Journal of Lasers, Optics & Photonics

Domínguez and Velásquez, J Laser Opt Photonics 2015, 2:2
http://dx.doi.org/10.4172/jlop.1000119

Research Article Open Access

Topical Gel Application and Low Level Laser Therapy on Related Soft Tissue Traumatic Aphthous Ulcers: A Randomized Clinical Trial

Ángela Domínguez[1]* and Sergio Andrés Velásquez[2]

[1]Department of Orthodontics, Faculty of Dentistry, Universidad del Valle, Cali 76001000, Colombia
[2]Department of Orthodontics, Institución Universitaria Colegios de Colombia (UNICOC), Cali 76001000, Colombia

Abstract

Objective: To evaluate the effect of low level laser and Fitostimuline gel® application on pain and healing of orthodontic related traumatic aphthous.

Materials and methods: In this double blind and randomized clinical trial, 60 subjects reported traumatic aphthous lesions and the same day they appear immediately they were placed in :G1: (control group) at 13 patients in which only the traumatic factor of the lesion was removed.G2: (Fitostimuline®) 14 patients treated with Fitostimuline® 3 times a day, until the lesion disappeared.G3: (Laser) 14 patients treated with LLLT (Low Level Laser Therapy). G4: (Laser + Fitostimuline®) 15 patients treated with LLLT application and Fitostimuline® 3 times per day, until the lesion healed completely. ANOVA was applied for parametric data, and non-parametric ANOVA (Kruskal-Wallis test - Friedman) and Mann-Whitney U test were made. Past statistical software version 2010 for Excel was used.

Results: Higher diameter aphthous ulcer measures and pain significantly reduced for the Fitostimuline Gel®and Laser treated groups or both combined if compared with the control group. The medicament effect its slow if compared to laser therapy, nonetheless when used simultaneously the effect does not differ from the one obtained by laser only application. Fitostimuline Gel® application does not increase laser effect on healing.

Conclusions: Topical Fitostimuline Gel® and LLLT therapy are highly efficient treatment options for aphthous ulcer and pain generated by orthodontic treatment, when compared to a control group. LLLT therapy, it's more effective than Fitostimuline Gel® for orthodontic related aphthous ulcer treatment. Combining therapies do not improve nor enhance treatment results.

Keywords: Low level laser therapy; Orthodontic appliances; Aphthous; Fitostimuline Gel®

Introduction

Traumatic aphthous ulcers (epithelial laceration that usually exposes nerve ending terminals and result in acute and severe pain) [1], are shown on a high percentage on either children or adults during orthodontic treatment [2,3].

Low level laser therapy (LLLT), it´s an international accepted designation defined as laser treatment, in which the outer energy is applied at a low intensity to produce on the tissues non thermal and bio stimulating effects [4].

LLLT has shown to have an increase in proliferation at the cellular level due to several mechanisms [5-20]. Anti-inflammatory properties are based on its decreasing effect on E2 prostaglandin, factor-alpha tumor necrosis, interleukin-1β, cyclooxygenase- 2mRNA and plasmin activator levels [21]. Analgesic properties are associated with its anti-inflammatory action and neuronal effect [22-24]. Summing all of the above, LLLT offers a potential solution and has been used in aphthous recurring stomatitis [25-28].

Fitoestimuline Gel® it´s an oral cavity application gel, each 100 g contain aqueous Triticum vulgare extract, 15 g, 2 fenoxietanol 1 g and carbopolcarbé Viano and Santiano [29]. searching for its action mechanism Fitostimuline® was applied over fibroblast and lymphocytes mouse cultures, finding an increase on ARNm and DNA synthesis. The authors concluded that this activity is the base for the action mechanism of the substances that are a part of it, achieving the proper stimulation for tissue regeneration.

This study's objective is to evaluate the effect of LLLT and Fitostimuline Gel® application on pain and healing of orthodontic related traumatic aphthous lesions..

