Reintroduction of maggot debridement therapy in the treatment of diabetic foot ulcers in Singapore: a single institution's initial experience

Key words:

- *Diabetic foot*
- *Foot ulcer*
- *Maggot debridement therapy*
- *Peripheral vascular disease*
- *Wound healing*

Background: Diabetes mellitus is often associated with peripheral vascular disease and limb ulcers. Among diabetics, the lifetime risk of developing a foot ulcer is approximately 15%. Maggot debridement therapy (MDT) uses sterile, medical-grade maggots for non-surgical treatment of necrotic or sloughy wounds. **Aim**: This study aims to ascertain the safety and efficacy of MDT using locally produced, sterile maggots of *Lucilia cuprina* as a means of biological debridement in diabetic foot ulcers (DFU).
Methods: We prospectively recruited patients with DFUs to undergo MDT. Baseline and interim wound characteristics, change in slough or necrotic tissue were studied. **Results**: Our results were promising with minimal side effects besides discomfort and mean visual analogue pain score was 3.3. All wounds showed reduction in slough, with an average reduction of 15% after one application and 45% after two applications ($p<0.001$). **Conclusion**: MDT has proven to be a safe and effective method of debridement, with the pain resulting from MDT easy to manage.

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Diabetes mellitus is a condition often associated with peripheral vascular disease and limb ulcers. Diabetic foot ulcers (DFU) are one of the most prevalent complications in patients who have suboptimal control of their diabetes. It is also a common cause for amputation of lower extremities (Oliver and Mutluoglu, 2020). There are 1 in 3 people aged 65 and above with diabetes and by the year 2050, up to 1 million Singaporeans are projected to be affected by diabetes (Ministry of Health Singapore, 2010). Among patients with diabetes, 2–3% will develop a DFU each year, while the lifetime risk of developing a DFU is approximately 15%. There has been a rising trend in lower extremity amputation rates in Singapore, related to complications arising from diabetes. The amputation rates increased from 26 per 100 000 residents in 2001 to 47 per 100 000 residents in 2007 and 55 per 100 000 residents in 2014. These high rates of lower extremity amputations in Singapore, compared with other Organization for Economic Co-operation and Development (OECD) countries (Organisation for Economic Co-operation and Development, 2015), not only have subsequent implications on patients' quality of life, but also have indirect costs on society, as a significant number of amputees are unable to return to work and require a long-term carer.

Maggot debridement therapy (MDT), using sterilised medical grade maggots, was described in 1832 for chronic wounds that have moist slough, where surgical debridement is not required (Larrey, 1832). There has also been emerging evidence for its use in wounds infected with multiple drug-resistant organisms (Naik and Harding, 2017). The technique has had a resurgence in recent times due to improved ways to deliver maggots to the wound bed (Paul, 2009). MDT in Singapore since has recently been reintroduced in the local healthcare system. It has been shown to be associated with faster growth of granulation

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tissue and greater wound healing rates when compared with conventional therapy (Sherman et al, 2000). MDT is also useful as a means for biological debridement in infected ulcers and helps to remove necrotic or sloughy tissue. It has also been used in regional countries such as Malaysia, with usage in both tertiary hospitals and primary health care settings, which has led to reductions in lower extremity amputation rates in these countries (WHO, 2018).

While MDT has been reported extensively in the UK and the USA where sterile maggots are readily available, there is a lack of published papers on the effectiveness of MDT in Singapore with only one prior report (Pettican and Baptista, 2012).

Aim

In this study, a locally produced Health Science Authority (HSA) approved medical device, *Lucilia cuprina* sterile maggots were used in the treatment of DFUs. The objective of the study was to ascertain the safety and efficacy of this locally developed for MDT, and evaluate whether MDT improves wound healing, in terms of reduction in wound area and reduction in slough percentage. We also evaluated whether MDT reduces the need for operative debridement. The findings of the research could be used to support the reintroduction of MDT as an adjunct wound therapy locally in Singapore and will also add to the growing body of literature on MDT in Asian patients.

