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Review / Derleme

Biosurgery: utility in chronic wounds

Biyocerrahi: kronik yara bakımındaki yeri

Ali Korhan Sığ¹

¹Hacettepe University, Faculty of Medicine, Department of Medical Microbiology, Ankara, Turkey

ABSTRACT

Biyocerrahi veya maggot debritman tedavisi veya larval terapi faydası özellikle kronik yara bakımında kanıtlanmış bir tamamlayıcı tıp uygulamasıdır. Uygulama neredeyse kronik yara bakımından istenen tüm nitelikleri taşımaktadır. Etki mekanizması temelde dört bölümde incelenebilir; 1) Mekanik debritman, 2) Antimikrobiyal etki, 3) Yara iyileşmesini uyarma, 4) Biyofilm yıkımı. Maggotlardan izole edilen çok sayıda protein yeni ilaçların üretilmesinde ciddi potansiyel taşımaktadır. Şu an için, bu uygulamanın etki mekanizmaları tamamen aydınlatılamamıştır ve uygulama salt bir tedavi yöntemi olarak değerlendirilmemekte; aslen, kronik yara bakımına çok disiplinli bir yaklaşımın parçası olarak sunulmaktadır.

Keywords: *Lucilia sericata*, kronik yara .bakımı, larva terapi, maggot debritman tedavisi

Corresponding Author: Ali Korhan Sığ, Hacettepe University, Faculty of Medicine, Department of Medical Microbiology, Sıhhiye, 06100, Ankara, Turkey

E-mail: dr_korhan@hotmail.com

Phone: +90 531 794 06 08

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INTRODUCTION

Biosurgery or maggot debridement therapy or larval therapy is a complementary – integrative medicinal method that is widely studied for a long time (1-3). *Lucilia sericata* larvae are actually important in forensic entomology, but their ability to feed from necrotic tissue and microorganisms makes them perfect candidates to be used in chronic wound care (4,5).

Recently, chronic wounds including diabetic foot are serious problems for healthcare, their financial burden is too high and unfortunately chronic wound prevalence is uprising (6-9). The main problems in these kind of wounds are; 1) Corrupted healing process, 2) Fruitless chronic inflammatory reactions, 3) Continuous producing of necrotic tissue, 4) Infecti-

ÖΖ

Biosurgery or maggot debridement therapy or larval therapy is a complementary – integrative medicinal method that it has proven utilities especially in chronic wound care. The method nearly provides every activity desired from a wound care. Its modes of action can be divided into four major titles; 1) Mechanic debridement, 2) Antimicrobial action, 3) Directing the tissue to wound healing, 4) Biofilm degradation. Furthermore, many isolated proteins from maggots showing various activities give a potential for future drugs. For now, whole effect mechanisms remain unclear and this therapy is not used as a single treatment method; it is actually a part of multidisciplinary approach to wound care.

Anahtar Kelimeler: *Lucilia sericata*, chronic wound care, larval debridement, maggot debridement therapy

Sorumlu Yazar: Ali Korhan Sığ, Hacettepe Üniversitesi Tıp Fakültesi, Tıbbi Mikrobiyoloji Anabilim Dalı, Sıhhiye, 06100, Ankara, Türkiye

E-posta: dr_korhan@hotmail.com

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ons, v) Biofilm formations (6,10-12). Without breaking this circle, it is actually impossible to make a proper wound treatment. Currently, there are many wound dressings or wound care methods with different specialties, and choosing the appropriate treatment method is debatable and mainly depends on etiology, wound type and existence of infection.

BIOSURGERY

Biosurgery was studied for several types of chronic wounds such as diabetic foot ulcers, venous stasis ulcers, pressure wounds. It acts mainly in four mechanisms; 1) Mechanic debridement, 2) Antimicrobial action, 3) Directing the tissue to wound healing, 4) Biofilm degradation. Maggots do these actions by

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their mechanical movements (i.e. eating) and with secretions/excretions containing several types of proteins, enzymes and chemicals (4,5). Furthermore, recent studies indicated that maggots behave in a specialized way to the wound and the infectious agent, that the proteins show wide variability according to the encountered wound and the infectious agent (13). This seems to be a perfect adaptation mechanism, which might provide physicians a "patient-specialized" treatment.

Mechanic debridement: Feeding from only necrotic tissue is the key point. The larva performs a socalled "search&destroy" activity, that it eats necrotic tissue and also it wanders onto the wound area in search of food. This behavior provides the advantage of debridement in even areas of the wound that are unreachable by surgical debridement (4,5,14). In addition, debridement is not achieved only by feeding, but also enzymatic reactions made by secretions/ excretions (15).

Antimicrobial action: Many studies were published indicating antimicrobial effects. Maggots do this action by simply eating the pathogen agent, killing the agent with secretions/excretions and alkalizing the wound area. Till now, bacteriostatic, bactericidal, antifungal and antileishmanial activities were obviously defined (13,14,16-30).

