Acupuncture and Wound Healing

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ABSTRACT
Acupuncture has been used in the treatment of wounds, but there are few experimental or clinical studies in the veterinary literature of wound treatment with acupuncture. In an experimental burn wound study of mice, two needles were inserted around the burn wound daily for 30 minutes (similar to the "circle the dragon" wound treatment used in acupuncture) for 14 days. Wound healing was monitored and compared to wound healing associated with the use of a conventional collagen wound dressing. Acupuncture significantly reduced the inflammatory response, wound size and increased the local expression of extracellular matrix proteins similar to the collagen dressing. In a clinical study of closed surgical incisions, two local points at each end of the incision and other acupoints were stimulated once post-operatively and had no subjective effects on incision healing. Most veterinary acupuncturists treating wounds would do multiple treatments and usually treat more acupoints. In an equine case series, local and acupoint stimulation with gold bead implantation resulted in healing of difficult to heal wounds on the distal limbs. Well-designed, controlled studies of acupuncture for different wound types are needed. Acupuncture is often less expensive than surgery, requires less specialized equipment and can be used safely with other treatment techniques. Inserting acupuncture needles in the region around the wound moves *Qi* and Blood in the region to minimize *Qi*/Blood Stagnation in acute wounds or relieve long-term Stagnation in chronic wounds. Further investigation is warranted to clarify the benefits and mechanisms of action of acupuncture for wound healing.

Key words: acupuncture, wound healing

ABBREVIATIONS

ECM	Extracellular matrix
bFGF	Basic fibroblast growth factor
TCVM	Traditional Chinese veterinary medicine

Whether wounds occur from trauma, burns or are surgically created, the goal in every case is rapid healing and a reasonably cosmetic appearance. The process of wound healing is complex, with multiple overlapping stages. Derangement of this carefully orchestrated process can lead to delays in healing, large scars or chronic lesions that never heal. There are many methods to aid the wound healing process, including bandaging, topical treatments, skin grafts and artificial grafting materials, but these treatments can be labor-intensive and expensive. Veterinary practitioners are always searching for new treatment methods that are economical and require less management, while maintaining a high standard of efficacy and safety. With these goals in mind, the use of acupuncture to hasten the wound healing process has been studied.

Mechanism of Wound Healing

Normal wound healing can be divided into three phases: inflammatory, proliferative, and remodeling (Figure 1). The inflammatory phase is sometimes further divided into two phases characterized by vascular and cellular responses.[1] The final product is scar tissue that is similar to, but never the same as normal tissue in appearance or strength. Disruptions in this process can prolong healing or result in chronic non-healing lesions.

The inflammatory phase of wound healing can last anywhere from 24 hours to 2 weeks, depending on the size and severity of the wound. The initial vascular response is characterized by vasoconstriction and hemostasis that is mediated by platelets. Platelets form a fibrin clot and trigger the coagulation cascade through the release of chemical mediators. In addition to hemostasis, fibrin clots also provide the physical scaffold on which other cells migrate at later stages in the process. The cellular response occurs quickly after initial hemostasis and is characterized by the migration of neutrophils and monocytes.

As the inflammatory stage progresses, macrophages, differentiated monocytes, become the predominant cell type.[1] The macrophages phagocytize cellular debris, apoptotic cells and bacteria. Macrophages also provide the necessary foundation for angiogenesis and granulation tissue formation and release cytokines that encourage cell migration, proliferation and matrix production. Macrophages produce chemotactic molecules that attract fibroblasts to the area that are vital for the next phase of the wound repair process.[1,2] One chemotactic molecule, basic fibroblast growth factor (bFGF), has been shown to stimulate fibroblasts and increase the production of fibronectin and other molecules important in the regulation of extracellular

