A COMPARATIVE STUDY OF THE EFFECTS OF VIBRATION AND ELECTRICAL STIMULATION THERAPIES ON THE ACCELERATION OF WOUND HEALING IN DIABETIC ULCERS

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ABSTRACT

Introduction: Diabetic ulcers accompanied by ischemia is difficult to treat. Such ulcers require therapy that can improve the blood flow. Previous studies have revealed that two therapies could improve blood flow and accelerate the healing of diabetic ulcers: vibration and electrical stimulation (ES). However, it is unknown which of these two therapies is best at accelerating wound healing in diabetic ulcers. The purpose of this study was to compare both therapies in relation to accelerating the wound healing of diabetic ulcers. Methods: This study was an experimental study involving diabetic rats. The rats were divided into two groups: vibration and ES. Vibration and ES were applied for 10 minutes per day for 7 days. Wound size, inflammation, intensity of fibroblast infiltration, area of necrosis and degree of re-epithelialisation were compared. The difference in wound size was analysed using an independent t-test, while the histological data were analysed using a Mann-Whitney U-test. Results: On day 5 onwards, there was a thin slough in the ES group which was not present in the vibration group. Day 4 onwards and the wound size was significantly smaller in the vibration group than in the ES group. The intensity of inflammation was significantly less, and the degree of fibroblast infiltration was significantly higher in the vibration group compared with the ES group. Re-epithelialisation was more advanced in the vibration group than the ES group. Conclusions: Our study revealed that wound healing in diabetic ulcers following vibration was better than after ES. We suggest that nurses should use vibration rather than ES in clinical settings.

Keywords: complementary therapy, diabetic ulcer, electrical stimulation, vibration, wound healing

INTRODUCTION

Indonesia has the tenth highest proportion of people with diabetes mellitus (DM) in the world (Shaw, Sicree and Zimmet, 2010). It is predicted that Indonesia will become number six by 2030 (Shaw, Sicree and Zimmet, 2010). Soewondo, Ferrario and Tahapary (2013) revealed that the prevalence of patients with DM in Indonesia had increased by 11% over 19 years, although this figure is likely to be higher since there are many unreported cases (Yusuf et al., 2016).

Diabetes mellitus causes many complications. Patients have a risk of limb amputation at a rate that is 40 times higher than people without DM (Brechow et al., 2013). After amputation, patients with DM also have a higher risk of limb re-amputation and rate of mortality (Moulak, Mtonga and Gill, 2003; Izumi et al., 2006). Armstrong, Wrobel and Robbins (2007) showed that the prevalence of deaths due to diabetic foot ischemia was higher than that due to cancer.

Considering the impact of diabetic ulcers on patients, a therapy that accelerates wound healing is urgently required. Wu et al., 2007 revealed that diabetic ulcers that heal with difficulty are accompanied by impaired blood flow (ischemia).

The presence of ischemia impairs the wound healing process, especially the angiogenetic phase, thus a therapy that improves blood flow would be of great benefit, including the use of drugs which act as vasodilators that improve blood flow or induce angiogenesis such as prostaglandins or basic fibroblast growth factor (Addison et al., 1972; Lees, 1994). However, the continuous administration of these drugs causes side effects such as cramping, the vasoconstriction of blood vessels and the acceleration of osteogenesis (Nagase et al., 2007). Because most patients with diabetic foot ulcers also have other complications due to high blood glucose, a therapy that has minimal side effects is not invasive and is comfortable for patients is required.

Previous studies have shown that two complementary therapies that are safe for application to patients are vibration and electrical stimulation (ES). A previous study revealed that a low vibration frequency can improve blood flow (Nakagami et al., 2007), and accelerate healing of stage I pressure ulcers (Arashi et al., 2010), deep tissue injury...
Sari, et al., (2015) and diabetic ulcers (Sari, Sutrisna and Hartono, 2016). Sari et al., (2015) revealed that the reduction of hypoxia and reduction of activation of matrix metalloproteinase-2 and matrix metalloproteinase-9 are the mechanisms that are responsible for the acceleration of wound healing following vibration.

Studies reveal that ES has been utilised for many health purposes because it can improve blood flow. Humans create a type of electricity called bioelectricity. Following an injury to the skin, a low current flows between the skin and underlying tissue, which is called the current of injury. This is important during the wound healing process (Kim, Cho and Lee, 2014). The electric current which is used in ES is a low current (microAmpere, μA).

Thus, the low current of ES therapy reflects the bioelectric current created by the body (Ud-Din and Bayat, 2014). Results of studies both in vitro and in vivo reveal that ES improves the healing process by promoting keratinocyte migration, improving wound perfusion, stimulating collagen synthesis (Kim, Cho and Lee, 2014), and inducing angiogenesis (Liebano and Machado, 2014). (Liebano and Machado, 2014). A previous in vitro study revealed that ES could also reduce inflammation (Cho et al., 2000). In results similar to the effect of vibration, previous studies have also shown that ES accelerates wound healing in pressure, ischemic and diabetic ulcers (Eriksson et al., 1981; Goldman et al., 2003; Koel and Houghton, 2014).

