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Assessment of Pain Perception After Conventional Frenectomy With Application of Cold Atmospheric Plasma

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ABSTRACT

Frenectomy is a surgical technique that purposes to remove the unusual frenum. There are a limited number of studies examining the effect of cold atmospheric plasma on periodontal tissues. The aim of this study was to investigate the effect of Cold Atmospheric Plasma (CAD) application on pain and discomfort in patients after conventional frenectomy operations. Eigthy-seven patients (38 male and 49 female, aged between 18-36 years) with mucogingival problems because of maxillary labial frenums were selected for this study. Patients were randomly divided into two groups: group 1(G1) frenectomy with conventional surgery and group 2(G2) frenectomy with conventional surgery+CAP. The frenum was held with a hemostat inserted to the depth of the vestibule and incision were placed on. After the triangular resected portion of the frenum was removed with the hemostat and wound were sutured. Conventional surgical technique was repeated for G2 and the surgical area was irradiated using CAP (kINPen 11). Visual Analog Scale (VAS) was used to rate postoperative degrees of pain and functional discomforts (chewing and speech) at 1st, 3rd, 7th and 10th days. VAS score for pain was significantly lower in the G2 group as compared to the G1 on 1st, 3th, 7th and 10th days. Similarly, when the chewing and speech VAS values are compared, the values in the G2 are lower than the G1 ($p>0.05$). According to these results, we can conclude that plasma reduces complications that may occur after frenectomy and these results may related to the positive effect of plasma on wound healing.

Key Words: Cold plasma, labial frenum, mouth mucosa, postoperative pain, oral surgery

Introduction

The labial frenum is characterized as triangular shape and extending from the interdental surface of the labial mucosa to the gingival mucosa and the underlying periosteum between the central incisors. Frenum is fold of enclosed muscle fibers and connective tissue and covered with a mucous membrane. Histologically, an ortho- or parakeratinized laminar epithelium demonstrated which covers thick and soft connective tissues with lymph vessels, blood vessels and minör salivary glands. Muscular fibers found in the structure of frenum originated from the orbicularis oris muscle of the lip (1,2) It has flexible anatomical structure and modulate and limit the labial movement.

Frenum is considered as normal anatomical structures that not has pathological effects. However, frenum cause some problems (diastema, gingival recession, loss of papilla, aesthetics and phonetic problems and also food retention) if it penerate the papilla and/or located too close to the gingival margin (3). The excess tension caused by the long frenum attachment leads to separate gingival margin from the tooth surface. These conditions disallow appropriate toothbrushing and cause to plaque accumulation, and also gingivitis occured (4). Frenum problems are generally observed in the facial region of central incisors and frenum are examined clinically by applying tension over it to consider the movement of papilla or decolor of tissue generated due to ischemia of the gingiva (5). According to Miller, the frenum should be described as pathogenic when it is extraordinarily extensive or there is no attached gingiva throughout the midline or the interdental papilla moves when the frenum is streched (6).

Frenectomy is a surgical technique that purposes to completely remove the unusual frenum including its attachment of the underlying bone

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Fig. 1.a: Preoperative photograph of maxillary anterior frenum extending to the interdental papilla of the central incisors; b: Immediately after conventional frenectomy; c: Wound closure by suture

and it can be performed with several methods (conventional method, soft tissue laser, etc.) (7,8). The conventional frenectomy method (periodontal knives and using scalpels) has been used for many years. On the other hand, this technique has certain disadvantages like causing large wound area where primary closure is not possible in the lower part and healing takes place by secondary intension and also patient compliance occurs (9). Therefore, it is very important to accelerate wound healing and decrease symptoms such as bleeding, pain and swelling after the frenectomy procedure.

In recent years, plasma technology has been used for medical therapies. Plasma is the fourth state of matter occurs as a result of partial ionization of the gas after application of high energy to any gas. Cold Atmospheric Plasma (CAP) is a non-thermal because it has electrons at a hotter temperature than the heavy particles and the temperature in the application area is below 40°C. Several different gases such as argon, nitrogen, helium and air only can be used while producing the CAP. The results of the studies showed that plasma promote wound healing, not only with its antibacterial properties, but also by directly affecting epidermal and dermal cells (10,11).