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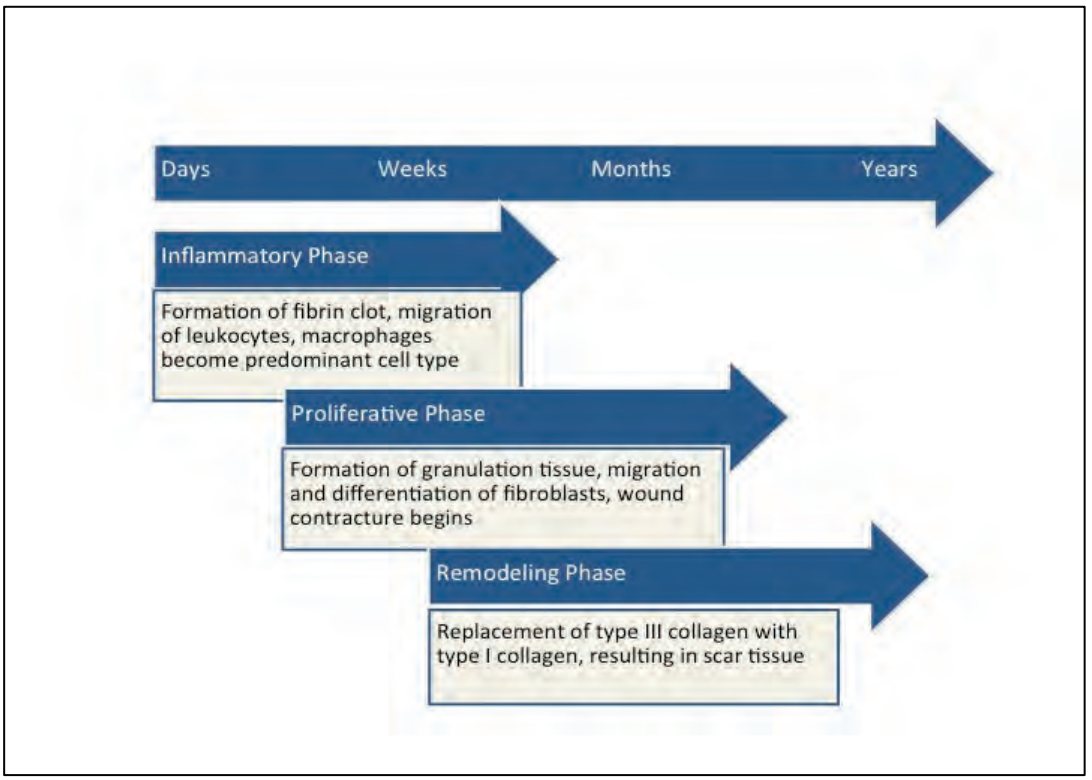

Figure 1: Phases of wound healing

matrix (ECM) synthesis and degradation.[3] Macrophages play a vital role in not only the inflammatory phase of the wound healing process, but also appear to be needed for the transition to the proliferative phase as well.[1]

The proliferative phase of wound healing is characterized by re-epithelialization to re-establish a permeability barrier, re-establishment of blood supply and fibroplasia to reinforce the dermal tissue.[1] Clinically, this is the stage in which granulation tissue appears, approximately three to four days after initial injury. The fibrin clot of the inflammatory stage is replaced with fibroblasts and endothelial cells that produce type III collagen and support capillary growth. The fibroblasts migrate from the wound edges into the center of the wound and produce collagen, fibronectin and other important molecules that form the foundation for new dermal tissue. Fibronectin enhances fibroblast migration by providing an adherent base that allows the cells to bind to the ECM. It also participates in wound contracture by providing a scaffold for collagen fibrils. During the fibroplasia process, fibroblasts differentiate into several subtypes that serve different functions during the rest of the healing process.[1,2]

The proliferative phase is also characterized by active wound contracture, which peaks at two weeks after the initial injury. While not as important for partial thickness wounds, contracture accounts for 40% of the decrease in wound size during the healing process.[1] Wound contracture is mediated by myofibroblasts, a fibroblast subtype. These cells have differentiated into a specialized cell type with actin microfilament bundles that allow the cells to contract, much like muscle cells, along the edge of the wound. Fibronectin aids the attachment of the myofibroblasts to collagen fibers along the wound edge. The cells contract, bringing the collagen fibers closer to the cells and contracting the wound.[1] Cell migration and wound contracture is further aided by several chemical factors, such as bFGF.

