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The Therapeutic Effects of Topical Application of Ozonized Olive Oil on Diabetic Ulcer Healing: A Literature Review

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Abstract

Diabetic ulcers is one of diabetic complications often experienced by patients with diabetes mellitus (DM). This problem lead to serious condition which usually have an effect on patients' quality of life. Application and research about wound care management in diabetic ulcer, specifically in ozone and olive oil, have been done already. However, exploration of how does the therapeutic effect of ozonized olive oils still limited. The purpose of this literature review is to determine the effectiveness of ozonized olive oil as topical treatment in diabetic ulcer. Source of databases in this literature review are Science direct, PubMed, and Google scholar. Articles were limited for 10 years from January 2009 to May 2019 which can be accessed full text in English. Type of literature included were review articles and research articles which the research area is in human. A qualitative analysis was performed to interpret the data. There were 5847 articles based on the keywords. Four studies met the inclusion criteria then were analyzed. Results of this review stated that it has been recently proved that ozonized olive oils are effective to care diabetic ulcer. It is useful as antiseptic, anti-fungal, topical antibiotics, anti-infections, and continued to be healing stimulator. This review provides clinical evidence which supports and recommends the benefits of ozonized olive oil in diabetic ulcer healing.

Keywords: diabetic ulcer, ozonized olive oil, wound healing

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1. Introduction

Diabetic ulcers is one of diabetic complications often experienced by patients with diabetes mellitus (DM). This problem lead to serious condition which usually have an effect on patients' quality of life. It is also identified as the main cause of hospitalization. Early identification of these problems should be done in order to prevent the more serious complication. So that, improving outcomes and decreasing the risk of progression as the target of healing will be accepted [1]. Diabetes patients more likely suffer from

lower extremity complications that include peripheral neuropathy, vascular problems, and ulcerations. It contribute to the incidence of diabetic ulcers, especially diabetic foot infections. More than 50% of diabetic wounds are at the risk of below-knee amputation. It significantly increases mortality because of a poor quality of life that lead to social, psychological, and economic consequences.

Diabetic Foot Ulcer (DFU) is one major chronic ulcer complication of DM in the lower limbs consists of lesions in the tissue associated with neurological disorders and peripheral vascular disease caused by several factors. Previous studies revealed that DFU's risk factors and related factors consist of dyslipidemia, DFU history or previous amputation, diabetes nephropathy, callus formation in the legs, duration of diabetes, Ankle Brachial Index (ABI), level of knowledge, and Body Mass Index (BMI) [2]. International Working Group on Diabetic Foot (IWGDF) mention that neuropathy and angiopathy are also the main factors causing DFU [3]

The incidence of neuropathy and angiopathy in the world reaches 40-70% of diabetics that they are at risk of developing DFU. The previous study by Kusumaningrum and Asriningati (2016) identifying DFU risks in diabetics which mentions 85.7% of people with diabetes with neuropathy has a high risk to become DFU (Kusumaningrum & Asriningati, 2016). Moreover, a study stated the prevalence of diabetic foot ulcer in Eastern Indonesia is 12% [3]. The more prevalence of DM, the higher the complications that happened.

Globally, it has been estimated that around 15-25% of diabetic patients will experience DFU during their lifetime. A study by Zhang [4], mentions that the prevalence of DFU in the world is as much 6.3% [4]. North America has a DFU prevalence of 13%, then followed by Africa (7.2%), Asia (5.5%), Europe (5.1%), and Ocenia (3%). DFU is one of the most feared problems in developing countries, because it is a major cause of disability, morbidity, and mortality among diabetic patients. Compared to diabetics without DFU, those diabetics with DFU have lower quality of life scores, especially in physical function and role limitations due to physical health and emotional function.

Patients with diabetic ulcers in Indonesia is increasing, especially in the big cities and the patients need an expensive cost for therapy. That's why we need an alternative therapy in the treatment of diabetic ulcers, using the alternative medicines. One of the alternative medicine which can be used to heal the ulcer is ozon. Application and research about wound care management in diabetic ulcer, specifically in ozone and olive oil, have been done already. However, exploration of how does the therapeutic effect of ozonized olive oils still limited. Therefore, the aim of this review was to evaluate the effectiveness of ozonized olive oil as topical treatment in diabetic ulcer. This review

will be beneficial as reference for wound care clinician to apply the topical therapy using ozonized olive oil in their intervention.

