium deposits can form as a result of decreased blood supply to the effected area.[27]

Absorption of the deposits through acetic acid iontophoresis was the focus of a study by Psaki and Carroll.[27] Each of 12 subjects received iontophoresis of a

3% acetic acid solution for 150-300 mA-min. When the subjects could raise their arm with minimal assistance, exercises were initiated.[27] The authors concluded the following; 1) Calcium deposits were decreased by hyperemia and hyperacidity in 40% of the cases, as this was identified through pre and post-treatment x-ray findings, 2) Joint pain and tenderness disappeared after acetic acid iontophoresis, and 3) ROM may be completely restored following iontophoreses of acetic acid.

Results comparable to these were reported in a case study by Wieder.[42] In a patient with myositis ossificans of the quadriceps femoris muscle, Wieder[42] reported a 98.9% reduction in the calcified mass and the return of full knee ROM following treatment. The iontophoresis consisted of 3 ml acetic acid (2%) for 80 mA-min followed by eight minutes of pulsed ultrasound and passive ROM. Treatment continued three times per week for three weeks.

Popkin[36] performed two case studies to determine the effect of hyaluronidase iontophoresis on scleroderma. Scleroderma is a progressive, systemic syndrome characterized by hardening and thickening of the skin and ultimately decreased ROM. Hyaluronidase hydrolyses hyaluronic acid[36] is a substance which plays a part in the arrangement of the collagen matrix. Popkin[36] performed two case studies to determine the effect of hyaluronidase iontophoresis on scleroderma. In both of the studies he

found that during treatment signs and symptoms were diminished and the subjects perceived substantial benefits including increased ROM. The benefits were determined to be only short-term.

The iontophoresis of iodine ion was used by Langley[43] to treat tendon adhesions, and Tannenbaum[44] in reducing post-surgical scar tissue. Both case studies utilized an Iodex ointment at and 80 and 100 mA-min of treatment respectively. After five consecutive daily treatments, Tannenbaum[44] found the return of normal ROM and an increase in muscle strength from trace to good. At a six month follow-up both ROM and strength were normal. Langley[43] found similar results after three daily treatments. These two case studies demonstrate the possibility of scar reduction through the use of iontophoresis.

TISSUE REPAIR

The physiological basis and the value of zinc ions in tissue repair has been discussed by various researchers.[4,45] When zinc is introduced into the tissue, insoluble precipitates are formed with tissue components, and this aids in the epithelialization of granular tissue.[45] Zinc ion is also considered to be antibacterial.

Cornwall[46] investigated the clinical effectiveness of zinc iontophoresis in healing ischemic ulcers. The subject had bilateral ulcers secondary to BK amputations. In this case study, zinc-oxide ointment (0.1 mole solution) was

applied proximal to the lesion and transferred into the underlying tissue with approximately 68 mA-min iontophoresis b.i.d. for 20 days. The author demonstrated >98% closure of both ulcers at the end of the 20 day period.

Abramson and associates[47] studied the effects of histamine iontophoresis on 14 subjects with various ulcers. The affected extremity was placed in a solution (0.0001%) of histamine diphosphate, and iontophoresis was administered at 60 mA-min two to three times per week. Complete healing of trophic changes occurred in four of the subjects with progressive systemic sclerosis (n=5), while the fifth subject showed some improvements. Subjects with sickle cell anemia (n=4), neurotrophic ulcers (n=1), and venous stasis ulcers (n=1) all demonstrated improvements, while those with ischemic ulcers secondary to arteriosclerosis (n=3) showed no improvements.

Recurrent herpes labialis (RHL) are lesions caused by herpes simplex virus (HSV).[48] If left untreated, HSV can lead to blindness, encephalitis, and cancer. Healing of the lesions usually requires seven to ten days which allows the lesions to transmit to other areas of the body or to other individuals through venereal contact. Burning, itching and severe scabbing generally accompanies healing.

