Journal of Photochemistry & Photobiology, B: Biology 159 (2016) 149–154

Contents lists available at ScienceDirect

Journal of Photochemistry & Photobiology, B: Biology

journal homepage: www.elsevier.com/locate/jphotobiol

The effect of He–Ne and Ga–Al–As lasers on the healing of oral mucosa in diabetic mice

Farahnaz Fahimipour [a,b,*], Behzad Houshmand [c], Parvin Alemi [d], Mohammad Asnaashari [e], Mahmoud Akhavan Tafti [f], Fatemeh Akhoundikharanagh [d], Seyed Emadeddin Najafi Farashah [d], Mohammad Aminisharifabad [g], Aghdas Setoudehnia Korani [d], Mina Mahdian [h], Farshid Bastami [d], Mohammadreza Tahriri [b]

[a] Dental Biomaterials Department, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran
[b] Department of Developmental Sciences, Marquette University School of Dentistry, Milwaukee, WI 53233, USA
[c] Department of Periodontics, School of Dentistry, Shahid Beheshti University of Medical Science, Tehran, Iran
[d] Dental Research Center, School of Dentistry, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[e] Department of Endodontic, School of Dentistry, Shahid Beheshti University of Medical Science, Tehran, Iran
[f] Department of Pathology, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
[g] Department of Computer Science, Wayne State University, Detroit, MI, USA
[h] Department of Oral health and Diagnostic Sciences, School of Dental Medicine, University of Connecticut, Farmington, CT, USA

ARTICLE INFO

Article history:
Received 25 July 2015
Received in revised form 12 March 2016
Accepted 14 March 2016
Available online 18 March 2016

Keywords:
Wound healing
Oral mucosa
Low level laser therapy
Diabetes

ABSTRACT

Delayed wound healing is one of the complications of diabetes mellitus. Low-level laser therapy (LLLT) has been used to accelerate wound healing however the effect of LLLT on the hard palate wound healing in streptozotocin-induced diabetic (STZ-D) mice has not yet been characterized. This study aims to determine the effect of LLLT (He–Ne and Ga–Al–As laser) on the process of wound healing in the hard palate among diabetic and non-diabetic mice. 90 adult male mice were divided into six groups. Type 1 diabetes mellitus was induced in three groups by means of injection of STZ. Of these, one group was irradiated with He–Ne laser (DH group), one with Ga–Al–As laser (DG group) and one did not undergo any LLLT (DC group). The remaining groups were non-diabetic which were allotted to laser therapy with He–Ne laser (NH group) or with Ga–Al–As laser (NG group) or no LLLT (NC group). Five animals from each group were killed on the third, seventh, and fourteenth days after surgery, and biopsies were made for histological analysis. On the 3rd and 7th days after the surgery, the number of polymorphonuclear (PMN) cells in NH, DH, NG, and DG groups was significantly lower than that of the control groups. On the 3rd, 7th and 14th days, the fibroblasts and new blood vessel counts and collagen fibers in diabetic laser treated groups (DG and DH) were significantly higher compared to that of NC, DC, NH and NG groups. On the 7th and 14th days, the fibroblasts and new blood vessel counts and collagen fibers in NH, DH, NG, and DG groups were also significantly higher than that of the control groups, and the fibroblast and new blood vessel counts and collagen density fibers in NH and DH groups were higher than that of the NG and DG groups. LLLT with He–Ne laser compared to Ga–Al–As laser has a positive healing effect on hard palate gingival wounds in STZ-D mice.

1. Introduction

Diabetes is one of the most common diseases in the world [1]. The incidence of this condition is increasing every year with a substantial morbidity and mortality rate. Delayed wound healing is one of the complications in diabetic patients resulting in 15% more amputation than normal population [2].

Wound healing is a complex process that involves a variety of cells, mediators and chemokines and various mechanisms such as fibroblast proliferation, angiogenesis, collagen rearrangement and tissue contraction. Hard palate ulcers can occur due to a variety of reasons including trauma, surgical wound following tooth extraction or tumor resection [3,4].

In the inflammatory phase, inflammatory cells migrate to the wound area followed by the proliferative phase in which the number of fibroblasts and macrophages increases while acute inflammatory reactants decrease. During the final phase of wound healing, fibroblasts mediate the granulation tissue formation via secretion of extra-cellular matrix and collagen the process of tissue reformation occurs fibroblasts help tissue to reformation extra cellular matrix and collagen which lead to create granulation tissue that perfuse with new formed vessels [5].

* Corresponding author at: Dental Biomaterials Department, School of Dentistry, Tehran, University of Medical Sciences, Tehran, Iran.

http://dx.doi.org/10.1016/j.jphotobiol.2016.03.020
1011-1344/

Table 1
The specification of the lasers has been used in this research.