2. Methods

This was a review of the literature study. A quasi-experimental, experimental, and randomized control trial studies were considered for the inclusion. Sample used Diabetes patients with diabetic ulcers. Data collection procedure: Source of databases in this literature review are Science direct, PubMed, and Google scholar. Articles were limited for 10 years from January 2009 to May 2019 which can be accessed full text in English. Type of literature included were review articles and research articles which the research area is in human. Data analysis used A qualitative analysis was performed to interpret the data.

3. Results

There were 5847 articles based on the keywords. Four studies met the inclusion criteria then were analyzed. Figure 1 provides a summary of these key papers.

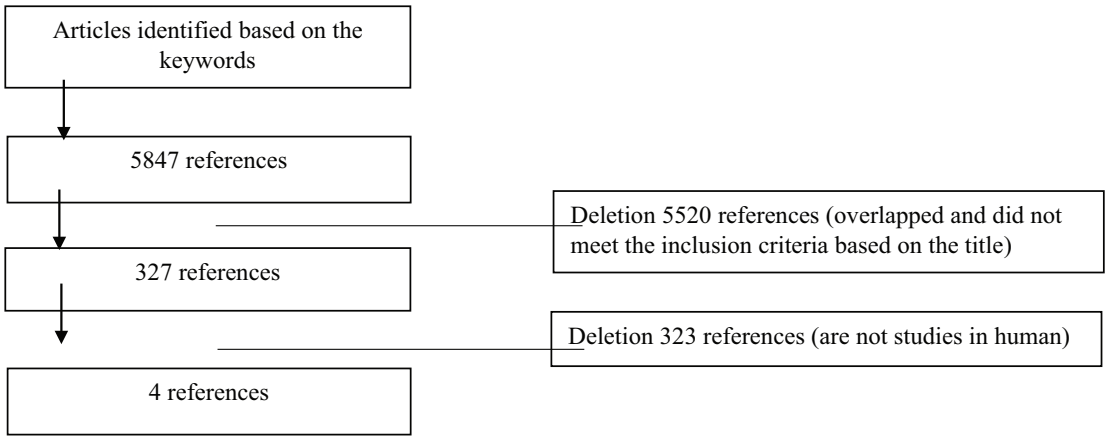

Figure 1: Flowchart of the search and selection process.

Four studies were included in the final analysis (table 1). Most of the studies had been conducted in Egypt. Three studies had a quasi-experiments and one study used a randomized control trial. All studies evaluated the effects of ozonized olive oil in diabetic ulcer healing. Two studies compared the effect of ozonized olive oil to other dressing on the healing of diabetic foot ulcers.

Results of this review stated that it has been recently proved that ozonized olive oils are effective to care diabetic ulcer. It is useful as antiseptic, anti-fungal, topical antibiotics, anti-infections, and continued to be healing stimulator.

4. Discusion

4.1. Ozonized olive oils and clinical studies on diabetic ulcers healing

The diabetic ulcer progress is caused by many factors. It is including peripheral vascular disease, peripheral neuropathy, and infection. Each condition have to be solved using appropriate treatment. A treatment already used in this case was ozonized olive oils.

Antifungal therapy is one of effective treatment in infection. However, it is less effective for colonization. It is depends on the sensitivity of microorganism [5]. Many studies have already proved that ozone therapy is more effective to treat colonization, in this case, ozone can inhibit the infection occurrence. Ozone can also support the role of antifungal treatment during infection.

Ozone can be used as a treatment of chronic wounds such as diabetic wounds. The application of ozonized oils might be useful in the treatment of foot ulcers in people with diabetes. Olive oil is used as a mediator of ozone to infiltrate inside the tissue. The using of ozonized olive oil will be minimized exudate production. The healing effect of ozone therapy can be observe from biological, physiologic, and metabolic activities that activated by the exposure of blood to ozone.

Based on this previous study in dentistry, it is proved that ozonized olive oil is a more effective antiseptic than chlorhexidine digluconate and povidone-iodine against S. aureus and the periodontal pathogen P. gingivalis [6]. An ozon application for this chronic wound is focused in inflammatory conditions. The inflammatory complication can be prevented as the exudate indicator have produced minimal [7].

