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The Effect of Negative Pressure Wound Therapy (NPWT) on Diabetic Ulcer Wound Healing
(Literature Review)

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ABSTRACT

Diabetes mellitus is a problem that constantly occurs in Indonesia and the world until now. Various complications arise if not treated and controlled properly such as diabetic ulcers. The main goal of diabetic ulcer treatment is to achieve healing as quickly as possible. Many wound care techniques are currently developing along with technological developments, one of which is Negative Pressure Wound Therapy/NPWT. This study was conducted to determine the effect of NPWT intervention on diabetic ulcer healing specifically. Scopus, Pubmed, Sage, ProQuest were used to find articles that matched the inclusion and exclusion criteria, then reviewed. There was an effect of giving NPWT as evidenced by a decrease in the wound area, leukocyte count, and Ang2 levels, an increase in the number of EPCs with a significant value of p<0.05). The use of NPWT attracts excess exudate by applying negative pressure to the wound so that the wound fluid is reduced and the wound heals faster. NPWT is safe to use on diabetic ulcers, especially to help reduce exudate, wound area, and depth, accelerate healing time, increase the number of growth factors in wound tissue regeneration. Further research is needed to prove other clinical benefits of using NPWT.
Keywords: Negative Pressure Wound Therapy (NPWT), Diabetic Ulcer, Wound Healing

INTRODUCTION

Until now, diabetes mellitus is a problem that often occurs in Indonesia and the world. Various complications can arise as a result of not being treated and controlled properly. Diabetic foot ulcers are one of the chronic complications of diabetes mellitus in the form of ulcerations affecting the lower limbs, with or without infection, which can cause damage to the underlying tissue (International Diabetes Federation, 2017). Diabetic ulcers are chronic wounds that are difficult to heal because they require patience in long-term treatment. Effective wound care is one part of a holistic approach that is needed optimally in treating diabetic ulcer patients.

According to the World Health Organization (WHO) in 2016, approximately 8.5% (422 million) of the world's adult population had diabetes, 25% (105.5 million) of that number would develop diabetic ulcers (Armstrong et al, 2017). More than 4.8 million adults in the UK have diabetes and 25% or around 1.2 million of these diabetics will develop diabetic foot ulcers (Armstrong et al, 2017; Diabetes UK, 2020). There were 7,545 amputations among diabetics in the UK between 2015 and 2018. It is known that 84% or approximately 6337 lower extremity amputations were due to complications of foot ulcers (Public Health England, 2019).

It takes a long time and comprehensive multidisciplinary treatment for diabetic ulcer healing. If the wound is not immediately treated and treated properly, it will have many impacts starting from infection, worsening ulceration, gangrene, resulting in increased treatment costs and is the main cause of amputation. The main focus of diabetic ulcer intervention is to prevent and avoid lower extremity amputation, so that maximum care and therapy are needed to treat diabetic ulcers. One of the interventions applied is to perform good and effective wound care for diabetic ulcer healing. Treatment of diabetic ulcers has the main goal of achieving healing as soon as possible and as an effort to prevent recurrence after healing is achieved.

Quite a lot of wound care techniques are now constantly evolving along with technological developments. The therapy that is currently very popular and has received much attention from researchers is negative pressure wound therapy (NPWT or what is often referred to as a vacuum wound (Vacuum Assisted Closure/VAC). Negative Pressure Wound Therapy (NPWT) or known as negative pressure wound care is the application of negative pressure to the wound of 50-175 mmHg either continuously or intermittently (Kartika, 2016). NPWT is a wound management therapy commonly called wound vacuum is a non-invasive method by applying negative pressure to the closed space of the wound so that the excess wound fluid can be reduced and clean the bacteria that cause infection.

The basic mechanism of how NPWT work is to attract fluid in the form of blood which is certainly toxic, irritant in the tissue area around the wound, and also changes the local microcellular environment to achieve faster and maximum wound healing. The NPWT consists of a pump, suction hose, s le dressing (granufoam), and a canister (liquid container bottle). The NPWT pu functions to maintain negative pressure wound therapy (NPWT) on the wound surface around -125 mmHg. In addition to keeping the humidity of the wound and around the wound with the use of granufoam, this NPWT therapy can stimulate tissue growth and absorb excess fluid exudate. The exudate is controlled by the dressing through a combination o sorption and moisture. Many empirical pieces of evidence have been shown by scientists worldwide that negative pressure wou therapy (NPWT) has greater efficiency in wound healing. Therefore, the authors are interested in conducting a literature review on the effect of the negative pressure wound therapy (NPWT) method in healing wounds, especially in diabetic ulcers.