Parameters of the lasers	He–Ne	Ga–Al–As
Peak power	5 mW	25 mW
Wavelength	632.8 nm	830 nm
Spot shape	Circular	Circular
Spot size	0.02 cm^2	0.1 cm^2
Frequency	Continuous	Continuous
Exposure time	16 s	16 s
Energy density	4 J/cm^2	4 J/cm^2

Low level laser therapy (LLLT) is a therapeutic method which was initially introduced by Mester [6]. It has been shown to improve wound healing; however, there is controversy in the literature regarding the wound healing efficacy of red and infra-red laser in human tissues [6].

The first laser that was used for this purpose was helium–neon (He–Ne) laser which is based on inert gas. After that, semiconductor diode lasers such as gallium–aluminum–arsenide (Ga–Al–As) were used [7]. A review of literature has shown that although the effects of LLLT on hard palate wound healing have been thoroughly studied in non-diabetic animals [8], the effect of LLLT on the hard palate wound healing in STZ-D mice has not yet been characterized. The results of such studies will assist the clinician in order to render the most efficient and effective treatment for ulcerated areas in the hard palate in diabetic patients. This study aims to determine the effect of LLLT (He–Ne and Ga–Al–As laser) on the process of wound healing in the hard palate among diabetic and non-diabetic mice.

2. Materials and Methods

2.1. Animals

This was a randomized controlled trial approved by the ethics committee of Iran center for dental research, Shahid Beheshti University of Medical Science, Tehran, Iran. The study consisted of ninety adult male albino mice with an average weight of 60 ± 1 g. The mice were housed in air-conditioned room with 22 c temperature and diurnal cycle (12 h light/12 h dark).

The mice were randomly divided to six groups; NC (non-diabetic, control), NH (non-diabetic, He–Ne laser), NG (non-diabetic, Ga–Al–As laser), DC (diabetic, control), DH (diabetic, He–Ne laser) and DG (diabetic, Ga–Al–As laser).

3. Induction of Type I Diabetes Mellitus (DM)

Type I DM was induced in groups DC, DH and DG via administration of 55 mg/kg of body weight pancreatin β-cell STZ (Zanosar Pharmacia and Upjohn Co., Kalamazoo, MI, USA) through intraperitoneal injection. Non-diabetic mice received control injections of distilled water. Presence of diabetes was confirmed by measuring blood glucose level after 7 days post-injection, and the mice with glucose levels above 250 mg/dl in a distal tail small injury sample were included in the study [9].

4. Wound Creation

The wound model was identical to that of D'Arcangelo's study [10]. Mice were anesthetized with intramuscular injection of ketamine hydrochloride (40 mg/kg) and diazepam (4 mg/kg) and then hard palate was disinfected with iodine solution. Subsequently, an incision (4 mm long and 2 mm deep) was made in the median raphe, 2 mm posterior to the lingual surface of incisor teeth using a scalpel number 15. Postoperative antibiotic was administered to the mice for 4 days.

5. Laser Therapy Application

In this study two types of lasers were used; helium neon laser (He–Ne) with wavelength 632.8 nm, peak power 5 mW, and spot size 0.02 cm^2 and gallium–aluminum–arsenide laser (Ga–Al–As) with wavelength 830 nm, peak power 25 mW, and spot size 0.10 cm^2(low-level laser apparatus). It is worth mentioning that the specification of the lasers has been used in this research are summarized in Table 1.

Lasers were applied to two areas of the wound at a 1 cm distance and perpendicular to it. Application time and dose of laser irradiation were 16 s and 4 J/cm^2 respectively [9]. NH and DH groups were irradiated with He–Ne laser and NG and DG groups with Ga–Al–As laser. The NC and DC groups did not receive any laser therapy. The four experimental groups received the first dose of irradiation immediately after the surgeries and were subsequently irradiated once a day every day following the surgery, identically.

6. Histologic Procedures

Five mice from each group were sacrificed on the 3rd, 7th, and 14th postoperative days using chloroform in a closed space and prepared for histologic analysis. The samples were fixed in 10% formalin (Merck, Darmstadt, Germany) for 24 h, dehydrated in gradate ethyl alcohol