Methodology

Maggot preparation process

Colonies of *Lucilia cuprina* flies were initially collected from the wild and allowed to reproduce in an Arthropod Containment Level 2 (ACL 2) insectary facility. Firstly, slivers of sheep offal are used as a bait to attract wild type blowfly populations, into a transparent box which can then be sealed for transportation back to the ACL 2 insectary. Then, trained staff identify the *Lucilia cuprina* species of blowfly and remove them and kill the other species of blowflies/ flies trapped within. When sufficient males and females wild-type *Lucilia cuprina* blowflies are collected, they are allowed to breed, lay eggs, hatch into larvae, pupate and emerge as adults to complete and continue the life cycle as Lab reared *Lucilia cuprina* blowflies.

Under ISO13485 certified protocols for medical device manufacture, lab reared *Lucilia cuprina* blowflies are kept in cages of 200–500 flies and fed a diet of carbohydrates and proteins essential to healthy growth and development. At a specific age, the lab reared blowflies become sexually active and thereafter females become gravid within a few days. A high protein substrate comprised of sheep or seafood offal is used to stimulate the gravid females to lay eggs which are visible as clumps of white eggs about 1–2mm in length. Trained staff remove these eggs clumps, separate them into individual eggs and rinse them in distilled water in preparation of the sterilisation process to generate the medical grade maggots.

The sterilisation process involves multiple washes in a buffered disinfection solution with vigorous agitation, conducted under aseptic protocols in a Biosafety cabinet. On each wash cycle, eggs that are not viable or damaged, will float to the top and are removed with a sterile pipette. On the final wash cycle, viable eggs remaining are carefully removed and placed onto prepared transportation vials containing a nutrient agar transport media and sealed for delivery. For quality control, all batches of sterilised eggs have a sampling of eggs and sampling of disinfection wash which are streak plated on Blood and Choc agar to select for fastidious microbes, then incubated at 36.9ºC for a minimum of 18 hours. They are observed for signs of microbial growth and findings recorded for traceability as stipulated in the ISO13485 protocols and HSA guidelines. The corresponding vials of hatched larvae are labelled and delivered to the designated medical facility for clinical use, with each vial containing about 200 *Lucilia cuprina* larvae.

Inpatient study protocol

Prescription of MDT was based on a multidisciplinary decision by the clinical team and wound care professionals. For baseline assessments, vascular assessments were routine and performed as part of existing workflow and standard of care.

Sterile, medical-grade HSA-approved maggots for MDT were applied onto the wound and were changed every 2–3 days. Each patient had 2 consecutive applications of MDT.

Patients were allowed to switch between MDT and conventional wound therapy, and not limited to MDT alone. Revascularisation and operative debridement or amputations were performed as part of standard of care. Standard clinical review with wound inspection, pain score and assessment of wound size and area was performed every time the MDT dressings were changed. Slough percentage was recorded at baseline, and after each application. Photographs of the wound were taken and

Table 1.s Patient demographics	
Demographics	**No. (%) or mean ± standard deviation**
Study population	11
Study period	1 year
Male:female	10 (90.9%) : 1 (9.1%)
Chinese : Malay : Indian : Other	8 (72.7%) : 1 (9.1%) : 1 (9.1 %) : 1 (9.1%)
Mean age (range)	64 (51–81) years
Cigarette smoking: current: ex: never	2 (18.2%) : 5 (45.4%) : 4 (36.4%)
Diabetes mellitus	11 / 11 (100%)
Mean Hbac (range)	7.1% (5.3 – 9.1%)
Peripheral vascular disease	9 / 11
Toe brachial pressure index	0.25 ± 0.16
Revascularisation performed before MDT application	9 / 11 (81.8%)
Type of revascularisation: angioplasty : bypass : hybrid procedure	6 : 2 : 1
Hypertension	10 / 11 (90.9%)
Ischaemic heart disease	8 (72.7%) : 3 (27.3%)
End stage renal failure	4 / 11 (36%)