Based on the above studies, both vibration and ES could improve wound healing. However, up to the present, there is no study that compares the effectiveness of the two complementary therapies, therefore, which therapy is better for accelerating wound healing of diabetic ulcer is still unknown.

MATERIALS AND METHODS

Research Design

This was an experimental study utilising post-test only, using a control group design approach.

Electrical Stimulation Device (Figure 1)

Electrical stimulation consisted of two main parts, the electrodes and power supply. The electrodes served as a distributor of electrical current to the skin and were constructed from corrosion-resistant metal that could easily be attached to the skin. The power supply provided electric current to both electrodes. The current generated was a square wave of electrical pulses whose amplitude and frequency could be varied (Sari, Sutrisna and Hartono, 2017).

The electrodes were attached to the skin as shown in Figure 2. Based on previous research, ES was applied for 10 minutes every day for 7 days (20 Hz, 320 μs, 50 μA) (Sari, Sutrisna and Hartono, 2017).
Vibration Device

The vibration device which was used in this study was originally constructed by our research team (Sari, Sutrisna and Hartono, 2016). In brief, the vibration bed consisted of 3 vibrating motors and its frequency can be varied by changing the velocity. The application of the use of vibration bed for the rat can be seen in Figure 3. The rats were given an application of vibration for 10 minutes once a day for 7 days.

Animal

This study used male Wistar rats aged 12-14 weeks. The rat’s body weight was in the range of 190-220 grams. The rats had free access to food and drink. The protocol of this study was approved by the research committee ethics for an animal study, of the Faculty of Medicine, Jenderal Soedirman University (1208/KEPK/III/2017).

The rats were divided into two groups, vibration-treated and electrical stimulation-treated. Every day, the wounds were washed with saline in both groups prior to being covered with a film dressing.

Induction of Rats

The rats were acclimatised for 7 days before the induction of diabetes by injection of Alloxan Monohydrate (Sigma Aldrich, USA) at a dose of 90 mg/kg. Blood was drawn from the tail vein 4 days after induction to assess whether the blood glucose concentration had increased. The rats were considered diabetic when their blood glucose was greater than 250 mg/dl. The rats were shaved the day prior to wounding. The rats were anesthetised with Ketamile (25-30 mg/kg body weight) during the shaving and wounding procedures. The procedure of wounding was according to the previous publication (Sari et al., 2015a). The diameter of each wound was 1 cm, extending to the Panniculus carnosus. The wounds were cleaned with normal saline, dried with gauze then covered with a parafilm dressing. The wound was monitored daily from day 0 to 7 and recorded with a digital camera.

Tissue Staining

The rats were sacrificed on day 7 using an overdose of ketamile. The tissue samples were fixed in 10% formalin then processed and embedded into paraffin. The samples were sectioned and then stained with a hematoxylin and eosin (H&E). Sections were observed using a light microscope. The inflammation and infiltration of inflammatory cells were indicated by blue staining in the H&E sections.

Wound Size

The size of the wound was measured by using ImageJ software from the National Health Institute. The wound area was determined based on the inner wound margins (Ueda et al., 2010) The relative wound areas were determined as (day n area – day 0 area) / (day 0 area). (Ueda et al., 2010)

Reepithelialisation

Reepithelialisation was indicated by the presence of new epithelial tissue in the epidermis layer. Reepithelialisation was observed with a light microscope. The result of the study was described qualitatively.

Statistical Analysis

Statistical analysis was performed by SPSS software, version 16. The data of the wound size was analysed by an independent t-test. The histological result was analysed by a Mann-Whitney U-test. The value of  p < 0.05 was considered to be significant.

RESULTS

The result of the macroscopical findings could be seen in Figure 4. On day 0, the visual appearance of the wound was similar in both groups. On day 1 to day 3, the wound base in both groups started to be filled with granulation tissue. On day 3, the wound size in the vibration group tended to be smaller

| Table 1. Intensity of inflammation and fibroblast between vibration and ES group |
|-----------------------------|-----------------|----------------|
| Groups                     | PMNs    | Fibroblasts |
| Vibration                  | 2*      | 3*          |
| Electrical stimulation     | 3       | 2           |

Values indicated median score
Rating scale : 0 = absent, 1= occasional, 2 = moderate, 3 = abundant, >3 = very abundant
* P< 0.05
PMNs = polymorphonuclear neutrophils
compared with the ES group. On day 5, the granulation tissue in both groups was increased. However, there was a thin layer of slough in the ES group, which was not present in vibration group. On day 7, the thin layer of the slough was still present in the ES group.

The difference of the wound size between two groups could be seen in Figure 5. There was no significant difference in wound size between vibration therapy and ES from day 0 to day 3. However, the wound size in the vibration group was significantly smaller than in the ES group on day 4 to day 7 (P=0.011 on day 4, P=0.025 on day 5, P=0.005 on day 6, P=0.0001 on day 7).