Materials and Methods

This is a clinical intervention study design, double blind and randomized clinical trial. The initial sample was 350 suitable patients under orthodontic treatment, starting in August 2013 and finishing in May 2014, at the Universidad del Valle (Cali, Colombia) clinics and in a private practice. From this sample, 60 subjects reported traumatic aphthous lesions and the same day it appear immediately they were placed in 4 groups as follows:

G1: 15 patients in which only the traumatic factor of the lesion was removed.

G2: 15 patients treated with Fitostimuline Gel® 3 times per day, until the lesion disappeared.

G3: 15 patients treated with LLLT.

*G4:*15 patients treated with LLLT and Fitostimuline® 3 times per day, until the lesion healed completely.

***Corresponding author:** Angela Dominguez, Department of Orthodontics, Faculty of Dentistry, Universidad del Valle, Cali 76001000, Colombia, USA, Tel: +57-2-3212100; Fax: +57-2-3169450; E-mail: angela.Dominguezc@gmail.com

Received May 11, 2015; **Accepted** June 25, 2015; **Published** June 27, 2015

Citation: Domínguez Á, Velásquez SA (2015) Topical Gel Application and Low Level Laser Therapy on Related Soft Tissue Traumatic Aphthous Ulcers: A Randomized Clinical Trial. J Laser Opt Photonics 2: 119. doi:10.4172/jlop.1000119

The distribution of the sample can be seen in the flow diagram, according to consolidated standards of reporting trials (CONSORT) (Figure 1). Randomization was made by including patient database in http://www.random.org/lists web page by a different operator from the ones that made the clinical interventions.

Inclusion criteria

- Ages from 18 to 40 years old.
- Traumatic aphthous lesion not bigger than 6 mm in diameter that allowed the placing of a digital caliper in the zone.
- No systemic compromised, epileptic, pacemakers or pregnant patients.
- No medication use during treatment time.

Exclusion criteria

- Completely failed to fill the VAS.
- To missing a follow-up appointment.

Laser irradiation protocol

Within the appointment in which the patient reported the aphthous lesion G3 and G4 were irradiated with Photon Lase III (AS-GA-Ir) (DMC equipments; Sao Carlos, Brazil) therapeutic laser, with a wavelength of 660 nm, 25 J/cm^2, 100 mW, during 14 seconds. Irradiation was made by one operator, applying laser by scanning the lesion 1 mm away two times each of seven seconds. Only one laser application per aphthous lesion was made.

G1 and G2 received a placebo application with the laser tip inactive, this in order to create a placebo effect aplication to prevent false effects and mainly to keep the registration process in the visual analog scale as true as possible.

Fitostimuline® aapplication

Fitostimuline Gel® was applied from the moment the lesion appeared using a Q tip 3 times a day until the lesion completely healed. The first application was made by an operator who clearly explains the process to the patients, and all the following applications were made by the trained patient. Only G2 and G4 receive topical medication.

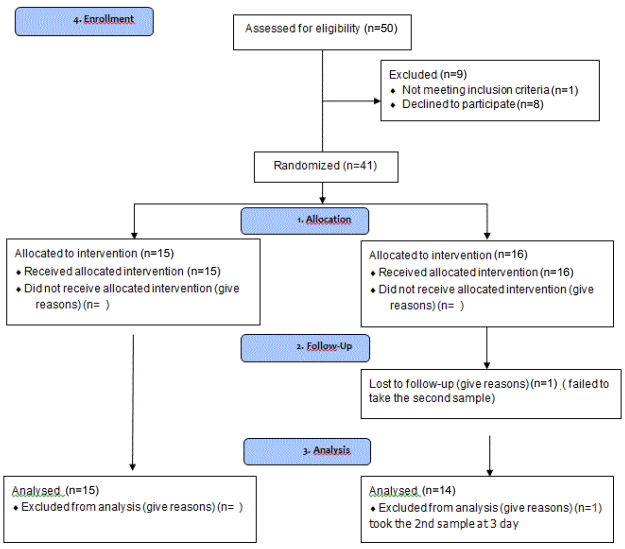

Figure 1: CONSORT flow diagram–traumatic aphthous ulcers.