The final phase of wound healing is the remodeling phase, which begins during the inflammatory stage and can last for several months to years. Depending on the size of the wound, it is possible to have several different phases of healing occurring at the same time. The remodeling phase is predominated by the replacement of the type III collagen-rich granulation tissue with scar tissue composed of type I collagen, the predominant collagen type in normal skin. The final result is a scar that has approximately 70% of the pre-injury tensile strength compared with normal skin.[1]

Treatment Options

The most common medical treatment options for wounds include bandages and casts, topical medications, and collagen dressings. Surgical interventions include primary closure, delayed closure, tension sutures and skin grafts. Depending on the wound, several of these techniques may be needed to achieve complete resolution. Many of these treatments and interventions are extremely time and effort intensive and require months of treatment. Surgical options may decrease the

overall healing time, but can also be prohibitively expensive.

Non-conventional treatment options have been gaining attention.[4-8] Honey is advocated as a low-cost option for treating diabetic foot ulcers in humans in conjunction with conventional treatments.[4] Aloe has also been shown to accelerate wound healing when used topically.[5] Other methods that have been gaining popularity include ultrasound therapy and laser therapy. Ultrasound treatments provide mechanical stimulation to the tissue via micro-massage and also have anti-inflammatory effects.[6] Laser therapy increases fibroblast activity, collagen production, and angiogenesis.[6] Electrical stimulation has also demonstrated efficacy in wound treatment. When the proper charge, density and total energy are applied to a wound, there is increased migration of macrophages, neutrophils, and epidermal cells, improved perfusion, inhibited bacterial growth and decreased edema.[7] One clinical study successfully treated chronic wounds that had not responded to conventional treatment via electrical stimulation delivered by needles inserted around wound edges.[8] In addition to these topical options, homeopathic remedies have been suggested to address pain, help expel foreign bodies, or resolve discharges from chronic wounds.[5]

Traditional Chinese veterinary medicine (TCVM), specifically acupuncture, has recently been investigated as a possible adjunct or stand-alone treatment for wounds.[9] The technique involves the placement of acupuncture needles around the wound, known as "circle or surround the dragon" technique. Needles are placed either transversely or obliquely along the edge of the lesion and directed toward the center.[9] This is combined with acupoints proximal and/or distal on the Channel(s) the wound is located.[10] Acupuncture has several advantages over conventional treatments. It is relatively less expensive than surgery, requires significantly less specialized equipment, and can be used safely with other treatment techniques.

Studies of Acupuncture Treatment Efficacy for Wound Healing

There is an unfortunate lack of rigorous scientific or clinical research on the use of acupuncture to aid wound healing. A Pubmed search yielded only three studies on the topic in the veterinary medical literature. These included an experimental study, a clinical study and a case series. Even though the standards of evidence-based medicine dictate that only randomized experimental or clinical studies provide the most rigorous hypothesis testing and evidence of efficacy, the case series is included in this discussion because of the relatively small number of available studies.

A randomized experimental trial report, from Lee et al, used an experimental model of burn injuries in mice and compared wound healing between two different treatment groups.[11] One group received a Duoderm collagen dressing[a] and the second group received acupuncture therapy alone. The acupuncture treatment consisted of daily placement of needles at two opposing locations one centimeter away from the burn area. The needles were maintained in place with sticky bandage material for 30 minutes. The tested hypothesis was there would be no difference between the two treatment groups. A control group that received burn injury and no treatment was included for comparison, as well as a sham group that underwent the initial sedation procedure, but received no burn. Several variables were measured that clearly demonstrated differences between the various groups. At seven days post-burn treatment, the number of circulating eosinophils was measured to investigate evidence of systemic inflammation. The sham treatment group had the lowest mean number of circulating eosinophils, while the untreated burn (control) group had the highest. Both treatment groups had fewer mean circulating eosinophils than the control group, but the investigators found the acupuncture group's mean number was significantly lower than the Duoderm group.[11] There is clear evidence that both treatments appear to lower eosinophil counts, providing evidence of acupuncture's ability to decrease systemic inflammation.

