

A Randomized Clinical Trial Comparing the Effects of Diode Laser and Diode Laser along with Topical Application of Glutathione as an Adjunct in the Management of Gingival Hyperpigmentation

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Abstract

Background: Pigmentation of the gingiva is a negative factor in an otherwise acceptable “smile window”. Recently, cryosurgery and laser techniques have gained popularity for depigmentation and seem to be the most reliable and satisfactory procedures. To our knowledge, this study is unique and is the first reporting comparison of diode laser and lasers along with topical application of glutathione in the literature.

Materials and Methods: This randomized controlled clinical trial included 24 patients who presented with a chief complaint of “black gums” and requested aesthetic therapy. They were randomly divided into group I and II based on split mouth design. Patients in group I and II were treated using a diode laser, with beam set at 1.30 W power, 200 J energy, in continuous mode. Patients in Group II were treated with 0.5% glutathione gel as an adjunct. Patients were followed for 1, 3 and 9 months. Standardized digital images were taken and pigmentation area and pigmentation index was measured at 0, 1, 3 and 9 months by using image analysis software.

Results: Statistical analysis of the data revealed a significant difference between pre and post-operative measurements of pigmented area, gingival pigmentation index and time ($p < 0.05$).

Conclusion: From the present study, during the 9-month follow-up, the depigmentation achieved using both the techniques were effective. Glutathione as an adjunct too had a role in delaying the repigmentation.

Keywords: Cryosurgery; Esthetics; Hyperpigmentation; Lasers

Introduction

Esthetics has become an important facet of dentistry, and clinicians have to face the challenge of achieving acceptable gingival esthetics, along with addressing biological and functional problems. The color of the gingiva plays an important role in overall esthetics. As seen clinically, it varies from person to person, in different areas of the mouth and appears to be consistent with the color of the skin [1]. High levels of oral melanin pigmentation are usually observed in individuals of African, East-Asian or Hispanic ethnicity [2].

An assortment of Depigmentation techniques have been employed in the management of hyperpigmentation with almost parallel results. Selection of the technique should be based on clinical experiences and individual preferences. One of the first and still popular techniques to be employed is the surgical removal of undesirable pigmentation using scalpels [3]. Moreover, laser ablation has been rec-

ognized as one of the most effective, comfortable and consistent techniques. Different lasers have been used for gingival depigmentation including carbon dioxide, diode, Nd: YAG, Er: YAG and Er, Cr: YSGG lasers with diverse success. The diode laser which has been introduced in dentistry few years back is a solid-state semiconductor laser that uses a combination of Gallium (Ga), Arsenide (Ar) to change electrical energy into light energy, has been employed in this study [4].

These agents are useful, but the recurrence of pigmentation is observed as early as 3months to 9 months in various studies [1]. To overcome this limitation, a fascinating agent, glutathione was used. It is a cysteine-glycine-glutamate tri-peptide, which exerts several effects on melanogenesis through different mechanisms involving the functions and cellular transport of tyrosinase. It is renowned that when glutathione or cysteine is added to melanocytes or melanoma cell lines, the melanogenetic pathway is shifted from eumelanin towards pheomelanin formation [5]. As per periodontal literature, no study on glutathione as an adjunct in the management of gingival hyperpigmentation was found till date. With this background, in the present study a comparison was done to evaluate the effectiveness diode laser and diode laser along with glutathione as an adjunct in the treatment of gingival hyperpigmentation.

Materials and Methods

Study Population

In this 9 month randomized controlled clinical trial, a total of 24 systemically healthy patients of age 18-40 years were selected from the outpatient Department of Periodontics, Kamineni Institute of Dental Sciences, Narketpally, Nalgonda (Dist), India. The study was conducted from April 2014 to August 2015. The research protocol was submitted to the Institutional Ethical Committee and Review Board of the NTR University of health sciences, Vijayawada, AP, India. After ethical approval, all patients provided written informed consent.

Selection criteria

- **Inclusion criteria** 1) Systemically healthy people with moderate to severe pigmentation based on Dummetts classification (1964) [6] 2) Patients of 18 - 40 years age group.
- **Exclusion Criteria** 1) Pregnant and lactating mothers 2) Acute Periodontitis patients 3) Family history of skin cancer.

