

The Effect of Ozone Therapy on The Healing Process of Diabetes Mellitus Wounds at Dd Care Clinic, Wound, Stoma and Continent Care Center Padang City

Wenny Lazdia¹, Faridah Mohd Said², Nisha Nambiar³, Evi Hasnita⁴

Lincoln University Collage, selangor Malaysia^{1,2,3}

Universitas Fort De Kock, Indonesia⁴

E-mail: w3nnylazdia@gmail.com*

KEYWORDS

Diabetes Mellitus
Wounds, Ozone
Therapy

ABSTRACT

Diabetes mellitus (DM) is a chronic disease that can cause various complications, including diabetic foot wounds. Wound healing in diabetic patients is often hampered, so effective therapy is needed. Ozone therapy has shown potential in accelerating the wound healing process through increased tissue oxygenation and antimicrobial effects. This study aims to determine the effect of ozone therapy on the wound healing process of diabetes mellitus at DD Care Clinic Padang City. This study used a quasi-experimental design with a one group pretest-posttest method. A sample of 10 people was taken with purposive sampling technique. Data were collected using the Bates-Jensen Wound Assessment Tool (BWAT) questionnaire and analyzed using the Wilcoxon signed ranks test. The mean diabetic wound healing score before ozone therapy was 41.1 (SD 7.34) and after therapy was 25.3 (SD 7.39). The statistical test showed a P value of 0.005, which indicated a significant difference between the scores before and after therapy. The results showed that ozone therapy is effective in accelerating diabetic wound healing. This therapy works by increasing oxygenation, reducing infection, and stimulating cell regeneration. This finding is in line with previous studies that show the benefits of ozone in wound management. There is a significant effect of ozone therapy on the wound healing process of diabetes mellitus at DD Care Clinic, with a P-value of 0.005. Therefore, it is recommended that healthcare professionals consider using ozone therapy in diabetic wound care protocols to improve clinical outcomes.

INTRODUCTION

Diabetes mellitus (DM) is a chronic disease that is very common worldwide. According to the latest data, in 2021, the number of adult diabetics reached about 537 million people, and it is expected to increase to 783 million people by 2045. One of the serious complications often experienced by people with diabetes is diabetic foot ulcers. Diabetic foot wounds occur in 15-25% of people with diabetes during their lifetime, and can lead to serious infection, amputation and even death. In addition to the physical impact, these wounds also have a major effect on the patient's quality of life, causing pain, disability and decreased mobility. This suggests the need for more attention to the prevention and management of foot wounds in people with diabetes to improve their quality of life and reduce the burden on the healthcare system. (Erdoğan et al., 2018) WHO estimates that, globally at the age of 20-79 years in 2021 is expected to reach 10.5% (536.6 million people),

increasing to 12.2% (783.2 million) in 2045. (WHO 2021). The International Diabetes Federation (IDF) in 2019 stated that there are currently 351.7 million people in the world aged 20-70 years with diabetes (IDF, 2019). Indonesia is ranked 7th in the world after Mexico with a percentage of diabetes mellitus reaching 10.7 million (11.5%) and is estimated to continue to increase until 2030, reaching 13.7 million (14.9%) and in 2045 reaching 16.6 million (18.2%). (IDF, 2019) (Astasio-picado et al., 2023).

Diabetes mellitus is not only a global and national problem, but also a problem in West Sumatra. The prevalence of diabetes mellitus in West Sumatra increased from 0.7% in 2007 to 1.3% in 2013, and in 2018 it increased again to 1.7% (Ministry of Health of the Republic of Indonesia, 2018) (Dewi, 2022). Padang City is the third city with the highest number of people with diabetes mellitus after Pariaman City and Padang Panjang, with the highest prevalence of type 2 diabetes. In 2018, the prevalence of type 2 diabetes in Padang City reached 9,357 cases. In 2019, there was an increase to 18,301 cases, but in 2020 there was a decrease to 11,148 cases (Kardela et al., 2022). In the context of wound management in diabetics, ozone therapy has shown significant benefits. Based on the literature, ozone therapy can improve wound healing through improved tissue oxygenation, which supports the cell regeneration process. In addition, it has antimicrobial effects, helps reduce wound infection, and accelerates the healing process. Thus, ozone therapy can be an effective option in wound management in diabetics, who often face challenges in wound healing.