To assess the speed of wound closure, the wounds were measured at 0, 3, 7 and 14 days after the burn treatment. The wound healing was more rapid in both the acupuncture and Duoderm treatment groups, but the acupuncture treated group consistently had the smallest mean wound area. By day 14, the mean wound area between the treatment groups (Duoderm and acupuncture) and the control group was significantly less. The mean wound area measurements in the acupuncture group were also significantly less than the Duoderm group starting at the 7th day of the post-burn treatment. The investigators concluded from these data that acupuncture was a superior treatment to Duoderm in stimulating burn wound closure.[11] The relative sizes of the wounds were very small and it is not possible to directly extrapolate these data to larger wounds, but further investigation of the treatment of burn wounds with acupuncture in other animals is warranted.

Histochemical measurements were performed to investigate possible mechanisms for accelerated wound healing. Both bFGF and fibronectin expression were determined using immunohistochemical and Western-blot techniques. The expression of bFGF was found to be significantly elevated in the acupuncture treated group, when compared to both the control and Duoderm treated groups. The fibronectin expression was similarly elevated in the acupuncture and Duoderm groups. From this evidence, the investigators suggested that acupuncture treatment modulates the local expression of extracellular matrix proteins, such as bFGF and fibronectin that stimulates and hastens wound healing.[11]

The investigators reached several conclusions at the end of the report. The study effectively demonstrated that acupuncture treatment produced results that were at

least comparable, if not clinically superior, to the Duoderm treatment and superior to no treatment. The acupuncture needle placement was deliberately not at any specific acupuncture point or Channel, yet the approach of using local treatment with minimal number of needles was still able to achieve measurable physiologic responses. Finally, evidence of the ability of acupuncture to modulate bFGF, fibronectin, and the inflammatory response was demonstrated. While not definitive, the mechanism of acupuncture's enhancement of the healing process may be related to these cellular modulations and bears further investigation.[11]

The second study, from Saarto et al, investigated surgical wound healing.[12] This was a randomized blinded clinical study involving pets undergoing various surgical procedures. Healthy pets were randomly assigned to one of two groups: acupuncture treatment or no treatment. Pets undergoing both soft-tissue and orthopedic procedures were included and there was no attempt to standardize anesthesia or post-operative medications. The surgeons were blinded to which group each pet was assigned and one person, who was also blinded, performed the post-operative assessments. The acupuncture treatment group received one treatment immediately following surgery using the following acupoints: GV-14, LI-4, LI-11, GB-34, SP-6 and two local points 0.5 cm distal from each end of the surgical wound. Needles were in place for 5 minutes except the GV-14 needle, which was left in place for 15 minutes. The acupuncture treatment group consisted of 15 animals (total of 17 surgical wounds) and the non-treated control group consisted of 14 animals (total 17 surgical wounds). Each animal was evaluated for edema formation, presence of scabs, exudate, hematoma and dermatitis at 3 and 7 days post surgery.[12] The null hypothesis for this study was there would be no difference between the two groups in any of the chosen parameters, thus showing no difference in wound healing with or without acupuncture treatment.

