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## REVIEW ARTICLE

## JOURNEY FROM BLACK TO PINK GUMS: MANAGEMENT OF MELANIN INDUCED PHYSIOLOGICAL GINGIVAL HYPER PIGMENTATION

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Smile is an expression of happiness, self-confidence, kindness and beauty. Along with teeth and lips, gingiva is also a vital component of smile. Melanin induced gingival hyper pigmentation may appear un-aesthetic especially when it is associated with high smile line, upper anterior labial segment and is uneven in appearance. It affects individuals from all races. Generally, it is believed that melanin induced gingival hyper pigmentation is confined to individuals from dark races. But studies have shown that Iranian, Indian, Italian, Arabian, Greek, German, French, Japanese, Chinese, Jewish, Thai, Malaysian and other ethnic groups also display clinical gingival pigmentation.<sup>1</sup> Gingival hyper pigmentation may result in psychological distress especially when the appearance is of utmost importance for the individuals. This article aims to focus on the physiology, clinical appearance and treatment options available for the melanin induced gingival hyper pigmentation along with the reported recurrence in the light of current literature.

**Keywords:** Gingival Hyperpigmentation; Physiological pigmentation; Gums; Black gums

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### INTRODUCTION

#### Physiology of melanin induced hyper pigmentation

Physiological hyper pigmentation is caused by melanin. Melanin granule is a non-haemoglobin derived pigment which is round in shape with approximate size of 0.3 micron and molecular weight of 20,000.<sup>2</sup> It is composed of 57% carbon, 9% nitrogen, 3.5% hydrogen, 30% oxygen and varying amounts of sulfur.<sup>3</sup>

Melanin is produced by melanocytes which are neuroectodermal in origin, from tyrosine through the action of tyrosinase and is stored in the vesicles “melanosomes”. Melanocytes resides in the basal and spinous layers of the epidermis and epithelium, leptomeninges of the central nervous system, uveal tract and in the retina of the eye.<sup>1</sup> Attached gingiva is the most commonly effected intraoral site. Melanin granules are phagocytosed and contained within other cells of the epithelium and connective tissue, called melanophages or melanophores.<sup>4,5</sup>

Melanin plays a vital role in the skin protection from the damaging effects of ultraviolet radiations. It dissipates about 99.9% of absorbed ultraviolet radiations, thus protecting the skin from ultraviolet B radiation damage and reducing the risk of skin cancer.<sup>6</sup> Inside the oral cavity, melanin may have a positive role in decreasing the progress of inflammatory process

within gingival tissues.<sup>7</sup> Oral melanocytes may act as scavenging antioxidants and prevent oxidative stress.<sup>8</sup> Studies have shown that individuals with gingival hyper pigmentation show a negative correlation with bleeding index, plaque score and gingival index.<sup>7,9,10</sup> Physiologically induced gingival hyper pigmentation is genetically determined and doesn't reflect a medical problem or disease.<sup>11</sup>

Various studies on human and animal genome have shown that there are at least 11 different genes responsible for normal pigmentation.<sup>11,12</sup> Individuals from different races and ethnic groups contain same number of melanocytes. It is the activity of melanocytes not their number which is responsible for differences in the colour among different populations.

#### Clinical Presentation

Clinically, melanin induced gingival hyper pigmentation appears as brown or blue black area mostly located on facial aspect of attached gingiva. The variation in colour is due to amount, distribution and depth of melanin. Blue discoloration represents melanin deposits in the connective tissue whereas brown discoloration is associated with superficial deposition in the epithelium.<sup>3</sup>

The pigmentation is more prominent in upper anterior segment and disappears or fades in posterior segment. It is either symmetric or irregular patchy area with well-defined borders.

**Differential Diagnosis**

Melanin induced gingival hyper pigmentation is a physiological condition and must be differentiated from other pathological conditions producing hyper pigmentation either due to endogenous or exogenous factors. Endogenous causes include inherited diseases or diseases due to hormonal disturbances, infections, carcinomas and inflammation. Exogenous causes include discoloration due to heavy metals, amalgam tattoos, smoking and certain medicines.<sup>13-15</sup> *Dandasa*, a walnut tree peel, used for teeth whitening also causes temporary discoloration of gingival and lips. (Table-1)