METHODS

This research is research using the literature review method. This type of literature review research is trying to find theoretical references that are relevant to the case or problem e raised. The type of research design used in this literature review is causal which is intended to examine the effect of negative pressure wound therapy on healing diabetic ulcers. This type of research uses quasi-experimental, qualitative research, cross-sectional studies, and randomized control trials methods.

Search Strategy

The search in this literature review uses both nursing and health research databases, using four databases with high and medium quality criteria, namely Scopus, Pubmed, Sage, and ProQuest. Researchers set the literature from the last 5 years in 2016-2020. The literature search was carried out in August-September 2020. The strategy used to search for articles was using PICOS. The found articles were then identified based on the inclusion and exclusion criteria.

Search selection

Inclusion criteria included a population of diabetic patients with foot ulcers. The sample of his study is more than 15 respondents. The research was conducted on humans. The intervention used was applying the Negative Pressure Wound Therapy (NPWT) technique. The study design and publication type use quasi-experimental studies, qualitative research, cross-sectional studies, and randomized control and trials which are published in 2016-2020 and the language used are English.

ta identification/ Data extraction

Search articles or journals using keywords and boolean operators (AND, OR NOT or AND NOT) which are used to expand or specify the search, making it easier to determine the articles or journals used when doing the research. Keywords in this literature review are a ted to Medical Subject Heading (MeSH). The keywords used are Effectiveness OR Effectiveness OR Efficacy AND Negative Pressure Wound Therapy OR Vacuum-Assisted Closure OR Topical Negative Pressure AND Wound OR Wounds AND Diabetic ulcer OR Foot ulcer OR Feet ulcer AND Healing OR Healings OR Dressing.

Table 1. Keyword Search Strategy in Database

Efectifity	***Negative Pressure Wound Therapy***	***Wound***	***Diabetic ulcer***	***Healing***
OR	*OR*	*OR*	*OR*	*OR*
Effectiveness	*Vacuum-Assisted Closure*	*Wounds*	*Foot ulcer*	*Healings*
OR	*OR*		*OR*	*OR*
Efficacy	*Topical Negative Pressure*		*Feet ulcer*	*Dressing*

Based on the results of a literature search through publications in four databases and using keywords that have been adapted to MeSH, the researchers found 720 articles that matche these keywords. The search results that have been obtained are then checked for duplication, it was found that 4 similar articles were removed and the remaining 716 articles. The researcher then conducted a screening based on the title (n = 57), abstract (n = 20), and full text (n = 15) which was adjusted to the theme of the literature review. The assessment was conducted based on the feasibility of the inclusion and exclusion criteria obtained as many as 15 articles that can be used in the literature review.

After the selection based on the inclusion and exclusion criteria is then extracted in the form of a PRISMA checklist table as follows:

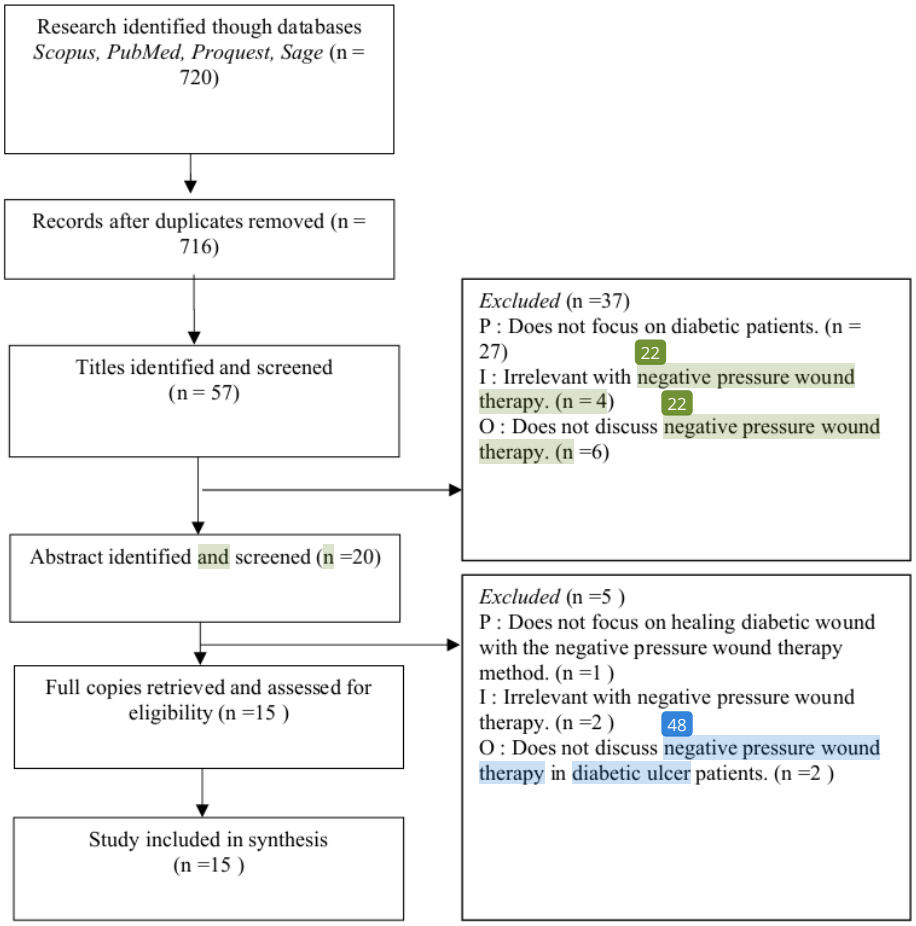

Figure 1. Flowchart of Literature Review Based on PRISMA 2009 (Polit and Beck, 2013)

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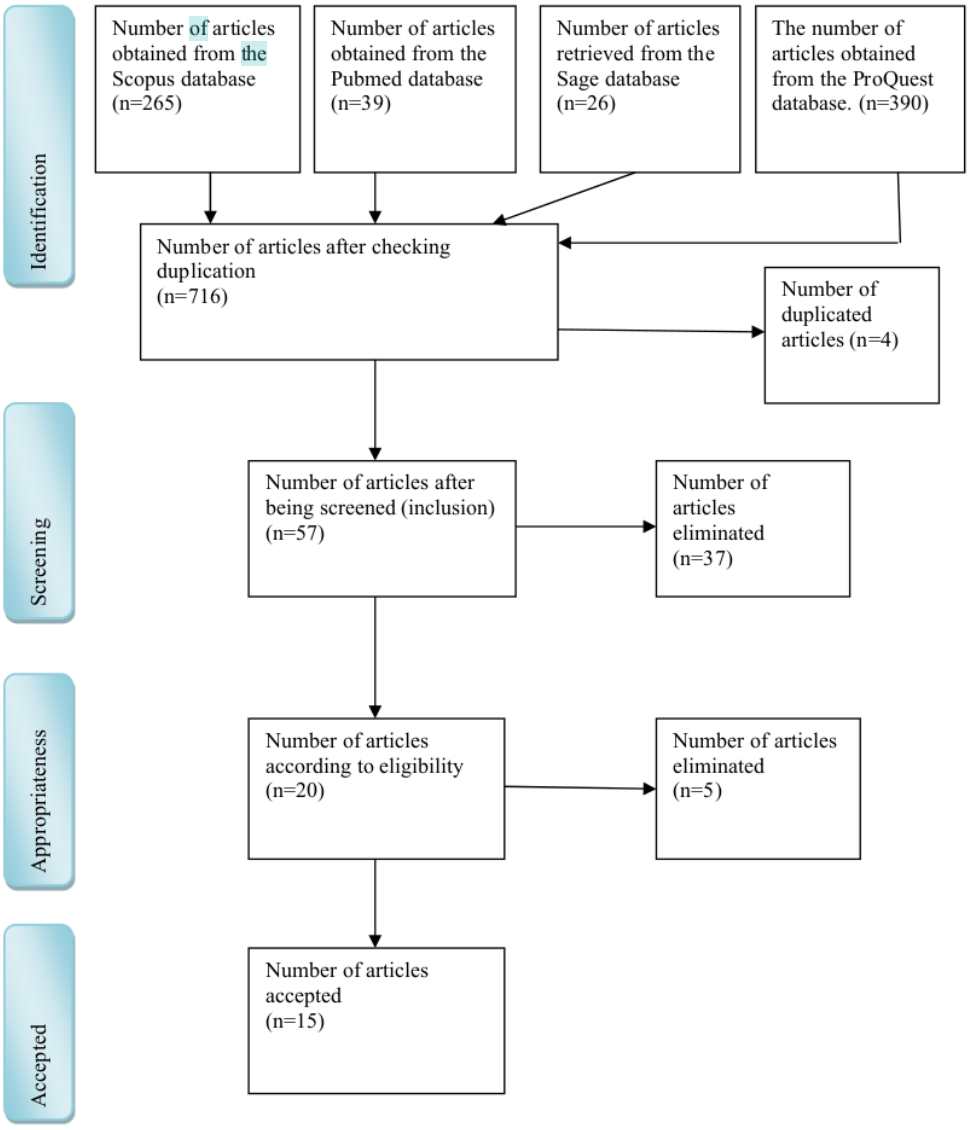