In general, stimulation of healing of the wound area and control of possible complications are very important for the comfort of the patient after periodontal surgery operations. There are a limited number of studies in the literature examining the effect of cold atmospheric plasma on periodontal tissues (12,13). The aim of this study was to investigate the effect of Cold Atmospheric Plasma application on pain and discomfort in patients after conventional frenectomy operations.

Materials and Methods

Eigthy-seven patients (38 male and 49 female, aged between 18 and 36 years) with mucogingival problems because of maxillary labial frenums who presented to the department of periodontology (Eskisehir Osmangazi University, Faculty of

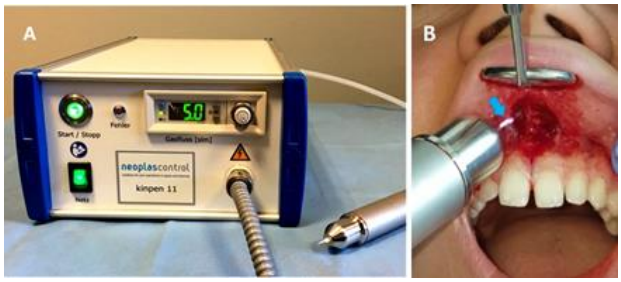

Fig. 2. kINPen 11 plasma jet. Argon gas is used as the carrier gas at a flow rate of 5 l/min at 2.5 Bar (A). Application of the kINPen 11 plasma jet (Blue arrow: Plasma jet) (B)

Dentistry) were selected for this study. The study protocol was reviewed and approved by the institutional review board (Approval number: 25403353-050.99-E.42818). Only maxillary anterior frenum extending to the interdental papilla of the central incisors were included in this study. Patients who had any systemic disease that could affect oral surgery, were being treated with analgesics or antibiotics during the previous three months, exhibited poor oral hygiene were excluded from the study. Patients were randomly divided into two groups and written consent was obtained from each patient: group 1 (G1) frenectomy with conventional surgery (n= 44, 19 male, 25 female, mean age 27,23±2,09) and group 2 (G2) frenectomy with conventional surgery + CAP application (n=43, 19 male, 24 female, mean age 27,12±2,53).

Surgical Procedure: A single operator performed all the frenectomies. The surgical area was anesthetized with a local infiltration by using 2% lignocaine with 1:80000 adrenaline. The frenum was held with a hemostat inserted to the depth of the vestibule and incision were placed on the upper and under surface of the hemostat with a #15 blade. After the triangular resected portion of the frenum was removed with the hemostat, a blunt dissection was done on the bone to relieve the fibrous attachment. The edges of the diamond shaped wound were sutured by using 4-0 black silk with interrupted sutures (Figure 1). Conventional surgical technique was repeated for group 2. After frenectomy the surgical area was irradiated using CAP. The CAP used for this study was the kINPen 11 plasma jet developed by the Leibniz Institute for Plasma Science and Technology, Greifswald, Germany, in cooperation with Neoplas GmbH, Greifswald, Germany. The plasma jet comprises a base station including the control unit and the power supply, together with a hand piece containing the electrical discharge system and the gas flow. The discharge system is supplied with argon plasma, with the pulses being

Table 1. Demographic Characteristics of the Patients Included in the Study

Demographic characteristics	Frenectomy	Frenectomy + CAP	*P* value
Male *n* (%)	19 (%50)	19 (%50)	0,925
Female *n* (%)	25 (%51)	24 (%49)	
Age (Mean±SD)	27,23±2,09	27,12±2,53	0,824

SD=Standard deviation; CAP= Cold atmospheric plasma
Chi-square (x2) test (*P*<0.05*)