Diabetes (DM) is a disease characterized by high blood glucose caused by impaired insulin function and production or both. High blood glucose affects many parts of the body and causes complications. With the increasing prevalence of diabetes, this disease is secondary, the complications caused by this disease are also increasing. Diabetic foot ulcers (DFU) are one of the complications due to various causes such as neuropathy, ischemia, and infection that contribute to morbidity and amputation. It has been found that lower extremity amputation increases the risk of death (Izadi et al., 2019).

Diabetes mellitus (DM) is a chronic metabolic disease with a high population of sufferers in the world including Indonesia. Diabetes mellitus (DM) which does not receive good treatment is very likely to cause complications, one of the complications that is often found in people with diabetes mellitus is diabetic foot ulcers (DFU). It is recorded that there are 131 million global population experiencing lower extremity complications due to diabetes mellitus (DM) where 18.8 million of them experience diabetic foot ulcers reaching 12% this percentage is higher than China, the country with the most diabetes mellitus sufferers in the world or the global prevalence which only reaches around 1.4% - 5.9%. (Hidayat, 2021)

Diabetes mellitus is characterized by metabolic disorders. This is a disorder of carbohydrate metabolism that results in hyperglycemia and glycosuria, due to inadequate insulin production or utilization. Long-term complications that cause early morbidity are characterized by microvascular disease with thickening of the capillary basement membrane, macrovascular disease with accelerated arterio hony sclerosis, neuropathy involving the somatic and autonomic nervous systems, neuromuscular dysfunction with muscle wasting, embryonic starch, and decreased resistance to infection. These chronic complications involve the eyes, kidneys, heart, nerves, and blood vessels.

Ozone therapy is a therapy composed of ozone. This gas is present in the atmosphere with various general effects: direct disinfectant and trophic effects and systemic antibacterial and antiviral effects. This gas also increases blood circulation, makes glucose metabolism more effective, increases erythrocyte metabolism and increases fatty acid metabolism. Ozone is produced by three main energy sources, namely electrical discharge, chemical electrolysis, and ultraviolet radiation. Ozone has the property of being able to react with inorganic and

organic substances until carbon oxides, higher oxides, and water are formed, namely until oxidation is complete. (Astasio-picado et al., 2023)

The general effects of this gas are that when used locally, it has a direct disinfectant and trophic effect, thanks to the formation of peroxide it has systemic antibacterial and antiviral effects, it improves the shape of red blood cells thus increasing blood circulation which favors the delivery of oxygen to the tissues, glucose metabolism becomes more effective, increasing erythrocyte metabolism (Astasio-picado et al., 2023).

According to the journal (Kushmakov et al., 2018) ozone causes platelets to aggregate, along with the release of specific growth factors known to heal wounds quickly. Furthermore, O₃ when applied to decubitus foot ulcers (DFU), eliminates pathogens and O₂ promotes fibroblast proliferation. This helps rebuild the intercellular matrix, healing the area around the decubitus foot ulcer (DFU). Bulynin et al. showed that ozone has antibacterial properties and developed a new method of treatment through hydropressive wound treatment. The flow of ozonized liquid was generated under a pressure of 350 ATM and the “OZh-2” apparatus was used. The wound was quickly cleaned, reducing the possibility of infection, and the treatment period.

A study showed that the use of hyperbaric oxygen therapy can improve skin wound healing. Travagli et al. Believe that the acceleration of wound closure trends in the younger population may be due to O₂ tension by ozone in the area around the wound which acts as an antibacterial agent to reduce bacterial infection. In the late 20th century, a team of German scientists used ozone on skin ulcers caused by diabetes. They used plastic bags for an average of 25 minutes with concentrations ranging from 10 to 80 µg/mL. The different concentrations mentioned above were used according to how severe the ulcer was. As the patient's ulcer healed, lower concentrations of O₂ were used.

