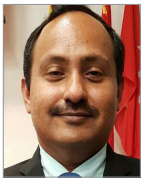
Maggot debridement therapy in the treatment of diabetic foot ulcers





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The incidence of diabetic foot ulcers (DFU) in Malaysia is about 15% of diabetic cases and is increasing in trend as the population ages. DFUs are one of the major complications of long-standing diabetes, which may lead to amputation if left untreated or undertreated. Management of the diabetic foot requires a thorough knowledge of the major risk factors for amputation, frequent routine evaluation and meticulous preventive maintenance. The most common risk factors for ulcer formation include diabetic neuropathy, structural foot deformity and peripheral arterial occlusive disease. Maggot debridement therapy (MDT) is a type of biological therapy involving the introduction of live, sterile maggots (fly larvae) into non-healing skin and soft tissue wounds of a human to clean out the necrotic (dead) tissue or slough within a wound, and at the same time promote granulation tissue and epithelisation. We recruited nine patients with DFUs and used MDT to debride the wounds. The wound bed was assessed and the percentage of wound healing was assessed. Pain score was also assessed and any side effects or complications such as myiasis and bleeding were documented. All wounds showed reduction in slough and necrotic tissue, with wound healing as assessed by area measurements. Pain reduction was noted and there were no untoward effects.

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Diabetes can lead to slow wounds healing in many patients. This happens primarily in older patients, the number of which is increasing, resulting in rising costs for the delivery of healthcare. It has been said that, the annual cost of managing these wounds exceeds 20 billion dollars (Harding et al, 2002), with a loss of over two million working days. Diabetic foot ulcers (DFU) are more difficult to treat and may lead to minor or major amputation of affected part if not treated or undertreated.

There are many treatments available in association with wound healing in patients with diabetes, such as biotherapies, photobiomodulation, topical oxygen therapy and various advanced dressings. The primary focus of this study is biological therapy using maggots. Maggot debridement therapy (MDT) is the application of live fly larvae to wounds to facilitate in wound debridement (cleaning), antimicrobial effect and/or healing. An infestation of maggots on a living host is called myiasis. When that infestation is limited to a wound, it is called wound myiasis. MDT is basically a therapeutic wound myiasis, controlled in ways that optimise efficacy and safety. The myiasis is carefully controlled by selecting the species and strain of fly (the species that being in this study is *Lucilia cuprina*), sterilising the larvae, using special dressings to maintain the larvae on the wound, and integrating quality control measures throughout the process (Nair et al, 2020). The Institute of Medical Research Malaysia found the species *Lucilia cuprina* to be the ideal maggot to be used in the therapy, as it is the endemic species of Lucilia in Malaysia.

Historically, military surgeons were the first to discover the beneficial effects of maggot-infested wounds. They noted that injured soldiers abandoned on the battlefield become better and that their wound recovery was improved

when those wounds were infested with maggots (Pechter and Sherman, 1983). William Baer, having observed maggot-infested wounds during his service, as an orthopaedic surgeon in World War I, was the first to apply maggots systematically to non-healing wounds while he was a professor at Johns Hopkins and Children's Hospital in Baltimore, Maryland (Baer, 1931).

This research determines the clinical efficacy of MDT in terms of wound healing in DFUs carried out in Hospital Kuala Lumpur's Wound Care Unit. The time period of this report is six months from the initial approval of the research proposal. The aim of this study was to observe wound-related pain associated with MDT, the possible complications that may arise such as myiasis and bleeding from the time of wound debridement to wound bed preparation.