Patient grouping

A randomized, split mouth controlled clinical trial was designed to compare the effectiveness of diode laser and diode laser along with topical application of glutathione as an adjunct in the treatment of gingival melanin hyperpigmentation. A total of 30 patients were screened, of which twenty four patients of age between 18 - 40 years were enrolled in the study and the 2 treatment protocols are allocated to each of the two quadrants randomly by coin toss method (Figure 1). These maxillary and mandibular segments again randomized into right and left segments to which glutathione gel is applied only on one side. The treatment groups were 1)Group I-Laser (L) 2)Group II- Laser + Glutathione (L+G) (Figure 2).

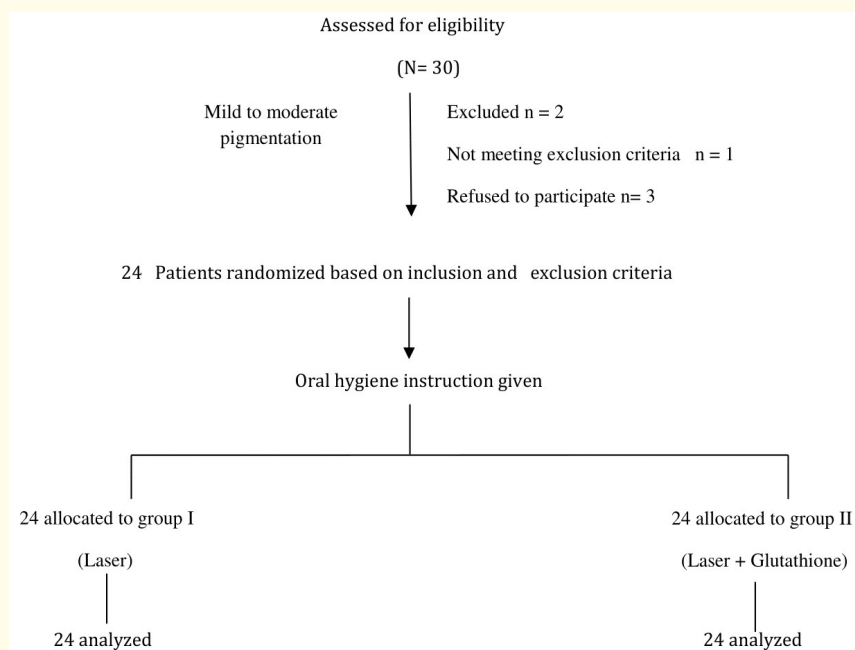


Figure 1: Flow Chart.

Clinical Evaluation

The following clinical parameters were recorded at baseline, one month, three months and nine months 1) Gingival pigmentation index (Dummett C.O, 1964) [6] 2) Area of pigmentation.

Image acquisition and analysis

Standard digital photographs were taken at baseline, 1, 3 and 9, months post-operatively with digital camera†, with 16 mega pixel, 1920 × 1080 resolution, shutter speed set at 30 seconds. For each photograph, the patient sat on a unique vertically positioned dental seat with the head positioned upright in a natural head position and the lips and cheeks opened using a cheek retractor. A standardized distance and angulation of the camera in relation to the participants was maintained at every appointment. The standardized images were entered in image analysis software‡ and pigmentation areas were traced manually from the mid-cervical region of the right canine to the left canine and the gridlines were superimposed on image and area of pigmentation was measured.

Preparation of glutathione gel

Glutathione gel was prepared by the Department of Pharmacology, Nalanda college of Pharmacy, Nalgonda. 5ml glass vials with proper air tight polypropylene caps were taken. Appropriate amounts of glutathione powder and solvent (distilled water) (50: 100) i.e. 50 mg glutathione water and 100ml of solvent were taken into glass vials. The contents were mixed. After initial mixing of the contents, Carbapol (a gelling agent) was added and set aside for one hour. After that contents were stirred (with stirrer) for 30 min to obtain glutathione gel and tri-ethanolamine was added to adjust the pH [5-7]. By this 0.5% concentration of glutathione gel was prepared.

Surgical Procedure

Diode Laser

Before operating the diode laser, the operating staff and the patients wore special laser-protective glasses. Highly reflective instruments or instruments with mirrored surfaces were avoided. The laser was used at 1.3 W power, 200J, in continuous mode. Local infiltration was used to minimize the patient discomfort. Laser ablation was started from the mucogingival junction working toward the free gingival margin, including the papilla. The motion of the ablation was circular with overlapping circles. Complete procedure from the time of initiation of laser complete removal of pigmented area from canine to canine was recorded in minutes by stop watch (Figure 2).