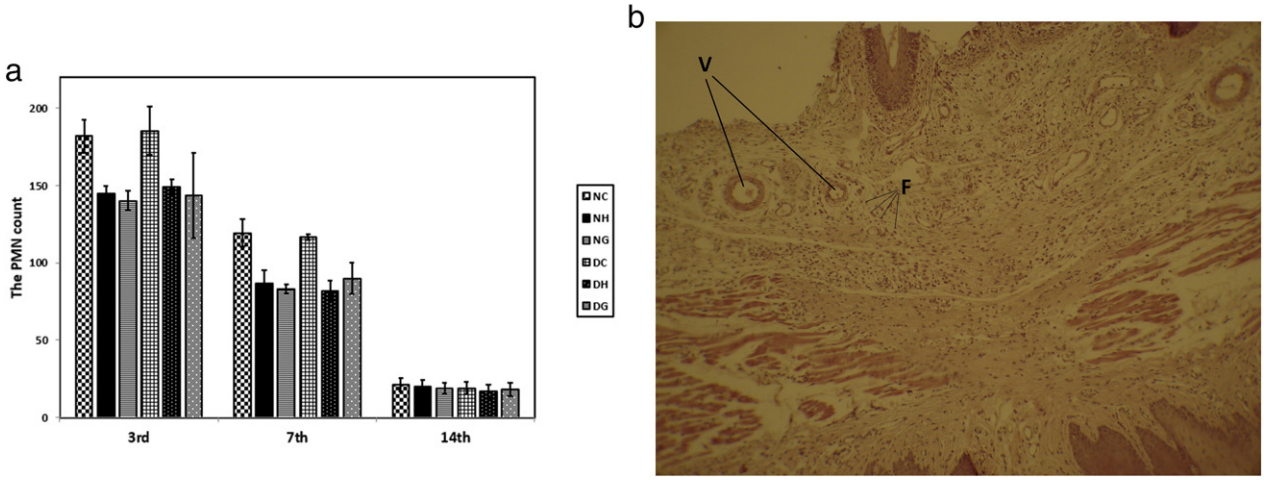

Fig. 1. (a) Mean ± SEM number of PMN cells on the 3rd, 7th, and 14th days post-operation and (b) a photomicrograph of oral mucosa in the control group on day 14 after surgery. On the 14th day, inflammatory cells could hardly be observed (F: fibroblast and V: blood vessel).