Zahumensky et al. stated that dismantling and removal of the area around the diabetic foot ulcer (DFU) is a key step in initiating therapy for neuropathic ulceration. Furthermore, the healing process can be accelerated with ozone, however, one should wear proper footwear to reduce unnecessary pressure on the foot. In non-healing wounds, O₂-O₃ combination therapy may be beneficial. A study showed that it can heal and reduce pain due to its inherent disinfectant properties and endogenous oxygen free radical scavenging properties. O₂-O₃ is known as a disinfectant because it is known to inactivate bacteria by destroying their envelope through the oxidation of certain proteins and lipids. (Kushmakov et al., 2018)

The results of the study conducted by Nabi et al. showed that topical and systemic ozone therapy is effective in reducing the size, wounds reduce the length of hospitalization, and produce more antioxidants in patients with diabetic foot ulcers (DFU). The study conducted by Zhang et al. reported that the efficacy rate, wound size reduction, and ulcer healing were much higher at the end of treatment in the ozone therapy group compared to the control group. studied the effects of ozone therapy in healing diabetic foot ulcers in two groups.

The control group only received routine diabetic foot ulcer treatment and the intervention group received routine treatment with ozone therapy twice a week. The results showed that ozone therapy was very effective in treating diabetic foot ulcers (DFU) and reducing recovery time in the intervention group compared to the control group. Teuvov et al. (2017) also showed that ozone therapy as a complementary method reduced the length of hospitalization in diabetic foot ulcer patients and accelerated their recovery. In a case report by Aytacoglu et al., the use of ozone therapy was reported to prevent leg amputation in a 67-year-old woman with diabetic foot ulcers (DFU) (Faraji et al., 2021).

The potential impact of this study is significant, both for nurses and healthcare workers caring for diabetic patients and for healthcare policy makers. The findings may encourage the adoption of ozone therapy as a more effective approach in the management of diabetic foot wounds, improve the quality of patient care, and reduce the overall burden on the health system.

RESEARCH METHOD

The method used in this study is using an experimental or quantitative method. This study was conducted using the Quasi-experimental method with a One Group Pre-test Post-test research design. The population of this study was 10 people and used a purposive sampling technique with research inclusion criteria.

This research was conducted at the DD Care Clinic, Wound, Stoma and Continence Care Center, Padang City from April 2024 to June 2024. And it was carried out according to the SOP in carrying out ozone therapy and was carried out twice a week for 3 weeks.

The research instrument used the Baters-Jensen Wound Assessment Tool (BWAT) sheet. Data were analyzed using the Denwilcoxson signed ranks test to analyze the difference in the average healing of diabetic wounds before and after ozone therapy. This study has received ethical approval from the Health Research Ethics Commission of Fort De Kock University Bukittinggi.

RESULT AND DISCUSSION

Characteristics Respondents

Table 1. Distribution frequency characteristics Respondent based on type gender and age

Characteristics	F	%
Gender		
a. Man	5	50
b. Woman	5	50
Age		
Pre-elderly (45-59 years)	4	40
Elderly (≥ 60 years)	6	60

From table 1 it can be seen that that from 10 respondent's half of its various sex man that is as many as 5 people (50%) and half of them Again various sex Woman (50%). While from aspect age, some big Respondent is in the category elderly as many as 6 people (60%) and some small be at the age pre-elderly as many as 4 people (40%).

Analysis Univariate

Average healing diabetes mellitus wound before being given therapy ozone

Table 2. Average healing diabetes mellitus wound before being given therapy ozone

Variables	N	Mean	SD	Min-Max
Before being given ozone therapy	10	41.1	7.34	33-51

From table 2 we can see the average healing rate. diabetes mellitus wound before being given therapy ozone namely 41.1 with standard deviation 7.34 and minimum value 33 and value maximum 51.

Average healing diabetes mellitus wound after being given therapy ozone

Table 3. Average healing wound after being given therapy ozone

Variables	N	Mean	SD	Min - Max
After being given ozone therapy	10	25.3	7.39	15 – 36

From table 3 we can see the average healing rate. diabetes mellitus wound after being given therapy ozone namely 25.3 with standard deviation 7.39 and minimum value 15 and value maximum 36.

Analysis Bivariate

Normality test of healing average diabetes mellitus wound before and after given therapy ozone

Table 4. Trial results average normality of healing diabetes mellitus wound before and after given therapy ozone

Treatment	<i>P</i> value (<i>Shapiro Wilk</i>)	Information
Before being given ozone therapy	0.05	Not Normal
After being given ozone therapy	0.44	Normal

Normality test results for average healing diabetes mellitus wound before being given therapy ozone is obtained Pvalue (Shapiro-Wilk) = 0.05 = α (0.05) (Data is not normal) and Pvalue (Shapiro-Wilk) after being given therapy ozone 0.44 > α (0.05) (Normal Data). Because data distribution before it is given therapy ozone abnormal and data after being given therapy normal ozone, then the appropriate further test for test average difference in healing diabetes mellitus wounds before and after being given therapy ozone is the Wilcoxon signed ranks test.

