# Home Care by Ozone Bagging towards Diabetic Foot Ulcers Healing

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Abstract: The global prevalence of DM patients in 2014 is 8.3% of the total population in the world. Increased prevalence of DM followed by increased incidence of diabetic foot ulcers. The American Diabetes Association mentioned that in 2010 there were approximately 73,000 cases of non-traumatic limb amputations with a diagnosis of DM. The purpose of this study was to determine the effect of home care with modern wound care: ozone bagging towards diabetic foot ulcers healing in Palembang. This research used quantitative and qualitative approach with mixed methodology design. The samples obtained 42 people by purposive sampling technique. Quantitative analysis used dependent samples paired t-test and qualitative used non-statistical analysis through logical inference based on actual considerations and conditions. The average before treatment were 36.21 with SD = 4.076 and after treatment were 37.17 with SD = 4.316. Home care with modern wound care: ozone bagging gave effect on wound healing of patients with diabetic foot ulcers (p = 0.026). All participants expressed feelings of great satisfaction. Therefore, it is necessary to develop further research, by developing design and intervention in several groups, so it can assess the effectiveness of ozone bagging for healing diabetic foot ulcers through home care.

## 1 BACKGROUND

Diabetes Mellitus (DM) was a chronic disease that occurs when the pancreas does not produce enough insulin or when unable to effectively use insulin (WHO, 2015). Diabetes Mellitus was a chronic hyperglycemic state accompanied by chronic abnormalities in the eyes, kidneys, and blood vessels, with lesions in the basement membrane in examination with an electron microscope (Darmono, 2007). Diabetes Mellitus which does not get optimal treatment will cause various complications, either simultaneous or a dominating problem such as diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, vascular abnormalities, and diabetic foot ulcers (Poerwanto, 2012).

American Diabetes Association mentions that Diabetes Mellitus that causes abnormalities in the blood vessels can cause stiff blood vessels and vasoconstriction causing blood flow in the tissue was disturbed. As a result of the disruption of blood flow causing the surrounding tissue to become ischemic, causing injury and causing diabetic foot ulcers (ADA, 2014). International of Diabetic Federation (IDF, 2015) states that the global prevalence rate of DM patients in 2014 was 8.3% of the total population in the world and will increase in 2014 up to 387 million cases of Diabetes Mellitus patients. Indonesia was the seventh country with 8.5 million DM patients after China, India and the United States, Brazil, Russia, Mexico.

The incidence of DM according to data Riskesdas (2013) increased from 1.1% in 2007 to 2.1% in 2013 from the total population of 250 million people. The prevalence of DM disease in South Sumatera Province based on integrated surveillance of non-communicable diseases (NCD) based on the community found that the number of people with diabetes mellitus in 2015 was 3180 people (Depkes, 2015), while the Health Service Data of Palembang in 2014 diabetes mellitus reached 1553 cases and increased by 2015 amounted to 1595 cases (Dinkes, 2015).

Increased prevalence of DM followed an increase of incidence of diabetic foot ulcers which is one part of complications caused by DM. The American Diabetes Association (ADA, 2014) mentions that in 2010 there were approximately

73,000 cases of non-traumatic limb amputations in adults over 20 years old with a diagnosis of DM. The prevalence of diabetic foot ulcers patients in the United States was 15-20%, the risk of amputation was 15 to 46 times higher than those not suffering from DM. Data Center and Information of PERSI in 2011, it is known that the number of visits DM clients with diabetic foot ulcers at Cipto Mangunkususmo Hospital in 2012 amounted to 111 patients. Amounts of amputation accounted for 35%, consisting of 30% major amputation and 70% minor amputation, while amputation death rate was about 15%.

Diabetic foot ulcers have several underlying risk factors, namely peripheral neuropathy, ischemia and infection (Clayton & Tom, 2009). Peripheral neuropathy was an important cause of the occurrence of diabetic foot ulcers. Peripheral neuropathy in the diabetic client concerns all the components of the nervous system, sensory, motor and autonomic nerves that each contribute to the development of diabetic foot ulcers (Chand et al., 2012). The most common type of diabetic neuropathy was the Distal Symmetric Polyuropathy (DSP). More than 50% of PDS is asymptomatic and clients at risk of unwitting injury to the foot resulting in foot ulcers (Boulton, 2005). Ischemia was a state of tissue lacking oxygen due to low oxygen supply in the tissue. It caused by the process of macroangiopathic on blood vessels so that blood circulation in the tissue decreases. This condition is characterized by the loss or decrease in pulse in the tibial artery, dorsalis pedis and popliteal, leg muscles experience shrinkage, cold and thickened nails.