Glutathione application

A thin layer of 0.5% glutathione gel was applied using a steel spatula, which formed film over the deepithelized area, which ranged from (2-4 gms), after which periodontal dressing was covered (Figure 2).



Figure 2: Surgical procedure. A) Pre- Operative B) Immediate post-operative with laser C) Glutathione gel application.

Post-operative instructions

For both groups, reinforcement of precautionary postoperative instructions, such as avoiding smoking and eating hot and spicy food for the first 24 hours, were given. Patients were prescribed analgesics as needed, if they experienced any pain.

Follow-Up

All patients were recalled after 1, 3, and 9 months for postoperative observation. Standard digital photo images were obtained pre operatively, 1, 3 and 9 months.

Statistical Analyses: A statistical software programme^s was used for data analysis. The results were averaged for each parameter at baseline, 1, 3 and 9 months. The significance of intergroup differences was assed using Analysis of variance (ANOVA) test, Kruskal wallis test and t- test.

Results

The intergroup comparison of area of pigmentation as revealed by one way ANOVA between four groups showed statistical significance at baseline, one month and three months ($p = 0.0004$, $p = 0.0002$, $p = 0.0001$) respectively (Figure 3). The inter group comparison of gingival pigmentation index as revealed by Kruskal Wallis test showed no statistical significance in mean gingival pigmentation index score for all groups at all time intervals (Figure 4 and 5).

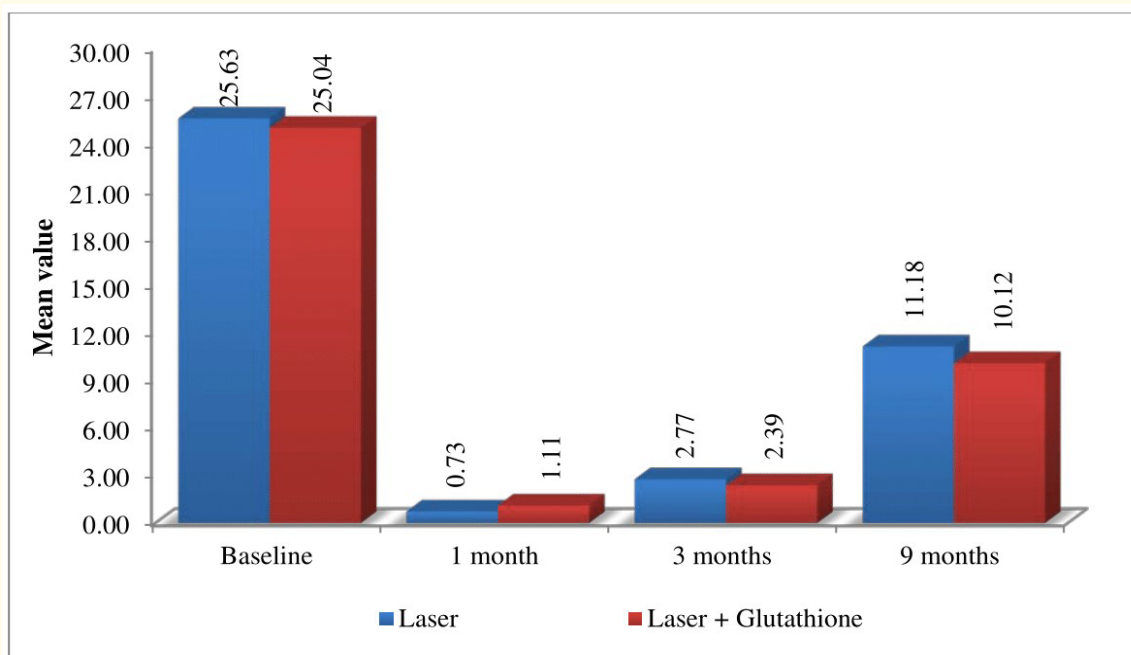


Figure 3: Comparison of four groups with respect to area of pigmentation in 50Pixels/mm at different time points.