Difference in healing rates diabetes mellitus wounds before and after being given therapy ozone

Table 5. Differences in average healing diabetes mellitus wounds before and after being given therapy ozone

Treatment	N	Mean	SD	<i>P</i> value
Before being given ozone therapy	10	41.1	7,340	0.005
After being given ozone therapy		25.3	7,394	

Based on Table 5 concludes that study of the 10 respondents, the average recovery was obtained diabetes mellitus wound before being given therapy ozone namely 41.1 with standard deviation 7.340 and average healing diabetes mellitus wound after being given therapy ozone namely 25.3 with standard deviation 7.394.

Wilcoxon signed ranks test results for analyze average difference in healing diabetes mellitus wounds before and after being given therapy ozone obtained P-value (0.005) $\leq \alpha$ (0.05) (H_a accepted). This means there is average difference in healing diabetes mellitus wounds before and after given therapy ozone in Padang City.

Discussion

Discussion Univariate

Average healing diabetes mellitus wound before being given therapy ozone

From table 2 it shows that the average score healing diabetes mellitus wound respondents before being given therapy ozone is 41.1 with standard deviation 7.34. Lowest score before being given therapy ozone is 33 and the highest is 51.

Diabetes mellitus is a condition medical important things that have an impact on life many people around the world. Disturbance metabolism chronic which is also called as “parent” all this disease marked with height level glucose blood consequence pancreas No produce enough insulin, so that impact negative term long to health. people who have diabetes tends to be a disease more difficult for healed If experience wounds in comparison with people who don't have diabetes.

People with diabetes if experience wound will need long time for cure the wound. (Rizky et al., 2024) Diabetic wounds are one of the significant and damaging complications. Wounds are disconnection continuity structure anatomy network a varied body start from the simplest like layer epithelium from skin, until the deepest layer like network subcutaneous, fat and muscle even bone along with structure other such as tendons, vessels blood and nerves, as from due to trauma (Primadina et al., 2019).

Ulcer diabetic is type wounds that can be found in patients with diabetes mellitus, where at first wound classified as normal and as usual but wounds in patients with diabetes mellitus if wrong handling and care cause difficult infection to be cured, so that become wound chronicle that can cause wound gangrene and has fatal consequences as well Can culminating in action amputation (Santoso et al., 2022).

Diabetic foot ulcer must get maintenance Because There is a number of reasons, for example for reduce risk infection and amputation, repair function and quality alive. Some researcher conveys that factor age is very influential to healing wounds. Sufferers who have enter carry on age of healing process the wound will A little slow compared to with sufferers whose age Still young. (Santoso et al., 2022) Healing diabetic wounds are obstructed by various factors, including infection bacteria, dysfunction macrophages, excess cytokines proinflammatory, high level species oxygen reactive, and hypoxic sustainable. Healing Diabetes mellitus wounds can also be influenced by blood sugar levels and nutrition daily. For speed up the healing process diabetes mellitus wounds are needed patient for notice nutrition dive maintenance wound namely protein, because can help repair network skin and tissue body others who experience damage.

Balance between synthesis and degradation network to form a healing process normal wound consisting of from separate events that are mutually exclusive relate including microcirculation transportation oxygen, response immune and inflammatory changes metabolism and systems neuroendocrine as well as involving a number of level organization like many kinds of type of cell. A wound stated healed in a way perfect If wound has return to structure anatomy network, function network and appearance normally in period appropriate time.

This result in line with study albatanony et al, 2019 who conveyed that healing diabetes mellitus wounds with use therapy ozone is very effective. It conveys that effect ozone to bacteria is with bother integrity capsule cell bacteria through oxidation, so that happen cell regeneration.

Average healing diabetes mellitus wound after being given therapy ozone

Table 3 shows that the average score healing Respondent Diabetic Wounds after being given therapy ozone is 25.3 with standard deviation 7.39 and mark lowest 15 and value highest 36. Regarding giving therapy ozone in the healing process wound diabetes, according to (Naziyah et al., 2022). ozone can stimulate antioxidants so that diabetic wounds heal quickly granulate and close. Therapy ozone capable kill all type gram positive bacteria and gram negative, including resistant bacteria to antibiotics, as appropriate with study previously. Impact processing ozone to organism microscopic is bother integrity receptacle cell bacteria through oxidation so that cause recovery cells and accelerate the healing process wound (Andini, 2024).