The angiopathic process in clients of diabetes mellitus often occurs in the lower legs, especially the feet, in the form of narrowing and blockage of peripheral blood vessels, due to perfusion of the distal tissue of the leg becomes reduced, causing the occurrence of diabetic foot ulcers (Tambunan, 2010). Diabetic Mellitus sufferers with diabetic foot ulcers were particularly vulnerable to infection. Infectious bacteria in diabetic foot ulcers were Staphylococcus or Streptococcus aerobic bacteria and anaerobic bacteria Clostridium Perfringens, Clostridium Noy and Clostridium Septicum (Kateel et al., 2018).

Complications caused by diabetic foot ulcers require good holistic penalization. PERKENI (2011) mentions that in the management of Diabetes Mellitus is holistic that includes metabolic, vascular, infectious, pressure, and educational controls. Wound control is a form of effort in the treatment of diabetic foot ulcers by performing cleansing and necrotomy action if necessary on infected tissues on a regular basis. Infection control is a preventive measure of the activity of microorganisms that can cause infection in diabetic foot ulcers. Measures that can be done include preventing port de entry to a minimum and perform wound care regularly with aseptic techniques PERKENI (2011).

Management of infection is very important in the healing process of diabetic foot ulcers (Pressman, 2007) reveals modern treatments that can be done in the healing process of diabetic foot ulcers one of them by using ozone bagging. The use of ozone as a complementary / alternative therapy is now popular in Indonesia and has been used since 1992 (Inggraini, 2007). As a molecule that has enormous energy, Ozone can inactivate bacteria, viruses, fungi and some types of protozoa. this may occur due to the presence of radical ions of ozone degradation results in water in the form of hydrogen peroxide (HO2) and hydroxyl (HO) (Zhafira, 2012).

The function of ozone in healing diabetic wounds is as an antimicrobial. It was generally believed that bacteria are destroyed by the protoplasm oxidation process. The oxidation of protoplasm will damage the capsid or outer skin of the microorganism comprising the unsaturated bond of phospholipid or lipoprotein, then penetrate into the cell membrane, react with cytoplasmic substances and convert the circular plasmid of closed DNA into an open DNA circular, which can reduce the efficiency of bacterial proliferation, directly activate cytoplasmic integrity, and disrupt some degree of metabolic complexity (Dewayanti et al., 2009). The purpose of this study was to determine the effect of home care with modern wound care: ozone bagging towards diabetic foot ulcers healing in Palembang.

## 2 METHODS

This research was a pre-experimental pretest – posttest used quantitative and qualitative research, which used together through the mixed methodology design approach model. The type of mixed methods used explanatory sequential.

This method carried out in sequence, quantitative research methods first then followed by qualitative research. Researchers use this design with the expectation of qualitative findings will help interpretation or contextualize the results of quantitative research.

This research conducted in Palembang on September 18 to December 25, 2017. The population

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of this research was respondent with diabetic foot ulcers total of 55 people. The samples obtained 42 people by purposive sampling technique according to the inclusion and exclusion criteria. The inclusion criteria of this research were: able to read and write; DM people with diabetic foot ulcers grade 3 and 4 (Wagner Classification); and never get therapy with ozone bagging. The exclusion criteria of this research were: DM people with contraindication: acute alcohol intoxication, acute myocardium infarct, multi organs bleeding, pregnancy, hypertoroid, thrombocytopenia, ozone allergy, and people with heparinization; unable to complete the process.

Determination of location based on recommendation and data of Muhammad Hoesin Hospital considering DM people which was control as outpatients in internist polyclinic. The independent variable in this research was home care with modern wound care: ozone bagging, and dependent variable was diabetic foot ulcers healing.

Quantitative data obtained by observation sheet using Leg Ulcer Measurement Tools (LUMT) and have been tested for validity and reliability with r table 0.82. Qualitative data obtained from the interview, observation and documentation of patient assessment about diabetic foot ulcers healing, to determine the rational validity of modern wound care model: ozone bagging. Then, validated the treatment that have been given to the respondent, especially with what is perceived by the respondent, both the pain associated with ulcers, the frequency of pain, the feeling during the treatment is done or the feelings about the quality of life of the respondents who will come.