Registration

Aphthous ulcers diameter measure (AUDM): It was taken from the day it appeared (T0) with a digital caliper Baker® SND-10 (maximum margin of mistake of 0.005 mm) Perpendicular to the widest point of lesion diameter and until the day before of its total healing by a blind operator.

Visual analog scale (VAS): It was explained to all patients how to properly register their pain perception in a 100 mm visual analog scale. Beginning the day that the lesion appeared (T0) consecutively at the same time, every day until the lesion completely disappeared. The distance from 0 to the patients mark was measured with a digital caliper Baker SND-10® by a blind operator. Registration was done in every patient, even when they reported 0 on VAS.

Aphthous lesion healing (ALH): The day that the lesion completely healed was registered on the chart, from the lesion intervention day (T1), until a maximum of 10 days (T11).

Ethical considerations

This is completely approved and cover by Resolution 8430 from 1993. In this legal setting this project was reviewed by the human ethical committee of the department of health of Universidad del Valle (Cali, Colombia). The research was classified as risk higher than minimum and approved by act number 015-013 of 2013.

Statistical analysis

After a proper registration of Aphthous ulcers diameter measure (AUDM) in mm, visual analog scale (VAS) in mm and Aphthous lesion healing (ALH) in days, ANOVA and U Mann-Whitney test were used for parametric data: (AUDM) and (ALH).

For the parametric data analysis the confidence interval was obtained using a 95% as the distribution, when there were a lot of zeros the data didn't fall under a Gaussian distribution.

For the pain data obtained from VAS analysis, non-parametric ANOVA (Kruskal-Wallis test) and Mann-Whitney U test were made. To evaluate group and time differences a non-parametric two way ANOVA (Friedman) test was used, and for even comparisons between groups a U Mann-Whitney test.

A significance level of P=0.05 was used for all the tests. In multiple comparing this value was modified according to Bonferroni as significant p value of $p<0.01$. Past statistical software version 2010 for Excel was used for the entire statistical analysis.

Results

Initial values

56 subjects compose the analyzed sample. 13 belonged to G1, 14 to G2, 14 to G3 and 15 to G4. The demographic characterization showed a homogenous sample according to age and gender as shown on (Table 1). Initial aphthous ulcer diameters (T0) showed a homogeneous and low variance among the groups G1: 4.23 ± 0.61, G2: 4.41 ± 0.65, G3:4.36 ± 0.82 and G4: 4.27 ± 0.63. After completing the Kruskal-Wallis ANOVA test, the initial value of pain (VAS median) among the 4 groups did not show a statistically significant value $p>0.05$.

Group	n	Man	Women	Age (years)	Age range
G1	13	5	8	26 ± 6	18 a 37
G2	14	7	7	25 ± 63	18 a 37
G3	14	7	7	26.7 ± 53	18 a 38
G4	15	6	9	26.3 ± 6	18 a 38

Table 1: Demographic sample description.

Times	G1	G2	G3	G4
T0 (before)	4.23 ± 0.61	4.41 ± 0.65	4.36 ± 0.82	4.27 ± 0.63
T1 (after)	4.23 ± 0.61	4.41 ± 0.65	4.36 ± 0.84	3.97 ± 0.63
T2 (day 1)	4.37 ± 0.63	3.47 ± 0.68	2 ± 1.22	0.52 ± 0.7
T3 (day 2)	4.32 ± 0.73	3 ± 1	0.83 ± 0.74	0.24 ± 0.44
T4 (day 3)	4 ± 0.66	1.84 ± 0.6	0.06 ± 0.24	0.036 ± 0.14
T5 (day 4)	3.56 ± 0.6	0.85 ± 0.73	0	0
T6 (day 5)	2.95 ± 0.78	0.25 ± 0.57	0	0
T7 (day 6)	2.14 ± 0.91	0.08 ± 0.3	0	0
T8 (day 7)	1.45 ± 1.1	0	0	0
T9 (day 8)	0.66 ± 0.9	0	0	0
T10 (day 9)	0.23 ± 0.56	0	0	0
T11 (day 10)	0	0	0	0

Table 2: AUDM (mm) (X ± S) by groups and days of the aphthous ulcers.