According to rahayu et, al., 2018 decline amount colonization bacteria in patients with diabetic wounds can influence healing diabetic wounds, treatment wound with therapy ozone can, lower amount colonization bacteria in people with diabetes. In vitro studies show that therapy ozone own antibacterial properties and can deactivate microorganisms, besides kill microorganisms' ozone also does not influence proliferation cell osteoblastic.

Ozone will late in fluid wounds and will produce radical free of hydrogen peroxide (HO₂) and hydroxyl (OH) which have potential relatively high oxidation, so that can oxidize bacteria very effectively and can cause lysis wall bacteria.

Research conducted by (Sakinah, 2019) states that healing Diabetic foot wounds are influenced by various factors factor local and also factor systemic, factors local is factors that are direct influence condition wounds, including is existence pressure on the wound, pressure on the injured leg injury must be reduced for reduce injury more continue. While factor systemic is overall condition or disease individuals who can influence healing wound among them hormones, stress, disease comorbidities and nutrition.

Research result This in line with Research conducted by the Prophet in 2016 showed that use therapy ozone own effect clinically proven in a way significant influence phase healing wound, as antioxidants and reduce the length of stay-at-home sick on treatment patient with diabetic foot ulcer.

Study This in line with research conducted by Tauvov (2017) which shows results giving therapy ozone accelerate the inflammatory-degenerative process become a regeneration process and reduce microbes. Research results the after being given therapy ozone Respondent in category 100% regeneration of things This shows the healing process diabetic wounds with therapy ozone effective, time maintenance shorter and causing comfort to respondents.

Study This in line with research conducted by Anwarista and Arifin, (2023) which shows that ozone as an antimicrobial that can very usefully remember action pathogenetic given bacteria in development and maintenance periodontal inflammation. Ozone as therapy addition No cause pain and can used as an antiseptic in non- surgical treatment periodontal disease.

According to assumption researcher from what has been discussed previously, therapy ozone proven effective in maintenance diabetes mellitus wounds (Andini, 2024). Where from a number of results study existence appointment network necrotic exudate in wounds, granulation and epithelialization. These things can be measured with the BWAT (Bates-Jensen Wound Assessment) format. The BWAT sheet is can be used for evaluate or measure healing wound.

Implementation process maintenance diabetes mellitus wounds with use therapy ozone can be done with a number of methods that is direct to ozone gas network applied direct to part sick body, in ozone gas intervention dissolved into the blood taken from patients and intramuscularly ozone gas is injected to auto. Replacement wrapping wound can be done depends condition wounds and comfort respondents.

Discussion Bivariate

Influence therapy ozone to healing diabetes mellitus wound

Table 5 shows that the average score healing wound Respondent before being given therapy ozone is 41.10 and the average score healing wound Respondent after 6 times given therapy ozone is 25.3. There is average score difference healing wound Respondent between before and after given therapy ozone is obtained Pvalue $(0.000) \leq \alpha (0.05)$ (H_a is accepted). This means there is average difference in healing diabetes mellitus wounds before and after being given therapy ozone in Padang City.

Diabetic wounds are wound difficult open for healed wound This is experienced by people with diabetes mellitus. This wound usually occurs in the part that holds body, such as palm or big toe. Diabetic ulcers are a disease caused by Because body experience insulin deficiency (type 1 diabetes) or body experience insulin resistance (type 2 diabetes).

Diabetic wounds can be caused by several things factor including neuropathy, trauma, foot deformity, pressure high on the soles of the feet and disease vascular. Examination and classification comprehensive and systematic diabetic wound care can help give adequate direction. Diabetes mellitus wounds can also be caused by continued pressure continuously or existence friction that results in damage to the skin, friction Can cause the occurrence abrasion and damage epidermis surface skin. Care the right wound is effort for help speed up the healing process wound so that need continue to be developed. Diabetic wounds that do not heal healed become factor risk infection and causes the main thing to do action amputation as well as death.