Figure 2. PRISMA Diagram

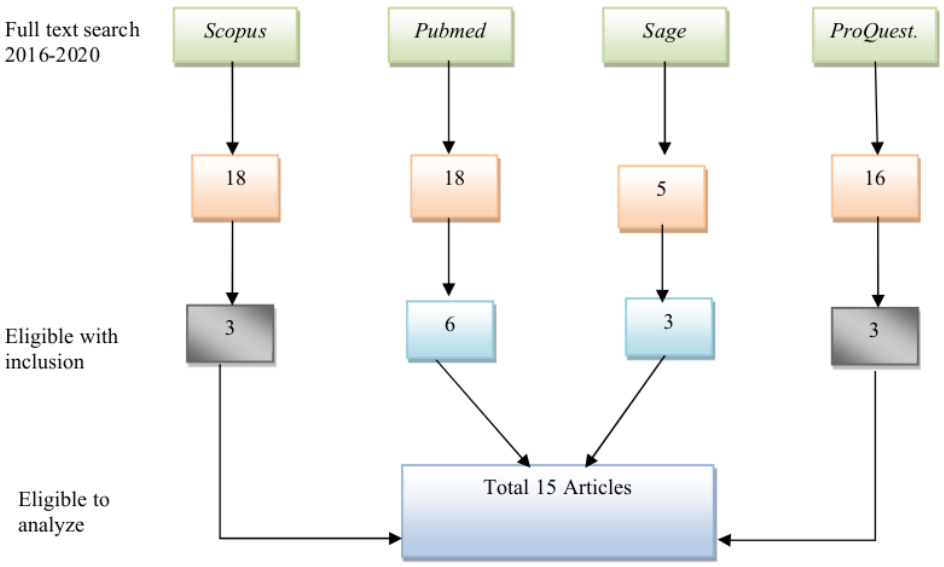

Figure 3. Article Selection Scheme Based on Inclusion and Exclusion Criteria

RESULTS

Table 1. Intervention Characteristics

Author/Year	Respondent Age	Number of Respondents	Material	P Value
Borys et al /2019	67,5- 69,0 years old	25 patient	- NPWT -Conventional therapy	0,028
Kirsner et al /2019	60,4-62,5 years old	115 patient	-s-NPWT -t-NPWT	0.018
Hohendorff et al /2019	62 - 70 years old	49 patient	- NPWT -Standar Therapy (ST)	0,02
Hu et al /2019	51-69 years old	70 patient	- VAC therapy -VAC and photon therapy	<0.0001
Seidel et al /2020	>18 years old	181 patient	- Terapi NPWT - Moist wound standard care	0.004
Mu et al /2019	±55,7 years old	56 patient	-NPWT	<0,01
Yang et al /2017	50 - 70 years old	20 patient	-Vacuum-Assisted Closure (VAC) -Moist wound therapy	<0,01
Lavery et al /2020	>21 years old	150 patient	-Traditional NPWT -NPWT with simultaneous irrigation (NPWT-I)	0,53
Chiang et al /2017	41-83 years old	22 patient	-Topical Negative Pressure (TNP) -Topical dressing	0,03
Wang, et al/ 2019	55-56 years old	13 patient	-NPWT after debridement	0,001