Table 2. Wound characteristics and study outcomes	
Wound characteristics	
Side of wound (Right : left)	2 (18.2%) : 9 (81.8%)
Depth of wound (superficial : deep)	25 (75.8%) : 8 (24.2%)
Type of wound (heel : single toe amputation : multiple toes amputation : trans-metatarsal amputation)	2 (18.2%) : 2 (18.2%) : 5 (45.4%) : 2 (18.2%)
Study outcomes	
Mean reduction in slough following 2 applications	45% (*p<0.001*)
Mean change in area of wound (cm^2) following 2 applications	+0.65 (*p=0.71*)
Number of vials used (1 : 2 : 3 : 4)	7 : 13 : 1 : 1
Mean number of vials used per application	1.81
Use of antibiotics (yes : no)	32 (97%) : 1 (3%)
Mean Visual Analogue Scale Score	3.3 (2.3 – 4.3, 95% CI)
Mean number of debridements required per inpatient (Total : post-MDT)	2 : 1
Complications as a result of MDT	0
Patients who did not complete prescribed length of therapy	1
Wound closure rate	45.5% (5/11)
Limb salvage rate	90.9% (10/11) 2 patients demised from non-wound related aetiologies with affected limb preserved
Mean time to wound closure	7.2 months (6 – 8.4, 95% CI)
Median time to wound closure	7 months

stored on the patient's electronic medical record as per existing clinical practice.

Analgesia was given and titrated as per World Health Organisation (WHO) Analgesic ladder, using combinations of paracetamol, nonsteroidal anti-inflammatory drugs (if no history of gastrointestinal bleeding) and weak opioids like tramadol. Additional potent opioids like subcutaneous fentanyl injection were prescribed as required for dressing changes.

Wound care after usage of MDT varied between negative pressure wound dressing to promote granulation tissue or conventional dressings like hydrofibres (AQUACELAg or ExufiberAg) or technology lipido-colloid (TLC) nano-oligosaccharide factor (NOSF) dressings (Urogostart) with an outer foam dressing.

Patients were also allowed to withdraw from participation in the study at any time without penalty or affecting their medical care. Clinical data that was collected up to the time of withdrawal was kept and analysed.

Statistical analysis was conducted using GraphPad Prism version 8.0.2 for Windows (GraphPad Software, San Diego, California, USA). Descriptive analysis was conducted for all demographical data. Student's t-test was used on continuous data to compare the means between two groups and one-way ANOVA was used to compare the means of three or more matched groups. A *p*-value <0.05 was considered statistically significant.

Ethics approval for the study was obtained from our hospital's Institutional Review Board (NHG DSRB Reference: 2020/00037). All patients consented to the study and the use of their data for publication purposes.

Results

Patient demographics

In this study, 11 patients with DFUs were prospectively recruited to undergo MDT. The participants were selected from inpatients admitted under the Tan Tock Seng Hospital Vascular Surgery Service. Of the 11 patients 9 had pre-existing peripheral vascular disease (requiring revascularisation) in addition to diabetes mellitus. Patients with non-revascularised and ischaemic wounds, wounds with exposed blood vessels or at risk of profuse bleeding (haemophiliacs) or rapidly advancing soft tissue infection mandating operative debridement were excluded.

Table 2 showing the wound characteristics and study outcomes. There was a reduction in slough percentage of 15% on average after the first application. By the second application, the average reduction in slough percentage increased to 45% (p<0.001) *(Figure 1)*, with all patients having reduction in slough after 2 cycles *(Figure 2)*. The length, breadth and area of the wounds were also recorded at baseline, and after each application. Change in wound length, breadth and area showed no clear trend, with some patients seeing a reduction in wound length, breadth and area, while others saw an increase in these measurements. The changes are reported in the individual patients' case study tables above. A total of 3 out of 11 patients (27.3%) had reductions in wound lengths and 4 out of 11 patients (36.4%) had reductions in wound breadths, after 2 applications. The change in total wound area was also calculated and reported in each individual case study, with a total of 2 out of 11 patients (18.2%) seeing a reduction in wound area after 2 applications of MDT.