Table 2. Comparison of VAS Scores Between the Groups

		VAS Scores Median (min - max)		*P* value
		Frenectomy G1	Frenectomy + CAP G2	
1st day	Pain	5 (4 - 9)*	3 (2- 7)*	0.001*
	Chewing	6 (5 - 8)*	4 (3 - 7)*	0.001*
	Speaking	6 (4 - 8)*	4 (3 - 6)*	0.001*
3rd day	Pain	2 (1 - 5)*	1 (1 - 3)*	0.001*
	Chewing	2 (1 - 3)*	1 (0 - 2)*	0.001*
	Speaking	2 (1 - 5)*	1 (1 - 3)*	0.001*
7th day	Pain	1 (0 - 2)*	0 (0 - 1)*	0.001*
	Chewing	1 (0 - 2)*	0 (0 - 1)*	0.001*
	Speaking	1 (0 - 2)*	0 (0 - 2)*	0.001*
10th day	Pain	0 (0 - 1)*	0 (0 - 0)*	0.001*
	Chewing	1 (0 - 1)*	0 (0 - 1)*	0.013*
	Speaking	0 (0 - 1)*	0 (0 - 0)*	0.001*

CAP= Cold atmospheric plasma, Mann-Whitney U test (*P*<0.05*)

generated at a frequency of 21 kHz with an applied voltage of 5 kV. Argon gas is used as the carrier gas at a flow rate of 5 l/min at 2.5 Bar. The distance between nozzle and tissue was approximately 5 mm. The device kINPen 11 has CE certification for fulfilling the electrical safety standards required for use on humans. The wounds were treated with the plasma jet moving in three different directions (vertical, horizontal and diagonal) over the wound surface. Approximately 1 cm^2 of wound surface was treated for 1 minute (14) (Figure 2). CAP application was performed in the same way in the group 1 for preventing placebo effect. However, the application did not occur because the start button was not pushing. After surgery, the patients were advised to be on soft/liquid diet for 1 week and they were told to use an analgesic if needed. Also patients were informed not to take analgesics within 24 hours before VAS evaluations.

Scoring Method: Visual Analog Scale (VAS) was used to rate postoperative degrees of pain at 1st, 3rd, 7th and 10th days after surgery. The degree of pain and functional discomforts, including chewing and speech were rated on a 10 cm horizontal VAS, separately. Immediately after the frenectomy, and at 3rd, 7th and 10th days each patient was asked to make a vertical mark on a 10 cm VAS. The scale was graded with values ranging from "0" to "10" from left to right. The left "0" point indicated no pain and no functional complications whereas the right "10" point indicated to worst pain and extreme functional complications (15).

Statistical Analysis: SPSS 21.0 Packet Data Program (SPSS 21.0 Software Package Program Inc. Chicago, IL) was used for statistical analysis. The data were analyzed for compliance with normal distribution with Shapiro-Wilk test. The data found to be compatible with the normal distribution was compared using the independent-samples T test and the data that did not fit the normal distribution was compared using the Mann-Whitney U test. Chi-square (x^2) test was used for categorical variable comparisons. P <0.05 was considered statistically significant.

Results

Demographic characteristics of the patients are shown in Table 1. There were no statistically significant differences between gender and age distribution by groups ($p>0.05$). The analysis showed that VAS score for pain was significantly lower in the frenectomy+CAP (G2) group as compared to the frenectomy group (G1) on 1st, 3th, 7th and 10th days. Similarly, when the chewing and speech VAS values are compared, there is a statistically significant difference between the two groups and on 1st, 3th, 7th and 10th days the values in the G2 group are lower than the G1 group ($p<0.05$) (Table 2). In addition, the comparison of the scores of pain, chewing and speech for each gender were analyzed. Similar to the results obtained before, when only data from females were evaluated, there were statistically significant differences between G1 and G2 groups in almost all scores ($p<0.05$). However, there is no significant difference between the VAS values of the chewing on the 10th day ($p=0.161$) (Table 3). When the data obtained only from males were compared, there were significant differences between all scores of pain ($p<0.05$) while there was no difference between chewing and speech VAS scores only on the 10th day ($p=0.271$, $p=0.096$) (Table 4).

