The purpose of this study was to test the effect of high voltage stimulation (HVS) on edema reduction in the rat hindpaw. The animals were divided into a control group (n = 20) and a treated group (n = 20). The right hindpaw volume was measured, and then the animal's paw was traumatized. The animals in the treated group were treated with HVS at 24, 48, and 72 hours posttrauma. Paw volume measurements were made on all animals at 0, 24, 48, 72, and 96 hours posttrauma. In addition, the paw volume was measured in the treated group both before and after HVS. The results showed that animals in both groups had a significant decrease in paw volume over the experimental period, but no significant difference was found between the two groups in the amount of edema reduction. The HVS treatment did not produce a significant change in paw volume immediately after treatment.

Key Words: Edema, Electric stimulation, Rats.

Alon suggested that high voltage stimulation (HVS) may be effective in reducing edema, but very few studies exist regarding the effectiveness of HVS in treating edema. No formal, experimental studies have been published on the effect of HVS on edema reduction. Several clinical reports, however, have discussed the use of electrical stimulation in the treatment of traumatic edema. Several clinicians have suggested that HVS may be of benefit in the treatment of ankle sprains, although they offered no scientific evidence to support their claims. Newton used HVS to reduce traumatic hand edema, and although the stimulation did not have any effect on volume reduction, it did increase range of motion. Other investigators also have reported success in the treatment of postoperative pain and edema, but gave no objective evidence to substantiate their claims.

Other types of electrical stimulators also have been used in an attempt to reduce edema or increase lymphatic flow. Ladd et al compared the effect of interference current therapy (ICT) with effects of cold compression and contrast baths in the treatment of subacute ankle injuries in 23 patients. After four days of treatment, they found no significant difference between the three types of treatments and their ability to decrease ankle swelling. Both the ICT and contrast bath treatments, however, significantly increased ROM, as compared with the cold compression treatment. Sixty-cycle, sinusoidal current stimulation has been shown to increase lymphatic flow in dogs, but the stimulation was less effective than passive ROM or massage in increasing lymphatic flow.

High voltage stimulation is in widespread use by many physical therapists and athletic trainers throughout the United States for the treatment of traumatic edema; however, very little scientific evidence exists to suggest that it has any therapeutic or physiological effect on the edematous condition. The purpose of this study, therefore, was to study the effect of HVS on reducing posttraumatic edema in the hind limbs of rats. The null hypothesis was that no difference in edema reduction would exist between the treated and control animals over the treatment period.

**METHOD**

Controlled studies of traumatic edema on human subjects are difficult to implement because obtaining an adequate patient sample with the same type of injury to the same anatomical location is extremely difficult. Rat paw edema (both traumatic and drug-induced) has been used extensively to test the effectiveness of anti-inflammatory agents on edema reduction. We, therefore, used rats in this study because rat paw edema commonly is used to study edema and because the experimental conditions could be well controlled.

**Instrumentation**

To measure the rat paw volume changes, a small-volume plethysmograph was constructed specifically for this experiment. The details of the construction and use of this device have been reported previously. This instrument does not require anesthetized animals and requires only one person to perform the paw volume measurements.

To measure the paw volume, the lateral malleolus of the animal's foot first was marked with waterproof ink. The animal then was wrapped in a towel, and the paw was dipped vertically into the immersion vessel of the plethysmograph to the level of the ink mark on the lateral malleolus. The paw immer-
sion causes a volume of fluid equivalent to the paw volume to be displaced in the immersion vessel. The paw volume then is determined by means of a dial incorporated into the plethysmograph.

The stimulator used for the study was an EGS 100-2* HVS stimulator. The EGS 100-2 delivers a twin peak pulse with a duration for each pulse of about 65 to 75 µsec. The stimulator has a variable output intensity of 0 to 500 V. The pulse rate can be varied from 1 to 120 pulses per second (pps). To accommodate the stimulator for use on small animals, the stimulation was accomplished by using two 5- × 5-cm carbon electrodes.

