Iontophoretic Treatment of Herpetic Whitlow

Louis P. Gangarosa, Sr., PhD, DDS, Larry J. Payne, MD, Kataro Hayakawa, MD, W.J. McDaniel, MD, Richard E. Davis, MD, Barry M. Thompson, MD


Herpetic whitlow can be a vector for spread of infection, especially among health care professionals. Until now, treatment has been inadequate. In two patients with documented herpetic infections of the finger, the antiviral drug idoxuridine was applied to the lesions by cathodal iontophoresis. Results were characterized by rapid relief of discomfort and swelling, rapid appearance and coalescence of vesicles, and rapid healing, with reduced pain and little or no paresthesia. No recurrences have been noted in the two patients after 42 and 38 months. The positive beneficial results indicate that aggressive iontophoretic treatment for herpetic whitlow is useful and justified.

KEY WORDS: Antiviral; Herpetic whitlow; Iontophoresis

Although herpes simplex viruses (HSV) are capable of infecting any tissue in the human body, they appear to have a preference for mucocutaneous junctions and other highly keratinized external surface tissues. The human finger is occasionally involved, especially among health professionals who contact HSV during patient examination and manipulation. Also, the finger may serve as a vector for spreading the virus, not only from the lesion site to other areas of the skin or mucosa, but also to other persons.

The term "whitlow" originally referred to a painful, pus-producing lesion; in fact, HSV are the usual cause of herpetic whitlow, and the lesions act like HSV lesions on any other surface area. They can be caused by either HSV-1 or HSV-2. They do not produce pus unless secondarily contaminated by bacteria. They usually produce a clear, opulent, serosanguinous fluid typical of HSV vesicular lesions. The initial symptoms—tingling and pain—are often followed by digital erythema and swelling. Associated symptoms include fever, lymphadenopathy, lymphangitis, malaise, and myalgia. Complications can include local hyposthenia, secondary ocular involvement, and systemic viremia. The lesions are most frequently seen on the thumb and the first and second fingers of the dominant hand. Recurrences are seen in 20% of patients.

Herpetic whitlow is not only painful but also a hazard and inconvenience for health professionals and for patients who are undergoing treatment. A recent report described an incident in which 20 of 46 patients contracted oral herpes infections from a dental hygienist with herpetic whitlow. Thus, there is a need for a specific and aggressive treatment for herpetic whitlow. Previous treatments have included elevation, immobilization, normal saline compresses, analgesics, and topical antibacterial and antiviral ointments and creams, none of which appear very useful. Patient protection is afforded by wearing gloves; unfortunately, the viruses proliferate in a moist environment within the glove, leading to increased suffering.

We report here two cases of health care workers who were treated with ophthalmic idoxuridine solution (Stoxil), using the iontophoretic method of application. Iontophoresis is a method of enhancing penetration of ionic drugs into surface tissues using an electric current. This is an old method, first suggested in the 1700s after early discoveries in electricity. Recent advances in technology and drug development provide a new opportunity to apply iontophoresis in a rational and safe manner, making it applicable to modern therapy. The iontophoretic method is based on carriage of charged drugs by direct current under an electrode of like charge; the electrode device consists of paper or cotton saturated with an aqueous solution containing no other ions except the drug. This device is attached to metal and the surface tissue, and is used for passage of the current. A similar, indifferent electrode containing sodium nitrate is connected to the opposite electrode and is placed anywhere else on the body surface. This method allows local concentration of drugs and avoids systemic effects. This method has been used successfully for cystic fibrosis diagnosis (pilocarpine nitrate), local anesthesia (lidocaine and epinephrine) for myringotomy for skin and oral mucosal anesthesia, treatment of hyperhidrosis, and for glucocorticosteroid introduction, as well as for many other uses. We reported on successful use of antiviral therapy for herpes infection (oralabialis, cutaneous, and zoster), and now we report a similar use for herpetic whitlow.

CASE REPORTS

Case 1. A 34-year-old dentist was first affected by herpetic whitlow in August 1983. He experienced burning and paresthesia underneath the nailbed of his left index finger at the tip of the fingernail. He noted extensive rubor, pain, enlargement of the left troclear nodes, and swelling of the involved finger to 1.5 times its normal size. The lesion was initially diagnosed as paronychia and it was drained. HSV-1 was identified by fluorescence microscopy. The pa-
tient then was instructed to apply acyclovir ointment (Zovirax), which he faithfully did, not only by repeated application with his right index finger, but also within a finger cot that he wore while working. In spite of intensive topical application, the vesicles persisted for three weeks, followed by dry crust and scab formation for two weeks. The patient still complained of loss of sensation in the affected finger 18 months later.

