International Journal of Infectious Diseases 25 (2014) 32–37

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

A systematic review of maggot debridement therapy for chronically infected wounds and ulcers

Xinjuan Sun [a], Kechun Jiang [a], Jingan Chen [a], Liang Wu [b], Hui Lu [c], Aiping Wang [a,*], Jianming Wang [b,c,*]

[a] Department of Endocrinology, The 454th Hospital of Chinese PLA, Nanjing, China
[b] Department of Epidemiology and Biostatistics, School of Public Health, Nanjing Medical University, Nanjing, China
[c] Department of Social Medicine and Health Education, School of Public Health, Nanjing Medical University, Nanjing, China

ARTICLE INFO

Article history:
Received 22 February 2014
Received in revised form 22 March 2014
Accepted 31 March 2014

Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Larva
Skin infection
Skin ulcer
Wound
Treatment
Debridement

SUMMARY

Objective: This study aimed to systematically evaluate maggot debridement therapy (MDT) in the treatment of chronically infected wounds and ulcers.
Methods: We performed a meta-analysis referring to the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). We searched for published articles in the following databases: PubMed, Web of Science, Embase, Wanfang (Chinese), and the China National Knowledge Infrastructure (CNKI). The latest search was updated on March 14, 2014. For dichotomous outcomes, the effects of MDT were expressed as the relative risk (RR) and 95% confidence interval (CI). For continuous outcomes with different measurement scales, we calculated the standardized mean difference (SMD). The pooled effects were estimated using a fixed effect model or random effect model based on the heterogeneity test. Subgroup analyses were performed according to the types of wounds or ulcers.
Results: MDT had a significantly increased positive effect on wound healing compared with conventional therapies, with a pooled RR of 1.80 (95% CI 1.24–2.60). The subgroup analysis revealed that the combined RRs were 1.79 (95% CI 0.95–3.38) for patients with diabetic foot ulcers (DFU) and 1.70 (95% CI 1.28–2.27) for patients with other types of ulcers. The time to healing of the ulcers was significantly shorter among patients treated with MDT, with a pooled SMD of −0.95 (95% CI −1.24, −0.65). For patients with DFU, the SMD was −0.79 (95% CI −1.18, −0.41), and for patients with other types of ulcers, the SMD was −1.16 (95% CI −1.63, −0.69).
Conclusion: MDT not only shortened the healing time but also improved the healing rate of chronic ulcers. Therefore, MDT may be a feasible alternative in the treatment of chronic ulcers.

1. Introduction

Chronic wounds, such as pressure sores and diabetic or vascular ulcers, are associated with high morbidity and, to a lesser extent, mortality.[1] Chronic wounds are notoriously difficult to treat because they usually take the form of non-healing ulcers with fibrotic tissue, dead necrotic slough, and multiple infections.[2] An important issue in wound management is the process called debridement,[3] which is defined as the removal of foreign debris and devitalized or contaminated tissues from a wound bed so that the surrounding healthy tissues are exposed.[4] Clinicians may debride wounds using various methods, including surgery, conservative sharp, high-pressure fluid irrigation, ultrasonic mist, autolysis, or enzymatic agents.[4]

One of the 'old' techniques in wound care is maggot debridement therapy (MDT). MDT is also known as maggot therapy, biodebridement, or larval therapy. In MDT, live and 'medical-grade' fly larvae are applied to the patient's wounds to achieve debridement, disinfection, and, ultimately, wound healing.[5] MDT is indicated for open wounds and ulcers that contain gangrenous or necrotic tissues with or without infection.[6]

MDT uses freshly emerged and sterile larvae of the common green-bottle fly, *Phaenicia* (*Lucilia*) *sericata*, which is a type of artificially induced myiasis raised under controlled clinical

* Corresponding authors.
E-mail addresses: wap454hospital@163.com (A. Wang), jmwang@njmu.edu.cn (J. Wang).

http://dx.doi.org/10.1016/j.ijid.2014.03.1397

conditions.[7] This type of larval therapy has several core beneficial effects on wounds and ulcers, including debridement, disinfection, and enhanced healing.[7] The beneficial effects of using larvae were first noted in 1557,[8] but with the introduction and widespread use of antibiotics in the 1940s, it was gradually neglected by doctors.[9] In recent years, with the rising incidence of drug resistance, there has been renewed interest in using maggots in chronic wound management,[9] particularly in treating wounds infected with methicillin-resistant *Staphylococcus aureus* (MRSA) and other drug-resistant pathogens.[1]

Current evidence supporting MDT for chronically infected lesions comes from several small clinical trials. To systematically summarize the overall effects of MDT in treating chronic wounds, we performed a meta-analysis by combining the results from different studies with the hope of providing scientific evidence for future clinical applications.

