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"Bio-Surgical Therapy" Overview

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Abstract
At the beginning of 21st century William Baer presented a dramatic work to bone and soft tissue infections with live maggots or warm or larva. Certainly numbers of therapists around the globe have rediscovered the benefits of maggot therapy. The principal vision for the in maggot therapy is the clean and clear debridement caused due to chronic wound which are not responding to current antibiotic or antimicrobial therapy. More over the advantage of maggot or warm therapy over existence is low cost, easy production, higher cure rate, lack of resistance and reliable therapy. Modern dressing materials have simplified the procedure and minimized the risk of escaping maggots. The development and establishment of biotech laboratories throughout the world make possible availability to millions of people. Various medical literatures are rapidly growing with scientific evidence demonstrating the efficacy and safety of maggot therapy for a variety of problematic wounds. Current review is prepared to focus various application and advantages of maggot debridement therapy with suitability for choric wounds.
Keywords: Maggot Therapy, Debridement, Chronic wound.

1. Introduction
Maggot (Warm) therapy was often considered as a traditional therapy; and has long been associated with battlefield wound and was widely used until early in the twentieth century [1]. Use of maggot therapy declined with the introduction of antibiotics and improvement in surgical debridement. The use of maggot therapy has been again coming in a picture due to antibiotics resistance and the potential adverse effects associated with the same. It is generally categorized as a "bio-surgical" therapy and considered a safe rapid and cost effective comparing with another measures [2].

The insect which is used in this therapy are sterile maggots and are specifically produced by specialized and authorized organizations like Zoo biotic Ltd (Bridgend, UK). Maggot therapy employs the use of freshly emerged, sterile larvae of the common greenbottle fly *Lucilia sericata.* Naturally seeded maggots cannot be used therapeutically [1]. These insects have been known for their potential from centuries to have a healing mechanism that can be used by the medical field. Ambroise Pare discovered the beneficial effect maggots as wound healing. Military physicians also discovered maggots' ability to eat only infected tissue in soldiers during battle. In the 1930's, William Baer started clinical trials on maggots resulting in very successful results in many of these studies [3]. During this time, hundreds of hospitals in the United States were using maggot debridement therapy (MDT) for the treatment of conditions such as osteomyelitis and chronic leg ulcers [3,4].

As the population ages, the number of patients suffering from chronic wounds attributable to diseases such as diabetes mellitus and peripheral vascular disease is on the rise. This poses a significant impact on the health care system, because of the chronicity of care required and the associated costs. A chronic wound does not progress through the four overlapping phases of wound healing. Instead, it is commonly arrested at the inflammatory phase, due to the presence of slough, necrotic debris and infection [4]. In addition, much research has been devoted to developing new techniques to enhance and speed the process of wound healing, including adjuvant growth factors, tissue-engineered products, hyperbaric oxygen and negative pressure wound therapy [4]. As an alternative to surgery, maggot debridement therapy (MDT) has been shown to provide rapid and effective wound debridement, thus speeding the process of wound healing and lowering the overall costs of management.

Traditionally, the principles of treatment for acute and chronic wounds include debridement and the application of dressings [4,5]. Sterile worms can be applied to a wound in a direct (free range) or indirect (contained) manner. In the direct contact manner, larvas are applied directly onto the wound with a hydrocolloid dressing on the surrounding healthy skin [1].

Fig No.1: Medical worms by monarch lab

After the worms are placed on the wound a nylon mesh is fixed to the hydrocolloid dressing to cage the worms within the wound and prevent them from escaping. In direct application the maggots should not be applied on communicating wounds like thoracic or abdominal. In the indirect contact manner, maggots are supplied within a closed polyester net with absorbent hydrophilic polyurethane foam. The manufacturer declares that based on scientific evidence the presence of tiny pieces of foam within the net provide a physical environment that appears to markedly stimulate the activity and development of the worms whilst assisting with exudates management [6]. Worms applied by the free range method should still be regarded as the treatment of choice [1].

2. Mode of action of maggots against debridement

The action of maggots on wound healing is via the production of potent photolytic enzymes [7]. Maggot secretion is sterile and fulfilled the required definitions of a sterile secretion during the process of dissolving fibrin and necrotic tissue, digest bacteria's including MRSA (Methicillin-resistant *staphylococcus aureus*) [2]. With regards to the increasing of antibiotic resistance, the action of maggots against MRSA is of particular interest and dramatic as it reduces the chances of spread of infection from the wound both systemically and from patient to patient and no issue of resistance [8]. However, in vivo maggots seem to be less effective against gram-negative infected wounds [1]. Wound debridement involves removing necrotic tissue, exudates, foreign material and bacteria so that the normal stages of wound healing can take place [4].

3. Limitations of current anti-microbial therapy

3.1. Local irritancy

This is exerted at the site of administration. Gastric irritation, pain and abscess formation at the site of I.M. Injection especially erythromycin, tetracycline, certain Cephalosporins and Chloramphenicol are irritants.