Discussion

Plasma has been used in many industrial fields for many years. In the recent years, with the discovery of the biological effects of plasma, it has also started to be used in medicine. Although it has just started to be used in dentistry, there is no in vivo study in today's literatüre. In vitro studies in dentistry were about modification (16), and decontamination (17) of implants' surfaces, the connectivity of dentine restorations (18), antimicrobial effect in root canals (19) and tooth whitening (20). Although there were so many studies about the the effects of plasma on wound healing in dermatology, there was no records the results of wound healing after periodontal surgery with application of plasma. In our study, it was aimed to determine the effects of CAP on patient comfort after the frenectomy.

Frenectomy is a surgical procedure aimed to eliminate the connection between the periosteum and bone under the frenulum and the complete removal of soft tissues that form the frenulum. Conventional technique in which the frenulum is excised using scalpel is an invasive surgical procedure. Although it is a cost-effective and easy-to-implement procedure, the conventional method also has some disadvantages. Due to the sutures thrown to close the surgical area and provide hemostasis, the patient may experience complaints such as restriction and discomfort in functional movements during speech and eating after the operation (7,21).

In this study, frenectomy+CAP group patients recorded significantly lower VAS score than the convensional frenectomy group, indicating that CAP group patients experienced less pain during post-operative time. Reducing pain and other complications in the patient after dental treatments (especially oral surgery), is very important for patient comfort and evaluating the success of the treatment. Pain is a sensitive sensation that is affected by many different physiological and psychological conditions and can vary from person to person. The data obtained as a result of studies showed that VAS is a reliable and valid method for assessing pain (22). In assessments with VAS, it has been shown that a regular distribution can be achieved. It is also show that it has sufficient sensitivity in the evaluation of treatment effects, can be repeated, and has been reported as a successful evaluation method in many studies (23).

In the medical field, the frequency of studies examining the effects of plasma on wound healing is remarkable. Kahnberg and Thilander investigated the healing of excisional wounds formed in the palate of the rats in their study, that the wound surface was reduced with contraction and epithelial cell migration of the wound margins and the defects was completely closed after 3 weeks (24). In another study, CAP was applied to acute cutaneous wound surfaces of 2 mm diameter created in 40 male mice for 1 minute daily and change in the surface area of the wound; epithelization; and amount of myofibroblast, macrophage, neutrophil and transforming growth factor (TGF55 β) were evaluated. In the macroscopic evaluation, the wound area of the test group was found to be smaller than that of the control group at all times between 4-15th days. In immunohistochemical evaluation, the presence of myofibroblast was observed in the test group on the 3rd day, but not in the control group and the researchers attributed faster wound healing to the formation of myofibroblasts in the test group (25).

Several kinds of reactive oxygen species (ROS) like ozone (O3) and nitric oxide (NO) were occurred with plasma application (26). ROS

Table 3. Comparison of VAS scores between the groups in females

		VAS Scores Median (min - max)		P value
		Frenectomy G1	Frenectomy + CAP G2	
1st day	Pain	7 (4 - 8)*	4 (3 - 8)*	0.001*
	Chewing	7 (5 - 8)*	5 (4 - 7)*	0.001*
	Speaking	6 (4 - 8)*	5 (2 - 8)*	0.001*
3rd day	Pain	2 (1 - 3)*	1 (1 - 2)*	0.001*
	Chewing	2 (1 - 5)*	1 (1 - 3)*	0.001*
	Speaking	2 (1 - 4)*	1 (0 - 2)*	0.001*
7th day	Pain	1 (0 - 2)*	0 (0 - 2)*	0.001*
	Chewing	0 (0 - 2)*	0 (0 - 1)*	0.003*
	Speaking	1 (0 - 1)*	0 (0 - 1)*	0.001*
10th day	Pain	0 (0 - 1)*	0 (0 - 0)*	0.001*
	Chewing	0 (0 - 1)	0 (0 - 0)	0.161
	Speaking	1 (0 - 1)*	0 (0 - 0)*	0.001*