As seen from the case studies, all patients showed a decrease in slough percentage, 18% of

Case 1

- A 64-year-old Chinese male, with a deep left heel wound
- They received 2 applications of MDT
- Overall reduction in slough percentage of 60%;, with a 8.5% increase in wound size.

Pre MDT		Post MDT	
Length : breadth : area	6.1 cm : 6.8 cm : 32.9 cm^2	Length : breadth : area	6.3 cm : 6.6 cm : 35.7 cm^2
Wound bed	100% slough	Wound bed	40% slough
Pain score	0/10	Pain score	2/10

Case 2			

- A 51-year-old Malay female, with a superficial wound over 3rd, 4th and 5th ray amputation sites on left foot; Fem — distal bypass with vein graft for revascularisation.
- She received 2 applications of MDT
- Overall reduction in slough percentage of 40%; 6.0% increase in wound size

Pre MDT		Post MDT	
Length : breadth : area	7.3 cm : 5.0 cm : 26.5 cm^2	Length : breadth : area	6.9 cm : 5.6 cm : 28.1 cm^2
Wound bed	80% slough	Wound Bed	40% slough
Pain score	4/10	Pain score	8/10

Wound healed 5 months post MDT

Case 3			

- A 60-year-old Chinese male, with a superficial wound over 1st and 2nd ray amputation sites on left foot, who underwent angioplasty for revascularisation
- He received 2 applications of MDT
- Overall reduction in slough percentage of 20%; 9.7% increase in wound size

Pre MDT		Post MDT	
Length : breadth : area	6.3 cm : 4.4 cm : 19.6 cm^2	Length : breadth : area	5.1 cm : 6.0 cm : 21.5 cm^2
Wound bed	80% slough	Wound bed	60% slough
Pain score	2/10	Pain score	10/10

the participants had wounds that were less than 5% covered in slough by their third visit, which was after the second application. Pain scores increased from an average of 2.6 on the first visit, to 3.4 on the second visit, and finally to 3.9 on the third visit. Across all visits, a total of 55% of the participants reported pain levels below 6 on the pain scale.

The participants came for a total of three visits, with the third visit being a follow-up with no MDT being administered. Over the 3 visits, there were 25 (75.8%) reports of superficial wounds and 8 reports of deep wounds (24.2%). Over the course of two applications, 7 patients used 1 vial, 13 patients used 2 vials, 1 patient used 3 vials and 1 patient used 4 vials. Of the 11

Case 4

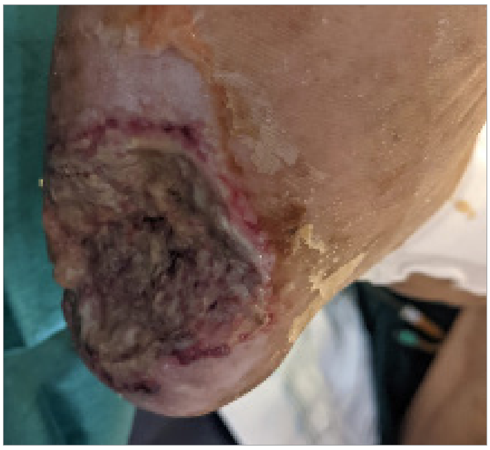
- A 65-year-old Chinese male, with a superficial wound over 1st, 2nd and 3rd ray amputation sites on left foot. He underwent a left common femoral endarterectomy and tibial vessel angioplasty
- He received 2 applications of MDT
- Overall reduction in slough percentage of 40%; 20.8% increase in wound size