Research by using ozone bagging was done for 15 weeks divided into 3 sessions. Each session for 5 weeks with 14 respondents. Before treatment with ozone bagging, wound care with NaCl solution and cleansed when there was exudate. Home care helped by 4 tools of ozone bagging for every day with duration of each respondent for 10 minutes.

After all data were collected, then analyzed using univariate and bivariate (dependent sample paired t test) and qualitative analyzed using non-statistical analysis through logical inference based on actual considerations and conditions. This research had been reviewed and certified for Ethical Approval with No. 666/KEKP-PTKMKS/XII/2017 on September 11, 2017 issued by Health Research Ethics Committee of Health Polytechnic Makassar.



ng Ozone Arrangem

Figure 1: Ozone bagging tools.

## **3 RESULTS**

#### 3.1 Quantitative Results

Table 1: Distribution of respondents based on demographic characteristic.

/		
Characteristics	Ν	%
Sex		
Men	17	40.5
Women	25	59.5
Total	42	100
Age		y
21-39 years	13	31
> 40 years	29	69
Total	42	100
Level Education		
Medium (High School)	23	54.8
High (University)	19	45.2
Total	42	100
Employment		
Not work	29	69
Work	13	31
Total	32	100

Table 1 explained most of respondents were women and more than 40 years old with medium level education, and not worked.

From Table 2, we can see that the average condition of diabetic foot ulcers before doing home care with modern wound care: ozone bagging was 36.21 and standard deviation = 4.076. The average condition of diabetic foot ulcers after home care with modern wound care: ozone bagging was 37.17 and standard deviation = 4.316.

Table 2: Distribution of average diabetic foot ulcers before and after treatment.

Number of Average Diabetic Foot Ulcers					
Pretest		Posttest			
Mean	SD	Mean	SD		
36.21	4.076	37.17	4.316		

Table 3: Distribution of average diabetic foot ulcers after treatment.

Variable	Mean	SD	SE	P Value
Diabetic foot ulcers Healing	- 0.952	2.677	0.413	0.026

Table 3 showed the result of statistic test got pvalue = 0.026, hence can be concluded treatment home care modern wound care: ozone bagging influence to wound healing of diabetic foot ulcers.

#### **3.2 Qualitative Results**

#### 3.2.1 Pain Scale

All of participant say did not feel anything on diabetic foot ulcers while home care treatment by ozone bagging.

"I did not fell anything on my diabetic foot ulcers, just like wind touch my leg and diabetic foot ulcers".

#### 3.2.2 Feelings about Ozone Bagging

All participants expressed feelings of great satisfaction with home care treatment by ozone bagging as the following statement:

"No one can take me for treatment again, I want to take help my children, but their home far away. They also work so afraid of burdening. So, if the nurses come to my home, we were very helpful"

"The nurses were diligent, care, patient, and friendly. Which makes comfortable, no need to queue and tired. I can set my own time when not bother. Different in hospital, my wound (diabetic foot ulcers) not well maintained ".

'I did not difficult to manage schedule. My wound looks better, the left one has changed and dried. The right will soon heal, but sometimes still a bit wet. "

## **4 DISCUSSION**

The research founded that 90% of respondents stated comfortable choosing home care and 10% of respondents said uncomfortable choose home care. According to the researchers there were respondents who stated uncomfortable because of using Home care more than five weeks so they did not familiar with home care service and feel disturbed. Based on the interviews it was found that there were patients who prefer to be treated at home rather than in the hospital because they closer to the family and the patient does not feel the activity is limited so it makes the patient prefer to choose home care.

Comfort is a concept that has a strong relationship in nursing. Some comfort types are defined as follows: (1) Relief, a state in which a recipient has a specific needs fulfillment; (2) Ease, a state of calm and pleasure; (3) Transcendence, a state in which an individual reach above the problem. Then derivate the above context into the following: (1) Physical, with respect to body sensations; (2) Psychospiritual, with respect to the internal self-consciousness, which includes selfesteem, self-concept, sexuality, the meaning of life to a relationship of higher needs; (3) Environment, with respect to the environment, conditions, external influences; (4) Social, with regard to interpersonal, family, and social relationships. Providing home care services can support patient comfort and independence at home (Kolcaba & DiMarco, 2005).

According Katrina M et al. (2013) the benefits of home care services for clients include the needs of clients fulfilled and people will be more comfortable and satisfied with professional nursing care. Meanwhile, according to Lechner et al. (2017) stated the environment at home felt more comfortable for some clients and compared the hospital treatment so healing of diabetic foot ulcers rapidly. It showed that comfort has a chance to influence in choosing home care for diabetic foot ulcers treatment.