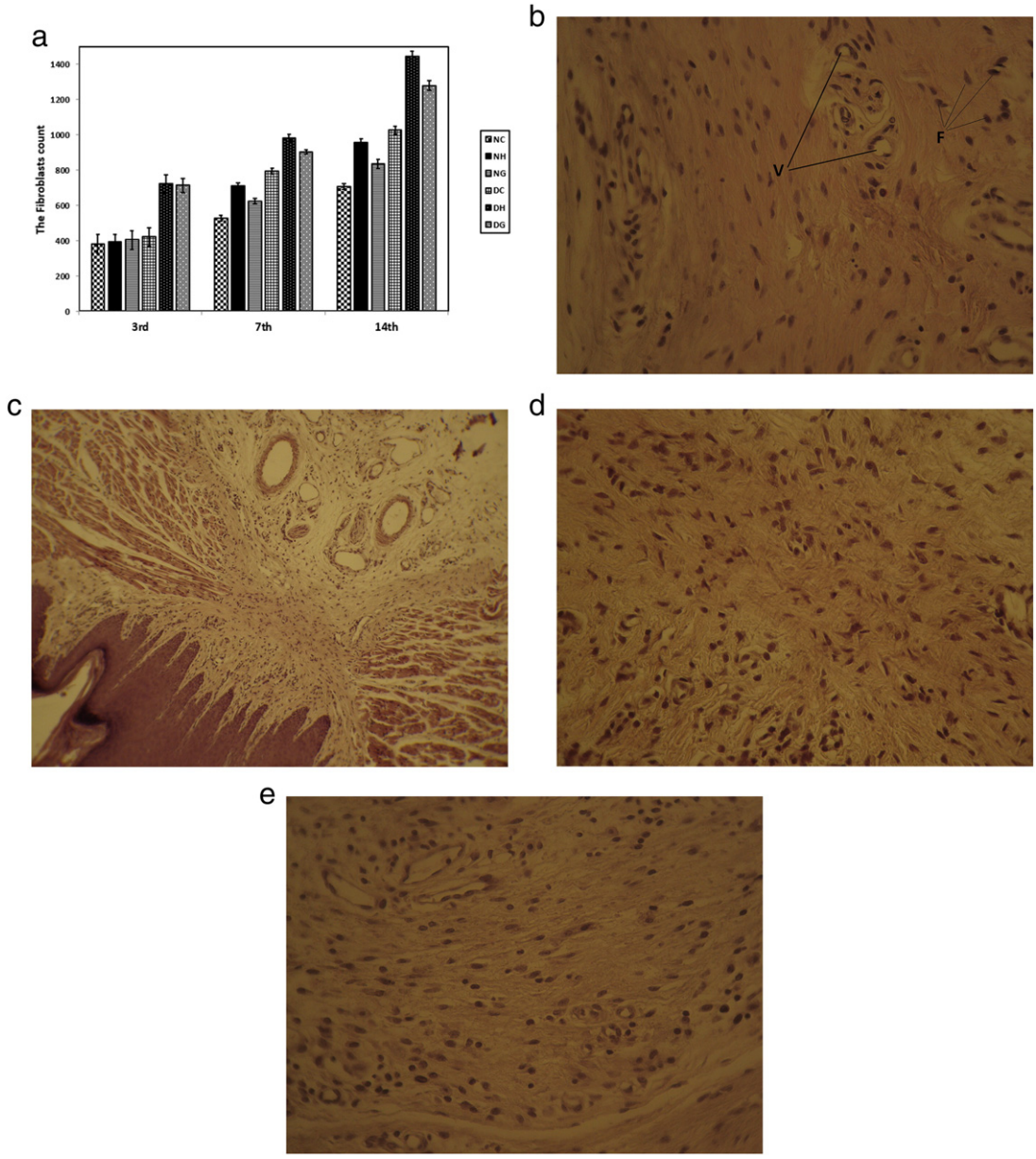

Fig. 2. (a) Mean ± SEM number of fibroblasts on the 3rd, 7th, and 14th post-operation days. Photomicrographs of the oral mucosa on day 14 after the surgery: (b) NC group, (c) DC group, (d) DH group and (e) DG group (F: fibroblast and V: blood vessel).

bath (100 and 70%), clarified in xylol, embedded in paraffin wax (Histosec; Merck) and sectioned in consecutive sequences with 5 μm intervals. we selected two sections of each wounded area randomly and stained them with hematoxylin and eosin (H&E) and Masson's trichrome (MT) for light microscopy evaluation. Ten zones from each sample was randomly selected and evaluated for polymorphonuclear cells, fibroblast proliferation, and vascularization by mean of a calibrated ocular on a Nikon light microscope at 400× magnification.

Fibroblasts were characterized as spindle shape cells with blue-stained nucleus, and new blood vessels were identified as small areas of capillary formation and assemblies of endothelial cells forming a lumen that contain erythrocytes [11].

The density of collagen fibers was graded according to the following scale: 1 = few collagen fibers, 2 = few and partially dispersed collagen fibers, 3 = few and fully spread collagen fibers, and 4 = dense collagen fibers [12]. To avoid observer bias, the pathologist was blinded to the study groups and also each sample was assigned a code and data were recorded accordingly.

7. Statistical Analysis

Data were submitted to SPSS software Version 12 for statistical analysis. The data were reported as mean ± SD. In all analyses, $p < 0.05$ was considered statistically significant. For scaled variables (the number of PMN cells, fibroblasts, and blood vessels), the difference between groups was analyzed using multivariate analysis of variance ($p < 0.05$). The density of collagen fibers was treated as an ordinal variable and Kruskal–Wallis test was applied for comparison among the groups. Tukey's test was performed as a post hoc test when ANOVA and Kruskal–Wallis rendered statistically significant difference among groups.

8. Results

The blood glucose level in non-diabetic rats was 97.31 ± 15.4 mg/dl. All diabetic rats showed clinical evidence of diabetes approximately 7 days after STZ injections. The blood glucose level at the start point