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			- Gauze bandage after debridement	
Chattinnakorn et al /2020	18 -70 years old	27 patient	NPWT	<0,001
Gonzalez et al /2017	18 - 80 years old.	72 patient	-*Vacuum-Assisted Device with debridement* -Debridement and regular wound cleaning	<0,05
Borys et al /2018	64-65 years old	53 patient	- NPWT - Standar Therapy	0.0001
Singh et al /2020	Not listed	86 patient	-Conventional VAC -Indigenous Low VAC - VAC TPOT	p> 0,05
Ludwig-Slomczynska et al /2019	64,9-68,3 years old	23 patient	-NPWT - Standar Therapy	FDR *(False Discovery Rate)*= 0.05

Based on the 15 articles obtained, the majority of respondents are aged 50-60 years on average and are multi-regional. The gender characteristics of the respondents are almost the same between men and women. Most of the respondents on each article are more than 25 people. Based on the results of the 15 articles found, an analysis related to the use of NPWT was applied to diabetic ulcer patients with a certain time span, and measurements of the wound area and wound depth using a measuring instrument that has been established. It was shown that NPWT has a significant effect on healing diabetic ulcers as indicated by significant results of each article is P <0.05, which means that there is an effect of NPWT treatment on diabetic ulcer wound healing.

DISCUSSION

1. Wound Healing before NPWT Intervention in Diabetic Ulcer Patients

Before NPWT, there were quite a lot of wound care techniques, one of which was conventional wound care methods which had the principle of maintaining moisture, warmth, and preventing trauma. However, the use of NaCl in this conventional wound care method is less able to maintain moisture because Nacl is volatile so that the gauze becomes dry. The dryness of the gauze causes the gauze to easily stick to the wound and this condition causes re-trauma to occur easily. Due to the lack of gauze in maintaining moisture, the wound healing process takes a long time. From the 15 journals obtained, before NPWT was performed, the wound had different characteristics. Before NPWT therapy, the number of leukocytes in diabetic ulcers tends to be high. One of the parameters measured in determining the response to tissue infection in wounds is high leukocyte levels (Gonzalez et al., 2017). Increased levels of white blood cells (leukocytes) occur due to the inflammatory process of diabetic ulcers. Increased production of leukocytes occurs when the body is trying to fight the infection process. Leukocytes are one of the components in the blood that detect the presence of infection, including in wounds. The area of the wound and the depth of the ulcer are severe causing peripheral vascular disruption to wound healing which will be hampered. The depth and area of the wound in diabetic ulcer patients vary depending on the severity and grade of the wound. A wound is said to be completely healed if the wound has returned to its normal anatomical structure, tissue function, and appearance within an appropriate period of time (T Velnar in Primadina et al., 2019). Damage to nerves and blood vessels due to uncontrolled blood sugar levels in diabetic patients triggers the occurrence of diabetic ulcers which are characterized by wounds, especially on the legs with a certain area and depth.

The number of EPCs in diabetic ulcer patients was still low before NPWT treatment. The amount of EPC is one of the indicators used to assess the rate of wound healing in diabetic ulcer patients. EPC (Endothelial Progenitor Cell) plays a role in accelerate wound healing. EPC play a role in the process of angiogenesis and neovascularization (Lalezari et al., 2017). Tissue vascularization in diabetic ulcers tends to be disrupted, thus affecting the length of wound healing. A wound is said to be healed if there is a complete re-epithelialization and neurovascularization process, namely the process of forming epithelial tissue to cover the entire wound surface and the process of forming new blood vessels.

Likewise, levels of angiopoietin (Ang) tended to be high before NPWT treatment. Angiopoietin levels also play a role in the process of angiogenesis or the formation of new blood vessels. Angiopoietin is an angiogenic factor needed for the maturation of blood vessels and can increase the process of angiogenesis (Xie et al., 2020).

The tissue where the formation of new blood vessels occurs usually looks red (erythema) due to the formation of capillaries in that area. Under physiological conditions, Angiopoietin 2 (Ang2) levels are low, Ang2 levels are elevated associated with chronic complications. As in diabetic ulcers, Ang2 levels tend to be higher. In the wound healing process, an increase in Ang2 in the absence of Vascular Endothelial Growth Factor (VEGF) is associated with impaired wound healing.