**MATERIAL AND METHODS**

Online database (MedLine/ PubMed) was thoroughly searched from 1990 to March 2014 for the studies describing treatment regime of melanin induced physiological hyperpigmentation along with recurrence of pigmentation and post-operative pain. Keywords used were “Melanin”, “gingival hyper pigmentation”, “treatment”, “re-pigmentation”, and “post-operative pain”. Inclusion criteria were

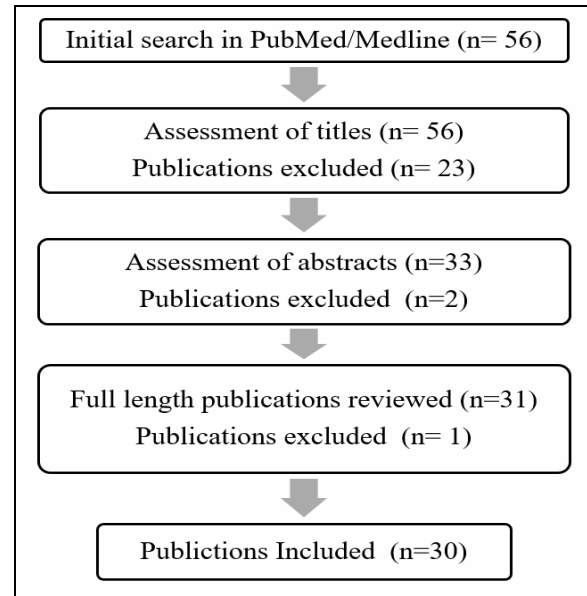
- Publications on human subjects
- Publications in English language only
- Publications describing management of Physiological melanin induced gingival hyper pigmentation

Titles and abstracts of retrieved articles were independently reviewed by authors (H.F and M.S.S, F.R.K) according to inclusion criteria. In case of any disagreement or confusion fourth author (F.T) made final decision regarding inclusion of the article.

In total 56 publications were retrieved. After thorough evaluation of titles and abstracts,

23 publications were excluded. The remaining publications were assessed in full length and 30 publications finally met the inclusion criteria. None of the study in the current review fulfils the criteria to be titled as “randomized controlled trial”. Those studies that compared two or more treatment modalities over time for their outcomes (recurrence of pigmentation and pain) were labelled as “comparative clinical studies” in this review. All others were either case report or case series (Table 2). Details of included studies are given in Table-3.

**Table-2: Literature search flowchart.**



**Table-1: Causes of gingival hyper pigmentation**

| Exogenous   | Endogenous   |
|---|--|
| <b>Heavy Metals:</b><br>Gold, Bismuth, Arsenic, Mercury, Silver, Lead, Copper     | <b>Genetic:</b><br>Peutz-Jeghers syndrome, Von Reckling Hausen’s disease (neurofibromatosis), Gaucher’s disease, Wilson’s disease, Primary hemochromatosis |
| <b>Tatoos:</b><br>Amalgam, Graphite, Intentional                                  | <b>Physiological:</b><br>Melanin induced Pigmentation  |
| <b>Smoking</b><br>Tobacco   | <b>Hyperplastic benign lesions</b><br>Ephelides (freckles), Lentigo , Mselanotic macules   |
| <b>Medications:</b><br>Antimalarial, Minocyclin, ketoconazole, Oral contraceptive | <b>Endocrine Disturbances :</b><br>Addision Disease, Albright Syndrome, Pregnancy  |
| <i>Dandasa</i>  | <b>Infection:</b><br>Human immunodeficiency virus (HIV)  |
|   | <b>Blood Disorders:</b><br>Thalassemia   |
|   | <b>Liver Disorder:</b><br>Jaundice   |
|   | <b>Secondary to other Disorders:</b><br>Secondary hemochromatosis  |
|   | <b>Neoplastic:</b><br>Nevi - Benign, Melonoma – Malignant, Brochiogenic carcinoma  |
|   | <b>Trauma</b>  |
|   | <b>Inflammation</b>  |