At the conclusion of the study, the results demonstrated no difference between the two groups in most of the evaluated parameters. The acupuncture treatment group differed from the control group only in the category of presence of edema at seven days after surgery. The treatment group had statistically significant reduction in edema (p = 0.008) when compared to the edema in the non-treated control group. There appeared to be greater hematoma formation in the acupuncture treatment group, but the finding was not statistically significant (p = 0.051).[12] These data upheld the null hypothesis that acupuncture treatment post-operatively would not change the normal course of surgical wound healing in healthy pets. There are a few aspects of the research design of the above clinical trial that are problematic. Acupuncture was only performed for 5 minutes (except for GV-14) one time, while most clinical acupuncture treatments last longer, are more frequent and local treatment usually involves more than two needles.[10] The method of outcome measurement was based on subjective scoring rather than objective measurements. Future trials should include more and longer treatment sessions and objective parameters need to be monitored in addition to the subjective ones. Surgical wounds are generally closed, clean wounds that heal quickly, as opposed to traumatic or open wounds. Because surgical wounds heal quickly, selecting a different wound type, such as acral lick granulomas, may allow for a longer study period. One could also argue that the use of standardized acupoint selection with all the patients may also have yielded less than ideal results. To achieve reproducible results, a standard approach is desirable, but not always feasible. This is an ongoing and troubling problem when designing studies of acupuncture efficacy in clinical settings.

The final article is a case series report describing gold bead implantation to aid wound healing in horses.[13] Injuries on the distal limbs of horses can be very difficult to manage because of the relative lack of sub-dermal tissue and difficulty in restricting movement of the tissue.[13] The report describes the treatment of 35 horses with a variety of wounds. The wounds were located at the level of the carpus/tarsus or distal, varied from acute to chronic (present as long as 6 months) and ranged widely in size (24 cm^2 to >300 cm^2). At the time of bead placement, the wound was surgically prepped and local anesthetics were applied. Gold plated beads were inserted 3–5 mm under the skin edge using a 14-gauge hypodermic needle with a metal plunger. The needle was inserted through the wound edges to avoid puncturing the skin surrounding the wound. The exact number of implanted beads was not specified. In some cases, *Ting* (*Jing*-well) points were also used depending on which Channels the wounds were located. The amount of time required for wound healing was not specified, but long-term follow up was conducted for 2–28 months.[13]

The exact protocol for wound treatment evolved during the course of the study. With each case, the author modified the timing of bead placement based on the results of the previous case. An example of this is the protocol for acute lacerations. The initial treatment consisted of debridement, suturing to appose skin edges when possible, bandaging and antibiotic and anti-inflammatory injections. Gold beads were implanted 7-9 days after the initial injury. These initial cases yielded positive results (control of granulation tissue formation and reasonable healing); therefore, the author began implanting beads at the initial examination. This resulted in even faster healing and better cosmetic results than the previous protocol. Chronic wounds also received a varied protocol of treatment. In cases of exuberant granulation tissue, the tissue was trimmed to below the level of the surrounding skin and beads were placed at the wound edge. Bandage placement and further topical treatment was variable or completely absent and did not appear to alter the final outcome. Cases of early exuberant granulation tissue formation (2–4mm above

skin edges) were not debrided. The bead placement was able to control the abnormal tissue. Though normal healing occurred, the author suspected a faster result could have been achieved with debridement.[13]

This equine case series highlights many of the possible advantages of using acupuncture, specifically gold bead implants, for a large variety of wounds that are difficult to treat. The wounds received initial conventional treatments, including debridement and suturing, but further care was sometimes minimal for several reasons, including financial constraints and temperament of the horse. Despite this minimal aftercare, good results were still achieved, even for large chronic wounds that had not responded to other conventional treatments. This treatment modality provides an option that can be performed at the client's facility and does not require extensive aftercare. Despite the apparent success of this treatment, there are some difficulties with the presentation. The author admits to inadequate placebo/control cases for direct comparison, but also states that in a clinical setting, it is unethical to withhold treatment.[13] This highlights another one of the difficulties in investigating new modalities of treatment in a clinical setting. The variability of the treatment protocols, including the lack of specifics on the number of beads implanted, exact location around the wounds and rationale for the inclusion or exclusion of *Jing*-well (*Ting*) points, makes it difficult to translate the protocol for clinical usage or experimental design by others. Such individual treatment is frequently needed in a clinical setting but is not considered reproducible "evidence" by the scientific medical community.