Gangarosa et al[48] performed a study which produced 20 separate trials, six control (C) and 14 experimental (E), from six subjects. The C group (non-blind) received no

treatment while the E group received 3-5 mA-min of idoxuridine solution (0.1%). Treatment duration was until healing was complete usually within 3.4 days (+-0.3) for E compared to 8.8 days (+-1.1) for C group. The lesions in the E group also healed with less discomfort and scabbing. MacCullum and Jensen[49] reported a comparable average of 8.9 days for healing in treatment by topical idoxuridine ointment without the assistance of iontophoresis. Gangarosa and associates[50] feel the reason that topical ointments are unsuccessful is not due to drug ineffectiveness, but secondary to lack of ion transfer without the assistance of iontophoresis.

Herpetic whitlow is another type of lesion generally caused from HSV.[51] The lesions occur on the fingers which provide for an easy method of transmission to additional body regions or other individuals. Gangarosa and collages[51] reported on two case studies involving the iontophoresis of idoxuridine (0.1%) in two subjects with herpetic whitlow. Each lesion was treated with at least 0.5 mA of current for ten minutes, and larger lesions received proportionately increased dosages. One subject exhibited a 60% decrease in healing time and an 80% reduction in severity. This subject experience no return of the lesions at 38 months post-treatment. A second subject experience decreased pain, resolved HSV lesions, and lacked recurrent lesions at 48 months post-treatment.

Twenty-seven subjects diagnosed with RHL of the oral region participated in a double blind, placebo controlled study conducted by Gangarosa and associates.[50] The study utilized one control group (C) and two experimental groups (E_1,E_2). E_1 received iontophoresis of vidarabine monophosphate (5.2% solution), E_2 received acyclovir (3.5% solution), and C received NaCl (0.9%) solution. These concentrations allowed for an equal number of ions per ml of solution. Current-time settings were at 4.0 mA-min for all subjects, and a total of eight treatments were administered over a three week period. The E_1 group had significantly lower ($P<0.05$) titers of the virus than either E_2 or C after a 24 hour period, but the number of healing days was not significantly different. The authors suggested that a single treatment with vidarabine monophosphate may be sufficient to offer significant benefits.

The purpose of three case studies by LaForest and Cofrancesco [52] was to study the treatment of burned ears with gentamicin sulphate iontophoresis. Two subjects (S_1 & S_2) were positioned in sideling with the burned ear immersed in a gentamicin sulphate solution (5mg/ml water) at 5-10 and 35 mA-min respectively. One subject (S_3) received gentamicin sulphate (8mg/ml water) iontophoresis at a dosage of 75 mA-min. S_3 used a solution soaked gauze pad electrode for ion transfer. S_1 experienced epithelialization after 12 treatments/7 days, and had no recurrence at 27 months.

Epithelialization for S_2 occurred after 24 treatments/13 days and the subject suffered no recurrence at 8 months. The ear of the final subject, S_3 had healed following 28 treatments over a 15 day period. This subject experienced no recurrence at 18 months post-treatment. Sela and associates[53] propose molding a prosthetic device for the ear to eliminated the need for ear immersion during iontophoresis.

The transfer of antibiotic ions is supported by Rapperport et al.[7] In a double blind study, they demonstrated significant ($P<0.01$) levels of penetration of penicillin through burn eschar. This research involved studies of both human and animal subjects.

The purpose of a study by Haggard et al[6] was to determine the effect of copper iontophoresis on fungal infections of the hands and feet. Iontophoresis was administered to 37 subjects who had been diagnosed with dermatophytosis. Each subject received treatment two or three times per week at a dosage of 80-120 mA-min if one extremity was treated or 160-200 mA-min if both extremities were treated simultaneously. If the hands were infected they were place in a 0.2% copper sulfate solution with the active electrode while the feet were place in a saline solution with the dispersive electrode. This arrangement was reversed if the feet were infected, and if both were infected the subject received two 20 minute treatments. Seventy percent

of the subjects obtained a clinical cure after an average of six treatments. Eighty-eight percent of these subjects ere followed for a period of three to six months, with 22% suffering some type of recurrence.