CAP= Cold atmospheric plasma, Mann-Whitney U test ($P<0.05$*)

Table 4. Comparison of VAS scores between the groups in males

		VAS Scores Median (min - max)		P value
		Frenectomy G1	Frenectomy + CAP G2	
1st day	Pain	5 (4 - 8)*	4 (3 - 8)*	0.001*
	Chewing	6 (5 - 8)*	5 (3 - 8)*	0.001*
	Speaking	5 (4 - 7)*	3 (3 - 8)*	0.001*
3rd day	Pain	4 (2 - 7)*	2 (2 - 5)*	0.001*
	Chewing	4 (2 - 6)*	2 (2 - 5)*	0.001*
	Speaking	4 (1 - 7)*	3 (1 - 6)*	0.001*
7th day	Pain	1 (0 - 2)*	0 (0 - 1)*	0.001*
	Chewing	1 (0 - 2)*	0 (0 - 2)*	0.005*
	Speaking	1 (0 - 2)*	1 (0 - 1)*	0.012*
10th day	Pain	0 (0 - 1)*	0 (0 - 1)*	0.012*
	Chewing	0 (0 - 1)	0 (0 - 0)	0.271
	Speaking	0 (0 - 1)	0 (0 - 0)	0.096

CAP= Cold atmospheric plasma, Mann-Whitney U test ($P<0.05$*)

accelerate wound healing by stimulating the heparin-induced epidermal growth factor release by stimulating MMPs directly, and activation of the mitogen activated protein kinase pathway, and accelerating wound healing and regeneration by increasing nitric oxide concentration (27). Plasma contribute to wound healing by providing stimulation, angiogenesis, contraction and coagulation of fibroblasts and keratinocytes (28). And also nitric oxide provides fibroblast proliferation, increases phagocytosis, keratinocyte proliferation and collagen synthesis. In this way accelerates wound healing and regulates immune response (29).

Many invivo and in vitro studies have been shown that CAP can reduce the amount of microorganisms and has an effect on biofilms without affecting living epidermal tissues (30,31). The agents with antimicrobial properties, used after periodontal surgery, accelerate wound healing by reducing bacterial plaque accumulation, postoperative pain and edema (32). Based on their contribution to healing of chronic infected wounds shown in medical studies, it may be

thought that plasma stimulated the gingival epithelialization process due to the antimicrobial activity.

In the study of Kalghatgi et al, CAP application has been shown to increase endothelial cell proliferation with release of fibroblast growth factor-2 (FGF-2) (33). In another study, the effect of plasma on the healing of burns in mice was evaluated and it was observed that the healing process improved with neovasculer vessels formed after plasma treatment (34). Similar to these studies, it has been reported by many researchers that angiogenesis was induced by plasma (35). Angiogenesis is a very important process in the second stage of wound healing related with ROS, NO, cytokines and growth factors which could be provided by CAP.

Histological and histomorphometric studies have shown that plasma application reduced microbial colonisation on the wound, stimulated the late phase of inflammation, increased epithelialization and wound contraction, and caused earlier wound closure (36).

All groups showed reduction in VAS with time also VAS was significantly lower in CAP-treated group as compared to control group ($p<0.05$). On the 1st and 3rd days, VAS rates were high in both groups, a rapid decrease was observed in the VAS after the 7th day. According to the results obtained from this study, on the 1st, 3rd and 7th postoperative days; CAP application in addition to conventional frenectomy method had significant advantages in terms of pain, speech, and chewing.

Since our study is a human study, histological evaluation is not as easy as in animal studies. For this reason, postoperative evaluations of healing in the wound area could only be made by comparing the patients' pain and other functional complaints. In line with these limitations, according to our data obtained from this study, we can conclude that plasma reduces complications that may occur after frenectomy and these results may be related to the positive effect of plasma on wound healing. However, more studies are needed to better understanding the mechanism of plasma effect on gingival wounds.

Conflict of interest: The authors declare that they have no conflict of interest.