Methodology

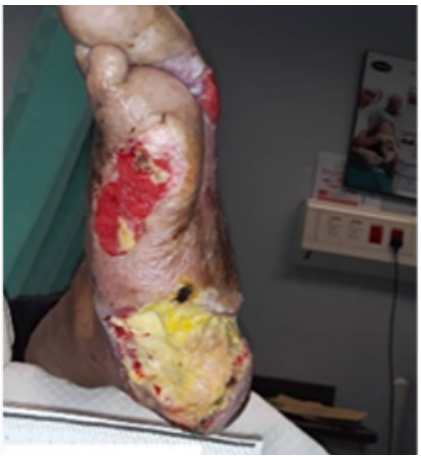
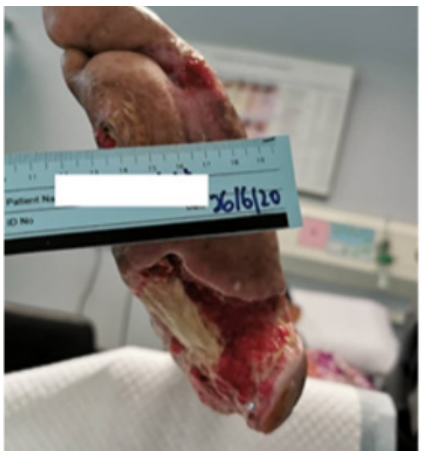
Wound dressing and treatment

Patients with DFUs were evaluated for MDT and written consent for treatment was obtained from those selected. The maggots (*Lucilia cuprina*) were obtained from the Medical Entomology Unit, IMR, Kuala Lumpur. Each vial contained 100–500 sterile maggots that were viable and used minimally for two to three MDT treatments. Distilled water was added to the vial containing maggots to loosen them. The maggots were pipetted out of the vial onto a piece of gauze. Assessment of the wound site along with pain score assessment was completed at every visit. The wound perimeter was surrounded with a cage-like dressing, made up of gauze and micropore, which was used to secure the gauze in place and prevent maggots from escaping. The gauze containing maggots was applied directly onto the wound bed. We used 10 maggots for every 1cm^2 of wound surface. The wound was then covered with light gauze to absorb the fluid, after this the entire foot was loosely bandaged with a crepe bandage. The bandage and gauze were changed as necessary before the washout. A washout of the wound was performed after 72 hours of maggot application using distilled water. Maggots were then reapplied as needed. If no change was seen after three consecutive applications then MDT was abandoned and other forms of debridement carried out as needed.

During the evaluation process, the patients will have their DFUs graded according to the

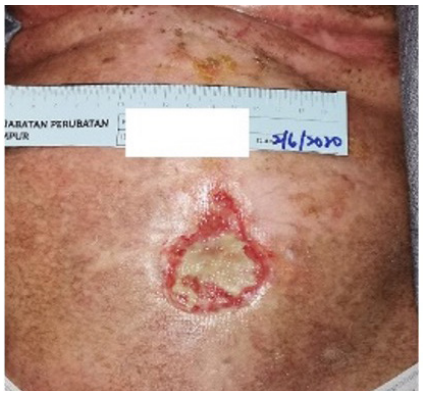
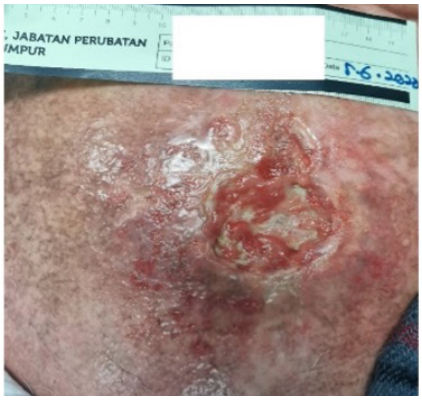
Case 1

- An 81-year-old Malay gentleman with underlying diabetes on treatment
- Had a diabetic foot ulcer for more than 6 weeks, which was getting worse
- Maggot debridement therapy (MDT) was performed six times, no side effects were observed (e.g. myiasis or bleeding)
- The wound improved by 31%

Pre-MDT	Post-MDT
Area (length x width): 102cm^2	Area (length x width): 70cm^2
Wound bed: Tendon exposed Sloughy tissue (100%)	Wound bed: Tendon exposed Granulation tissue (80%)
Pain score: 3	Pain score: 1
	