Jersild and Plesner[54] followed-up 35 subjects who had received copper iontophoresis (0.001% solution) in the treatment of epidermophytia of the hands and feet. Iontophoresis was administered at 100-300 mA-min every other day for a total of two to five treatments (85%) or six to 11 treatments (15%). Of these 35 subjects, 87.5% had experienced no reappearance of the epidermophytia.

It has been demonstrated that silver ions are effective bactericidal agents.[55,56] Becker and Spadaro[55] studied the effects of silver ion on chronic osteomyelitis with non-union of the bone. Prior to iontophoresis, surgical debridement was used to remove necrotic tissue and drain infection. Two separate treatment protocols were used. One of the protocols consisted of a pure silver wire electrode that was implanted into the bone if wounds could be surgically closed. These subjects received continuous iontophoresis at 1 microampere per centimeter of exposed wire for the first 24 hours. The dosage was then reduced to 100 nanoampers. This dosage was maintained for approximately six weeks until 1.5 to 2.5 joules of total energy were delivered. An alternate protocol was used when the wound was required to be left open. This involved using a silver

impregnated nylon fabric as the electrode. This nylon material was packed into the wound site and wrapped with a sterile dressing. Current was regulated at 0.9 volts.

Control of the infection was achieved in 12 out of 15 treatments. Healing of non-unions also occurred in these 12 subjects after a period of 3-36 months. Control of the infection was not complete in the remaining three treatments.

Satyanand and associates[56] used procedures very similar to the first treatment technique used by Becker and Sparado.[55] Out of the 50 subjects treated, 22 experienced good outcomes, 18 fair, and ten poor. The best results were experienced by those with Staphylococcus infections (38%), and the poorest results by subjects with Proteus infections (14%).

The silver impregnated fabric method of ion transfer is supported by Falcone et al.[57] They demonstrated significantly larger inhibitory zones when the silver iontophoresis was versus control groups.

MOVEMENT OF FLUIDS

Iontophoresis may be used to effect fluid flow in an attempt to: 1) Control edema; 2) Increase blood flow and nutrients to an injured area; or 3) In some cases, such as hyperhidrosis, the clinician wants to decrease the flow of fluids.

The purpose of a study by Schwartz[58] was to determine

the effectiveness of hyaluronidase by iontophoresis in treating lymphedema. Hyaluronidase decreases the viscosity of fluids allowing them to move freely within the circulatory system. The subjects (n=5) extremity was wrapped in a cloth containing hyaluronidase dissolved in an acetate buffer solution. Control iontophoresis treatments (inert buffer solution) were randomly substituted for the hyaluronidase treatments throughout the study. Each subject received 400-600 mA-min of iontophoresis. Volumetric measurements were taken pre and post treatment. Results indicate that the treatment was effective, but carry over between treatment required the use of an elastic compression wrap over the effected extremity. The control treatments (mean=4.8) had and 18.4 cc mean reduction in volume compared to the hyaluronidase treatment (mean=20.6) which had a 224.1 cc mean reduction in volume.

Kahn[33] demonstrated elimination of soft tissue edema after four treatments in a single case study involving a subject with gouty arthritis. The iontophoresis consisted of a 2% solution of lithium chloride delivered at 100 ma-min per treatment.