Procedure

Forty male Sprague-Dawley rats weighing 156 to 240 g were used for the study. The animals were maintained at a controlled temperature and were provided with rat chow and water ad libitum throughout the experiment. The procedure used in this study was approved by the animal resource facility director at the University of North Dakota before the experiment.

The animals were assigned randomly to either the control group (n = 20) or the treated group (n = 20). The right hindpaw was used for all measurements and treatments.

On the first day of the experiment, a volume measurement was performed on the right hindpaw of each animal. The right hindpaw of each animal then was traumatized by dropping a 50-g, 0.5-cm diameter weight from a vertical distance of 50 cm onto the dorsum of the paw. The weight was dropped onto the paw midway between the first tarsometatarsal joint and the lateral malleolus. The details of the procedure have been described by other investigators.

Paw volume measurements were made on each animal before the trauma (0 hours) and before treatment at 24, 48, 72, and 96 hours posttrauma. We measured the paw volume of the animals in the treated group both before and immediately after the treatment with HVS.

Each animal was prepared for treatment by shaving the hair from its back and right hind-limb area. The positive electrode was coated with conductive gel† and taped in place just lateral to the vertebral column and directly superior to the right hip joint. The negative electrode was folded to form a rounded cuff that then was filled with conductive gel, placed over the right hindpaw, and taped in place.

For the actual treatment, the unanesthesitized animal was secured in a cone-shaped, polyethylene restrainer. Small openings were cut into the restrainer over the animal's back and right hindpaw to allow access to the animal for electrode placement. The stimulator electrodes then were taped in place, and the openings were taped shut. During treatment, the animal's right hindpaw was inside the restrainer in a flexed position similar to the left hindpaw. Because the restrainer was constructed of clear polyethylene, the electrodes always were visible to ensure that good contact was maintained.

The animals in the treated group were treated three times with HVS. The HVS treatments were given at 24, 48, and 72 hours posttrauma. The HVS was applied for a period of 20 minutes.4,5,14

No established guidelines existed previously as to the most effective HVS stimulus characteristics for the treatment of traumatic edema. The stimulator settings, therefore, were chosen to correspond with settings suggested by both the stimulator manufacturer and clinical reports.4,5,14 During the HVS treatment, the stimulator was set on continuous mode with a pulse rate of 80 pps. The output intensity was set at 40 V, which corresponded to an average current flow of 35 µA as read by a standard ammeter placed in the output circuit of the stimulator.

This stimulator intensity was chosen because in the preliminary studies we determined that at voltage levels greater than 40 V the animals became visibly agitated and attempted to chew on the restrainer. At the 40-V level, we observed no visible motor response, and the animals could tolerate a 20-minute session of stimulation without undue agitation or biting behavior. Some investigators have suggested that a low-intensity sensory response (subthreshold to a muscle contraction) may be beneficial in the treatment of edema with HVS.4,5 The stimulus characteristics in our study, therefore, were chosen somewhat arbitrarily because this is the first study to test objectively the effect of HVS on edema reduction.

After the 20-minute treatment session, the animal was removed from the restrainer, and the posttreatment paw volume was determined. The animal then was returned to its cage until the next treatment session. This same treatment was given to the animal once a day for three days.

The original protocol for this experiment involved traumatization of both the right and left hindpaws of each animal. The left hindpaw was to be the treated paw, and the right hindpaw was to serve as the control. Using that protocol in a preliminary study of five animals, both hindpaws were traumatized as described. Paw measurements were made on both paws before the trauma and before treatment at 24, 48, 72, and 96 hours posttrauma. The treated hindpaw also was measured immediately after treatment.

The preliminary study showed that the paw volume remained very high in both paws even 96 hours after trauma. Other investigators also have observed this same phenomenon when edema was produced in both hindpaws of the same animal.5,13 The investigators have suggested that bilateral edemas have some sort of mutual influence on each other, although the mechanism of this influence is not understood. The preliminary study indicated that when both hindpaws were traumatized, not only was the volume of edema produced greater, but also the course of the edema was prolonged in comparison to unilateral edema. Subsequently, therefore, the protocol of the experiment was changed so that only one paw was used of each animal from the control group and the treated group.