2. Wound Healing after NPWT Intervention in Diabetic Ulcer Patients

Based on the results of the literature review that has been carried out by researchers in general, it is explained that the use of NPWT has succeeded in influencing the healing of diabetic ulcers. This is proven from the results of the analysis of the fifteen articles which showed that after being given the NPWT intervention and measurements were made using various instruments to assess the condition of the wound, the results showed that there was an improvement in the wound area, wound depth, inflammation response, pain score, and tissue granulation acceleration. A study conducted by (Singh et al., 2020) showed a significant reduction in wound size, infection control in all three groups receiving NPWT. There was no statistically significant difference in the wound area and depth reduction between the three treatment groups ($P > 0.05$). In line with research conducted by (Wang et al., 2019) showing that NPWT plays a role in reducing wound infection and accelerating diabetic wound healing. The number of neutrophils was much smaller in the NPWT group compared to the control group with a P-value = 0.001.

A study conducted by (Gonzalez et al., 2017) showed that the number of leukocytes decreased on the 10th day of NPWT administration. A decrease in leukocytes indicates a reduction in both tissue and local infection of the wound. This NPWT/VAC technique controls the tissue inflammatory response by reducing interstitial fluid, increasing angiogenesis, reducing bacterial growth by isolating the wound from the environment and increasing the rate of granulation tissue in response to mechanical forces (Morykwas in Gonzalez et al, 2017). Leukocytes that are in normal limits indicate that the infection process is reduced in diabetic ulcers. The decrease in leukocyte levels within normal limits proves that after NPWT treatment, there is an effect on the healing of diabetic ulcers.

Research conducted by (Mu et al., 2019) showed an effect on healing diabetic ulcers with NPWT intervention ($p<0.01$) with ($\alpha<0.05$). The number of circulating EPCs increased significantly in the NPWT group. Granulation tissue growth was significantly higher in the NPWT group. NPWT given for 1 week can significantly increase the number of EPCs (Endothelial Progenitor Cells) in peripheral blood in diabetic patients with mild ischemic foot ulcers ($P=0.05$).

The use of NPWT can significantly increase the number of EPCs in peripheral blood in diabetic patients with diabetic ulcers. NPWT results in an increase in a number of growth factors associated with the angiogenesis process through VEGF stimulation and an increase in the number of endothelial progenitor cells (EPC) as a linking mechanism between the Vascular Endothelial Growth Factor (VEGF) pathway and angiogenesis (Lalezari et al., 2017).). The increase in the number of EPCs indicates an increase in endothelial function in both tissues and blood vessels in diabetic ulcers towards cell regeneration and wound healing.

Research conducted by (Hohendorff et al., 2019) stated that after NPWT treatment, the decrease in Angiopoietin 2 (Ang2) levels was more significant with $p = 0.01$. A decrease in Ang2 indicates better wound healing. The role of angiopoietin 2 (Ang2) in the process of angiogenesis depends on VEGF. In the presence of VEGF, Ang2 acts as a proangiogenic, whereas when VEGF is inhibited, Ang2 acts as an antiangiogenic (Hohendorff et al., 2019). The process of angiogenesis in diabetic ulcers is not the same as the process of wound angiogenesis in general, it is caused by a decrease in growth factors, one of which is VEGF in diabetic ulcers. Increased levels of VEGF during the normal wound healing process will stimulate the formation of neoangiogenesis directly. Angiopoietin is associated with inflammatory markers as well as leukocytes (white blood cells). The use of NPWT has benefits on angiopoietin levels. The mechanism of action of NPWT is to reduce exudate fluid and infectious materials such as bacteria by sucking them continuously, thereby reducing the humidity of the wound environment.

Research conducted by (Chattinnakorn et al., 2020) showed that the pain score of patients who were given cold air on NPWT was slightly reduced than those who used sterile room temperature on the NPWT tube (4 vs 5.67) with $P < 0.003$. The pain scores of patients given cold air on the NPWT tube were significantly worse than those on the NPWT tube (4 vs 6.59) with $P < 0.001$. This shows that presenting sterile cold water to the NPWT tube before dressing change can reduce pain scores than using nothing or using only room temperature sterile water.