Pre MDT		Post MDT	
Length : Breadth : Area	3.4 cm : 5.5 cm : 13.0 cm^2	Length : Breadth : Area	3.7 cm : 5.6 cm : 15.7 cm^2
Wound bed	80% slough	Wound Bed	40% slough
Pain score	5/10	Pain score	5/10

Case 5

- A 64-year-old Chinese male, with a superficial right heel wound. Bypass performed for revascularisation
- He received 2 applications of MDT
- Overall reduction in slough percentage of 100%; 12.4% increase in wound size

Pre MDT		Post MDT	
Length : Breadth : Area	5.5 cm : 6.3 cm : 25.0 cm^2	Length : Breadth : Area	6.3 cm : 6.5 cm : 28.1 cm^2
Wound bed	100% slough	Wound Bed	0% slough
Pain score	3/10	Pain score	5/10



Case 6

- A 52-year-old Chinese male, with a superficial wound over trans-metatarsal amputation site on left foot. Underwent angioplasty for revascularisation
- He received 2 applications of MDT
- Overall reduction in slough percentage of 40%;12.4% increase in wound size

Pre MDT		Post MDT	
Length : Breadth : Area	7.3 cm : 8.1 cm : 49.0 cm^2	Length : Breadth : Area	7.7 cm : 9.1 cm : 55.1 cm^2
Wound bed	80% slough	Wound Bed	40% slough
Pain score	4/10	Pain score	0/10

Case 7

- A 65-year-old Chinese male, with a superficial wound over 3rd, 4th and 5th ray amputation sites on left foot. Underwent angioplasty for revascularisation
- He received 2 applications of MDT
- Overall reduction in slough percentage of 20%; 12.0% increase in wound size

Pre MDT		Post MDT	
Length : Breadth : Area	10.1 cm : 3.2 cm : 27.4 cm^2	Length : Breadth : Area	11.6 cm : 4.0 cm : 30.7 cm^2
Wound bed	80% slough	Wound Bed	60% slough
Pain score	0/10	Pain score	5/10

Case 8

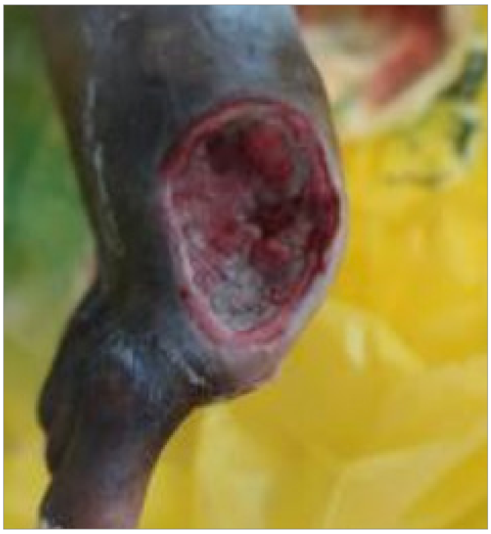
- An 81-year-old Chinese male, with a superficial wound over 3rd, 4th and 5th ray amputation sites on left foot. Underwent angioplasty for revascularisation
- He received 2 applications of MDT
- Overall reduction in slough percentage of 40%;13.9% increase in wound size

Pre MDT		Post MDT	
Length : Breadth : Area	2.3 cm : 6.4 cm : 11.5 cm^2	Length : Breadth : Area	2.8 cm : 5.9 cm : 13.1 cm^2
Wound bed	100% slough	Wound Bed	60% slough
Pain score	3/10	Pain score	2/10

Case 9

- A 66-year-old male, with a superficial wound over big toe ray amputation site on right foot
- He received 2 applications of MDT
- Overall reduction in slough percentage of 40%; 7.5% reduction in wound size