Nursing Law no 38 of 2014 in one article set about the practice board nurse. If the nurses want to open independent practice, they must establish a nameplate, if they do not put a nameplate, the nurse practice is considered illegal practice (nursing law no 38, 2014). Nursing practice can apply in hospitals, clinics, health centers and also at home clients as home care. Health care activities in home care included: medical services, nursing services and care, medical rehabilitation services, nutrition services, maternity visits, maternity visits, high risk infant visits, installation or replacement of medical devices such as gastric hoses, catheters, respiratory tubes and others, certain laboratory preparations, wound and stoma treatments, drug delivery via muscular and intra-vein, and infant massage (Karota 2012)

Alavi et al. (2014) explained diabetic foot disorders occur because the control of sugar levels was not well and lasted continuously for years. The main causes were nerve damage (diabetic neuropathy) and blood vessel disorders. Nerves that have been damaged make diabetes patients unable to feel pain, heat, or cold on the hands and feet. In Indonesia, there are 1785 diabetic patients with neuropathy complications (63.5%), retinopathy (42%), nephropathy (7.3%), macrovascular (16%), microvascular (6%), diabetic foot injuries (15%). Wound treatment techniques using a moist bandage aims to maintain the insulation of the wound environment that remains moist. Wound conditions that remain moist will help the wound healing process as much as 45% and reduce infectious complications and residual tissue growth.

Wound care aims to get the wound healed and prevent and overcome the infection so as not to spread to other organs. Deaths from wound infections that spread to the heart will not occur if wound care is done early on. There were 7 factors that inhibit wound healing consists of age, infection, hypovolemia, hematoma, foreign body, ischemia, diabetes and treatment (Lefrancois et al., 2017).

Modern wound care was a wound treatment that uses the principle of maintaining the wound environment to keep it moist. In maintaining the wound moisture, the dressing used ideally is a closed or occlusive dressing. Closed dressing is a bandage that prevents air from entering the wound or lesions and maintains moisture, temperature and body fluids and provides benefits, including: reducing the surface of the necrotic wound, preventing the wound from drying out, reducing pain, stimulating growth factor, activating the required enzymes for debridement as well as preparing wound protection (Vowden & Peter, 2017).

Ozone has a role in wound healing, which is as an antimicrobial and can accelerate the formation of growth factors. Ozone which is a powerful oxidant can kill microorganisms by destroying the microorganism's capsid consisting of an unsaturated bond of phospholipid followed by damage to RNA and DNA from the corresponding microorganism (Leusink, 2010).

The process of mechanics in the ozone is to inactivate bacteria, viruses, fungi, yeasts and protozoa: Ozone therapy interferes with the integrity of bacterial cells through the oxidation of phospholipids and lipoproteins. In fungi, ozone inhibits cell growth at some stage. In the virus, ozone destroys the viral capsid and disrupts the reproductive cycle by disrupting the virus-to-cell contact by peroxidation. The weak enzyme layers in cells that make them vulnerable to invasion by viruses make them susceptible to oxidation and elimination from the body, which subsequently replaces them with healthy cells (Elvis & Ekta, 2011). Diabetic complications are associated with oxidative stress in the body, ozone is found to activate antioxidant systems that affect glycemic levels. Ozone prevents oxidative stress by normalizing organic peroxide levels by activating superoxide dismutase (Zeng & Lu, 2018).

Stimulation of oxygen metabolism: Ozone therapy causes an increase in the rate of red blood cell glycolysis. This leads to а 2.3diphosphoglyceric stimulation that causes an increase in the amount of oxygen released into the tissues. Ozone activates the Krebs cycle by increasing the oxidative carboxylation of pyruvate, stimulating the production of ATP. It also causes significant decrease in NADH and helps oxidize cytochrome C. There is a stimulation of enzyme production that acts as a free radical scavenger and cell wall protector: glutathione peroxidase, catalase dismutase. and superoxide Production of prostacyclin, vasodilator, also induced by ozone (Viebahn-Hänsler, 2015). Immune activation: Ozone given at concentrations between 30 and 55 µg/cc led to the greatest increase in interferon production and the largest output of tumor necrosis factor and interleukin-2. Production of interleukin-2 launches the entire subsequent immunological reaction (Zeng & Lu, 2018).

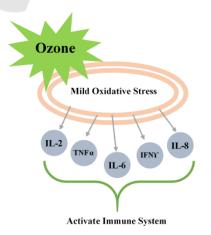


Figure 2: Mild oxidative stress induced by ozone therapy.