Times	G1	G2	G3	G4
T0 (before)	3.8-4.6	4-4.77	3.9-4.8	3.9-4.6
T1 (immediately)	3.8-4.6	4-4.77	3.9-4.8	3.6-4.3
T2 (day 1)	4-4.7	3.1-3.85	1.32-2.68	0.14-0.9
T3 (day 2)	3.9-4.8	2.44-3.56	0.4-1.2	0.02-0.5
T4 (day 3)	3.6-4.4	1.5-2.17	0-0.2	0-0. 11
T5 (day 4)	3.2-3.9	0.44-1.26	0	0
T6 (day 5)	2.5-3.4	0-0.57	0	0
T7 (day 6)	1.6-2.6	0-0.18	0	0
T8 (day 7)	0.8-2.1	0	0	0
T9 (day 8)	0.14-1.2	0	0	0
T10 (day 9)	0-0.55	0	0	0
T11 (day 10)	0	0	0	0

Table 3: Estimated confidence intervals of 95% .

Aphthous ulcers diameter measure (AUDM) VS time

To evaluate the treatment effect after a period of time and its evolution in G1, averages, measures in mm with standard deviations were used for every group from T0 to T11. (Before treatment, immediately after therapy, and from day 1 to day 10). The results are shown in (Table 2). 95 % Confidence intervals were set for all the groups from T0 to T11 (Table 3).

To represent the superior limit of the interval (to show the worst case scenario, 95% confidence) (Figure 2), is clearly shown that in every case the aphthous ulcer diameter reduced in size with time, but the G1 the process was much slower taking up to 10 days to heal. Combined treatment using LLLT and Fitostimuline Gel® produced a 1mm diameter reduction on day 1.

LLLT only reduces aphthous ulcer diameter faster than Fitostimuline Gel® on its own. Laser treatment reaches a 0 value on day 3 and Fitostimuline Gel® until day 6. Combining the two therapies did not potentiate the therapeutic effect, but works better than Fitostimuline Gel® on its own.

Comparing diameter changes thru time with a paired t test shows non-significant differences only for G1 in between T0 and T3. For groups G2 and G3 the differences are statically significant among all the times registered (p<0.0001) as for G4 but con p<0.00001.

VAS vs time

The VAS median calculation on mm is shown in Table 4. Of 29 subjects in the LLL therapy group, 25 (86.2%) reported 0 pains immediately after treatment, 13.8% soft pink (between 1and 2 VAS) and a 100% reported 0 pain after 2 days. As the diameter, pain diminished when comparing T1 with T10. The control group took 7 days to completely resolve pain. G2 resolve on day 4, and in G3 and G4 it took 2 days. (There was no difference between G3 and G4). Friedman´s Two way non parametric ANOVA showed differences among groups and times, which led to U de Mann-Whitney test for paired groups.

In G1, pain resolution began on day 3 (T4) p=0.0002, from T5 con p<0.0001. Other groups showed a significant pain reduction from day 1 (T2). For G2 p<0.001, comparing G3 and G4 using all the times, the differences were statically significant up<0.00001.

Aphthous lesion healing (ALH)

G1 showed a time range between 8 to 10 days for lesion resolution. G2 from 4 to 7days, G3 from 2 to 5 days and G4 from 1 to 3 days. Standard deviations and medians are shown in Table 5.

U Mann-Whitney test showed significant differences when comparing G1 with all the groups, as between G2 with G3 and G4 (p<0.01).