Kovacs et al[59] have established that Acetyl-B-Methyl-Choline (ABMC) is a strong vasodilator. Macht and associates[60] studied the effectiveness of ABMC (0.2%) iontophoresis on blood flow. A total of 31 separate experiments were performed on six subjects. Blood flow was

measured using a venous occlusion fluid-air plethysmograph. The subjects initially rested in a temperature controlled experiment room for one hour. The hand was then placed in the temperature controlled ABMC bath for 30 minutes, after which a baseline blood flow measurement was taken. Iontophoresis was then carried out at 300-540 mA-min with blood flow measurements taken at five to ten minute intervals. Significant increases in blood flow (up to 20 times the control) were demonstrated by the iontophoresis of ABMC. The 2 controls (ABMC immersion without current and iontophoresis of saline solution) experienced no significant changes in blood flow. Parameters very similar to these were used by Abramson et al[61] with the exception of decreased current-time dosages (5-15mA for 10-20min). This study included tests on the forearm (n=17), leg (n=8), and foot (n=5). It was demonstrated that the increased blood flow during ABMC iontophoresis returned to near baseline after an average of 33-58 minutes post-treatment. The study also showed that the vasodilatation which occurred during iontophoresis was primarily in the superficial/cutaneous circulation rather than in the deeper vessels.

Abramson et al[47] conducted a study on 16 subjects to determine the effect which histamine iontophoresis has on blood flow and blood oxygen content. Blood flow was measured with a segment type venous occlusion plethysmograph, and blood oxygenation was measured by the manometric method. The

oxygen uptake was calculated using the Fick principle. The histamine diphosphate solution (0.0001%) was transferred using 140-300 mA-min iontophoresis. The results of this experiment show a significant increase in blood flow during treatment which continued for approximately 65 minutes after the iontophoresis ended. In 93% of the experiments, calculated oxygen uptake fell during early treatment. While 60% of these remained below the baseline throughout treatment, 40% rose back to baseline or above. The authors offered several possible explanations for this occurrence.

Hyperhidrosis is a condition in which the individual experiences excessive, abnormal sweating of the hands, feet, axilla and/or trunk.[62] Shrivastava and Singh[63] researched the use of tap water iontophoresis in hyperhidrosis. Thirty subjects with plantar and palmar hyperhidrosis completed this study. The 30 subjects were divided into three groups, each with two subgroups. Group 1 received iontophoresis with both electrodes in the same pan, and one subgroup received a dosage of 400 mA-min compared to 625 mA-min for the remaining subjects. In group 2 the electrodes were not placed in the same pan, and treatment time varied providing a dosage of 150 mA-min for one subgroup and 250 mA-min for the other. Treatment dosage for group 3 varied from 150-400 mA-min depending on the subjects tolerance. Water level in all treatments was adjusted to just cover the palmar or plantar surface. Anhidrosis was experienced by all 30

subjects. Variation in treatment dosage did not demonstrate significant increased benefits ($P>0.05$), but the number of treatments required for anhydrosis was significantly less ($P<0.01$) when electrodes were place in separate pans. Mean duration of anhydrosis was 5.86 months, but this varied from subject to subject and treatment group to group.

Other researchers[64,65] have demonstrated that tap water iontophoresis provided only short term benefits, and was not as effective as using an anticholinergic solution. Grice et al[64] compared the iontophoresis of tap water to a poldine methosulphate (PMS) solution (.05%-.075% solution) in the treatment of palmar, plantar, and axillary hyperhidrosis. Method of current delivery was similar to that used by Shrivastava and Sing[63], but subjects with axillary hyperhidrosis were treated with a gauze covered electrode soaked in the chosen solution. Iontophoresis was administered weekly for six to eight weeks. The dosage for the hands and feet was 15-20 mA-min and 10-15 mA-min for the axilla. Nine subjects received PMS iontophoresis while the other received tap water iontophoresis. In each subject, one side of the body received iontophoresis while the other did not, thus providing a control.

Neither tap water nor PMS provided adequate control of axillary hyperhidrosis. While PMS provided quicker and generally a longer duration of anhidrosis, neither treatment provided long term relief. These authors agree with Morgan[66]

in that there is a possibility for a systemic effect and side-effect when using anticholinergic solutions. Table 1 summarizes research studies on iontophoresis.