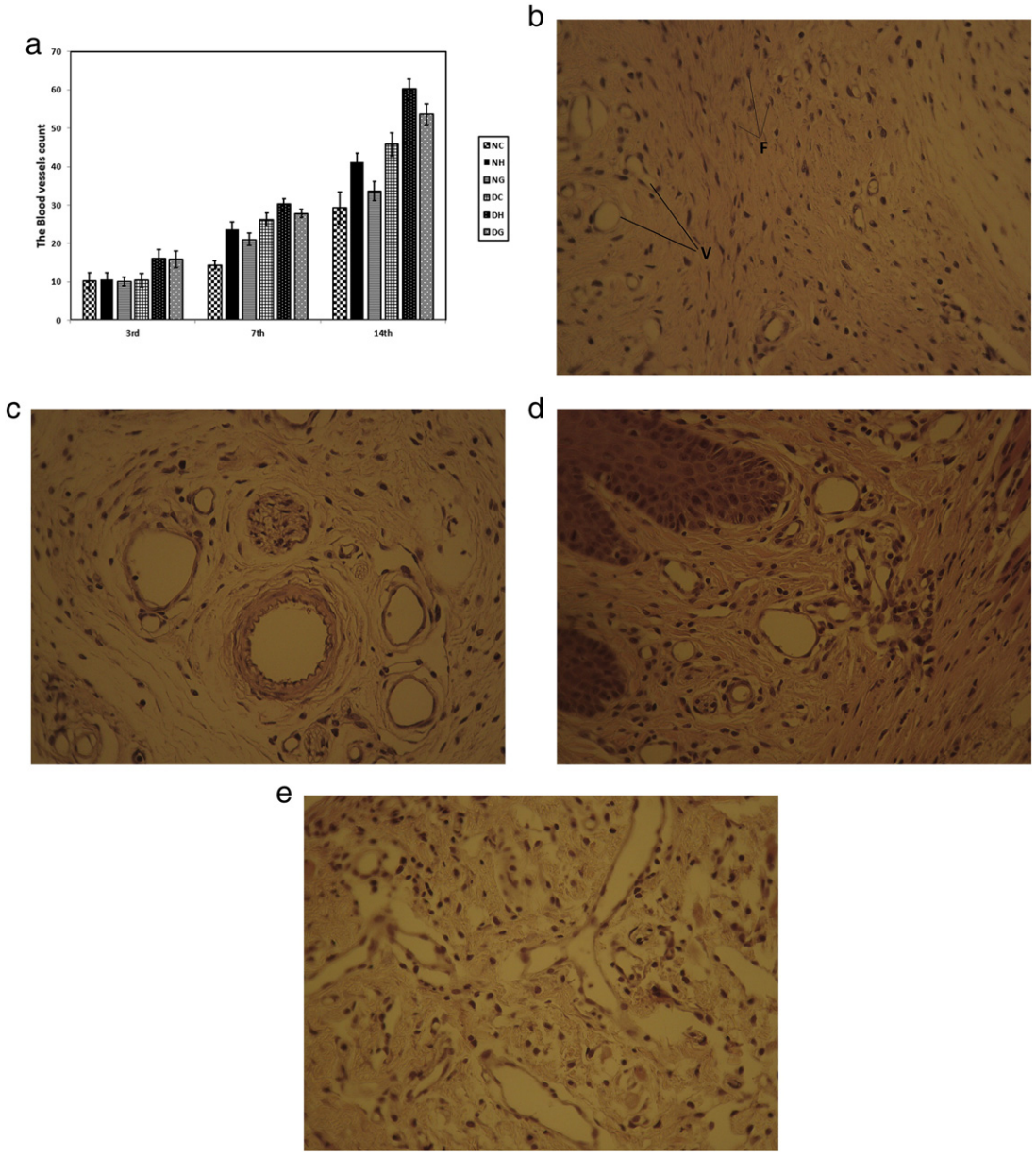

Fig. 3. (a) Mean ± SEM number of blood vessels on the 3rd, 7th, and 14th post-operation days. Photomicrographs of the oral mucosa on day 14 after the surgery: (b) NC group, (c) DC group, (d) DH group and (e) DG group (F: fibroblast and V: blood vessel).

of the study in the diabetic rats was recorded as 472.48 mg/dl before sampling. No evidence of infection was noted in the wounds.

8.1. Inflammatory Phase

Fig. 1a presents a comparison between the mean values of the numbers of PMN cells among the study groups. Inflammation was statistically more prominent in the non-diabetic and the DC group compared to the NH, NG, DH, and DG groups on days 3 and 7 ($p < 0.05$) with no statistical difference between the treatment groups. There were no differences between non-diabetic and diabetic control group.

The number of PMN cells had a markedly significant decreases on day 7 compared to day 3, however the inflammatory cells could hardly be observed on day 14 (see Fig. 1b).

8.2. Proliferative Phase

The granulation tissue formation was seen in the histological sections obtained on day 7 and day 14. The mean values for fibroblast count and new blood vessel formation are represented in Figs. 2a and 3a. The numbers of fibroblasts and new blood vessel in diabetic laser treated groups (DG and DH) were statistically higher compared to that of NC, DC, NH and NG groups on days 3, 7 and 14; ($P < 0.05$) however there were no statistical differences between NG, NH, NC and DC groups on day 3. The histological sections for days 7 and 14 marked an statistically increased proliferative activity in diabetic groups compared to non-diabetic groups ($P < 0.05$). The amount of fibroblast proliferation and new blood vessel formation in the DH and NH groups were statistically more prominent compared to those of the DG and NG groups respectively ($P < 0.05$). Histological evaluations of the samples on day 14 demonstrated a statistical increase in the fibroblast proliferation and new blood vessel formation in all groups compared to day 7 ($P < 0.05$) (see Figs. 2b–e and 3b–e).