References

1. Chaubey KK, Arora VK, Thakur R, Narula IS. Perio-esthetic surgery: using LPF with frenectomy for prevention of scar. J Indian Soc Periodontol 2011; 15: 265–269.
2. Neiva TGG, Ferreira DCD, Maia BGF, Blatt M, Nogueira Filho GR, Tunes UR. Frenectomy technique associated with mastigatory mucosa graft: clinical case report. Rev Dental Press Periodontia Implantol 2008; 2: 31–36.
3. Díaz-Pizán ME, Lagravère MO, Villena R. Midline diastema and frenum morphology in the primary dentition. J Dent Child 2006; 26: 11-14.
4. Shetty K, Trajtenberg C, Patel C, Streckfus C. Maxillary frenectomy using a carbon dioxide laser in a pediatric patient: a casereport. Gen Dent 2008; 56: 60–63.
5. Gottsegen R. Frenum position and vestibule depth in relation to gingival health. Oral Surg 1954; 7: 1069-1072.
6. Miller PD Jr. The frenectomy combined with a laterally positioned pedicle graft; functional and aesthetic consideration. J Periodontol 1985; 56: 102-106.
7. Fiorotti RC, Bertolini MM, Nicola JH, Nicola EM. Early lingual frenectomy assisted by CO2 laser helps prevention and treatment of functional alterations caused by ankyloglossia. Int J Orofacial Myology 2004; 30: 64‐ 71.
8. Bullock N Jr. The use of the CO2 laser for lingual frenectomy and excisional biopsy. Compend Contin Educ Dent 1995; 16: 1118-1120.
9. Haytac MC, Ozcelik O. Evaluation of patient perceptions after frenectomy operations: A comparison of carbon dioxide laser and scalpel techniques. J Periodontol 2006; 77: 1815‐ 1819.
10. Laroussi M. Sterilization of contaminated matter with atmospheric pressureplasma. IEEE Transactions on Plasma Science 1996; 24: 1188-1191.
11. Heinlin J, Zimmermann JL, Zeman F, et al. Randomized placebo-controlled human pilot study of cold atmospheric argon plasma on skin graft donor sites. Wound Repair and Regeneration 2013; 21: 800-807.
12. Kleineidam B, Nokhbehsaim M, Deschner J, Wahl G. Effect of cold plasma on periodontal wound healing—an in vitro study. Clinical oral investigations 2019; 23: 1941-1950.
13. Küçük D, Savran L, Ercan UK, et al. Evaluation of efficacy of non-thermal atmospheric pressure plasma in treatment of periodontitis: a randomized controlled clinical trial. Clinical Oral Investigations 2020; 1-13.
14. Arndt S, Schmidt A, Karrer S, von Woedtke T. Comparing two different plasma devices kINPen and Adtec SteriPlas regarding their molecular and cellular effects on wound healing. Clinical Plasma Medicine 2018; 9:24-33.
15. Matthews DC, McCulloch CAG. Evaluating patient perceptions as short-term outcomes of periodontal treatment: A comparison of surgical and non-surgical therapy. J Periodontol 1993; 64: 990-997.