Directing the tissue to wound healing: Although Debridement and antimicrobial actions of biosurgery can already break the chain of choric wound, studies indicated that secretions/excretions of larvae may directly effect in a positive way on wound healing and neoangiogenesis. These reactions are mainly depends on enzymatic reactions. It seems maggot secretions/excretions provokes many immunologic processes in multiple ways that results the wound to get out of chronicity chain (31-34).

Biofilm degradation: Unfortunately, infectious agents of chronic wounds have always a potential to create biofilms, which results with extended treatment durations or even treatment failure. Only a few studies were published on this issue about biosurgery, but preliminary reports seem to be very promising. It was observed that biofilms of *S. aureus, S. epidermidis, K. oxytoca, E. faecalis, E. cloacae* and *P. aeruginosa* can be degraded by this method. Of note, these bacteria are the most encountered species in chronic wound infections (35,36).

The method is applied in two forms; free-range and biobag. These methods have advantages and disadvantages over each other, but the mechanism is totally the same. The choice actually depends on the patient and physician. The studies did not show any significant side effect of biosurgery, only the main



problem seems to be patient comfort, which is very subjective and tolerable comparing to the estimated results (4,14,37).

CONCLUSION

Biosurgery is an effective, cheap, easily-applicable method in chronic wound care. Although effect mechanisms remain unclear, several actions were reported in many studies. These activities cannot be separated and should be evaluated as one-chained reaction circle. Besides, this therapy is not a single treatment method; it is actually a part of multidisciplinary approach to wound care.

DECLARATION OF CONFLICTING INTERESTS

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REFERENCES

- 1. Sherman RA, Hall M, Thomas S. Medicinal maggots: an ancient remedy for some contemporary afflictions. Annu Rev Entomol 2000; 45: 55-81
- 2. Sherman RA, Wyle FA. Low-cost, low-maintenance rearing of maggots in hospitals, clinics, and schools. Am J Trop Med Hyg 1996; 54: 38-41.
- Stoddard S, Sherman R., Mason B, Pelsang D, Sherman R. Maggot debridement therapy. An alternative treatment for nonhealing ulcers. J Am Podiatr Med Assoc 1995; 85: 218-21.
- 4. Sherman RA, Mumcuoglu KY, Grassberger M, Tantawi TI. Maggot Therapy. In: Grassberger M, Sherman RA, Gileva OS, Kim CMH, Mumcuoglu KY (eds). Biotherapy-history, principles and practice: A practical guide to the diagnosis and treatment of disease using living organisms. Springer Science & Business Media, Amsterdam 2013; 5-29.
- 5. Fleischmann W, Grassberger M, Sherman RA. Maggot therapy: A handbook of maggot-assisted wound healing. Thieme Publification, London, 2004.
- 6. Trøstrup H, Bjarnsholt T, Kirketerp-Møller K, Høiby N, Moser C. What Is New in the Understanding of Non Healing Wounds Epidemiology, Pathophysiology, and Therapies. Ulcers 2013; 8: 1-6.
- 7. Sood A, Granick MS, Tomaselli NL. Wound dressings and comparative effectiveness data. Adv Wound Care 2014; 3: 511-29.
- 8. Nunan R., Harding KG, Martin P. Clinical challenges of chronic wounds: searching for an optimal animal model to recapitulate their complexity. Dis Model Mech 2014; 7: 1205-13.
- 9. Cazander G, Jukema GN, Nibbering PH. Complement activation and inhibition in wound healing. Clin Dev Immunol 2012; 8: 1-14.