3.2. Systemic toxicity

Almost all anti-microbial agents produce dose-related and predictable organ toxicities. Tetracycline: - Liver and kidney damage, Chloramphenicol- Bone marrow depression. Polymyxin B- Neurological and renal toxicity. Vancomycin- Hearing loss, kidney damage. Amphotericin B - Kidney, bone marrow and neurological toxicity.

3.3. Hypersensitivity reaction

Practically all Anti-microbial agents are capable of causing hypersensitivity Reactions. These are unpredictable and unrelated to dose. The more commonly involved anti-microbial agents are Penicillin's, Cephalosporins Sulfonamides Fluoroquinolones.

3.4. Drug resistance

It refers to unresponsiveness of a microorganism to an Anti-microbial agent and this phenomenon of tolerance is seen in higher organisms.

There are the two types of resistance.

3.4.1. Natural resistance

Some microbes have always been resistant to certain AMAs. They lack the metabolic process or the target site which is affected by a particular drug e.g. Gram-negative bacilli are normally unaffected by penicillin or *Mycobacterium tuberculosis* is insensitive to tetracycline's.

3.4.2. Acquired resistance

It is the development of resistance by an organism due to the use of an AMA over a period of time. e.g. *Staphylococci, coliforms, tubercle bacilli*. Other likes streptococci resistance may be developed by mutation or gene transfer.

3.4.3. Superinfection (Suprainfection)

This refers to the appearances of a new infection as a result of Anti-microbial therapy Use of most AMAs causes some alteration in the normal microbial flora of the body. The normal flora contributes to host defense by elaborating substances called Bacteriocin.

3.5. Nutritional deficiencies

Some of the B-complex group of vitamins and Vit K synthesized by the intestinal flora is utilized by man. Prolong use of AMAs which alter this flora may result in these vitamin deficiencies.

Neomycin causes morphological abnormalities in the intestinal mucosa – steatorrhoea and malabsorption syndrome can occur.

3.6. Masking of an infection

A short course of AMAs may be sufficient to treat one infection but only briefly suppress another one contacts concurrently. e.g. Tuberculosis masked by a short course of streptomycin given for trivial respiratory infection.

3.7. Dose-related toxicity

3.7.1 Liver damage

Fatty infiltration of liver and hepatitis occurs occasionally. Tetracycline's are risky in pregnant women; can precipitate acute hepatic necrosis which may be fatal.

3.7.2. Kidney damage

It is prominent only in the presence of existing kidney disease. All tetracycline's, except Doxycycline, accumulated and enhance renal failure.

3.7.3. Phototoxicity

A sunburn –like or another severe skin reaction on exposed parts is seen in some individuals. A higher incidence has been noted with Demeclocycline and Doxycycline. Distortion of nails occurs occasionally.

3.7.4. Teeth and Bones

Tetracycline's have chelating property. Calcium–tetracycline chelate gets deposited in developing teeth and bones. Given during late pregnancy or childhood, tetracycline's can cause temporary suppression of bone growth.

3.7.5. Antianabolic effect

Tetracycline reduces protein synthesis and has an overall catabolic effect. They induce negative nitrogen balance and can increase blood urea [9].

4. Clinical indication / application of maggot's therapy

Maggot therapy is suitable for most kinds of wounds that contain adherent slough or soft necrotic cells or tissues, or clinically infected wounds that are not responding to antibiotic treatment. Maggot debridement therapy is principally used for the cleaning and disinfection of chronic wounds which are sloughy, necrotic, and infected. Various clinical studies have demonstrated the efficacy of Maggot debridement therapy in treating wounds that fail to respond another therapy. Maggot therapy is effective with only a single application of worms for 1 to 4 days.

The wound score was determined by and proportional to slough coverage, exudation, malodors, granulation and inflammation of surrounding skin. Larvae were effective in removing necrotic tissue and exudation without a damaging adjacent healthy tissue. These actions stimulate the tissue granulation and reduced offensive odors brought about by infections. The benefits of MDT have been reported for a variety of chronic wounds. With the emergence of antibiotic resistance, MDT has been demonstrated to be useful in surgical wounds infected with MRSA. Compared to conventional hydrogel therapy; MDT was more effective for chronic venous ulcers, diabetic ulcers, and pressure ulcers. In a controlled study on diabetic foot ulcers and complete debridement was achieved in 4 weeks. In another study on venous ulcers, 12 patients were randomized to receive MDT or conventional therapy [4]. Medical Maggots and maggot debridement therapy (MDT) are indicated for: debridement of non-healing necrotic skin and soft-tissue wounds such as pressure ulcers, neuropathic foot ulcers, chronic leg ulcers, or non-healing traumatic or postoperative wounds [10].

4.1. Types of wounds/lesion for which maggot therapy may be used: [11-13]

Infected wounds of all types that have failed to respond to conventional treatments.