Pre MDT		Post MDT	
Length : Breadth : Area	3.8 cm : 4.4 cm : 13.4 cm^2	Length : Breadth : Area	3.8 cm : 4.1 cm : 12.4 cm^2
Wound bed	40% slough	Wound Bed	0% slough
Pain score	0/10	Pain score	0/10



Case 10

- A 66-year-old Indian male, with a superficial wound over 5th ray amputation site on left foot. Underwent angioplasty for revascularisation
- He received 2 applications of MDT
- Overall reduction in slough percentage of 60%; 12.1% increase in wound size

Pre MDT		Post MDT	
Length : Breadth : Area	3.9 cm : 3.3 cm : 9.9 cm^2	Length : Breadth : Area	4.5 cm : 3.5 cm : 11.1 cm^2
Wound bed	100% slough	Wound Bed	40% slough
Pain score	3/10	Pain score	6/10

Case 11

- A 66-year-old Chinese male, with a deep wound over trans-metatarsal amputation site on left foot. Underwent angioplasty for revascularisation
- He received 2 applications of MDT
- Overall reduction in slough percentage of 40%; 31.2% reduction in wound size

Pre MDT		Post MDT	
Length : Breadth : Area	7.4 cm : 8.7 cm : 51.6 cm^2	Length : Breadth : Area	6.0 cm : 7.4 cm : 35.5 cm^2
Wound bed	100% slough	Wound Bed	60% slough
Pain score	5/10	Pain score	0/10

patients, only one was started on antibiotics from the second visit onwards, with the rest being on antibiotics throughout the duration of the study.

In this study, the use of MDT has halved the average number of inpatient debridements, as seen in *Table 2*. It is also noteworthy that there were no complications experienced by patients

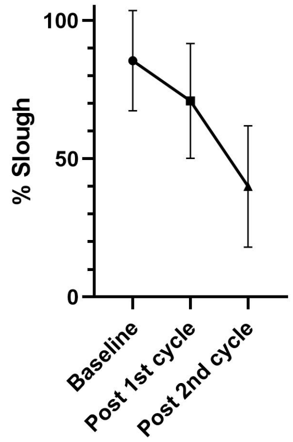


Figure 1. The mean percentage slough pre, during and post MDT (n=11). Error bars indicate standard deviation. There was 45% reduction in slough following the 2nd cycle of MDT compared with baseline (*p<0.001*).

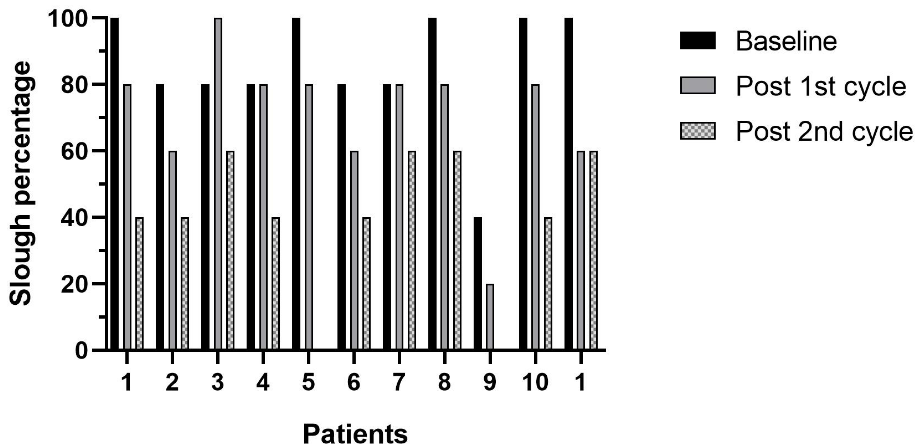


Figure 2. Slough reduction by patient

in this study. The mean change in area of wound was an increase of 0.65 cm^2. The mean pain score reported was 3.3 (±1.0) out of 10 at the 95% confidence interval. Only one out of the 11 patients in this study did not complete their prescribed length of therapy. Of the 11 patients 10 were on antibiotics for the full duration of the study, and one patient was administered antibiotics from their second visit onwards.