In the proliferative phase, collagen fiber formation was also evaluated. Fig. 4 shows the mean score for collagen formation among the groups. The histomicrographs of wound area in the diabetic and non-diabetic control group on days 7 and 14 demonstrates immature and unorganized collagen fibers, however in the DG, DH, NG and NH groups

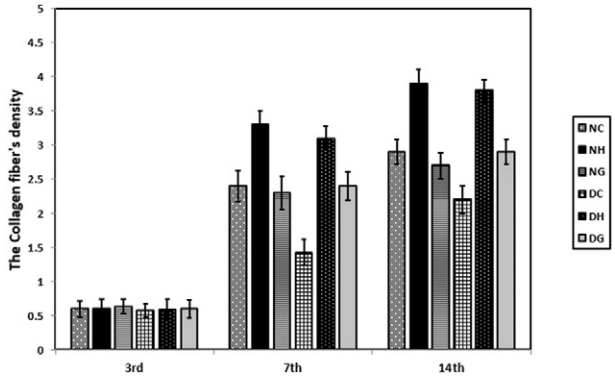

Fig. 4. Mean ± SEM score of collagen density on the 3rd, 7th, and 14th days after the surgery.

well-arranged and dense collagen fibers were formed with statistically high density ($p < 0.05$). Furthermore, the collagen fiber in the DH and NH groups were statistically denser compare to those of DH and DG, respectively ($p < 0.05$). Additionally, the density of collagen fibers in all groups on day 14 statistically increased compared to day 14 ($p < 0.05$).

9. Discussion

In this study we evaluated the effectiveness of two different types of low level laser therapy (He–Ne and Ga–Al–As lasers) at 4 J/cm^2 dose on the healing process of hard palate wound in diabetic and non-diabetic mice.

Wound healing is a complex process that involves a variety of cells and mediators. It is generally divided into three phases including inflammatory (1–3 postsurgical days), proliferative (3–7 postsurgical days) and remodeling phase (up to several months after surgery) [13].

The margins of an ulcer in the hard palate are dense and the healing process is long. Furthermore, other factors such as diminished cellular capacity, altered growth factor response and decreased angiogenesis and blood flow, impair the wound healing process in diabetic patients [14]. The efficacy of laser radiation used in this study and efficacy of LLLT on diabetic mice have been shown in previous studies [15–18]. However, we aimed to compare the effectiveness of two types of LLLT on hard palate wound healing in diabetic and non-diabetic mice.

He–Ne laser has been shown to be more effective in enhancing the wound healing process compared to Ga–Al–As laser. Studies demonstrate that He–Ne laser (632.8 nm) causes a series of respiratory chain reactions, whereas the Ga–Al–As laser (830 nm) induces a molecular pathway in the cell membrane that triggers photochemical response in the tissue [19,20].

Evans et al. evaluated the response of fibroblasts in normal and wounded tissue to three different types of lasers i.e. He–Ne laser (632.8 nm), diode laser (830 nm) and Nd-YAG (1064 nm) laser with energy densities of 5 and 16 J/cm2 in vitro. Their results showed that laser therapy can stimulate human fibroblast proliferation and they were also able to demonstrate that He–Ne laser with energy density of 5 J/cm^2 is more effective than the other two types of lasers. [21].

In Reddy's study, both He–Ne and Ga–Al–As lasers had positive stimulatory effect on wound healing process in diabetic rats but He–Ne laser was proven to be more effective than Ga–Al–As laser [22]. In the present study, we applied He–Ne laser (632.8 nm) and Ga–Al–As laser (830 nm) on diabetic and non-diabetic mice and our findings were in line with Reddy's.

10. Inflammatory Phase

This phase is characterized by immigration of inflammatory cells, specifically PMN cells, to the wounded area [23]. Two different mechanisms have been explained for the effect of LLLT on the inflammatory phase. Nagashima et al. presented that, LLLT inhibits sever inflammatory response and can induce increased collagen formation whereas according to Kami's study, laser initiates mild inflammation and leads to increased blood flow [24,25]. The findings of the present study confirm the former hypothesis.

11. Proliferative Phase

Fibroblast proliferation, neovascularization, and collagen Synthesis are characteristic features of the proliferative phase [26]. Schindl et al. found that low-intensity laser enhances endothelial proliferation and angiogenesis and also promotes wound healing process [27] in another study it has been shown that LLLT can reduce inflammatory phase and promote fibroblast proliferation and angiogenesis [28]. Sharifian et al. demonstrated that, pulsed LLLT at 0.2 J/cm^2 accelerated the wound healing process in both non-diabetic and diabetic rats [9].

In a study by Saygun et al., LLLT was shown to increase proliferation of human gingival fibroblasts (HGFs) and release of the growth factors and thus, can have an important role in periodontal wound healing [29]. In the present study, the numbers of fibroblasts and new blood vessels in the diabetic groups that received laser therapy, were significantly higher than the control groups and non-diabetic laser treated groups. The amount of fibroblast proliferation and neovascularization in the He–Ne groups was significantly higher compared to the Ga–Al–As groups in both diabetic and non-diabetic mice. Our results support the previous studies.