The microscopical difference between the vibration and ES group in the epidermis and dermis layers can be seen in Figure 6. The intensity of inflammation in both the epidermis and dermis layer in the vibration group was less compared to the inflammation in the ES group. The intensity of the fibroblasts was higher in the vibration group than in the ES group. The difference in the histological findings can be seen in Table 1. The intensity of inflammation was significantly less in the vibration compared with the ES group (P=0.034), and the fibroblast intensity was higher in the vibration compared with the ES group (P=0.045).

**DISCUSSION**

This study is the first study in the literature that compares vibration and electrical stimulation in accelerating the wound healing of diabetic ulcers. In this study, we found that wounds heal better if treated with vibration therapy compared with electrical stimulation.

The previous study revealed that ES could reduce inflammation, improve blood flow, reduce the bacterial burden, reduce pain and edema, decrease muscle spasms, and improve TGF-β1, collagen-I, and muscle
A Comparative Study of the Effects of Vibration... (Yunita Sari et al.)

contraction (Demir, Balay and Kirnap, 2004; Sebastian et al., 2011; Kim, Cho and Lee, 2014; Torkaman, 2014).

Recent research by the author has shown that compared with the standard treatment, wounds treated with ES showed a reduction in inflammation and an increase in re-epithelialisation (Sari, Sutrisna and Hartono, 2017). A reduction in inflammation following ES in diabetic ulcers might be due to the ability of ES to enhance phagocytosis (Cho et al., 2000). The improvement of reepithelialization might be due to the ability of ES to promote keratinocyte migration (Kim, Cho and Lee, 2014).

Based on previous studies, vibration could also accelerate the healing of diabetic ulcers, such as in pressure ulcers stage I, deep tissue injuries, and diabetic ulcers (Arashi et al., 2010; Sari, Sanada, et al., 2015; Sari, Sutrisna and Hartono, 2016). Vibration therapy that can accelerate the healing of diabetic ulcer is a vibration which is applied at a low frequency. If the vibration is applied at a high frequency, it will cause tissue damage (Sari, Sutrisna and Hartono, 2016). A high frequency of vibration might cause an excessive increase of reactive oxygen species and nitric oxide that causes the vasoconstriction of blood vessels (Hughes et al., 2009).

In this study, the author used a vibration of 40 Hz and ES with a frequency of 20 Hz, pulse width of 320 Hz at a current of 50 µA. These values were chosen after previous studies by the author, and other researchers found that wounds healed using those ranges of frequency and currents (Torkaman, 2014; Sari, Sutrisna and Hartono, 2017). The previous study revealed that a vibration below 50 Hz could accelerate the wound healing of chronic ulcers (Arashi et al., 2010; Sari, et al., 2015). The author investigated a vibration frequency range and determined that a frequency of 40 Hz accelerated the healing of diabetic ulcers (Sari, Sutrisna and Hartono, 2016). In relation to ES, the author also found that the frequency of 20 Hz, the pulse width of 320 Hz and a current of 20 µA could accelerate the healing of diabetic ulcers (Sari, Sutrisna and Hartono, 2017).

In this study, we found that wound healing in diabetic ulcers using vibration was better than using ES. The wound sizes were smaller when treated with vibration and showed a greater reduction in inflammation compared with the wounds treated using ES. However, the mechanism for this difference remains unknown. In this study, the vibration was experienced by the entire body, and so it is possible that blood flow might increase systemically and not only to the wound area. However, blood flow is likely to increase only in the wound area during ES, since the electrodes were placed directly on the wound. In patients with DM, increased blood flow around the body is important since high blood glucose frequently causes plaque that can result in impaired blood flow. Another study is needed to elucidate the mechanism as to why

Figure 6. The histological findings of the epidermis and dermis layer between the vibration and ES groups. Hematoxylin and Eosyn staining in the epidermis layer (upper part) and dermis (lower part) between vibration and electrical stimulation (magnification of 400X)

Figure 7. Re-epithelialisation between the vibration and ES group. Re-epithelialisation was longer in the vibration group than in electrical stimulation group (arrow line indicates length of reepithelialisation, magnification of 100X)
the wound healed better in vibration compared with ES.

In this study, all of the animals with diabetic ulcers survived during the observation of wound healing. However, ES can sometimes cause skin tearing. It is, therefore, reasonable to suggest that vibration therapy is safer than ES.

The results of this study are very important since it is the first study that establishes that vibration accelerates wound healing in diabetic ulcers to a greater extent than ES. Nurses should consider using complementary therapies such as vibration to accelerate the healing of diabetic ulcers instead of using ES.

CONCLUSIONS

This study is the first study in the literature to investigate the comparison of the effect of vibration therapy and electrical stimulation therapy in accelerating the wound healing of diabetic ulcers. In this study, we revealed that wounds treated with vibration therapy healed better than by ES therapy.

Besides, this is the first study in the literature that compares the effect of vibration therapy with electrical stimulation therapy in relation to the wound healing of diabetic ulcers. We have demonstrated that the wounds treated with vibration therapy healed better than by ES therapy, and so we suggest that nurses in clinical settings use complementary vibration therapy instead of ES when treating wounds.

In this study, we used animals since we wanted to investigate the healing of the wounds in diabetic ulcers in deep tissue. In the future, we will compare the effects of vibration and ES in human subjects.

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REFERENCES