Discussion

Maggots perform debridement by physically feeding on dead tissue, cellular debris and exudate present in sloughy wounds. Their feeding action physically breaks up necrotic or sloughy tissue, which is then consumed and digested. This process is mediated by proteolytic enzymatic digestion through a process of extracorporeal digestion. Collagenases, trypsin-like and chymotrypsin-like enzymes are secreted which breakdown devitalised tissue into a semiliquid form which the larvae can ingest. The larvae of *Lucilia sericata* do not digest living human tissue. This selective process is one of the major advantages of larval debridement therapy as it spares the healthy tissues necessary for healing (Gottrup and Jørgensen, 2011; Fforwm and Meinwe, 2013).

Additional mechanisms of action include an antibacterial effect within the wound as bacteria contained in liquefied material is ingested and digested, reducing the bioburden within the wound and larval secretions that prevent the formation of, and reduce pre-formed biofilms (Harris et al, 2007; Cazander et al, 2009).

Based on the results of our study, 100% of the participants experienced a reduction in slough percentage. The average reduction in slough percentage after 2 applications of MDT was recorded at 45%, with patient 5 and patient 9 reporting 0% slough after the 2 applications. These results demonstrate that MDT is effective in removing necrotic tissue — a finding also supported by other similar studies that have shown that MDT is able to debride and disinfect wounds that are sloughy and infected (Chan et al, 2007). These promising results support the use of MDT as a non-surgical alternative to wound debridement.

The average change in wound size was an increase of 0.65cm^2 ($p=0.71$). 2 out of a total of 11 participants showed reductions in wound area from baseline. Patient 9 and Patient 11 reported a 1.0cm^2 and 16.1cm^2 reduction in wound size respectively. The remaining patients showed increases in wound size ranging from 1.2–6.1cm^2. This could possibly be attributed to the type of tissue present at the wound edges, which would vary from patient to patient. Maggots used for medicinal purposes secrete digestive enzymes that selectively dissolve necrotic tissue (Sherman, 2003), and the wound edges with more necrotic tissue present would thus experience a transient increase in wound size post-MDT before the wound can re-epithelialise outward in.

The limb salvage rate was 90.9% (10/11), while the wound closure rate was 45.5% (5/11) in this challenging patient population, 2 patients died during follow-up due to non-wound related aetiology (myocardial infarction) at 1 week and 4 months following MDT. Both patients had preservation of the affected limb with no need of amputation above the metatarsal level at their time of demise.

In our study, MDT did not give rise to any major adverse effects or complications, but there were reports of discomfort secondary to pain from the participants; 45% of the participants reported pain levels above 5 on the pain scale, which is corroborated by other studies that also report increased pain levels experienced in up to 30% of patients undergoing MDT. (Sherman et al, 2001). Albeit an undesirable effect, there are several effective treatment modalities for pain, which can be tailored to each individual patient's requirements. In patients who present with severe pain before the initiation of MDT, pain control measures can also be preemptively taken. Examples of such pain control measures include administration of analgesia, shorter periods of application of maggots, applying smaller-sized maggots, and applying a smaller quantity of maggots during each MDT session. (Mumcuoglu et al, 2012).

From the results, locally produced MDT is an effective method of non-surgical wound debridement in this series of challenging diabetic foot wounds. Although there was an increase in wound size noted, the large reductions in slough tissue still result in improved wound healing outcomes.