4.2. Application of ozonized olive oil for diabetic ulcer treatment

A study compare between ozonized olive oil and conventional dressing on the grade I Diabetic Foot Ulcers healing revealed that the these dressing techniques (ozonized olive oil and povidon-iodin 10% wet dressing) were effective on the healing process of grade I diabetic foot ulcer. The topical application of ozonized olive oil had better healing effect than conventional dressing [8].

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Table 1

No.	Authors (year)	Title	Research objective	Design	Sample	Finding/ results	Conclusion
1.	Aziza E S, Nahad E, Nabila A B, and 'Wael Sh (2011)	Comparative Study of Ozonated Olive Oil Ointment versus Conventional Dressing Methods on the Healing of Grade I Diabetic Foot Ulcers	To compare the effect of ozonated olive oil ointment versus conventional dressing techniques on the healing of diabetic foot ulcers grade I	Quasi experimental	50 adult diabetic patients who had grade I foot ulcers (divided into two groups) in the Vascular Surgery Unit and Diabetic Foot Ulcer Unit at Alexandra main University Hospital	This study revealed that, although the two dressing techniques (ozonated olive oil ointment and betadine 10%wet dressing techniques) were effective on the healing process of grade I diabetic foot ulcers, yet ozonated olive oil solution had better healing effect than conventional solution.	Based on the results of the study, it is recommended that,ozonated olive oil ointment should be used on a daily basis time to treat grade I diabetic foot ulcers, In the vascular out –patient clinics it's preferable to use both dressing techniques in the management of patients with diabetic foot ulcer and increase nurses' awareness about ozonated olive oil ointment dressing technique.
2.	Enas Mohammed Ali (2013)	Ozone application for preventing fungal infection in diabetic foot ulcers	To determine the efficiency of ozonation in degrading mycotoxins produced by most dominant mycotoxigenic fungal species	Quasi experimental	60 people with diabetes and foot ulcer hospitalized in National Diabetes and Endocrinology Institute, Cairo University, Egypt	Among them, 72% (43/60) had yeast and mold infections. The pathogenic yeasts were noted in 60% of the patients, of which Candida (C.) species predominated. The observation of DFU documented extensive yeast conidia and fungal hyphae in association with infection. The gradual increase in ozone concentration induced progressive retardation of the spore viability of C. albicans. The diameter of mycelial growth of A. flavus was determined. At the beginning of the study there were no significant differences among the three groups. At the end of treatments, a decrease in WSA was achieved in all groups. However, compared with the antifungal treated group, the ozone treated group reached a significant WSA decrease.	Antifungal therapy is efficacious in infection, but not in colonization, and depends on the sensitivity of fungus species (problem of resistance). On the contrary, ozone therapy is better for colonization and in this case, ozone can prevent infection. Also, ozone can help support antifungal therapy during infection. 15Diabetologia

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Table 1: Continued.

No.	Authors (year)	Title	Research objective	Design	Sample	Finding/ results	Conclusion
3.	Hend Abdelmonem Elshenawie, Wael Elsayed Ahmed Shalan, Aziza Elsaeed Abdelaziz (2013)	Effect of Ozone Oil Ointment Dressing Technique on the Healing of Superficial and Deep Diabetic Foot Ulcers	To measure the effect of ozonated olive oil ointment technique on the healing of superficial and deep diabetic foot ulcers.	Quasi experimental	30 adult patients who had foot ulcers at Alexandria Main University Hospital	The study results showed that, after 3 weeks during follow up period the abnormal findings of ulcer wound healing in study group were significant decrease than in control group. Also, The results revealed no abnormalities or sign and symptoms of infection were found at the end of follow up period in study group. while in the control group at the third week and fifth week of follow up period, presence of some abnormalities such as increased of surface area measurements of the wound, unchanged surface area of the wound and absence of healing epithelial edge were observed. This findings may be due to the irritant effect of povidon-iodine. The study results showed the presence of relation between depth of ulcer and duration of follow up period during wound healing process in studied group patients" in the study group, after three weeks of follow up period the patient with grade III of foot ulcer had complete healing while the patient with grade V of foot ulcer had complete healing at the end of follow up period As control group, there were no one of all grades of diabetic foot ulcers had complete healing during follow up period while as, the majority of patients had partial healing with grade III at the end of follow up period This finding was illustrated by Willem(2011) (40) who found that. Duration of healing and foot ulcer depth (penetration through to exposed tendon, ligament bone or joint) were the most important factor for predicting out come.	Ozone ointment has shown effectiveness and safety dressing technique on the healing process of all grades of diabetic foot ulcer, which has Wounds with potential for infection, infected wounds, and poorly healing wounds. While as the conventional dressing technique is an antibacterial agent but it retards ulcer healing than ozone ointment dressing.