Table 1. Substances Delivered by Iontophoresis

Substance	Polarity[a,b]	Purpose/Pathology	Reference
Acetic Acid	NEG	Calcium Deposits, calcified tendinitis	27,42
Acyclovir	POS	Herpes simplex	50
Atropine sulfate	POS	Hyperhidrosis	62
Calcium	POS	Frozen joints	1
Chlorine	NEG	Muscle pain	34
Citrate	NEG	Rheumatoid arthritis	32
Copper	POS	Fungus infection	6,54
Dexamethasone	POS	Inflammation, myofascial syndromes arthritis, TMJ	9,19-21,23,25 28
Glycopyrronium Bromide	POS	Hyperhidrosis	62,66
Gentamicin sulfate	POS	Ear chondritis, antibiotic	52,53
Histamine	POS	Ulcers, blood flow	47
Hyaluronidase	POS	Absorption enhancement, edema, scleroderma, lymphedema	36,38,58
Hydrocortisone	POS	Arthritis, tendinitis, myositis, bursitis, chronic pain, TMJ	1,22,26,30
Idoxuridine	NEG	Herpes simplex	48-51
Iodine	NEG	Sclerotic, fibrosis, adhesions, scar tissue, trigger finger	43,44
Lidocaine	POS	Inflammation,Skin anesthesia, TMJ, pain, arthritis	9,20,23,25,26 28,29,35
Lithium chloride	POS	Gouty tophi	33
Magnesium	POS	Muscle relaxant, vasodilator, pain, inflammatory conditions	1, 24
Mecholyl	POS	Vasodilator, ulcers, arthritis, ischemia edema	34,59-61
Penicillin	NEG	Infected burn wounds, antibiotic	7
Poldine methylsulfate	NEG	Hyperhidrosis	62,64
Salicylate	NEG	Analgesic, scar tissue,adhesive joints, pain, inflammation, edema	1,34,35,43
Silver	POS	Chronic osteomyelitis, bactericidal, ulcers	55-57
Vidarabine Monophosphate	POS	Herpes simplex	50
Vincristine/-blastine	POS	Chronic pain, post-herpetic neuralgia, trigeminal neuralgia	37-41
Water	POS/NEG	Hyperhidrosis	62,63
Xylocaine	POS	Shin splints	9,26
Zinc	POS	Asepsis, ulcers, dermatitis, wound healing	4,45,46

[a] NEG = Negatively Charged Substances
[b] POS = Positively Charged Substances

CHAPTER 3

CONCLUSION

Iontophoretic procedures as used in physical therapy related conditions have been explored. Numerous studies concentrated on decreasing pain and increasing ROM in various pathological conditions. Several relatively objective studies on primarily acute pain indicate favorable results, but other research is not in total agreement. The relief of chronic pain is well documented and supported by various researchers, but the effects may be only short term. Iontophoresis use by physical therapists to assist in tissue repair is not new. Conditions commonly treated include ulcers, burns, HSV lesions, and fungal infections. Iontophoresis has also been used as a bactericidal agents. Research supports the use of iontophoresis in treating neurotrophic and venous stasis ulcers. Iontophoresis has also been used in an attempt to control edema, increase blood flow, and decrease sweat production. While most research indicated favorable results, the effects were not always found to be long term.

Repeated research on a single condition, with a specific drug, were rather limited. In my opinion, the

majority of these studies were non scientific, with no control groups. Most studies did not include specific treatment guidelines. Although the studies contained clinically applicable information, most of them were unable to demonstrate any level of cause and effect.

From this independent study I have formulated two recommendations. First, that clinicians continue to perform research while striving to conduct it in a more scientific manner. This is needed to provide proof of efficiency to those who are currently requiring it. Second, I would recommend that therapist utilizing iontophoresis do so in an informed manner. The decision to use iontophoresis should be based on an experimental foundation considered specifically for the ion and pathological condition in question.

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