USE OF MEDICINAL MAGGOTS IN WOUND HEALING

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Key Points

- Most effective for the debridement phase of wound healing
- Have antimicrobial properties, attract fibroblasts, and promote granulation tissue formation
- Success determined in large part by case selection and proper bandage application

History

Maggot biotherapy was likely an accidental discovery, as flies have always been with mankind, and deposited their eggs on necrotic, foul-smelling wounds. The earliest written mention of maggot presence in wounds is in the Old Testament of the Bible (Job 7:5). However, various ancient cultures including the Mayans are known to have attracted maggots to dressings which were then applied to wounds. In 1829, Napoleon’s surgeon in chief reported that maggots developing in infected wounds prevented further infection and accelerated wound healing. John Forney Zacharias documented application of maggots to Civil War wounds.

W.S. Baer is credited as the founder of modern maggot therapy. He used maggots during WWI, then reported high cure rates of juvenile osteomyelitis in practice. He kept a colony of flies, and was the first to realize that Clostridium sp. could be introduced via maggot application. He developed sterilization procedures to address this risk, and due to his efforts, more than 300 US hospitals were using maggots between 1930-1940. With the advent of penicillin and other commercially available antibiotics in the late 1940s, maggot therapy quickly went out of fashion.

In the 1980s, biosurgery was “rediscovered”. Multidrug resistant bacteria had hit the scene, and novel means of combating these public health hazards were applied. The use of medicinal maggots increased throughout the 90’s, and in 1996 the first international conference on biotherapy was held (International Biotherapy Society). http://biotherapy.md.huji.ac.il/

Life Cycle

Medicinal maggots are the larvae of Calliphoridae flies, the most common species employed being Lucilia sericata (Green Bottle Fly/Green Blowfly). Calliphoridae flies represent the first wave of faunal succession on corpses, and have become instrumental in various forensic applications. These larvae are ideal for use in wounds, as they exclusively affect necrotic tissue and leave healthy tissue behind. This property is known as “facultative myiasis”. Under extremely rare circumstances, as with sheep strike, clinical disease in living animals is seen.

Adult gravid females lay 2000-3000 eggs on a food source. Under optimal conditions, the eggs will hatch in 18-24 hours. The first instar larvae, which are 1-2 mm long, begin the feeding cycle. After 4-5 days of feeding, the larvae will have undergone two molts, and grown to approximately 1 cm in length. The engorged larvae then leave the wound and look for a dry place to pupate, typically burrowing into the ground. Adults then emerge from the pupae 7-20 days later.

Medicinal maggots are by definition sterile. They are available in the human medical field by prescription only. Monarch Laboratories (Irvine, CA) is the exclusive US supplier of medicinal maggots at this time. www.monarchlabs.com In order to produce this product, Lucilia sericata eggs are surface disinfected, then placed in sterile containers. A sterile food source (soy
protein and brewer’s yeast) is provided, and first instar larvae are delivered to the customer. Approximate cost $100.00 for 250-500 larvae, or $150.00 for 500-1000 larvae.

Mechanisms of Action\textsuperscript{1,2}

A multitude of qualities beneficial to wound healing have been attributed to the medicinal maggot. Maggots feed via extracorporeal digestion; that is, they secrete proteolytic enzymes into the surrounding wound that liquefy necrotic tissue, which they then ingest. In this fashion, they remove cellular debris, dead contaminated tissue, microbes and foreign material. As \textit{L.sericata} larvae rely on aerobic conditions, they will not penetrate tissues deeply. The larvae disturb wound surfaces by crawling around using their hook-like mouthparts. Maggot secretions raise the wound pH through secretion of sodium bicarbonate, thereby inhibiting the growth of bacteria. The secretions have also been shown to contain substances with healing properties, such as allantoin, and bactericidal components, such as urea.

\textit{In vitro}, maggot secretions have been shown to disrupt biofilms created by \textit{Staphylococcus epidermidis}, \textit{Staphylococcus aureus}, and \textit{Pseudomonas aeruginosa}. Application of maggots to pure cultures of various bacteria and fungi have resulted in a zone of lysis (cell death) which persists for days. Using fluorescence studies, the first instar larvae have been shown to ingest Escherichia coli as well, thereby decreasing surface bacterial load.

Chemotactic factors that affect migration of fibroblasts have been isolated from maggot secretions, and extracted fatty acids have been shown to induce granulation tissue formation in mice. Experimental hydrogels containing maggot secretions have shown increased speed of closure of defects in fibroblast cell cultures. There is also suggestion that maggot biosurgery may increase tissue oxygenation.

Storage

The manufacturer recommends that the medicinal maggots be applied to a wound within 24 hours of receipt. Multiple studies have shown that the larvae can be refrigerated, which extends their viability from less than 24 hours to an average of 60 hours. These studies measured maggot motility, and do not necessarily represent equal debridement efficacy.

Wound Selection

A mnemonic garnered from the human literature that is useful regarding the need for wound debridement is \textit{TIME}. \textit{T} stands for the amount of devitalized or otherwise deficient tissue. \textit{I} represents the presence and severity of infection and/or inflammation. \textit{M} refers to a moisture imbalance in the wound. Finally, \textit{E} indicates an expanding or undermined wound edge. Sharp surgical debridement results in the most efficient removal of large volumes of necrotic tissue. However, due to proximity of vital structures, overall condition of the patient, inability of the patient/owner to pursue surgery, lack of a surgeon for the procedure, and progressive declaration of wound tissue other options may need to be utilized. It is in these situations which maggot therapy is most effective in human medicine. That being said, maggot therapy can be used in conjunction with other means of debridement. In addition, maggots can be used in the face of systemic antibiotics and topical silver permeable dressings without any ill effects.