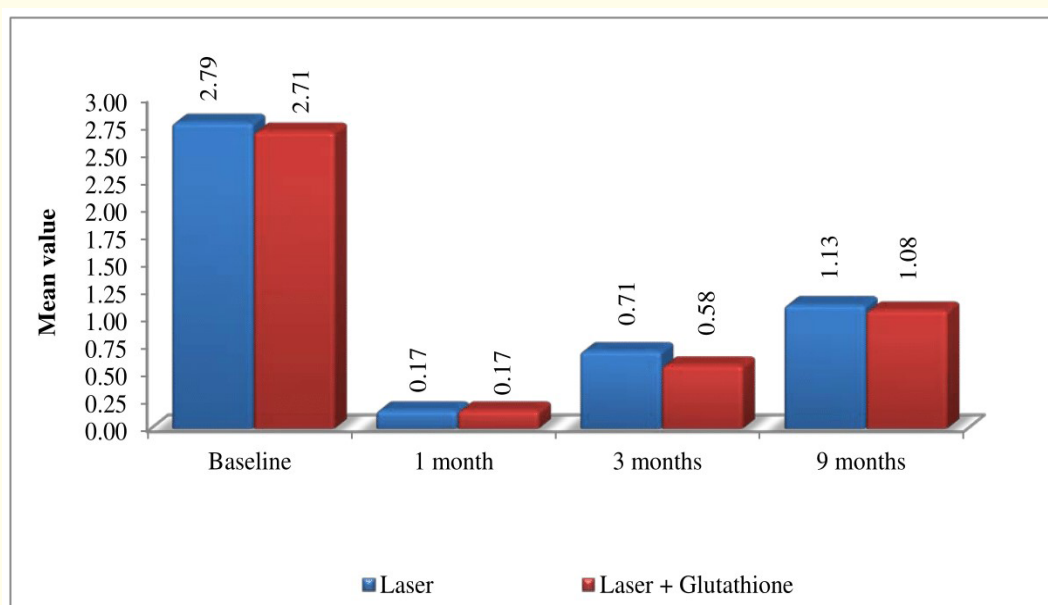


Figure 4: Comparison of two groups with respect to gingival pigmentation index (GP) scores at different time points.

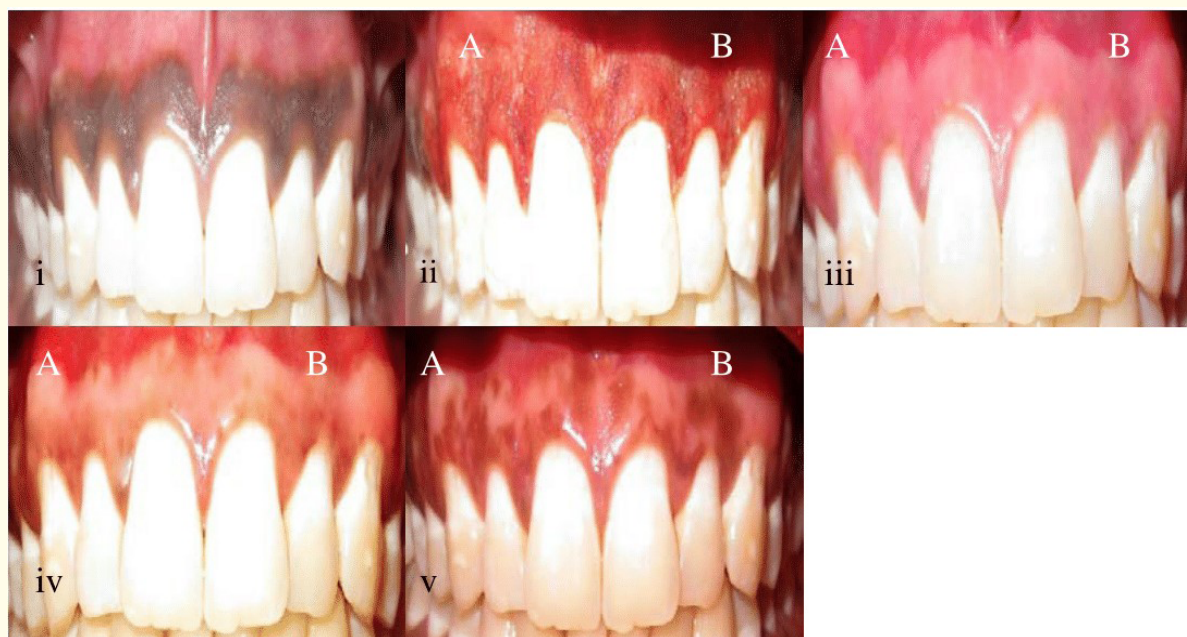


Figure 5: i) Pre-operative, ii) Immediate post-operative A- Laser treated, B- Laser with glutathione. iii) One Month Post-operative, iv) Three months Post-operative v) Nine months post -operative.