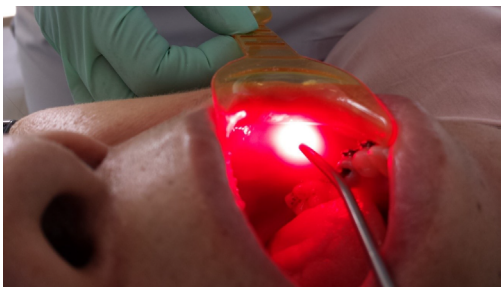

Figure 2: Laser irradiation with AsGaAl.

Times	G1	G2	G3	G4
T0 (before)	6.6	7	7.45	7
T1 (immediately)		6.91	0	0
T2 (day 1)	6.3	6	1.1	1.2
T3 (day 2)	6	3.8	0	0
T4 (day 3)	5.4	1	0	0
T5 (day 4)	3.57	0	0	0
T6 (day 5)	2.5	0	0	0
T7 (day 6)	2	0	0	0
T8 (day 7)	0	0	0	0
T9 (day 8)	0	0	0	0
T10 (day 9)	0	0	0	0
T11 (day 10)	0	0	0	0
*VAS: Visual Analog Scale mm				

Table 4: VAS Median by groups and days.

Group	Median	Range	x ± S
G1	8	7 a 10	8.46 ± 5.34
G2	5	4 a 7	5.28 ± 5.57
G3	3	2 a 5	3.21 ± 7
G4	2	1 a 3	2.93 ± 7

Table 5: Days until total healing of the lesion.

The only group comparisons, that showed no healing time related significant difference, was G3 vs G4 ($p>0.05$). As the two variables ANOVA test showed significant differences for groups and times (from 0 to 5 days included in the ANOVA) and the significant interaction, the Bonferroni´s t test for comparing multiple averages was used. Time median for ALH: G1 was 8 days. G2 5 days, 3 days for G3 and 2 days for G4 ,even though there was no significant difference between the last 2 groups.

Discussion

The objective of this study was to evaluate LLLT and the medication Fitoestimuline Gel® effect on pain control and healing effect over traumatic aphthous ulcers caused by orthodontic treatment.

The parameters that allowed evaluating the evolution of the 4 groups were: lesion diameter, pain registration on VAS and total number of days necessary for complete healing. This parameters were reproducible and recently used by Anand et al. [1] in 2013 to evaluate the effectiveness of 940 nm diode laser application in two patients with recurrent aphthous stomatitis, showing satisfactory and acute results on lesion healing.

The results showed that AUDM and pain significantly reduced for the Fitostimuline Gel® and Laser treated groups or both combined if compared with the control group. The medicament effect its slow if compared to LLLT, nonetheless when used simultaneously the effect does not differ from the one obtained by LLLT only. Fitostimuline Gel® application does not increase laser effect on healing.

This is also relevant when comparing the time needed to achieve total healing of the aphthous ulcer. A lesion without therapeutic treatment has an average healing time from 8 to 10 days, for G2 from 4 to 7 days, G3 from 2 to 5 days, and G4 from 1 to 3 days.

The data obtained in this study showed astonishing results analyzed with confidence intervals up to 95% allowing a great therapy evolution and clinical application for the 2 treatment alternatives.

It's important to outline that pain for the patients of the 2 laser treated groups disappeared immediately in 25 out of 29 patients and for the 100 % in 2 days. This compared to the 7 days that took on the control group is statistically significant and clinically relevant if pain is consider a priority on the clinical practice, and according to Kvam et al. [2] report were the aphthous ulcers for a high percentage of patients are considered the most uncomfortable part of treatment for the pain that they generate.

LLLT has been proven to be effective in recurrent aphthous stomatitis treatment [30-33], there are not any reports of orthodontic treatment related aphthous ulcers in terms of analgesia, prevention, and fast healing promotion.

It's important to clarify that not all lasers have the same healing parameters for aphthous ulcers. The main limitation of this study is the employment of only one laser equipment (DMC) (Figure 2) which allows a great evolution towards healing, but not an immediate healing response without pain as can be obtained by using recently appeared equipment.