Mechanism of Action From a Conventional Perspective

When acupuncture is used to treat a wound locally, needles are inserted into the local area around the wound with no regard to actual documented points.[9] There are important biochemical reactions that stimulate the healing process. For most wound treatments, acupuncture points are not used. Instead, needles are inserted into the local area around the wound with no regard to actual documented points. Despite this seemingly random procedure, there are important biochemical reactions that stimulate the healing process.

Insertion of an acupuncture needle creates micro-trauma to the tissue, resulting in tissue damage and local inflammatory response (Figure 2). Tissue damage causes the release of proteins that stimulate vasodilation and this effect can last from 2 minutes to 2 weeks. Neuromodulators and chemotactic proteins are also released that attract inflammatory cells. Mast cells are stimulated to release histamine, heparin, and platelet activating factor that further enhance vasodilation and inflammatory cell migration. Even without stimulating a documented acupoint, needle insertion creates a small,

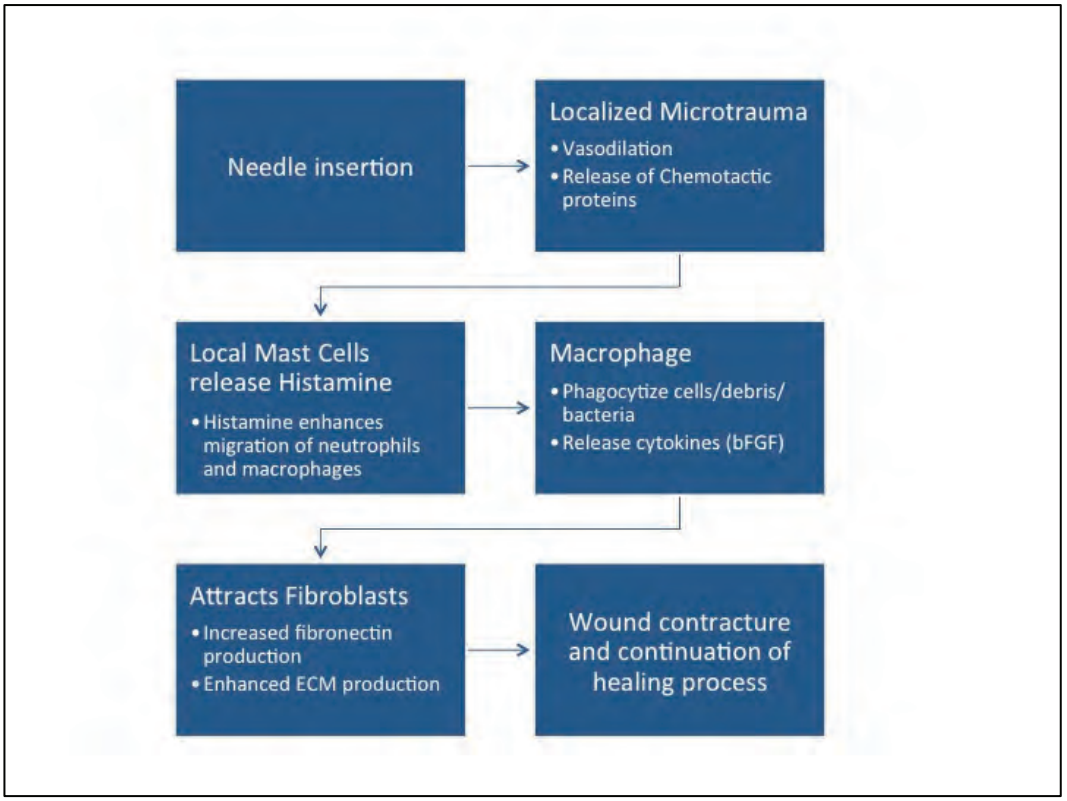

Figure 2. Proposed mechanism of action – how acupuncture influences wound healing from the conventional perspective