1. Infected chronic ulcers, such as pressure ulcers, leg ulcers diabetic feet
2. Sloughy wounds
3. Traumatic wounds

4. Amputation sites
5. Dehisced surgical wounds
6. Slow wounds
7. Wounds with Osteomyelitis
8. Necrotising fasciitis
9. Wounds containing MRSA
10. Surgical wounds
11. Malignant wounds
12. Venous ulcers.
13. Neuropathic ulcers (non-diabetic ulcers).
14. Arterial/ischemic ulcers.
15. Thromboangiitis obliterans.
16. Pyoderma gangrenosum.
17. Excised ulcer on malleolus.
18. Pilonidal sinus.
19. Infected wound after forearm replantation.
20. The wound of exposed knee prostheses.
21. Wound infection after breast surgery.
22. Infected gunshot wound.
23. Burns.
24. Non-healing surgical wound.
25. Methicillin-resistant Staphylococcus aureus–infected Wound.
26. Subacute mastoiditis.

5. Preparation of maggots for maggot therapy

The larvae of the green-bottle fly *Lucilia (Phaenicia) sericata* are the most commonly used for wound management. This fly belongs to the diptera order of insects, which are known to be able to infect living hosts and parasitize host tissue. Fly larvae were sterilized by washing the eggs for eight minutes in 0.05 percent sodium hypochlorite and placing them in a sterile container to hatch Within 24 -48 hours after hatching, They were ready to place on wounds. The young 2mm long maggots were covered with porous sterile dressings and left in place for 48-72 hours “cycles” one or two cycles applied each week [14]. Whenever possible maggots should be used on the day of delivery and if not possible in exceptional circumstances they can be stored over night in the cool place. If maggots must be stored in this way they may be placed in the bottom of the fridge but not near to the ice making section. Unless ambient temperature is particularly high there are no need store worms in this way if they are to be applied to 8 hours of receipt. If maggots are stored in a fridge it is recommended that they are allowed to return to room temperature before use [10,12].

6. Therapy protocol [14]

6.1. How to Apply Maggots

Currently, there are 2 modes of application of MDT. First direct application of freely crawling maggots can be applied to the wound bed and covered by nylon net. On the top of this is placed a gauze bandage to keep the maggots captured in the wound and to let them breathe freely. A quantity of up to 10 maggots per square centimeter wound surface for 3 days continuously is used. After this period, the maggots should be removed by washing out the wound with saline.

The second mode is indirect method where, maggots are captured and enclosed in special bio bag containing a polyvinyl alcohol spacer. The network of the bio bag is porous and permits the migration of maggot ES (excretions/secretions) to the wound. This bag facilitates the application of MDT and also the inspection of the wound bed during the treatment at any time. The effectiveness of the MDT captured in bags or in free-range application seems to be equal, but in the case of complicated undermined cavity, wound-free maggots may be preferable. It is advisable that using a quantity of 5 to 10 maggots per square centimeter wound surface for 3 to 4 days following after which the bags containing maggots should be replaced in combination with a saline cleaning of the wound. Furthermore, it is necessary to use a physiological saline solution daily to keep the surface wet. Maggot therapy should only be undertaken by an individual who has previous practical experiences in the management of wounds and a thorough understanding of the wound healing process and has received the appropriate training [12,15].

6.2. Skin preparation

Cut a hole in a hydrocolloid sheet the size and shape of the wound and place securely onto the surrounding skin. Alternatively cut strips of hydrocolloid dressing and place around the wound. If the wound is small and shallow a double layer of hydrocolloid may be applied to form a deeper cavity. If the wound is relatively small and a limited depth a double layer of hydrocolloid may be applied to form a shallow chamber into which the maggots are introduced.

6.3. Removing maggots from their container

Add 5ml of sterile saline to the pot containing the maggots gently agitate the pot. Pre-moisten a piece of sterile gauze with normal saline. Place the sterile nylon net (LARVE NET) that is supplied with each pot over the saline-soaked sterile gauze. Slowly pour the saline containing the maggots onto the part of wound.

6.4. Apply the free-range maggots to a wound

Invert the net over the wound and that securely to the hydro colloidal sheet using the waterproof of adhesive tape contained in the pack. The maggots will not fall off the net when it is inverted as they will be held in place by surface tension. The central part of the net must remain unconcluded in order to permit free drainage of exudates and allow the maggots to obtain an adequate supply of maggots.

6.5. Completing the dressing

Apply a gauze swab moistened but net saturated with saline over outside of the net. Complete the dressing with the surgical pad held in place with tape or bandage was appropriate occlusive or film dressing should not be used. Any unused larvae should be disposed of they are no longer sterile [2].

6.6. Duration of Maggot therapy

Maggots should be left on a wound for 3 days (bags -4 to 5 days) because under the ideal condition they will be fully grown by this time some time however if their growth rate is reduced it may be appropriate to leave them an additional day. If pain becomes a problem it may be necessary to remove them earlier. [14,16]. The average duration of therapy was 2 to 7 weeks, 2 cycles of maggot therapy per week, and every cycle took 48 to 96 hours. [17]

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