**Table-3: Clinical studies for the management of melanin induced physiological gingival hyper pigmentation**

| Author & Year                      | Method of treatment  | Study Design               | Sample size                | Follow up   | Reported Success Rate (Occurrence of Re-pigmentation)  | Post-Operative Pain  |
|------------------------------------|--|----------------------------|----------------------------|---|--|--|
| Ribeiro FV, 2014 <sup>19</sup>     | Nd:YAG laser on one side and scalpel technique on other side   | Comparative clinical study | 11 patients                | 6 months  | Not reported   | Higher extent of discomfort/pain experienced in the side treated by the scalpel technique compared to the Nd: YAG laser  |
| Kumar S, 2013 <sup>25</sup>        | Cryosurgery by tetrafluoroethane   | Case Report                | 5 patients                 | 12 months   | No recurrence  | Mild pain and discomfort in one patient  |
| Parwani S, 2013 <sup>18</sup>      | scalpel surgery and electro-surgery  | Case Report                | 3 patients                 | 3 months  | No recurrence  | No Pain  |
| Hegde R , 2013 <sup>20</sup>       | Surgical stripping, Er:YAG laser and CO2 laser   | Comparative clinical study | 140 sites from 35 patients | 6 months  | <b>Surgical stripping sites</b><br>15 of 70<br>3 of 20<br><b>Er:YAG-laser treated sites</b><br>10 of 35<br>6 of 20<br><b>CO2-laser-treated sites</b><br>8 of 35<br>4 of 20 | Statistically significant values for Er: YAG laser   |
| Simşek Kaya G , 2012 <sup>32</sup> | Gallium aluminium arsenide Diode and Er:YAG lasers   | Comparative clinical study | 20 Patients                | 6–24 months   | No recurrence  | No pain  |
| Shirazi AS , 2012 <sup>33</sup>    | Cryosurgery with liquid Nitrogen   | Case Series                | 15 patients                | 3, 12, and 24 months  | No recurrence  | No pain  |
| Kasagani SK,2012 <sup>34</sup>     | Electro-surgery; Scalpel surgery; and bur abrasion   | Case Series                | 3 patients                 | one month and 12 months for electro surgery and scalpel surgery and one month and six months for bur abrasion | Small areas of re-pigmentation with electro surgery<br>No recurrence in other cases  | No pain with scalpel and bur abrasion<br>Not reported for electro surgery  |
| Talebi M, 2012 <sup>35</sup>       | Cryosurgery  | Case Report                | 1 patient                  |   | No recurrence  | No pain  |
| Thangavelu A , 2012 <sup>36</sup>  | scalpel, electro surgery, and diode lasers   | Case Series                | 3 patients                 | 3 months  | remnants of pigmentation in scalpel surgery  | No pain  |
| Murthy MB 2012 <sup>37</sup>       | scalpel surgery, abrasion with rotary abrasive and a diode laser                                       | Case series                | 3 patients                 | 3 months  | No recurrence  | No pain for rotary abrasive and scalpel surgery<br>Not reported for diode laser  |
| Kathariya R,2011 <sup>38</sup>     | combination of scalpel de-epithelization on one side and bur abrasion or electro surgery on other side | Comparative clinical study | 6 patients                 | 24 weeks for scalpel<br>12 weeks for bur abrasion<br>Not reported for electro surgery                         | No recurrence for scalpel de-epithelization and bur abrasion   | No post-operative pain for scalpel de-epithelization and bur abrasion<br>Mild post-operative burning for electro surgery |
| Bhusari BM , 2011 <sup>39</sup>    | Electro surgery on one side & scalpel surgery(Partial split thickness flap) on other side              | Comparative clinical study | 3 patients                 | 1 week  | Not mentioned  | No post-operative pain   |
| Gupta G, 2011 <sup>28</sup>        | Semiconductor Diode Laser  | Case Report                | 1 Patient                  | Fifteen months  | No recurrence  | No post-operative pain   |