Research conducted by Agosti et al. (2016) shows care reports on youths who have had traffic accidents and amputations in the tibia and fibula dextra suggesting injuries to rehabilitation for treatment. At that time the wound was ulcerated but afebrile without signs of inflammation and negativity to the blood test. At 2 months of trauma despite proper care and dressing, the wound gradually improves and the patient complains of pain. For this reason, other than the standard dressing he undergoes ozone therapy. After 5 weeks of treatment, the wound healed. In patients with nonhealing injuries, ozone-oxygen therapy can help speed healing and reduce pain thanks to disinfectant properties and with enhancement of endogenous oxygen free restorer properties. Compared with standard dressings and other treatments reported in the literature, this shows a shorter course of action.

Oxidative stress has an important role in the development of complications in diabetes. Because ozone therapy can activate the antioxidant system, affect the level of glycemia and some markers of endothelial cell damage, the purpose of this study was to determine the therapeutic efficacy of ozone in the treatment of type 2 diabetic patients and diabetic feet and to compare ozone with antibiotic therapy. Ozone treatment increases glycemic control, prevents oxidative stress, normal levels of organic peroxide, and activated superoxide dismutase. The pharmacodynamic effects of ozone in the treatment of patients with neuroinfection. Diabetic feet may be considered to be derived from the possibility of being a superoxide scavenger. Superoxide is considered a link between four metabolic routes associated with diabetic pathology and its complications. Furthermore, healing of lesions improved, resulting in fewer amputations than in the control group. No side effects. These results suggest that medical ozone treatment may be an alternative therapy in the treatment of diabetes and its complications (Martínez-Sánchez et al., 2005).

Research in vitro evaluation of wound healing and antimicrobial potential of ozone therapy performed by (Borges et al., 2017), although ozone therapy is widely applied when wound repair and antimicrobial effects, little is known about the cellular mechanisms of this process. The effects of ozone on cell migration are evaluated through initial wound healing and trans well migration tests. The minimum inhibitory concentrations for Candida Staphylococcus albicans and aureus were determined. Ozone does not show cytotoxicity on the cell line, while chlorhexidine significantly reduces cell viability. Although no significant

differences between control cells and ozone treated cells were observed in the initial test, a substantial increase in migration of fibroblasts was observed in cells treated with an ozonation solution of 8 mg/ mL. In addition, a study conducted by (Weinstein, 2012) which concluded based on research conducted in two groups of respondents in the ozone group showed the healing process in foot ulcer is very significant for 12 weeks.

## 5 CONCLUSIONS

Home care by ozone bagging affects the wound healing of diabetic foot ulcers and all participants expressed do not feel anything in the wound when home care is applied with modern wound care: ozone bagging, as well as expressing a very satisfied feeling.

Modern wound care treatment: ozone bagging for healing diabetic foot ulcers through home care needs to be done further development. Further development is expected to be done in several groups and can be followed the development of diabetic foot ulcers healing with several measurements. as well as a series of ozone bagging tools can be made more simple and portable when home care therapy

# REFERENCES

- ADA, (American Diabetes Associatin), 2014. Standards of Medical Care in Diabetes 2014. *Diabetes Care2*, 37(1), p.S14.
- Agosti, I.D. et al., 2016. Effectiveness of a Short-Term Treatment of Oxygen-Ozone Therapy into Healing in a Posttraumatic Wound. *Case Reposrt in Medicine*, 2016.
- Alavi, A. et al., 2014. Diabetic foot ulcers: Part I. Pathophysiology and prevention. *Journal of the American Academy of Dermatology*, 70(1), p.1.el-1.e18. Available at: https://www.sciencedirect.com/science/article/pii/S01 90962213008207 [Accessed March 6, 2018].
- Borges, G.A. et al., 2017. In vitro evaluation of wound healing and antimicrobial potential of ozone therapy. *Journal of Cranio-Maxillo Facial Surgery*, 45, pp.364–370.
- Boulton, A.J.M., 2005. Diabetic Neuropathies. A Statement by the American Diabetes Association. *Diabetes Care*, 28(1).
- Chand, G. et al., 2012. Diabetic Foot. Clinical Queries: Nephrology.
- Clayton & Tom, 2009. A Review of The Pathophysiology; Clasification and Treatment of Foot Ulcer in Diabetic

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Patient.