- 10. Kumar V, Abbas AK, Aster JC. Robbins and Cotran pathologic basis of disease, 9th Ed., Elsevier Publification, London, 2015.
- 11. Nathan C, Ding A. Nonresolving inflammation. Cell 2010; 140: 871-82.
- Van der Plas MJA. Effect of maggot secretions on microbiological, haemotological and immunological processes. Maggot Therapy's Modes of Action. EZ Leiden, Leiden University Publification 2009; 9-35.
- Pöppel AK, Vogel H, Wiesner J, Vilcinskas A. Antimicrobial peptides expressed in medicinal maggots of the blow fly *Lucilia sericata* show combinatorial activity against bacteria. Antimicrob Agents Chemother 2015; 59: 2508-14.
- Mumcuoglu KY. Clinical applications for maggots in wound care. Am J Clin Dermatol 2001; 2: 219-27.
- 15. Pöppel AK, Kahl M, Baumann A, Wiesner J, Gokcen A, Beckert A. A Jonah-like chymotrypsin from the therapeutic maggot *Lucilia sericata* plays a role in wound debridement and coagulation. Insect Biochem Molecular Biol 2016; 70: 138-47.
- Andersen AS, Sandvang D, Schnorr KM, et al. A novel approach to the antimicrobial activity of maggot debridement therapy. J Antimicrob Chemother 2010; 65: 1646-54.
- Barnes KM, Dixon RA, Gennard DE. The antibacterial potency of the medicinal maggot, *Lucilia sericata* (Meigen): variation in laboratory evaluation. J Microbiol Methods 2010; 82: 234-7.
- Bexfield A, Bond AE, Roberts EC, et al. The antibacterial activity against MRSA strains and other bacteria of a < 500Da fraction from maggot excretions/secretions of *Lucilia sericata* (Diptera: Calliphoridae). Microbes Infect 2008; 10: 325-33.
- Bexfield A, Nigam Y, Thomas S, Ratcliffe NA. Detection and partial characterisation of two antibacterial factors from the excretions/secretions of the medicinal maggot *Lucilia sericata* and their activity against methicillin-resistant *Staphylococcus aureus* (MRSA). Microbes Infect 2004 ;6: 1297-304.
- Huberman L, Gollop N, Mumcuoglu KY, Block C, Galun R. Antibacterial properties of whole body extracts and haemolymph of *Lucilia sericata* maggots. J Wound Care 2007; 16: 123-7.
- 21. Huberman L, Gollop N, Mumcuoglu KY, et al. Antibacterial substances of low molecular weight isolated from the blowfly, *Lucilia sericata*. Med Vet Entomol 2007; 21: 127-31.
- 22. Valachova I, Majtan T, Takac P, Majtan J. Identification and characterisation of different proteases in *Lucilia sericata* medicinal maggots involved in maggot debridement therapy. J Appl Biomed 2014; 12: 171-7.
- Valachova I, Takac P, Majtan J. Midgut lysozymes of Lucilia sericata-new antimicrobials involved in maggot debridement therapy. Insect Mol Biol 2014; 23: 779-87.
- 24. Kerridge A, Lappin-Scott H, Stevens J. Antibacterial properties of larval secretions of the blowfly, *Lucilia sericata*. Med Vet Entomol 2005; 19: 333-7.
- Chernysh SI, Gordja NA, Simonenko NP. Diapause and immune response: induction of antimicrobial peptides synthesis in the blowfly, *Calliphora vicina* R.-D. (Diptera: Calliphoridae). J Entomol Sci 2000; 3: 139-44.
- 26. Erdmann G, Khalil S. Isolation and identification of two antibacterial agents produced by a strain of *Proteus mirabilis* isolated from larvae of the screwworm (*Cochliomyia hominivorax*) (Diptera: Calliphoridae). J

Med Entomol 1986; 23: 208-11.

- 27. Greenberg B. Model for destruction of bacteria in the midgut of blow fly maggots. J Med Entomol 1968; 5: 31-8.
- Robinson W, Baker F. The enzyme urease and the occurrence of ammonia in maggot-infected wounds. J Parasitol 1939; 25: 149-55.
- 29. Pöppel AK, Koch A, Kogel KH, et al. Lucimycin, an antifungal peptide from the therapeutic maggot of the common green bottle fly *Lucilia sericata*. Biol Chem 2014; 395: 649-56.
- 30. Polat E, Cakan H, Aslan M, et al. Detection of antileishmanial effect of the *Lucilia sericata* larval secretions in vitro and in vivo on *Leishmania tropica*: first work. Exp Parasitol 2012; 132: 129-34.
- Armstrong DG, Salas P, Short B, et al. Maggot therapy in "lower-extremity hospice" wound care: fewer amputations and more antibiotic-free days. J Am Podiatr Med Assoc 2005; 95: 254-7.
- 32. Dumville JC, Worthy G, Soares MO, et al. VenUS II: a randomised controlled trial of larval therapy in the management of leg ulcers. Health Technology Assessment 2009; 1-220.
- 33. Sun X, Chen JA, Zhang J, Wang W, Sun J, Wang A. Maggot debridement therapy promotes diabetic foot wound healing by up-regulating endothelial cell activity. J Diabetes Its Complications 2016; 30: 318-22.
- 34. Zhang J, Sun XJ, Chen JA, et al. Increasing the miR-126 expression in the peripheral blood of patients with diabetic foot ulcers treated with maggot debridement therapy. J Diabetes Its Complications 2017; 31: 241-4.
- 35. Cazander G, Van de Veerdonk MC, Vandenbroucke-Grauls CM, Schreurs MW, Jukema GN. Maggot excretions inhibit biofilm formation on biomaterials. Clin Orthop Relat Res 2010; 468: 2789-96.
- 36. Van Der Plas MJ, Jukema GN, Wai SW, et al. Maggot excretions/secretions are differentially effective against biofilms of *Staphylococcus aureus* and *Pseudomonas aeruginosa*. J Antimicrob Chemother 2008; 61: 117-22.
- 37. Mudge E, Price P, Neal W, Harding KG. A randomized controlled trial of larval therapy for the debridement of leg ulcers: Results of a multicenter, randomized, controlled, open, observer blind, parallel group study. Wound Repair Regen 2014; 22: 43-51.