localized area of improved immunity and perfusion.[14] This localized environmental change enhances the body's ability to proceed with the normal wound healing process.[15] Vasodilation allows important cellular factors to arrive at the wound, such as neutrophils, monocytes, and fibroblasts. Histamine is also an important element in wound healing. A study on wound healing was conducted with histidine decarboxylase gene-knockout mice (HDC-/-); these mice are incapable of converting histidine to histamine. When histamine was topically applied to wounds on the HDC-/- mice, healing was measurably accelerated, when compared to that of the HDC-/- mice that did not receive histamine. It was also found that the expression of bFGF within the wounds of the histamine treated mice was statistically significantly elevated compared to the bFGF expression in the untreated mice. The authors concluded that histamine enhanced cellular migration to the wound, particularly macrophages. This influences the production of important chemicals that continue the healing process, especially bFGF.[15]

The importance of understanding the exact mechanism of how acupuncture may influence wound healing can help further refine the techniques applied. In the case series, the author modified the technique over time because the results could be improved. Understanding the underlying biochemical processes may allow the clinician to better manipulate and speed the process. Research should be directed towards refining the technique to discern if the number or proximity of the needles to the wound edge influences healing and if these responses can be maximized with electrical stimulation.

Mechanism of Action from a TCVM Perspective

From the TCVM perspective, wounds result from localized trauma, which leads to *Qi*/Blood Stagnation causing reduced *Qi*/Blood flow and *Qi*/Blood Deficiency to local tissues.[10] There can also be a localized invasion of Heat and Heat Toxin, commonly referred to as inflammation and infection in conventional medicine.[10] Chronic local *Qi*/Blood Stagnation can also transform into Heat or Heat Toxin. While stimulation of acupuncture points can create various reactions throughout the body, the "circle the dragon" technique does not necessarily employ acupuncture points. Instead, needling the region around the wound serves to stimulate the flow of *Qi* and Blood within and around the wound to promote healing of affected tissues. Using the "circle the dragon" technique can minimize Stagnation in acute wounds or relieve long-term stagnation in chronic wounds.

Further relief of *Qi* and Blood Stagnation is achieved by using distal acupoints located on Channels associated with the wound.[10,13] With horses, *Jing*-well (*Ting*) points are frequently used. Distal acupoints can also clear Heat and Heat Toxins.[13] These pathogenic factors accumulate in the wound and contribute to the blockage of *Qi* and Blood flow; drainage of these toxins through distal acupoints relieves this Stagnation. Acupoints LI-4, GV-14, LI-14, *Wei-jian* can also be used to clear Heat and release Toxins during the inflammatory phase.[10] In individual patients, other acupoints can be selected to address underlying problems, such as Spleen *Qi* or Liver Blood Deficiencies, which may further contribute to *Qi*/Blood Stagnation.

Conclusion and Areas of Further Research

The studies discussed above unfortunately offer variable conclusions about the effects of acupuncture to enhance wound healing. Each of the studies, however, has shortcomings in their design or the ability to apply their results to the clinical setting. This should not deter clinicians from offering this treatment to patients they think will benefit, but it does require the clinician to be careful in their patient selection and provide full disclosure of the procedure's non-conventional and experimental nature.

There is also an opportunity for researchers, both scientific and clinical, to help fill the information void by conducting well-designed and scientifically rigorous studies to validate the efficacy of acupuncture for wound healing. The current studies suffer from multiple design problems, but, with some modification, can be used as models for further projects. Further investigation can elucidate the underlying biochemical reactions that occur when wounds are stimulated by local needles. This information will help refine the procedure, such as defining the number or placement of needles. Clinical trials provide evidence of efficacy, but need to include objective measures of outcomes. The use of standardized acupoint selection for all patients may yield less than ideal results, but future studies might eliminate this problem by only using local points around the wounds.

FOOTNOTES

[a] Duoderm CGF (controlled gel formulation), 11mm in diameter; Convatec, USA

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