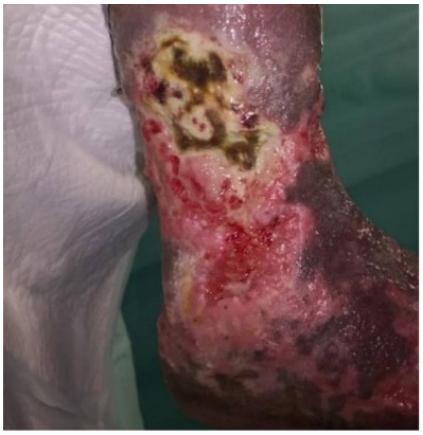
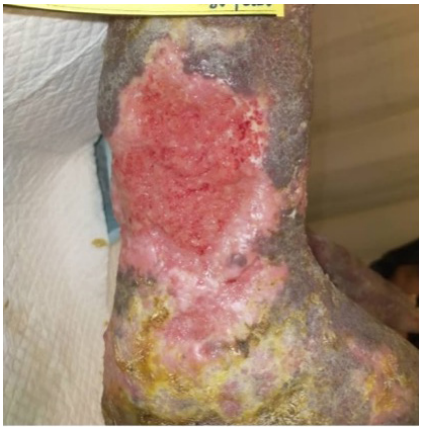
Case 2

- A 71-year-old Chinese gentleman with diabetes and mycosis fungoides stage II (mycosis fungoides is a cutaneous T-cell lymphoma) being treated by chemotherapy
- Patient claimed the wound originated from a radiotherapy session
- Treated with one round of maggot debridement therapy (MDT), no side effects were observed (e.g. myiasis or bleeding)
- The wound improved by 12%

Pre-MDT	Post-MDT
Area (length x width): 31.35cm^2	Area (length x width): 27.5cm^2
Wound bed: Sloughy tissue (70%) Granulation tissue (30%)	Wound bed: Sloughy tissue (30%) Granulation tissue (70%)
Pain score: 2	Pain score: 2
	

Case 3

- A 65-year-old Malay gentleman, being treated for diabetes and hypertension since 2014
- Unresolved right cellulitis and goitre, referred to Wound Care Clinic for further management
- Treated with five rounds of maggot debridement therapy (MDT), no side effects were observed (e.g. myiasis or bleeding)
- The wound improved by 36%

Pre-MDT	Post-MDT
Area (length x width): 55cm^2	Area (length x width): 35cm^2
Wound bed: Sloughy tissue (50%) Granulation tissue (30%) Epithelialisation (20%)	Wound bed: Granulation (70% Epithelialisation (30%)
Pain score: 3	Pain score: 2
	

University of Texas Medical Branch (UTMB) grading (Armstong et al, 1996). Treatment was considered complete once the wound had healed, defined as the wound/ulcer being suitable enough for split-thickness skin grafting (STSG), flap coverage or self-healing as judged clinically. DFUs found suitable for desloughing and STSG or flap coverage at the same setting were also considered to be healed.

Pain was measured using the Visual Analog Scale (VAS).

Results

Assessment of all nine patients who were enrolled in this study showed positive outcome were achieved in 66% . There are six patients who have completed the study, their data showed:

- Successful debridement of wound surface area in which less than 5% of wound bed was covered by slough or necrotic tissue after MDT
- Improved healing rate, most wound were suitable for wound closure by STSG or flap coverage within one week
- Time to heal reached optimal results with good wound bed preparation with minimum of two application, where there was a reduction in slough and necrotic tissue
- Reduction in wound-related pain from 3–2 to 2–0.