According to (Ismiati et al., 2023) therapy ozone is treatment alternative that uses ozone gas. This is used for overcome various problem health, including infection, anti-virus, anti- bacterial, anti- fungal, anti- inflammatory, anti- pain, and binding rubbish metabolism body and poison body. Therapy ozone use ozone in gas form, which can enter to in body through infusion, injection intramuscular, or injection vessels blood. Ozone gas can also mix with oxygen and inserted to in body in a way direct through skin. Therapy ozone can increase performance immunity, reduce viral load, and speed up the healing process wound (Andini, 2024).

Study This in line with results research conducted by Amir et al., (2022) stated that there is difference healing wound before and after given therapy ozone. This state that therapy ozone is very effective in help healing diabetes mellitus wounds. According to assumption researcher existence influence therapy ozone towards the healing process diabetes mellitus wounds due to existence decline average score before and after given therapy ozone is 41.1 to 25.3. There is a decrease degrees diabetes mellitus wounds are caused by administration therapy ozone Because therapy ozone own antibacterial properties and can deactivate microorganisms, besides kill microorganisms' ozone also does not influence proliferation cell osteoblastic.

Besides that, speed healing Wounds are also influenced by age and width wound. Respondent with older age young will experience healing wound more fast compared to Respondent elderly. This is because of cells owned by the respondents with age young more active in divide and regenerate so that the healing process wound in progress more fast

compared to Respondent with older age old specifically elderly. In addition, the width wounds also affect speed healing wound. The wider wound so the cells needed for regenerate wound naturally more many and need time longer for healed.

Besides that, healing Diabetes mellitus wounds can also be affected from protein intake consumed patient like white eggs and fish. Healing This diabetes mellitus wound can also be influenced from support family, support family this is very important because with support family patient feel Spirit For healed. Giving therapy ozone in the healing process diabetes mellitus wounds, can be seen from the occurrence decline score BWAT sheet as per the amount exudate, amount necrosis, and color edge wound. Healing wound with use therapy ozone No only affects diabetic wounds but can also be used.

CONCLUSION

Based on research conducted on 10 respondents, it can be concluded that the average wound size of diabetes mellitus before ozone therapy was 41.10 with a standard deviation of 7.340. The average wound healing of diabetes mellitus after ozone therapy was 25.3 with a standard deviation of 7.394. There is an effect of ozone therapy in healing diabetes mellitus wounds in Padang City, with a P value $(0.005) \leq \alpha (0.05)$, so the alternative hypothesis (H_a) is accepted. From the results of this study, there are several recommendations and practical implications. First, health workers and nurses are advised to consider using ozone therapy as part of the diabetic wound care protocol, given its effectiveness in accelerating the healing process. Second, clinic managers need to provide adequate training and resources to implement ozone therapy safely and effectively. Third, it is important for policy makers to consider the integration of ozone therapy in clinical guidelines and health policies related to wound management in diabetic patients, to improve the quality of care and clinical outcomes.

REFERENCES

- Andini. (2024). Effectiveness Ozone Therapy Against Healing of Diabetic Foot Wounds in Type II DM Patients . 4(02), 7823–7830.
- Anzali , B.C., Goli, R., Torabzadeh , A., Kiani, A., Rasouli, M., & Balaneji , S.M. (2023). Healing refractory diabetic foot ulcers (DFUs) by ozone therapy and silver dressing: A case report. *International Journal of Surgery Case Reports*, 105(February), 107970. <https://doi.org/10.1016/j.ijscr.2023.107970>
- Astasio -picado, Á., Babiano , A. Á., Miriam, L., & Lozano, R.R. (2023). Use of Ozone Therapy in Diabetic Foot Ulcers.
- Dewi, et al . (2022). Prevalence Study in Patients with Diabetes Mellitus . *Journal Devotion To the Community (JPKM) - Aphelion*, 3(September), 207–212. <http://jurnal.globalhealthsciencegroup.com/index.php/JPM>
- El Meligy , O.A., Elemam , N.M., & Talaat, I.M. (2023). Ozone Therapy in Medicine and Dentistry: A Review of the Literature. *Dentistry Journal*, 11(8). <https://doi.org/10.3390/dj11080187>
- Erdoğan, A., Düzgün, A.P., Erdoğan, K., Özkan, M.B., & Coşkun, F. (2018). Efficacy of Hyperbaric Oxygen Therapy in Diabetic Foot Ulcers Based on Wagner Classification. *Journal of Foot and Ankle Surgery*, 57(6), 1115–1119. <https://doi.org/10.1053/j.jfas.2018.05.011>
- Faraji, N., Goli, R., Choobianzali , B., Bahrami, S., Sadeghian, A., Sepehrnia , N., & Ghalandari , M. (2021). Ozone therapy as an alternative method for the treatment of diabetic foot ulcers: a case report. *Journal of Medical Case Reports*, 15(1), 1–8. <https://doi.org/10.1186/s13256-021-02829-y>