Regarding the effect of lasers on collagen regeneration, controversial results have been reported in the literature. In a study by Reis et al., an increase in collagen density and extracellular matrix distribution with following irradiation of Ga–Al–As laser (4 J/cm^2) has been reported [30]. Similarly, Lopes et al. concluded that LLLT promotes collagen Arrangement and accelerates wound healing [31]. On the other hand, Gavish et al. irradiated porcine aortic smooth muscle cells with a titanium–sapphire (Ti–Sa) laser (780 nm, 200 mW, 2 J/cm^2) for 18 min and reported that LLLT increases the activity of matrix metalloproteinase-2, which is involved in collagen degradation and remodeling [32]. Also, Fahimipour et al. reveled an acceleration of the wound healing process of experimental wounds in the hard palate mucosa of mice at LLLT with a He–Ne laser at energy densities of 3 and 7.5 J/cm^2 [33]. In the present study, the histomicrographs of the wound area in the diabetic and non-diabetic control groups on days 7 and 14 presented immature and unorganized collagen fibers, whereas in all the laser treated groups well-arranged and dense collagen fibers were formed with statistically high density ($P < 0.05$). Furthermore, the collagen fibers in the DH and NH groups were statistically denser compared to those of DG and NG respectively ($P < 0.05$).

12. Conclusion

In conclusion, the obtained experimental results ascertained that Low-level laser therapy with He–Ne laser compared to Ga–Al–As laser has a positive healing effect on the hard palate gingival wounds in STZ-D mice.

References

[1] D.E. Laaksonen, H.M. Lakka, L.K. Niskanen, G.A. Kaplan, J.T. Salonen, T.A. Lakka, Metabolic syndrome and development of diabetes mellitus: application and validation of recently suggested definitions of the metabolic syndrome in a prospective cohort study, Am. J. Epidemiol. 156 (11) (2002) 1070–1077.
[2] A.K. Arya, R. Tripathi, S. Kumar, K. Tripathi, Recent advances on the association of apoptosis in chronic non healing diabetic wound, World J. Diabetes 5 (6) (2014) 756.
[3] K.J. Bryant, K. Moore, J.F. McAnulty, Angularis oris axial pattern buccal flap for reconstruction of recurrent fistulae of the palate, Vet. Surg. 32 (2003) 113–119.
[4] I.R. Luskin, Reconstruction of oral defects using mucogingival pedicle flaps, J. Clin. Tech. Small Anim. Pract. 15 (2000) 251–259.