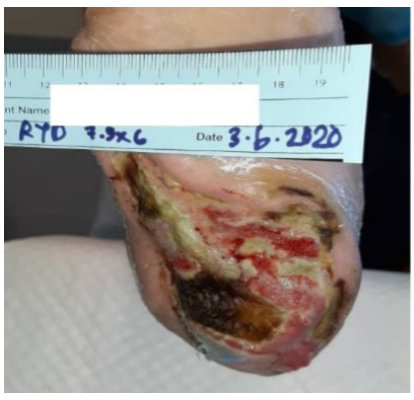
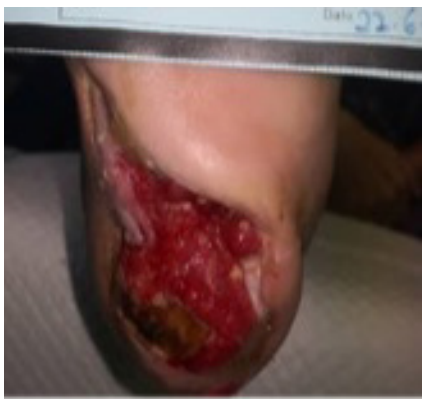
The other three patients showed a significant improvement with at least 40% of slough debrided within the time frame. Furthermore, MDT was not harmful, with no side effects reported in this study. The details of the DFU aetiology and treatments can be seen in ***Cases 1–9***.

Discussion

Wound healing is a physiological process of repairing, regenerating and remodelling of the injured tissue which consist of four components: homeostasis, inflammation, proliferation, and remodelling. (Cowan et al, 2007). In each phase, new cells are produced and transported into the injured tissue to aid healing, or cells already present alter their activity to secrete new cytokines or perform different tasks, in response to changing conditions in the wound, such as bleeding, hypoxia, alterations in cytokine concentrations. The cells will then undergo apoptosis, programmed cell death, and are engulfed by macrophages to be removed once no longer needed. Normally, these four stages in the healing process progressed quickly and smoothly based on its natural sequences. However, in certain cases such as presence of

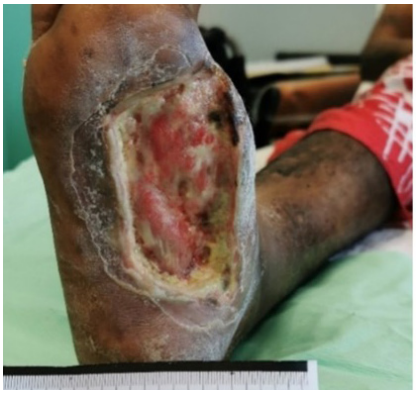
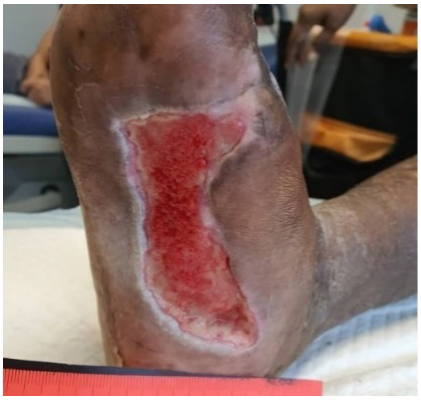
Case 4

- A 59-year-old, Malay gentleman. Known case of diabetes, with hypertension on treatment.
- Treated with three rounds of maggot debridement therapy (MDT), no side effects were observed (e.g. myiasis or bleeding)
- The wound improved by 67%

Pre-MDT	Post-MDT
Area (length x width): 45cm^2	Area (length x width): 15cm^2
Wound bed: Bone exposes Sloughy tissue (60%) Granulation tissue (40%)	Wound bed: Bone exposed Granulation tissue (100%)
Pain score: 1	Pain score: 0
	