16. Shibata Y, Hosaka M, Kawai H, Miyazaki T. Glow discharge plasma treatment of titanium plates enhances adhesion of osteoblast-like cells to the plates through the integrin-mediated mechanism. International Journal of Oral & Maxillofacial Implants 2002; 17.
17. Koban I, Holtfreter B, Hübner NO, et al. Antimicrobial efficacy of non-thermal plasma in comparison to chlorhexidine against dental biofilms on titanium discs in vitro–proof of principle experiment. Journal of clinical periodontology 2011; 38: 956-965.
18. Chen M, Zhang Y, Driver MS, Caruso AN, Yu Q, Wang Y. Surface modification of several dental substrates by non-thermal, atmospheric plasma brush. Dental Materials 2013; 29: 871-880.
19. Zhou X, Xiong Z, Cao Y, Lu X, Liu D. The antimicrobial activity of an atmospheric-pressure room-temperature plasma in a simulated root-canal model infected with enterococcus faecalis. IEEE Transactions on Plasma Science 2010; 38: 3370-3374.
20. Wang G, Ye G, Yang X, et al. The Efficacy, Safety, Stability, and Mechanism of Tooth Whitening by a Cold Atmospheric Pressure Air Plasma Microjet Assisted With or Without Hydrogen Peroxide. IEEE Transactions on Plasma Science 2014; 42: 1623-1628.
21. Butchibabu K, Koppolu P, Mishra AP, Pandey R, Swapna LA, Uppada UK. Evaluation of patient perceptions after labial frenectomy procedure: A comparison of diode laser and scalpel techniques. Eur J Gen Dent 2014; 3: 129-133.
22. Bıçakcı H, Çapar İD, Genç S, İhtiyar A, Sütçü R. Influence of rotary instrumentation with continuous irrigation on pain and neuropeptide release levels: a randomized clinical trial. Journal of endodontics 2016; 42: 1613-1619.
23. Güzeldemir E. Pain assessment methods. Sendrom 1995; 7: 11-21.
24. Kahnberg KE, Thilander H. Healing of experimental excisional wounds in the rat palate: (I) Histological study of the interphase in wound healing after sharp dissection. International journal of oral surgery 1982; 11: 44-51.
25. Nakajima Y, Mukai K, Rahayu HSE, et al. Cold plasma on full-thickness cutaneous wound accelerates healing through promoting inflammation, reepithelialization and wound contraction. Clinical Plasma Medicine 2014; 2: 28-35.
26. Schmidt-Bleker A, Winter J, Iseni S, Dünnbier M, Weltmann KD, Reuter S. Reactive species output of a plasma jet with a shielding gas device-combination of FTIR absorption spectroscopy and gas phase modelling. J Phys D: Appl Phys 2014; 47: 145201.
27. Bender CP, Hübner NO, Weltmann KD, Scharf C, Kramer A. Tissue tolerable plasma and polihexanide: are synergistic effects possible to promote healing 192 of chronic wounds? In vivo and in vitro results. In: Plasma for Bio-Decontamination, Medicine and Food Security: Springer 2012: 321-334.
28. Dobrynin D, Wu A, Kalghatgi S, et al. Live pig skin tissue and wound toxicity of cold plasma treatment. Plasma Med 2011; 1.
29. Malone-Povolny MJ, Maloney SE, Schoenfisch MH. Nitric oxide therapy for diabetic wound healing. Advanced healthcare materials 2019; 8(12): 180121.
30. Isbary G, Morfill G, Schmidt HU, et al. A first prospective randomized controlled trial to decrease bacterial load using cold atmospheric argon plasma on chronic wounds in patients. British Journal of Dermatology 2010; 163: 78-82.
31. Moreau M, Orange N, Feuilloley MGJ. Non-thermal plasma technologies: new tools for bio-decontamination. Biotechnology advances 2008; 26: 610-617.
32. Liu YCG, Lerner UH, Teng YTA. Cytokine responses against periodontal infection: protective and destructive roles. Periodontol 2000 2010; 52: 163-206.
33. Kalghatgi S, Friedman G, Fridman A, Clyne AM. Endothelial cell proliferation is enhanced by low dose non-thermal plasma through fibroblast growth factor-2 release. Ann Biomed Eng 2010; 38: 748-757.
34. Hirata T, Kishimoto T, Tsutsui C, Kanai T, Mori A. Healing burns using atmospheric pressure plasma irradiation. Japanese Journal of Applied Physics 2014; 53: 010302.
35. Haertel B, Eiden K, Deuter A, Wende K, von Woedtke T, Lindequist U. Differential effect of non-thermal atmospheric-pressure plasma on angiogenesis. Lett. Appl. NanoBioSci 2014; 3: 159-166.
36. Chatraie M, Torkama G, Khani M, Salehi H, Shokri B. In vivo study of non-invasive effects of non-thermal plasma in pressure ulcer treatment. Scientific reports 2018; 8: 1-11.