Conclusion

With stringent quality control measures in place for the sterilisation of live maggots by the Health Sciences Authority, as well as trained professionals handling the application of maggots, MDT has proven to be a safe and effective method of debridement. Pain resulting from MDT can also be easily managed. A major consideration would be that this form of therapy is dependent on the availability of sterile maggots, and our ability to get a ready, uninterrupted supply for treatment. The short life cycles of maggots result in their limited shelf life, which pose a challenge. Our study adds to the growing body of research that has been done on MDT and has demonstrated the efficacy and safety of this modality in the local context. WAS

Declaration of interest

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This was an investigator-initiated clinical *trial with support from Cuprina Pte Ltd*

References

Cazander G, van Veen KE, Bouwman LH et al (2009) The influence of maggot excretions on PAO1 biofilm formation on different biomaterials. *Clin Orthop Relat Res* 467(2): 536–45. https://doi.org/10.1007/s11999-008-0555-2

Chan DC, Fong DH, Leung JY et al (2007) Maggot debridement therapy in chronic wound care. *Hong Kong Med J* 13(5):382–6

Gottrup F, Jørgensen B (2011) Maggot debridement: an alternative method for debridement. *Eplasty* 11:e33.

Fforwm NH, Meinwe CG (2013) All Wales Guidance for the use of: Larval Debridement Therapy. All Wales Tissue Viability Nurse Forum.https://tinyurl.com/jccw3bt (accessed 10 July 2022)

Harris LG, Bexfield A, Nigam Y et al (2007) Disruption of Staphylococcus epidermidis biofilms by medicinal maggot Lucilia sericata excretions/ secretions. *Int J Artif Organs* 32(9):555–64. https://doi.org/10.1177/039139880903200904

Larrey DJ (1832) Observations on Wounds, and Their Complications by Erysipelas, Gangrene and Tetanus: and on the Principal Diseases and Injuries of the Head, Ear and Eye. https://wellcomecollection.org/works/bgvww8vf (accessed 18 July 2022)

Ministry of Health Singapore (2011). National Health Survey 2010. https://tinyurl.com/4hw225nn (accessed 10 July 2022)

Mumcuoglu KY, Davidson E, Avidan A, Gilead L (2012) Pain related to maggot debridement therapy. *J Wound Care* 21(8):400–5. https://doi.org/10.12968/jowc.2012.21.8.400

Naik G, Harding K (2017) Maggot debridement therapy: the current perspective. *Chronic Wound Care Management and Research* 4:121–8. https://doi.org/10.2147/CWCMR.S117271

Oliver TI, Mutluoglu M. (2020) Diabetic Foot Ulcer. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan- Present. https://www.ncbi.nlm.nih.gov/books/NBK537328/

Organisation for Economic Co-operation and Development. (2015). Health at a Glance 2015 : OECD Indicators. https://doi.org/10.1787/health_glance-2015-en (accessed 18 July 2022).

Pettican A, Baptista C (2012) Maggot debridement therapy and its role in chronic wound management. *Singapore Nursing Journal* 39(1):27–33

Paul AG, Ahmad, NW, Lee HL et al (2009) Maggot debridement therapy with Lucilia cuprina: a comparison with conventional debridement in diabetic foot ulcers. *Int Wound J* 6:39–46. https://doi.org/10.1111/j.1742-481x.2008.00564.x

Sherman RA, Shimoda KJ (2004) Presurgical maggot debridement of soft tissue wounds is associated with decreased rates of postoperative infection. *Clin Infect Dis* 39(7):1067-70, https://doi.org/10.1086/423806

Sherman RA (2003) Maggot therapy for treating diabetic foot ulcers unresponsive to conventional therapy. *Diabetes Care* 26:446–51. https://doi.org/10.2337/diacare.26.2.446

Sherman RA, Hall MJR, Thomas S (200) Medicinal maggots: an ancient remedy for some contemporary afflictions. *Annu Rev Entomol* 45: 55–81. https://doi.org/10.1146/annurev.ento.45.1.55

Sherman RA, Sherman J, Gilead L et al (2001) Maggot debridement therapy in outpatients. *Arch Phys Med Rehabil* 82(9):1226–9. https://doi.org/10.1053/apmr.2001.24300

World Health Organisation. (2018). Saving limbs from Amputations. https://tinyurl.com/yn2nf2zv accessed 10 July 2022)