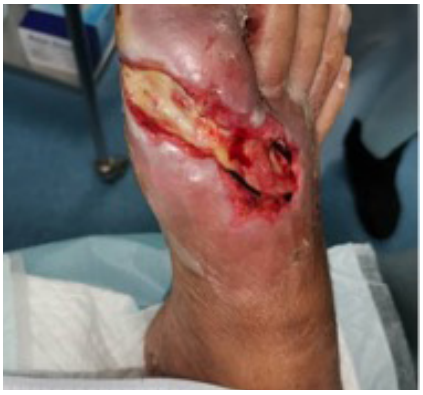
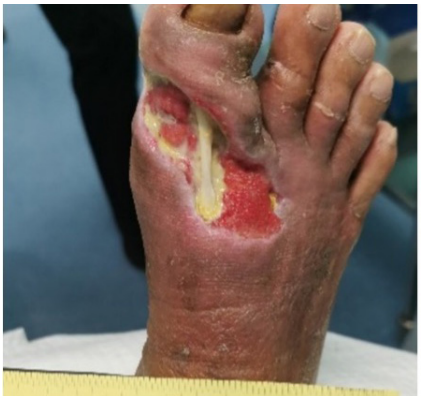
Case 5

- A 51-year-old Indian lady with underlying diabetes on treatment
- Wound debridement done under the Orthopaedic department, Hospital Kuala Lumpur
- Treated with four rounds of maggot debridement therapy (MDT), no side effects were observed (e.g. myiasis or bleeding)
- The wound improved by 36%

Pre-MDT	Post-MDT
Area (length x width): 36cm^2	Area (length x width): 22.5cm^2
Wound bed: Sloughy tissue (40%) Granulation tissue (60%)	Wound bed: Sloughy tissue (80%) Granulation tissue (20%)
Pain score: 2	Pain score: 0
	

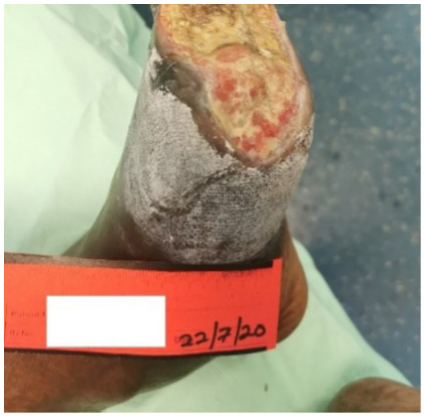
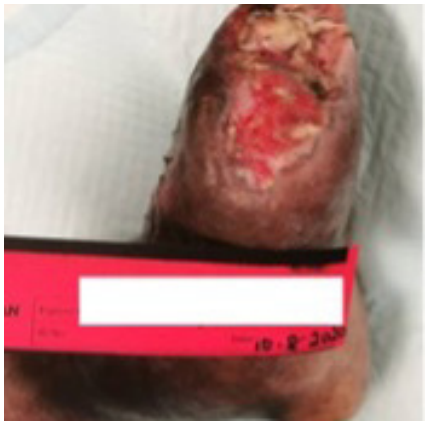
Case 6

- A 57-year-old Malay gentleman with underlying diabetes for 2 years, on treatment
- Develop an ulcer on the right big toe on 15.6.2020 because of blister due to pressure
- Treated with five rounds of maggot debridement therapy (MDT), no side effects were observed (e.g. myiasis or bleeding)
- The wound improved by 50%

Pre-MDT	Post-MDT
Area cm (length x width): 24cm^2	Area cm (length x width): 12cm^2
Wound bed: Sloughy tissue (40%) Granulation tissue (60%)	Wound bed: Sloughy tissue (80%) Granulation tissue (20%)
Pain score: 2	Pain score: 0
	

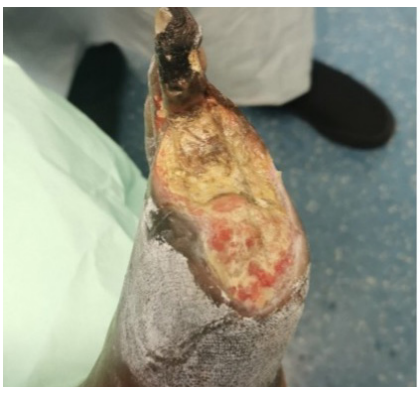
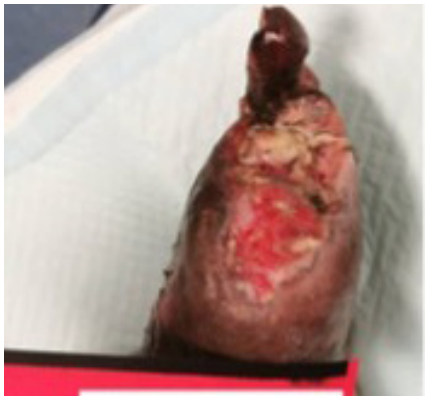
Case 7