- Hasan, M. (2023). Combination Ozone Therapy And Nutrition As Alternative Treatment Diabetic Foot Ulcers . 3, 10662–10673.
- Haskas , Y., Restika , I., Nursing , P., & Nani Hasanuddin Makassar, S. (2021). Evaluation of Various Wound Care Methods in Patients With Diabetic Ulcers : Literature Review. *Journal Priority Nursing* , 4(2), 12–28.
- Hidayat, N. (2021). Effects Giving Ozone Therapy in the Healing Process Diabetic Foot Ulcer : Literature Study . *BIMIKI (Periodic Scientific Student Knowledge Indonesian Nursing)* , 9(2), 74–81. <https://doi.org/10.53345/bimiki.v9i2.209>
- Ismiati , I., Harahap , WA, & Oktarina , E. (2023). Therapy for Healing of Ulcers Diabetikum : Literature Review . *Journal Scientific Journal of Batanghari Jambi University*, 23(2), 2193. <https://doi.org/10.33087/jiubj.v23i2.4124>
- Izadi, M., Kheirjou , R., Mohammadpour, R., Aliyoldashi , M.H., Moghadam, S.J., Khorvash, F., Jafari, N.J., Shirvani, S., & khalili , N. (2019). Efficacy of comprehensive ozone therapy in diabetic foot ulcer healing. *Diabetes and Metabolic Syndrome: Clinical Research and Reviews*, 13(1), 822–825. <https://doi.org/10.1016/j.dsx.2018.11.060>
- Kardela , W., Bellatasie , R., Rahmidasari , A., Wahyuni, S., & Wahyuni, F. (2022). Assessment Health- Related Quality of Life in Diabetes Mellitus Patients Type 2 In Health Center Andalas City of Padang. *Higea Journal of Pharmacy* , 14(2), 110. <https://doi.org/10.52689/higea.v14i2.496>
- Kushmakov , R., Gandhi, J., Seyam , O., Jiang, W., Joshi, G., Smith, N.L., & Khan, S.A. (2018). Ozone therapy for diabetic feet. *Medical Gas Research*, 8(3), 111–115. <https://doi.org/10.4103/2045-9912.241076>
- Nirenjen , S., Narayanan, J., Tamilanban, T., Subramaniyan, V., Chitra, V., Fuloria , N.K., Wong, L.S., Ramachawolran , G., Sekar, M., Gupta, G., Fuloria , S., Chinni, S. V., & Selvaraj, S. (2023). Exploring the contribution of pro-inflammatory cytokines to impaired wound healing in diabetes. *Frontiers in Immunology*, 14(July). <https://doi.org/10.3389/fimmu.2023.1216321>
- Primadina , N., Basori , A., & Perdanakusuma , DS (2019). *Qanun Medika- Medical Journal Faculty of Muhammadiyah Surabaya. Wound Healing Process Reviewed From Aspects Mechanism Cellular And Molecular* , 3(1), 31.
- Rizky, A., Tanjung, D., & Khairunnisa, K. (2024). The Effect of Ozone Therapy Stimulation on Diabetes Wound Healing Process. *Contagion: Scientific Periodical Journal of Public Health and Coastal Health*, 6(1), 480. <https://doi.org/10.30829/contagion.v6i1.19602>
- Sakinah. (2019). No TitleEAENH . *Αγ αη*, 8(5), 55.
- Santoso, P., Rahayu, D., & Irawan, H. (2022). Analysis of the Implementation of Gangrene Wound Treatment for Patients Diabetic Ulcers : Literature Review. *Journal Nursing* , 14(1), 171–178. <https://doi.org/10.32583/keperawatan.v14i1.40>
- Sri Temu , Untung Sujianto , MN (2021). The Healing Process Diabetic Foot Ulcer through Ozone Bagging Therapy. *Journal.Stikeskendal. Ac.Id*, 2(1), 2745–8555. <http://journal.stikeskendal.ac.id/index.php/PSKM/article/view/645>