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TABLE 1: Continued.

No.	Authors (year)	Title	Research objective	Design	Sample	Finding/ results	Conclusion
4.	Zohreh Karimi, Mohammad Behnam-moghadam, Hossein Rafiei, Naeem Abdi, Mohammad Zoladi, Mohammad Sharif, Talebianpoor, Arash Arya, Maryam Khastavaneh (2019)	Impact of olive oil and honey on healing of diabetic foot: A randomized controlled trial	(1) To examine the impact of honey on diabetic foot; (2) To examine the effect of olice oil on diabetic foot; and (3) to compare the impact of honey and olive oil in the healing of diabetic foot	A randomized clinical trial	45 patients with grade I or II diabetic foot who were referred to hospitals affiliated to Yasuj University of Medical Sciences	Demographic characteristics of patients in the three groups were similar. Mean scores of tissue around the wound, wound grade, wound drainage, and wound healing were similar before intervention in all three groups. After intervention, means score of tissue around the wound, wound grade, wound drainage, and wound healing were significantly higher in patients in the honey and olive oil groups compared to patients in the control group.	The results of this study reveal that honey is as effective as olive oil in the treatment of diabetic foot. Given the few studies on this topic, further investigation is needed.

A study also concluded that ozonized olive oil has shown its effectiveness. An appropriate dressing on the healing process of all grades of diabetic ulcer will protect wound condition in order not to be infected that result on poorly healing wounds. Moreover, compared to the conventional dressing technique, as an antibacterial agent, the using of ozonized olive oil is more effective to increase the healing process.

5. Conclusion

This review provides an evidence which supports and recommends the benefits of ozonized olive oil in diabetic ulcer healing. It is suggested that topical using of ozonized olive oil should be used routinely to treat diabetic ulcer.

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References

[1] Packer, C. F., & Manna, B. (2019). *Diabetic Ulcer* (March 24,). Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK499887/

[2] Bortoletto, M. S. S., de Andrade, S. M., Matsuo, T., Haddad, M. D. C. L., González, A. D., & Silva, A. M. R. (2014). Risk factors for foot ulcers–a cross sectional survey from a primary care setting in Brazil. *Primary Care Diabetes*, *8*(1), 71–76. https://doi.org/10.1016/j.pcd.2013.04.003

[3] Yusuf, S., Okuwa, M., Irwan, M., Rassa, S., Laitung, B., Thalib, A., ... Sugama, J. (2016). Prevalence and Risk Factor of Diabetic Foot Ulcers in a Regional Hospital, Eastern Indonesia. *Open Journal of Nursing*, *6*(January), 1–10. https://doi.org/10.4236/ojn.2016.61001

[4] Zhang, P., Lu, J., Jing, Y., Tang, S., Zhu, D., & Bi, Y. (2017). *Annals of Medicine Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis*. *3890*. https://doi.org/10.1080/07853890.2016.1231932

[5] Enas Mohamed Ali. (2013). Ozone Application for Preventing Fungal Infection. *Diabetalogia Croatica*, *42*(1), 3–22.

[6] Montevecchi, M., Dorigo, A., Cricca, M., & Checchi, L. (2013). Comparison of the antibacterial activity of an ozonated oil with chlorhexidine digluconate and povidone-iodine. A disk diffusion test. *New Microbiologica*, *36*(3), 289–302.

[7] Karateeva, S. Y., & Milkov, B. O. (2009). OZONOTHERAPY IN THE COMPLEX TREATMENT OF PURULENT – INFLAMMATORY COMPLICATIONS IN. *Clin. and Experim. Pathol.*, *8*(4), 113–116.

[8] Aziza, Nahad, Nabila, & Wael. (2011). Comparative Study of Ozonated Olive Oil Ointment versus Conventional Dressing Methods on the Healing of Grade I Diabetic Foot Ulcers. *Researchers*, *3*(8), 16–30.

[9] Elshenawie, H. A., Shalan, W. E. A., & Abdelaziz, A. E. (2013). Effect of Ozone Olive Oil Ointment Dressing Technique on the Healing of Superficial and Deep Diabetic Foot Ulcers. *Journal of American Science*, *9*(11), 235–250.