Maggots, then, are best suited to chronic wounds. As these wounds are often deep, it is important to not allow wounds to close over the maggot population. Healthy skin should be avoided, as maggot secretions may cause irritation and sores. Body cavities and exposed organs should also not be subjected to maggot therapy. Finally, large vessels should also be spared, and
caution exercised in the face of anticoagulant therapy, since hemorrhage can occur. It is also important to remember that maggot therapy is not a substitute for appropriate wound therapy; systemic antibiotics should be used if needed, and surgical debridement pursued in cases of rapidly progressing wounds, as seen in necrotizing fasciitis.

Maggot Application and Bandaging

The most critical aspect of maggot application is the creation of a proper bandage. Commercially available bandages are available from the medicinal maggot supplier, but are not necessary for successful use. Our technician who specializes in wound care calls her maggot containment bandages “screen porches”. As maggots are aerobic organisms, it is essential that sufficient oxygen reaches the wound surfaces. Similarly, they must be kept moist to prevent dessication, but not too soupy, as they will suffocate. Finally, if the wound is over a weight-bearing surface, pharmacologic or physical restraint procedures must be used to ensure that the maggots are not crushed. The maggots are left in place under appropriate dressings for 48-72 hours. Around that time period, they become satiated and move to the surface or periphery of the dressing, and are happy to be removed. Sterile saline irrigation or manual forcep removal of a few stragglers may be required in rare cases.

A hydrocolloid dressing, or plastic sheet/drape should be used to protect the surrounding normal skin. Prior to application, a wound-sized hole is cut in the dressing. Colostomy paste can be applied in areas that are uneven, or around bony prominences. Propylene glycol is toxic to maggots, so it is important to ensure that the dressing chosen does not contain this ingredient. Maggots are then applied to the wound at a dose of 5-8 maggots per square centimeter of wound surface. A mesh dressing (chiffon, or panty hose can be used) is then secured circumferentially to the bandage, completely covering the wound and trapping the larvae. This will allow air to circulate to the wound surface, and will also permit leaching of exudates. A two ply gauze layer is then placed over the mesh. Again, this allows circulation of air, but soaks up exudate. It is this layer of the bandage that is changed as needed during the 48-72 hours of maggot debridement. After removal, the maggots should be disposed of in accordance with your institution’s infectious (red bag) waste policy.

Side-Effects

More than 20,000 human patients have been treated with medicinal maggot therapy worldwide, without serious adverse effects. Few cases of severe hemorrhage requiring transfusion have been reported, but mild bleeding is common. Some people also report pain with maggot therapy.

Other possibilities include anaphylactic reactions to the insects themselves, or to the food sources in the supplied media. Theoretically, as ammonia is a byproduct of maggot digestion, patient can become hyperammonemic, and show encephalopathic signs.

Human Clinical Support

Maggot therapy has been safely used in thousands of human subjects, many of whom are critically ill with other metabolic diseases. In one study, 72% of patients were classified as ASA III/IV. Numerous case reports and small case series exist in the literature. Few large case control studies exist, and very little prospective evidence is available.

Generally, 50% of human leg ulcers are healed in 16 weeks with standard therapy. In a study of 103 case-controlled patients, 80% of wounds treated with maggots were completely
debrided in five weeks, compared to 48% with hydrogel. On examination at day 21, maggot treated wounds had 1/3 the amount of necrotic tissue and two times the granulation tissue of the hydrogel controls.3

Another case-control study determined that people were three times more likely to require limb amputation due to diabetic foot ulcers when subjected to conventional therapy than those whose wounds were treated with larval therapy. This same study showed a statistically significant increase in antibiotic-free days in the larval group as well. A case report describes the use of maggot therapy to salvage a re-implanted forelimb traumatically amputated in a crush injury. In another report, use of medicinal maggots in cases of necrotizing fasciitis was shown to decrease the number of surgical debridements.

A single prospective, randomized multicenter parallel group trial has been published comparing larval therapy with hydrogel application for venous and mixed arterio-venous leg ulcers. This study is known as the VenUS study, and included data from 23 hospitals. Inclusion criteria included non-healing wounds with at least 25% wound necrosis. Patients were followed to time of healing, and for at least six months afterward. When maggots were applied directly to the wounds, an average of 14 days was required for debridement, compared to 72 days for the hydrogel group. This difference is statistically significant.4

Veterinary Clinical Support

Most reports of maggot debridement in the veterinary literature involve non-companion species. Case reports including skin lesions in donkeys, and wounds in a buffalo and bull have been published.5 Morrison has an illustrative review of the use of medicinal maggots for equine laminitis,6 whereas Kočišová et. al. described the use of larvae in ovine foot rot.7 These studies are descriptive, and support the use of maggots for their debridement efficacy. However, they do not include a control population, making any statement on improved healing time difficult.

Two practitioner surveys, one to large animal practitioners and one to small, have also been published.8,9 These papers include short summaries of each case treated, including historical information, specific injury, and additional treatments. Maggot therapy was determined to be safe and effective in these descriptives.

References