Temperatures below 13.6°C can reduce the speed of conduction of nerve impulses which reduces pain relief (Bugaj in Chattinnakorn, 2020). Low temperatures can reduce the speed of conduction of nerve impulses resulting in reduced pain relief. The decrease in tissue temperature also acts in the peripheral nervous system by

reducing the speed of transmission in the nerves and thereby increasing the pain threshold and pain tolerance along the same nerve.

3. The Effect of NPWT Intervention on Diabetic Ulcer Healing

Based on the analysis of fifteen journals in general, it is explained that there is an effect of NPWT intervention on improving the condition of diabetic ulcers, including wound surface area, wound depth, acceleration of wound healing time, and an increase in several wound healing factors. From 15 journals that were obtained and analyzed, the average administration of NPWT affected healing diabetic ulcers. The effect of NPWT on wound healing is that it can decrease and reduce the area of the wound and accelerate wound closure.

Based on the results of 4 articles ((Borys et al., 2019), (Borys et al., 2018), (Kirsner et al., 2019), (Chiang et al., 2017)) which were found to be related to a reduction of wound area and wound depth Diabetic ulcer patients after receiving NPWT showed the same results with the significance of each article P> 0.05, which means that it indicates that the NPWT intervention affects healing diabetic ulcers characterized by the development and healing of wounds with a reduction in wound dimensions (area, depth, and volume).

Likewise with research conducted by (Hu et al., 2018) showed that there was a change in wound surface area in the experimental group receiving VAC ($p<0.001$, $\alpha<0.05$). The area and depth of the wound were also reduced and improved after the application of NPWT in the combined group of ulcer patients who received NPWT treatment combined with photon therapy also experienced changes in the wound surface area. Photon Therapy is a clinical application of the use of electromagnetic energy which has a wavelength of 100-10,000 nanometers. Light energy is transmitted through space as a wave that has a collection of energy called photons (Satria Nugraha et al., 2019). The nature of photons is collimation (travel in one direction without divergence), coherence (all waves converge in a phase with monochromaticity (single wavelength). This causes the photon beam to directly reach the mitochondria of the cell membrane, nucleus, and cytosol to increase the metabolic function of the cell which aims to normalize cell function, dry wounds, and accelerate wound healing. NPWT works on wound healing in several ways, one of which is by promoting contraction of the wound margins to facilitate closure and encourage the formation of granulation tissue (Kartika, 2016). Combination therapy (a combination of VAC with photon therapy) accelerates wound healing but does not affect long-term efficacy. VAC therapy combined with photon therapy is effective and safe in the treatment of diabetic ulcers.

In addition to affecting the surface area of the wound, NPWT also affects wound healing time. This is evidenced by a study conducted by (Seidel et al., 2020) the effect of using NPWT on diabetic wound healing by showing wound closure time in patients treated with NPWT was shorter than the Standard Moist Wound Care (SMWC) intervention ($p = 0.004$) with ($\alpha=0.05$). Likewise, research conducted by (Lavery et al., 2020) showing that NPWT shortens wound healing. The study stated that NPWT-I/NPWT with simultaneous irrigation took 50.7 days to heal. Meanwhile, conventional NPWT takes 56.3 days to heal ($p=0.53$ with $\alpha =0.05$). The average wound healing time in simultaneous irrigation NPWT was faster than conventional NPWT. Simultaneous NPWT irrigation used 0.1% polyhexanide betaine as simultaneous irrigation at a speed of 30 cc/hour.

In principle, the irrigation period can be repeated as often as desired. The period of administration of the solution (saline, antiseptic, or antibiotic) is approximately 10–30 seconds. The dwelling periods depend on the time it takes for the solution to become effective, usually 20 minutes. The suction period is 2 to 3 hours. Mechanically, irrigation will help remove foreign objects and reduce the concentration/inoculates of bacteria in the tissue by up to 80% (Wiguna & Putra, 2020). There was no significant difference between conventional NPWT and simultaneous irrigation NPWT. Both simultaneous irrigation NPWT and conventional NPWT have the same goal which is reducing exudate in diabetic ulcers. NPWT irrigation technique and conventional NPWT both only clean the wound and attract exudate. The addition of simultaneous irrigation did not change the clinical outcome of patients with diabetic ulcers which was superior to the use of conventional NPWT. The most commonly used pressure on the NPWT is 125 mmHg. Low pressures of less than 125 mmHg may be ineffective, whereas high pressures of more than 125 mmHg may be painful and harm the microcirculation. An initial pressure application of 125 mmHg was used in the first few days due to a large amount of initial exudate. The determination of the pressurization mode can be applied in continuous or intermittent mode. Negative pressure is most often applied in continuous mode. Intermittent mode involves switching on and off repeatedly (usually 5 minutes to 2 minutes).