[5] W. Posten, D.A. Wrone, J.S. Dover, K.A. Arndt, S. Silapunt, M. Alam, Low-level laser therapy for wound healing: mechanism and efficacy, Dermatol. Surg. 31 (3) (2005) 334–340.
[6] E. Mester, Experimentation on the interaction between infrared laser and wound healing, J. Z. Exp. Chir. 2 (1969) 94.
[7] J.R. Basford, Low-intensity laser therapy: still not an established clinical tool, Lasers Surg. Med. 16 (4) (1995) 331–342.
[8] F. Fahimipour, M. Mahdian, B. Houshmand, M. Asnaashari, A.N. Sadrabadi, S.E.N. Farashah, ... A. Khojasteh, The effect of He–Ne and Ga–Al–As laser light on the healing of hard palate mucosa of mice, Lasers Med. Sci. 28 (1) (2013) 93–100.
[9] Z. Sharifian, M. Bayat, M. Alidoust, R.M. Farahani, M. Bayat, F. Rezaie, H. Bayat, Histological and gene expression analysis of the effects of pulsed low-level laser therapy on wound healing of streptozotocin-induced diabetic rats, Lasers Med. Sci. 29 (3) (2014) 1227–1235.
[10] C. D'Arcangelo, F. Di Nardo Di Maio, G.D. Prosperi, E. Conte, M. Baldi, S. Caputi, A preliminary study of healing of diode laser versus scalpel incisions in rat oral tissue: a comparison of clinical, histological, and immunohistochemical results, Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod. 103 (6) (2007) 764–773.
[11] D. Altavilla, A. Saitta, D. Cucinotta, M. Galeano, B. Deodato, M. Colonna, V. Torre, G. Russo, A. Sardella, G. Urna, G.M. Campo, V. Cavallari, G. Squadrito, F. Squadrito, Inhibition of lipid peroxidation restores impaired vascular endothelial growth factor expression and stimulates wound healing and angiogenesis in the genetically diabetic mouse, Diabetes 50 (3) (2001) 667–674.
[12] D.U. Talas, A. Nayci, S. Atis, A. Polat, U. Comelekoglu, C. Bagdatoglu, N. Renda, The effects of corticosteroids on the healing of tracheal anastomoses in a rat model, Pharmacol. Res. 45 (4) (2002) 299–304.
[13] T. Velnar, T. Bailey, V. Smrkolj, The wound healing process: an overview of the cellular and molecular mechanisms, J. Int. Med. Res. 37 (5) (2009) 1528–1542.
[14] H. Brem, M. Tomic-Canic, Cellular and molecular basis of wound healing in diabetes, J. Clin. Investig. 117 (5) (2007) 1219.
[15] S.M. Safavi, B. Kazemi, M. Esmaeili, A. Fallah, A. Modarresi, M. Mir, Effects of low-level He–Ne laser irradiation on the gene expression of IL-1beta, TNF-alpha, IFN-gamma, TGF-beta, b FGF, and PDGF in rat's gingival, J. Lasers Med. Sci. 23 (3) (2008) 331–335.
[16] K. Nomura, M. Yamaguchi, Y. Abiko, Inhibition of interleukine-1beta production and gene expression in human gingival fibroblasts by low-energy laser irradiation, J. Lasers Med. Sci. 16 (3) (2001) 218–223.
[17] S. Fernando, C.M. Hill, R. Walker, A randomized double blind comparative study of low-level laser therapy following surgical extraction of lower third molar teeth, Brit. J. Oral Maxillofac. Surg. 31 (1993) 170–172.
[18] V.L. Busnardo, M.L. Biondo-Simoes, Effects of low-level helium–neon laser on induced wound healing in rats, Rev. Bras. Fisioter 14 (1) (2010) 45–51.
[19] G.K. Reddy, Photobiological basis and clinical role of low intensity lasers in biology and medicine, J. Clin. Laser Med. Surg. 22 (2) (2004) 141–150.
[20] K.C. Smith, The photobiological basis of low-level laser radiation therapy, Laser Ther. 3 (1991) 19–24.
[21] D.H. Evans, H. Abrahamse, Efficacy of three different laser wavelengths for in vitro wound healing, J. Photodermatol. Photoimmunol. Photomed. 24 (2008) 199–210.
[22] G.K. Reddy, Comparison of the photostimulatory effects of visible He–Ne and infrared Ga–As lasers on healing impaired diabetic rat wounds, Lasers Surg. Med. 33 (5) (2003) 344–351.
[23] P.M. Carrinho, A.C. Renno, P. Koeke, A.C. Salate, N.A. Parizotto, B.C. Vidal, Comparative study using 685-nm and 830-nm lasers in the tissue repair of tenotomized tendons in the mouse, Photomed. Laser Surg. 24 (6) (2006) 754–758.
[24] T. Nagashima, H. Kidokoro, H. Isigaki, Intra-arterial infusion of PGE1 in peripheral arterial disease, J. Gendai Iryou 14 (1982) 1000–1013.
[25] T. Kami, Improvement of flap survival by application of hypobaric oxygen training, Keio J. Med. 39 (1990) 6–13.
[26] T. Velnar, T. Bailey, V. Smrkolj, The wound healing process: an overview of the cellular and molecular mechanisms, J. Int. Med. Res. 37 (5) (2009) 1528–1542.
[27] A. Schindl, H. Merwald, L. Schindl, C. Kaun, J. Wojta, Direct stimulatory effect of low-intensity 670-nm laser irradiation on human endothelial cell proliferation, Br. J. Dermatol. 148 (2) (2003) 334–336.
[28] M. Dyson, S. Young, Effect of laser therapy on wound contraction and cellularity in mice, Lasers Med. Sci. 1 (2) (1986) 125–130.
[29] I. Saygun, S. Karacay, M. Serdar, A.U. Ural, M. Sencimen, B. Kurtis, Effects of laser irradiation on the release of basic fibroblast growth factor (bFGF), insulin-like growth factor-1 (IGF-1), and receptor of IGF-1 (IGFBP3) from gingival fibroblasts, Lasers Med. Sci. 23 (2008) 211–215.
[30] S.R. Reis, A.P. Medrado, A.M. Marchionni, C. Figueira, L.D. Fracassi, L.A. Knop, Effect of 670-nm laser therapy and dexamethasone on tissue repair: a histological and ultra structural study, Photomed. Laser Surg. 26 (4) (2008) 307–313.
[31] N.N. Lopes, H. Plapler, R.V. Lalla, M.C. Chavantes, E.M. Yoshimura, M.A. Silva, M.T. Alves, Effects of low-level laser therapy on collagen expression and neutrophil infiltrate in 5-fluorouracil-induced oral mucositis in hamsters, Lasers Surg. Med. 42 (6) (2010) 546–552.
[32] L. Gavish, L. Perez, S.D. Gertz, Low-level laser irradiation modulates matrix metalloproteinase activity and gene expression in porcine aortic smooth muscle cells, Lasers Surg. Med. 38 (2006) 779–786.
[33] F. Fahimipour, M. Nouruzian, M. Anvari, M. Akhavan Tafti, M. Yazdi, M. Khosravi, Z. Dehghannayeri, S.S. Sabounchi, M. Bayat, Effect of low-level laser therapy on experimental wounds of hard palate mucosa in mice, Indian J. Exp. Biol. 49 (5) (2011) 357–361.