Then it is suggested, to experiment in new randomized clinical trials that allows to compare different action mechanism for a diode laser, CO_2 and latest technology equipment.

Conclusions

- Topical Fitostimuline Gel® application and LLLT therapy are highly efficient treatment options for aphthous ulcer and pain generated by orthodontic treatment, when compared to a control group.

- LLL therapy, it's more effective than Fitostimuline Gel® for orthodontic related aphthous ulcer treatment. - Combining therapies do not improve nor enhance treatment results.

References

1. Anand V, Gulati M, Govila V, Anand B (2013) Low level Laser therapy in the treatment of aphthous ulcer. Indian J Dent Res 24: 267-70.
2. Kvam E, Gjerdet NR, Bondevik O (1987) Traumatic ulcers and pain during orthodontic treatment. Community Dent Oral Epidemiol 15: 104-700.
3. Kvam E, Bondevik O, Gjerdet NR (1989) Traumatic ulcers and pain in adults during orthodontic treatment. Community Dent Oral Epidemiol 17: 154-157.
4. Lim H, Lew K, Tay D (1995) A clinical investigation of the efficacy of low level Laser therapy in reducing orthodontic post adjustment pain. American Journal of Orthodontics and Dentofacial Orthopedics 108: 614-22.
5. Sroka R, Schaffer M, Fuchs C, Pongratz T, Schrader-Reichard U, et al. (1999) Effects on the mitosis of normal and tumor cells induced by light treatment of different wavelengths. Lasers Surg Med 25: 263-71.
6. Zhang J, Xing D, GAO X (2008) Low-power Laser irradiation activates Src tyrosine kinase through reactive oxygen species-mediated signaling pathway. J Cell Physiol 217: 518-28.
7. Miyata H, Genma T, Ohshima M, Yamaguchi Y, Hayashi M, et al. (2006) Mitogen-activated protein kinase/extracellular signal-regulated protein kinase activation of cultured human dental pulp cells by low-power gallium-aluminium-arsenic Laser irradiation. Int Endod J 39: 238-44.
8. Gao X, Chen T, Xing D, Wang F, Pei Y, et al. (2006) Single cell analysis of PKC activation during proliferation and apoptosis induced by Laser irradiation. J Cell Physiol 206: 441-8.
9. Kujawa J, Zavodnik L, Zavodnik I, Buko V, Lapshyna A, et al. (2004) The effect of low-intensity (3.75-25 J/cm^2) near infrared (810 NM) Laser radiation on red blood cell ATPase activities and membrane structure. J Clin Láser Med Surg 22: 111-7.
10. Kujawa J, Zavodnik L, Zavodnik I, Bryszewska M (2003) Low intensity near-infrared Láser radiation-induced changes of acetylcholinesterase activity of human erythrocytes. J Clin Laser MED Surg 21: 351-5.
11. Kujawa J, Zavodnik IB, Lapshina A, Labieniec M, Bryszewska M (2004) Cell survival, DNA, and protein damage in B14 cells under low-intensity near-infrared (810 nm) Laser irradiation. Photomed Láser Surg 22: 504-8.
12. Lirani-Galvão AP, Jorgetti V, Silva OL (2006) Comparative study of low-level Laser therapy and low-intensity pulsed ultrasound effect on bone in rats. Photomed Láser Surg 24: 735-740.
13. Coluzzi DJ (2000) An overview of Laser wavelengths used in Dentistry. Dent Clin N Am 44: 753–765.
14. Demir H, Yaray S, Kirnap M, Yaray K (2004) Comparison of the effects of Laser and ultrasound treatments on experimental wound healing in rats. J Rehabil Res Dev 41: 721-728.
15. Koichiro K, Shimizu N (2000) The effect of low-energy Laser irradiation on bone remodeling during experimental tooth movement in rats. Laser Surg Med 26: 282-291.
16. Ueda Y, Shimizu N (2003) Effects of pulse frequency of low-level Laser therapy (LLLT) on bone nodule formation in rat calvarial cells. J Clin Láser Med Surg 21: 271-277.
17. Almeida-Lopes L, Rigau J, Zângaro RA, Guidugli-Neto J, Jaeger MM (2001) Comparison of the low level Laser therapy effects on cultured human gingival fibroblasts proliferation using different irradiance and same fluence. Lásers Surg Med 29: 179-84.
18. Pereira AN, Eduardo Cde P, Matson E, Marques MM (2002) Effect of low-power Laser irradiation on cell growth and procollagen synthesis of cultured fibroblasts. Lasers Surg Med 31: 263-267.
19. Kreisler M, Christoffers AB, Willershausen B, d'Hoedt B (2003) Effect of low-level GaAlAs Laser irradiation on the proliferation of human periodontal ligament fibroblasts: an in vitro study. J Clin Peridontol 30: 353-358.