Indications of NPWT with intermittent suction may be useful for wound healing in the formation of new granulation tissue but in the intermittent suction mode, it can result in higher pain occurrence in treated patients. The intermittent mode results in mechanical stimulation on the base of the wound and greater stimulation of blood circulation, oxygenation, and angiogenesis, and possibly a lower risk of ischemic damage. It is suggested that the therapy can be applied in continuous mode for the first 24 hours and if the above effect is desired, the intermittent mode can be applied. Recommendations for starting and stopping the use of NPWT (Apelqvist et al., 2017) are the use of NPWT for exudate management starting immediately after debridement and discontinuing as soon as possible until wound closure is achieved and exudate reduction in the direction of wound drainage. The NPWT dressing is changed every 2-4 days.

Hospitals are the best places to treat patients with NPWT because they provide the best conditions for application, including rooms, sterile procedures, optional anesthesia, rapid availability of analgesics, and trained staff, and continuous patient observation. On initial application of NPWT, the patient and bandage should be monitored closely for at least 24 hours to ensure that possible bleeding and other complications are detected. Aside from the hospital, the NPWT application can also be done at home as long as the patient's condition allows them for home care treatment.

NPWT also showed a local increase in the number of growth factors such as EPC and TGF-β. Research conducted by (Mu et al., 2019) showed that the number of EPCs after NPWT treatment increased by 85.3 x10-6 cells from the original 34.1 x10-6 cells. In line with the research conducted by (Yang et al., 2017) showed an increase in the optical density of TGF-β1 on day 7 of 0.30 µm from the original optical density of TGF-1 on day 0 of 0.26 µm. TGF-β is involved in tissue regeneration. TGF-β also stimulates endothelial cells to form capillary loops, which is commonly referred to as the process of angiogenesis (Primadina et al., 2019). Compression of small blood vessels by negative pressure on NPWT will stimulate the growth of new blood vessels (angiogenesis). TGF-β and EPC are important growth factors and promoters in wound healing. Diabetic ulcers are chronic wounds that cause tissue hypoxia. Growth factors such as TGF-β and EPC are produced in response to tissue hypoxia which will play a role in the process of angiogenesis. NPWT is involved in gene-level expression changes. In line with the research conducted by (Ludwig-Slomczynska et al., 2019) showed that the wound area was much better in the NPWT group (FDR = 0.05). NPWT also induces gene expression during wound healing. The molecular mechanism that shows the effect of NPWT use down to the gene level is still unclear, but several proliferative genes were found after NPWT use. NPWT aids wound healing by removing excess exudate and influencing the inflammatory phase of cells. It is plausible when the exudate is taken out from the wound could promote the complex regulation of cell interactions and progression of the wound to the healing phase. Therefore, several proliferative genes were found after treatment with NPWT.

CONCLUSION

Before NPWT intervention, diabetic ulcers had different characteristics including high leukocytes, the depth of the wound, appearance of large wound areas, presence of exudate, low number of EPC (Endothelial Progenitor Cells), and length of time for wound closure. After NPWT treatment, the development of wound healing in a better direction was marked by a decrease in the number of leukocytes, a reduction in the depth and area of the wound, an increase in wound closure time, and an increase in the number of EPCs (Endothelial Progenitor Cells) which play a role in the angiogenesis process neurovascularization. NPWT affects healing diabetic ulcers, especially helping to reduce exudate, reducing wound surface area and wound depth, accelerating wound healing time, reducing wound infection, increasing the number of several growth factors in accelerating wound tissue regeneration. Suggestions for health workers and services are expected to increase the knowledge and skills of nurses in the use of NPWT to treat diabetic ulcer patients. For people with diabetes to further improve their health by consulting and seeking treatment in health care settings to get more up-to-date treatment, such as using NPWT for diabetic wound care to accelerate the ulcer healing process. For further researchers, can continue this literature review study more deeply with variables that do not exist in this literature review.

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