2. Methods

2.1. Data collection

This meta-analysis was conducted in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA).[10] We searched for published articles in electronic databases including PubMed, Web of Science, Embase, Wanfang (Chinese), and the China National Knowledge Infrastructure (CNKI) using the following terms and their combinations: ['maggot therapy' OR 'maggot debridement therapy' OR 'larval therapy' OR 'larval debridement therapy' OR 'biodebridement' OR 'biosurgery'] AND ['wound' OR 'ulcer']. The latest search was updated on March 14, 2014. Additional studies were identified from the references listed in the articles retrieved.

2.2. Selection criteria

Studies were included in this meta-analysis if they met the following criteria: (1) provided at least one of the following outcomes: healing rate, time to healing, incidence of infection, amputation rate, antibiotic-free days, or antibiotic usage; (2) compared maggot or larval therapy with other therapies (i.e., conventional therapy); (3) treated chronic wounds or chronically infected lesions; and (4) a relative risk (RR) with a 95% confidence interval (CI) or a mean with a standard deviation was reported or could be calculated from the data presented in the article. The exclusion criteria were (1) duplicated publications, and (2) studies published in any language other than English or Chinese.

2.3. Data extraction

Two graduate students independently read articles and extracted data using a standardized form. Extracted information included the name of the first author, year of publication, country, ulcer or wound type, study design, intervention and control methods, age, number of study subjects, and clinical outcomes. If published data were not available for validity assessments or outcome estimations, we contacted the authors to obtain more information. Discrepancies were resolved by discussion among the research group members.

2.4. Quality assessment

We evaluated the included studies using the quality checklist recommended by the Cochrane handbook for randomized controlled trials (RCTs).[11] The risk of bias among clinical trials was assessed based on the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias. In addition, the Newcastle–Ottawa Scale (NOS) was used to evaluate the non-RCTs.[12] The maximum score was 4 for the selection of study groups, 2 for the comparability of groups, and 3 for the ascertainment of outcomes or exposures. The maximum NOS score was 9, and studies with a score $\geq$6 were considered to be of relatively high quality.

2.5. Statistical analysis

We carried out statistical analyses using Stata 11.0 software (StataCorp LP, College Station, TX, USA). For dichotomous outcomes, the effects were expressed as the RR and 95% CI. For continuous outcomes with different measurement scales, we calculated the standardized mean difference (SMD) and 95% CI.[11] We used Cochran's Q test (significance cut-off point $p = 0.10$) and I^2 ($I^2 < 25\%$, no heterogeneity; $I^2 = 25$–50%, moderate heterogeneity; $I^2 > 50\%$, strong heterogeneity) to test the heterogeneity between the studies.[13,14] The pooled effects were calculated using a fixed effect model or a random effect model based on the heterogeneity test.[15,16] A Galbraith plot was used to detect the potential sources of heterogeneity.[17] A sensitivity analysis was performed by removing one study at a time to assess the stability of the results.[18] Publication bias was assessed using a funnel plot and Egger's test.[11]

3. Results

3.1. Characteristics of studies

Figure 1 illustrates the study selection procedure. In the initial search, 339 potentially relevant articles were identified. After reading the titles and abstracts, we excluded 59 articles that were duplicated publications. We next carefully read the full texts and excluded another 268 studies, including 72 reviews, 84 uncontrolled trials, 22 non-relevant studies, 69 other types of studies such as news, letters, or portraits, and 21 studies published in languages other than English and Chinese. Finally, 12 studies were included in this meta-analysis. The characteristics of these studies are listed in Table 1. The sample size for each study ranged from 12 to 267, with a median sample size of 76. These studies originated

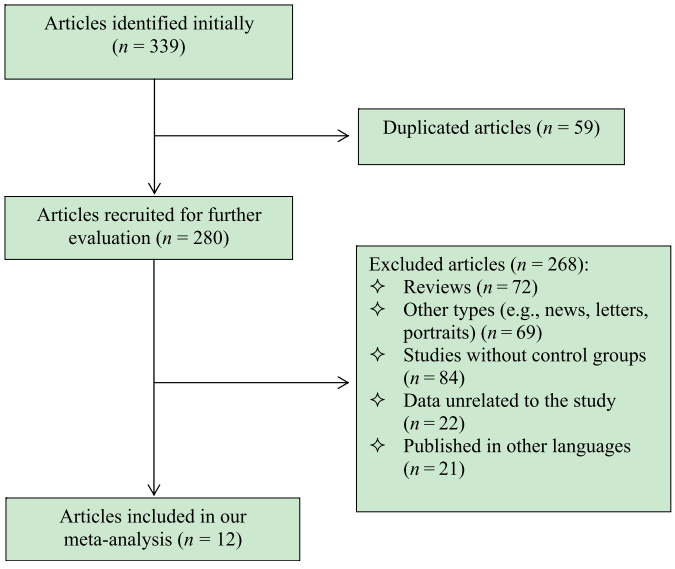

Figure 1. Flow diagram of the study selection procedure.