Data Analysis

After the experiment, the pretreatment and posttreatment paw volume changes of the treated and control animals over the treatment period were analyzed using a two-factor (time and treatment) analysis of variance (ANOVA) for repeated measures on one factor (time). The Student's paired t test was used to compare paw volume changes before and after treatment in the treated group. A probability level of 0.05 was used for all analyses.

RESULTS

Table 1 gives the descriptive statistics for paw volume changes in the treated and control animals before, during, and after the treatment period. The ANOVA

---

* Electro-Med Health Industries, Inc, 6240 NE 4th Ct, Miami, FL 33138.
† Codman & Shurtleff, Inc, Randolf Industrial Park, Randolf, MA 02368.
‡ Aquasonic 100, Parker Laboratories, Inc, 307 Washington St, Orange, NJ 07050.
results for the treatment period are presented in Table 2. The data analysis indicated that a significant decrease occurred in mean paw volume during the treatment period (24–96 hours posttrauma) in both the control and treated animals. The data analysis, however, also indicated that a significant difference did not exist in paw volume reduction between the control and treated animals over the treatment period. That is, both groups experienced a significant decrease in paw volume over the treatment period, but neither group had a significantly greater decrease in paw volume as compared with the other group. Table 3 indicates that although the treated group as a whole had a significant decrease in paw volume over the treatment period, a significant change did not exist in paw volume after each individual treatment session.

The mean percentage of change in paw volumes after the trauma treated groups had a comparable mean increase in paw volume of about 16%. After a sharp increase in paw volume 0 to 24 hours posttrauma, a rapid decrease occurred in paw volume 24 to 48 hours posttrauma in both groups. The initial paw volume changes after the trauma were quite variable from animal to animal. At 24 hours posttrauma, the control group had paw volume increases of 7% to 32%, and the treated group had increases of 8% to 23%. Overall, the mean change in paw volume at 24 hours posttrauma (about 16%) was similar in both the control and treated groups, indicating that the method of trauma induction seemed to be reliable. Although not significant, the group treated with HVS did show slightly lower mean paw volumes as compared with the control group during the treatment period.

**DISCUSSION**

Edema has been defined as "an abnormal accumulation of extravascular interstitial fluid." Although many causes of edema may exist, all cases involve a disturbance in the balance of the Starling’s forces, which govern fluid exchange across capillaries. Several factors may be involved in upsetting the balance of fluid exchange: 1) an increase in capillary hydrostatic pressure, 2) a decrease in capillary oncotic pressure or an increase in tissue oncotic pressure, 3) an increase in permeability of the capillary wall leading to loss of proteins, 4) an increase in venous pressure, or 5) a decrease in lymphatic flow. Under normal conditions, the capillary filtration pressure is slightly positive, and a net outflow occurs from the capillary beds into the interstitium. Normally, the excess tissue fluid is recirculated by the lymphatic system.

After trauma, edema results primarily from an increase in capillary permeability, causing a leakage of protein and, in some cases, an inflammatory response with an increase in leukocytes. The interstitial protein concentration increases, causing an increase in tissue oncotic pressure. The increase in tissue oncotic pressure causes an increased movement of fluid into the interstitium and a resultant swelling effect. The overall result is an increase of both proteins and fluid in the interstitial space. After normal capillary permeability is reestablished, the proteins cannot move back into the capillaries and must be removed by the lymphatic and proteolytic systems. The interstitial fluid, however, can be removed by both the vascular and lymphatic systems.