- A 65-year-old, Malay gentleman with underlying diabetes and hypertension, which have been undertreatment since 2014
- Unresolved left cellulitis and referred to the Wound Care Clinic for futher management.
- Treated with four rounds of maggot debridement therapy (MDT), no side effects were observed (e.g. myiasis or bleeding)
- The wound improved by 66%

Pre-MDT	Post-MDT
Area (length x width): 35cm^2	Area (length x width): 12cm^2
Wound bed: Necrotic tissue (80%) Sloughy tissue (20%)	Wound bed: Granulation tissue (100%)
Pain score: 2	Pain score: 0
	

Case 8

- A 76-year-old, Indian gentleman with underlying diabetes on treatment
- Wound debridement and Ray amputation done in hospital
- Treated with three rounds of maggot debridement therapy, no side effects were observed (e.g. myiasis or bleeding)
- The wound improved by 34%

Pre-maggot debridement therapy	Post-maggot debridement therapy
Area (length x width): 24cm^2	Area (length x width): 12cm^2
Wound bed: Sloughy tissue (80%) Granulation tissue (20%)	Wound bed: Sloughy tissue (20%) Granulation tissue (80%)
Pain score: 3	Pain score: 2
	

infection, biofilm or ischaemia, the healing may cease, leading to a non-healing wound. Wound healing may cease at any phase (or even while undergoing a combination of phases), but commonly it is within the inflammatory phase: dead, infected debris may not be adequately removed from the wound bed, and/or it might not be possible for the body to eradicate the local infection, and/or the proteases and other destructive products of inflammation by clearing the newly formed cellular and extracellular matrix as fast as it is being laid down (Cowan et al, 2007). It is in this context that debridement, disinfection, or cellular proliferation and migration are so important, as they can push the non-healing wound into the next phase of healing.

There have been several studies conducted to determine how the maggots increase granulation in the wound bed. A study conducted in 2006 demonstrated an increased migration (but not proliferation) of the fibroblasts which was attributed to the action of serine and metallo-proteinases (Horobin et al, 2006). Another study found high levels of gamma interferon and interleukin-10 in the excretions of maggots that were thought to increase granulation tissue formation (Prete, 1997).

About 5–30% of wounds treated with MDT have some pain or discomfort according to a number of studies. (Sherman et al, 2001; Sherman, 2002;2003.) At the same time, these patients also have chronic wound pain even before treatment with MDT. Therefore, they are likely to experience pain or discomfort during and after treatment, and also can be readily identified, warned, and treated appropriately with analgesics if needed. Commonly, pain generally occurs after the first 24 hours, as the maggots increase in size. An analgesic is a good choice to control the pain, but if not, taking out the dressing and removing of the maggots will reduce and halt the pain or discomfort in no time.

Finally, MDT is a great modality to be used in managing DFUs, especially for wound debridement; however, a more robust trial should be conducted to show the significance of MDT. WAS

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Case 9

- A 53-year-old, Indian lady with underlying diabetes being treated for more than three years
- Rays amputation done under Orthopaedic Surgeon in Klang on 22 June 2020, at presentation her tendon was slightly necroctic and sloughy
- Treated with four rounds of maggot debridement therapy (MDT), no side effects were observed (e.g. myiasis or bleeding)
- The wound improved by 58%

Pre-MDT	Post-MDT
Area (length x width): 108cm^2	Area (length x width): 45cm^2
Wound bed: Tendon exposed Sloughy tissue (60%) Granulation tissue (40%)	Wound bed: Granulation tissue (80%) Epithelialisation (20%)
Pain score: 3	Pain score: 2