Discussion

Gingival hyperpigmentation is seen as an inherited peculiarity in some populations, and is more aptly termed physiologic or racial gingival pigmentation [6]. Distribution of melanin pigmentation is quite unique in South Indian population who has darker skin color owing to more melanin content, and tends to have more oral pigmentation than their counterparts in North and Northeast India [7,8]. The study conducted by Ponnaiyan, *et al.* [8] showed that majority of south Indian population had pigmentation in the attached gingiva and interdental papilla (25.4%) and least in the marginal gingiva (10.2%). This finding is in contrast to a Jewish population study, in which the authors found that attached gingiva is only the most common pigmented anatomic division [9].

A variety of treatment modalities have been employed for esthetic correction of gingival pigmentation which can be achieved either by removal of the pigmented layer or by masking of the pigmented gingiva. Removal of the pigmented layer has been tried in the form of scalpel surgical technique [10], bur abrasion [11], cryosurgery [12], electrosurgery [13], lasers [14] and chemical treatment [15] (90% phenol, 95% alcohol). Masking the pigmented gingiva can be achieved by free gingival grafts (FGGs) or acellular dermal matrix allografts. Each of the treatment modalities has their own advantages and limitations. Lasers have become widely used in medicine and surgery since the development of the Ruby laser by Maiman in 1960. The diode lasers used in dentistry have wavelength spectrum ranging from 800 to 980 nm, which allows high levels to be absorbed by soft tissue, water, and chromophores, such as melanin and oxyhemoglobin and considered ideal for depigmentation procedure.

In the present study, glutathione gel was used as a depigmentation agent, which inhibit tyrosinase pathway and inhibit the formation of melanin.

The results observed with diode laser in the present study was similar to other studies conducted by Doshi, *et al.* [16,17], Udatta and Khan [18], Upasana, *et al.* [19], which showed that diode laser is minimally invasive treatment option for elimination of unaesthetic gingival melanin pigmentation even though repigmentation is the frequent dilemma with this technique.

In the present study, topical application of glutathione is used as an adjunct for additional advantage. Glutathione is a ubiquitous compound found in our bodies. Aside from its many ascribed biologic functions, it has also been implicated in skin lightening. On analyzing the results, the mean reductions in area of pigmentation in Group I (L) and II (L+G), were found to be statistically significant at one month 3 months and 9 months. The reduction achieved in group L+G was higher than that in L at all time intervals.

On analyzing the results, the mean reductions in the gingival pigmentation index in Group I (L) and II (L+G), found to be statistically significant at, one month, 3 months and 9 months. The reduction achieved in Group L+G higher than that in Group L at all time intervals. In the present study the techniques used for gingival depigmentation along with glutathione results in repigmentation at the end of 9 months. In all the two groups repigmentation is seen after three months which in accordance with other studies done earlier. But the continuation of the study, which was done by Tal., *et al.* [12] reported two cases with limited areas of repigmentation without any cosmetic significance after 3 years of the treatment. In present study repigmentation starts after 3 months in 25% of cases and increased in intensity by the end of 9 months in 75% of the sample.

The repigmentation is described as spontaneous. The mechanism of repigmentation is not understood; but according to the migration theory, active melanocytes from the adjacent pigmented tissues migrate to the treated areas, causing repigmentation. The repigmentation appeared in different areas in different individuals at varying times during the observation period [1]. In this study, the pigmentation started to reappear after 3 months and during the 9 months follow-up period which is patchy in distribution. The patchy pigmentation could be a result of the ongoing process of repigmentation. The decreased intensity of pigmentation may be due to less production of pigments. The intensity may increase with time and may reach to pretreatment level as it depends on the racial background of the patient. Kon., *et al.* [20], study was consistent with our findings, who demonstrated that permanent results cannot be offered when gingival depigmentation procedures are performed for cosmetic reasons.

Conclusion

From the present study, during the 9-month follow-up, the depigmentation achieved using both the techniques were effective. Glutathione as an adjunct too had a role in delaying the repigmentation.

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