Given those conditions, therapy to reduce edema must be aimed at three processes: 1) decreasing initial loss of fluid to the interstitium and reducing the inflammatory response, 2) increasing lymphatic flow, and 3) increasing circulation after the capillary bed has repaired itself. In theory, facilitation of those three processes should aid in edema reduction.
One of the factors involved in the treatment of traumatic edema is the correct timing of the treatment regimen. The conventional practice has been to apply ice for the first 24 to 48 hours posttrauma or until the tendency for swelling has diminished.\textsuperscript{17,20,21} The reasons for this treatment are 1) to decrease the initial inflammation by decreasing the metabolism\textsuperscript{17} and 2) to decrease the fluid filtration by vasoconstriction\textsuperscript{20,21}. After the tendency for swelling has diminished (usually within 24–96 hours posttrauma), heat may be recommended to increase circulation and to help remove fluid from the interstitium.\textsuperscript{22,23} In practice, the length of time that cold treatment is indicated depends on the extent of the injury; thus, heat application may be started sooner in less severe injuries. These treatment regimens tend to be based on clinical observations, however, and do not seem to be well substantiated by experimental evidence.

Based on those clinical observations, it would appear that the timing for HVS in this study was satisfactory. The greatest measured paw volume occurred at 24 hours posttrauma in both the treated and control animals and then declined rapidly 24 to 48 hours posttrauma (Figure). This finding would seem to indicate that no further vascular leakage existed and that a modality capable of increasing circulation may be indicated.

As stated previously, the stimulus characteristics used in this study were chosen somewhat arbitrarily and were based on clinical observations and the stimulator manufacturer’s suggested guidelines. A different set of stimulus characteristics may have yielded different results. We have shown in a prior study that the circulation response to HVS is related to the intensity of stimulation.\textsuperscript{24} That is, the greater the intensity of stimulation, the greater the increase in circulation. Because the circulatory response theoretically is desired in the treatment of edema to remove fluid, a stronger stimulus may have been more beneficial, although a stronger stimulus in this study may not have been tolerable to the animals. If an increase in lymphatic flow were desired, a stronger stimulus capable of inducing a muscle contraction may produce a better lymphatic pumping effect.\textsuperscript{7} In addition, the pulse rate used in this study may have been too high to give the most efficient muscle\textsuperscript{25,26} or lymphatic\textsuperscript{7} pumping effect. Based on our previous study, the 80-pps rate is capable of increasing blood flow, but a lower pulse rate and an intermittent muscle contraction may produce a better “muscle pump” action.\textsuperscript{24} The results of this study, however, are in agreement with other studies on the lack of effectiveness of electrical stimulation in the treatment of edema.\textsuperscript{5,6}

Based on the results of other studies, electrical stimulation may be indicated (or at least not contraindicated) in the treatment of traumatic edema.\textsuperscript{7,24,26} Our previous study showed that HVS could cause an increase in blood flow to the stimulated limb, an effect that should be beneficial in edema reduction.\textsuperscript{24} Other studies, using stimulators other than HVS stimulators, have shown that electrical stimulation could increase venous return\textsuperscript{26} and increase lymphatic flow.\textsuperscript{7} Theoretically, increased limb blood flow, increased venous drainage, and increased lymphatic flow should help remove excess interstitial fluid and proteins. Those studies, therefore, lend some indirect experimental evidence to suggest that electrical stimulation may be of some benefit, although further research is needed.

If the use of HVS for traumatic edema reduction is to be justified clinically, further studies must be conducted of both the effect and the optimal treatment protocols and stimulus characteristics required. Specifically, the timing of the HVS treatment and the number of treatments required to obtain the best outcome are important to determine. In addition, further studies on stimulation characteristics such as intensity, pulse rate, and treatment time will be required to determine which characteristics are the most effective for the treatment of traumatic edema.

**CONCLUSION**

The results of this study demonstrated that HVS did not cause a significant reduction in traumatic paw edema in the treated animals, as compared with the control animals. We, therefore, would conclude that further research using other stimulation characteristics and treatment protocols will be required to determine whether HVS is effective in the treatment of traumatic edema. Our results did not suggest that HVS is contraindicated in the treatment of traumatic edema.

**REFERENCES**