When the patient was first seen in our clinic (September 1984), he was suffering from a second outbreak. This occurrence was on the right index finger, a rather unusual site for a recurrence. In this instance, the patient again started using acyclovir ointment for seven days by the same method as above, with little or no effect. He then sought treatment at our clinic. Iontophoresis using 0.1% idoxuridine ophthalmic solution was performed at 0.25mA for ten minutes at the negative electrode, as described previously for herpes labialis. After treatment on a Saturday, the patient noted an immediate decrease in inflammation, pain, and discomfort. On the same day the vesicles ooze a clear fluid from the area. Coalescence of vesicles was noted almost immediately after treatment. The patient was instructed to keep the lesion dry (with only dry cotton in the finger cot) and to expose to the lesion to air as much as possible when not working. On Monday morning, the lesion appeared almost healed, and the patient returned to his work schedule, using dry cotton batting in a finger cot and rubber gloves. By Wednesday, the lesion exacerbated and more vesicles appeared. A dermatologist was seen and the following therapy prescribed: (1) erythromycin 250mg, qid; (2) 50mg zinc daily; (3) lysine 500mg, bid; and (4) Aristocort ointment applied daily. The patient then continued working with gloved hands; he called back on Friday, at which time the finger was no better. It was decided to start a series of three daily treatments using idoxuridine ointment. Also, the patient was asked to take four full days off from work so that the lesion would have adequate time to dry and heal. After the second treatment, the lesion again displayed coalescence of vesicles; also, there was oozing and rapid relief from pain. Several days after the three treatments there was an apparent successful resolution, and the patient returned to work. He continued using the finger cot and gloves as a precaution for his patients. Inflammation reappeared one week later, with the entire finger appearing red and swollen rather than vesicular. This was diagnosed by the patient as a secondary infection, which responded well to systemic corticosteroids for Crohn disease. The patient's symptoms started with prodrome and vesicle development. Iontophoretic treatment with idoxuridine was performed.

After treatment by idoxuridine iontophoresis, the patient noted that his mildest previous outbreak had been two days old and had gone through prodrome and vesicle development. Iontophoretic treatment with idoxuridine was performed. After treatment by idoxuridine iontophoresis, the patient noted that the lesion was greatly reduced. However, an apparent secondary infection occurred one week after the herpetic whitlow cleared, probably due to continuous wearing of gloves; thus, the overall result was difficult to assess. Nevertheless, he has not had a recurrence in 42 months. Results are clearer for the patient in case two. He obtained a very positive, beneficial effect (60% reduction in time, and 80% reduction in severity) with no sequelae. No recurrences have been noted for 38 months, which is far better than expected, based on his previous history.

RESULTS

Both patients were healthy young men, although the second patient had Crohn disease, which was under control. Each patient had had positive diagnostic tests for HSV-1 during earlier occurrences of herpetic whitlow. We were able to compare results from iontophoretic idoxuridine treatment with previous treatments only by the patients' experience. The patient in case one experienced rapid pain relief and resolution of HSV infection after the two sets of treatments, and the total duration of disease was reduced. However, an apparent secondary infection occurred one week after the herpetic whitlow cleared, probably due to continuous wearing of gloves; thus, the overall result was difficult to assess. Nevertheless, he has not had a recurrence in 42 months. Results are clearer for the patient in case two. He obtained a very positive, beneficial effect (60% reduction in time, and 80% reduction in severity) with no sequelae. No recurrences have been noted for 38 months, which is far better than expected, based on his previous history.

DISCUSSION

Herpetic whitlow is a problem occasionally encountered in health care professionals and in others. Trivial trauma, such as nail bites, nicks, and needle sticks, may be predisposing factors. In addition to the associated pain, the condition can
Course of herpetic whitlow in patient in case 2. Photo A, taken before the first treatment, shows numerous small, indurated vesicles (appearing as centrally located brown spots). The finger was very painful, with pain spreading up the arm. Photo B, taken ten minutes after first treatment, shows four pencil marks outlining area of treatment. Lesions were coalescing and vesicular fluid became more prominent. Patient noted some oozing of fluid for several hours after first treatment, was relatively pain free, and the condition improved for the next 48 hours. A second treatment was given 24 hours later. Photo C, taken 48 hours after first treatment and after a third treatment, shows lesions in the late dry crust state; pain was almost absent and no spreading (lymphangitis) was noted. Photo D, taken 72 hours after first treatment, shows only a few small areas of dry crust; no pain or adverse sequelae from the whitlow were noted. After two days, finger appeared normal.
cause the loss of valuable time from work. Not only is this expensive and painful, but also the infected finger may serve as a vector for transferring the disease. Past treatments for herpetic whitlow have been unsatisfactory, providing limited success in pain relief and not effectively attacking the infecting viral agent. The moist environment caused by wearing gloves and/or use of ointments may delay healing; the rational therapy for herpes simplex should be directed toward drying.