- Darmono, 2007. Naskah Lengkap: Diabetes Mellitus Ditinjau dari Berbagai Aspek Penyakit Dalam, Semarang: CV: Agung Semarang.
- Depkes, R., 2015. Prevalensi Penyakit Tidak Menular, Jakarta.
- Dewayanti, A., Ratnawati, H. & Puradisastra, S., 2009. Perbandingan Pengaruh Ozon, Getaj Jarak Cina (Jatropha Multifida L) dan Povidone Iodine 10% terhadap Waktu Penyembuhan Luka pada Mencit Betina Galur Swiss Webster.
- Dinkes, K.P., 2015. Data Kesehatan Kota Palembang, Palembang.
- Elvis, A.M. & Ekta, J.S., 2011. ozone Therapy: A Clinical Review. Jouornal of Natural Science, Biology, and Medicine, 2(1).
- IDF, (International of Diabetic Federation), 2015. International of Diabetic Federation: Prevalency.
- Inggraini, 2007. Ozone: The Silent Healer.
- Karota, B.E., 2012. Perawatan Kesehatan Rumah (Home Health Care), Medan: Universitas Sumatera Utara.
- Kateel, R. et al., 2018. Clinical and microbiological profile of diabetic foot ulcer patients in a tertiary care hospital. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, 12(1), pp.27–30. Available at: https://www.sciencedirect.com/science/article/pii/S18 71402117302795 [Accessed March 6, 2018].
- Katrina M, R., Steven M, H. & Harry, H., 2013. Home Care: More Than Just A Visiting Nurse. *BMJ Qual Saf*, 22(12), pp.972–974.
- Kolcaba, K. & DiMarco, M., 2005. Confort Theory and its application to Pediatric Nursing. A Pediatric Nuraing, 31, pp.187–94.
- Lechner, A. et al., 2017. Dry skin and pressure ulcer risk: A multi-center cross-sectional prevalence study in German hospitals and nursing homes. *International Journal of Nursing Studies*, 73, pp.63–69. Available at:

https://www.sciencedirect.com/science/article/pii/S00 20748917301165 [Accessed March 6, 2018].

- Lefrancois, T. et al., 2017. Evidence based review of literature on detriments to healing of diabetic foot ulcers. *Foot and Ankle Surgery*, 23(4), pp.215–224. Available at: https://www.sciencedirect.com/science/article/pii/S12 68773116300157 [Accessed March 6, 2018].
- Leusink, J., 2010. How does ozone kill bacteria? Available at: http://www.ozonesolutions.com/journal/2010/howdoes-ozone-kill-bacteria/ [Accessed January 3, 2018].
- Martínez-Sánchez, G. et al., 2005. Therapeutic efficacy of ozone in patients with diabetic foot. *European Journal* of Pharmacology, 2005(523), pp.151–161.
- PERKENI, 2011. Konsensus Pengelolaan dan Pencegahan Diabetes Mellitus Tipe 2 di Indonesia, Jakarta: PERKENI.
- Poerwanto, A., 2012. Mekanisme Terjadinya Gangren pada Penderita Diabetes Mellitus, Surabaya: FK-UWK.
- Pressman, S., 2007. The Story of Ozone.

Riskesdas, (Riset Kesehatan Dasar), 2013. Riset

Kesehatan Dasar, Jakarta.

- Tambunan, M., 2010. Perawatan Kaki Diabetes, Jakarta: FK UI.
- Viebahn-Hänsler, R., 2015. The use of ozone in medicine: Mechanisms of action.
- Vowden, K. & Peter, V., 2017. Wound dressings: principles and practice. *Surgery* (*Oxford*), 35(9), pp.489–494. Available at: https://www.sciencedirect.com/science/article/pii/S02 63931917301370 [Accessed March 6, 2018].
- Weinstein, J., 2012. Diabetes; Reports from University Medical Describe Recent Advances in Diabetes. Obesity, Fitness & Wellness Week, p.959.
- WHO, 2015. No Title. World Health Organization, p.1.
- Zeng, J. & Lu, J., 2018. Mechanisms of action involved in ozone-therapy in skin diseases. *International Immunopharmacology*, 56, pp.235–241. Available at: https://www.sciencedirect.com/science/article/pii/S15 67576918300407 [Accessed March 6, 2018].
- Zhafira, N.A., 2012. Pengaruh Waktu Inkubasi dan Dosis Ozon pada Disinfeksi Hama Bakteri Xanthomonas oryzae pv. oryzae dengan Kombinasi Proses Ozonisasi dan Adsorpsi dengan Zeolit Alam. Universitas Indonesia.