20. Choi EJ, Yim JY, Koo KT, Seol YJ, Lee YM, et al. (2010) Biological effects of a semiconductor diode Laser on human periodontal ligament fibroblasts. J Periodontal Implant Sci 40: 105-10.

21. Saygun I, Karacay S, Serdar M, Ural AU (2008) 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. Lásers Med Sci 23: 211-215.

22. Chung H, Dai T, Sharma SK, Huang YY, Carroll JD, Hamblin MR (2012) The nuts and bolts of low-level Láser (light) therapy.Ann Biomed Eng 40: 516-533.

23. Dederich DN (1991) Laser/tissue interaction. Alpha Omega 84: 33-36.

24. Hashmi JT, Huang YY, Sharma SK, Kurup DB, De Taboada L (2010) Effect of pulsing in low-level light therapy. Lásers Surg Med 42: 450-466.

25. Sarver DM, Yanosky M (2005) Principles of cosmetic dentistry in orthodontics: Part 3. Láser treatments for tooth eruption and soft tissue problems. Am J Orthod Dentofacial Orthop 127: 262-264.

26. De Souza TO, Martins MA, Bussadori SK, Fernandes KP, Tanji EY, et al. (2010) Clinical evaluation of low-level Laser treatment for recurring aphthous stomatitis. Photomed Láser Surg 28: S85-8.

27. Misra N, Maiti D, Misra P, Singh AK (2013) 940 nm diode Laser therapy in management of recurrent apthous ulcer. BMJ Case Rep.

28. Tezel A, Kara C, Balkaya V, Orbak R (2009) An evaluation of different treatments for recurrent aphthous stomatitis and patient perceptions: Nd: YAG Láserversus medication. Photomed Láser Surg 27: 101-6.

29. Viano I, Santiano M (1978) Study of the mechanism of action of phytostimulines. Batteriol Virol Immunol 71: 176-180.

30. Albrektson M, Hedström L, Bergh H (2014) Recurrent aphthous stomatitis and pain management with low-level Láser therapy: a randomized controlled trial. Oral Surg Oral Med Oral Pathol Oral Radiol 117: 590-4.

31. Prasad RS, Pai A (2013) Assessment of immediate pain relief with Laser treatment in recurrent aphthous stomatitis. Oral Surg Oral Med Oral Pathol Oral Radiol 116: 189-193.

32. Zand N, Fateh M, Ataie-Fashtami L, Djavid GE, Fatemi SM (2012) Promoting wound healing in minor recurrent aphthous stomatitis by non-thermal, non-ablative CO (2) Laser therapy: a pilot study. Photomed Láser Surg 30: 719-23.

33. Aggarwal H, Singh MP, Nahar P, Mathur H, Gv S (2014) Efficacy of low-level Laser therapy in treatment of recurrent aphthous ulcers - a sham controlled, split mouth follow up study. J Clin Diagn Res 8: 218-21.

Citation: Domínguez Á, Velásquez SA (2015) Topical Gel Application and Low Level Laser Therapy on Related Soft Tissue Traumatic Aphthous Ulcers: A Randomized Clinical Trial. J Laser Opt Photonics 2: 119. doi:10.4172/jlop.1000119