Acyclovir (ACV) may be considered a more specific antiviral therapy, but the ointment has not proven consistently effective in topical therapy,23; the ointment creates a moist atmosphere, which could have a negative effect.24 Recently, we reported that ACV cathodal iontophoresis was unimpressive in eliminating virus in double-blind studies of orolabial herpes simplex, although Ara-AMP (the monophosphate derivative of adenine arabinoside) iontophoresis caused a virological effect within 24 hours that was statistically better than placebo or ACV iontophoresis ($p < .001$).25 Another antiviral agent, idoxuridine, has been used topically for herpetic keratitis of the cornea for over 25 years. It appears to be a useful agent for treating HSV infections, when penetration is assured by iontophoresis.26–28 This therapy has the advantage of active antiviral treatment followed by drying. Although local application of 40% idoxuridine in dimethyl sulfoxide has been reported to be somewhat successful in treating herpetic whitlow,29 the 0.1% solution or 0.5% ointment have generally failed for all topical applications except to the cornea.30–32 However, drug penetration may have been the underlying problem. Iontophoresis can improve the penetration of many drugs, in laboratory animals, enhanced penetration of idoxuridine has been noted.33 Idoxuridine moved toward the positive pole during paper electrophoresis, allowing us to predict that idoxuridine should be delivered at the negative electrode. Actually, we found that either the positive or negative electrode would deliver idoxuridine to mouse skin, but the cathode was more efficient.34 One report35 claimed an increased incidence of allergic reactions after cutaneous application of idoxuridine ointments. This has not been noted using iontophoresis, which avoids the more prolonged exposure to the drug required in topical therapy. Iontophoretic application allows concentration at the site of application, while only a few brief exposures are required. Also, idoxuridine can have myelosuppressive effects. Iontophoresis circumvents the problems of systemic side effects, since minuscule amounts of the drug enter the bloodstream. Iontophoresis is a noninvasive technique that is painless. The technique can be performed rapidly and with minimal training. The technique can be valuable in treating herpetic whitlow, for which no other effective treatment exists. Four studies have reported success using idoxuridine iontophoresis for herpes labialis.1,10,16,18 One contraindication is for pregnant women; we also exclude patients who are electrically sensitive (cardiac problems), and those who refuse treatment after reading the package insert. These contraindications are used for avoidance of spurious medicolegal problems.

Although most herpetic infections are self-limiting, some involve greater morbidity, and therefore require more aggressive treatment. We believe herpetic whitlow is in this category, and that idoxuridine iontophoresis should be instituted as soon as possible. The iontophoresis procedure may be of great help in treating other herpes simplex lesions, and certainly deserves further study.

Acknowledgments: The authors wish to acknowledge the advice and assistance of Dr. James M. Hill, formerly at the Medical College of Georgia but now at the Louisiana State University Eye Center, New Orleans, LA; and Dr. J. Peter Rissing, VAMC, Department of Medicine, Medical College of Georgia, Augusta, GA.

References

17. Leduc S: Electric ions and their use in medicine. London, R. E. & Sons Ltd., 1–70, 1908
22. Package Insert: Motion Control Inc, Salt Lake City, UT

Suppliers
a. Smith Kline & French Laboratory, Division of Smith Kline Beckman Corp, Philadelphia, PA 19101
b. Burroughs-Wellcome Co, Research Triangle Park, NC 27709
c. Lederle Laboratories, Wayne, NJ 07470
d. Motion Control Inc, Salt Lake City, UT 84121
e. Dentelect Inc, Lutz, FL 33549

The Awards and Prizes Committee of the American Congress of Rehabilitation Medicine is seeking nominees for the newly established Edward W. Lowman, MD Award which honors the late physician who was a president of ACRM and a staunch advocate for the rights of handicapped citizens. The Lowman Award will be presented to members of the Congress who have "distinguished themselves by energetically promoting the true interdisciplinary spirit of rehabilitation medicine." Nominations should specify the reasons why a candidate is being nominated, eg, for clinical accomplishments, leadership, personal characteristics, philosophy of interdisciplinary care, etc. Names of nominees and data supporting the nominations should be sent to Robert H. Meier, III, MD, University of Colorado, Health Sciences Center, 4200 East Ninth Avenue, Box C-243, Denver, CO 80262

DEADLINE FOR RECEIPT OF NOMINATIONS: JUNE 30, 1989