| Author & Year                     | Method of treatment  | Study Design               | Sample size | Follow up       | Reported Success Rate (Occurrence of Repigmentation)   | Post-Operative Pain                     |
|-----------------------------------|--|----------------------------|-------------|-----------------|--|---|
| Lee KM, 2011 <sup>40</sup>        | Er:YAG laser on the right side rotary round bur on other side  | Comparative clinical study | 2 patients  | 4 weeks         | No recurrence  | Mild Pain in both cases                 |
| Ko HJ, 2010 <sup>29</sup>         | Nd: YAG laser and a high speed rotary instrument   | Comparative clinical study | 3 patients  | 1 month         | Pigmentation remained in 1 patient at site treated with Nd:YAG laser   | Mild Pain in 2 cases                    |
| Shimada Y, 2009 <sup>17</sup>     | Ascorbic acid 2-glucoside gel (AS-G gel) vs placebo gel as control   | Comparative clinical study | 73 subjects | 12 weeks        | Not reported   | Not reported                            |
| Arikan F, 2007 <sup>26</sup>      | Cryosurgery with tetrafluoroethane.  | Case series                | 21 patients | 30 months       | No recurrence  | No pain                                 |
| Azzeh MM, 2007 <sup>41</sup>      | Er:YAG laser   | Case series                | 6 patients  | 6 and 18 months | No recurrence  | No Pain                                 |
| Rosa DS, 2007 <sup>42</sup>       | Er:YAG laser   | Case series                | 5 patients  | 3 months        | Recurrence in 1 patient  | Not reported                            |
| Pontes AE, 2006 <sup>43</sup>     | Acellular dermal matrix allograft and Bur Abrasion   | Comparative clinical study | 15 patients | 12 months       | 8-15 sites treated with acellular dermal matrix allograft 15 out of 15 sites treated with bur abrasion   | Not reported                            |
| Roshna T, 2005 <sup>44</sup>      | scalpel surgery  | Case Report                | 1 patient   | 1 year          | No recurrence  | Not reported                            |
| Deepak P, 2005 <sup>45</sup>      | Bur abrasion/scraping, electro surgery and partial thickness flap  | Case series                | 3 patients  | 3 months        | remnants of pigmentation in patient treated with bur abrasion/scraping and electro-surgery No remanant pigmentation/repigmentation in case of partial thickness flap | Not reported                            |
| Esen E, 2004 <sup>8</sup>         | (CO2) laser  | Case series                | 10 patients | 24 months       | Two cases of partial repigmentation  | Mild post op pain                       |
| Tal H , 2003 <sup>46</sup>        | Er:YAG laser   | Case series                | 10 patients | 6 months        | no recurrences.  | Mild pain/itching in 1 <sup>st</sup> wk |
| Almas K ,2002 <sup>24</sup>       | Scalpel surgery  | Case Report                | 1 patient   | 6 months        | No recurrence  | No pain                                 |
| Atsawasuwan P, 2000 <sup>27</sup> | Nd:YAG laser   | Case series                | 4 patients  | 11-13 months    | No recurrence  | Mild post op pain                       |
| Ozbayrak, 2000 <sup>47</sup>      | CO2 laser  | Case series                | 8           | 18 months       | No recurrence  |   |
| Yeh CJ , 1998 <sup>23</sup>       | Cryosurgery by liquid Nitrogen   | Case Series                | 20 patients | 24 months       | No recurrence  | Not reported                            |
| Tamizi M,1996 <sup>1</sup>        | Free gingival Autograft in recipient site with either partial thickness recipient bed preparation or full thickness dissection | Comparative clinical study | 10 patients | 4.5 years       | Recurrence in 1 patient after 1 year in which partial thickness recipient bed was prepared   | Not reported                            |
| Bergamasch O, 1993 <sup>31</sup>  | Gingivectomy   | Case Series                | 5 patients  | 5years          | Recurrence of pigmentation in all patients   | Not reported                            |

## DISCUSSION

For the treatment of gingival hyper pigmentation various treatment modalities (as shown in Table III) are available. Broadly, these treatment modalities can be classified as:

- Non-Surgical Methods
- Surgical Methods
  - **Gingivectomy**
  - **Free gingival grafts**
  - **Acellular dermal matrix allografts**
  - **De-epithelialization** by bur abrasion, laser, cryosurgery, radiosurgery, electro surgery

### Non-Surgical Methods

Certain pharmacological agents have been prescribed in the past for gingival depigmentation. In 1955, the use of 90% phenol in combination with 95% alcohol was described by Hirschfeld.<sup>16</sup> This combination resulted in induction of chemical burns and epithelium sloughing. Not only had this technique resulted in re-pigmentation shortly after procedure in all cases, it was painful and caused tissue necrosis.

### Ascorbic Acid Gel

Recently, a study investigated the effects of ascorbic acid on gingival depigmentation both in vitro and in vivo and concluded that ascorbic acid due to its inhibitory effects on tyrosinase activity and melanin formation has a potential for the management of gingival hyper pigmentation.<sup>17</sup> Although a significant change in gingival colour after 4 weeks was observed but the long term follow up was not reported.

### Surgical Methods

A variety of surgical methods are reported in the literature for the treatment of gingival de pigmentation. Some methods are simple while others require sophisticated equipment and expertise of clinician.

### Gingivectomy

One of the most common techniques used for the treatment of gingival hyper pigmentation is surgical removal of epithelium along with a layer of underlying connective tissue with a scalpel blade. A surgical pack is placed over denuded area which later on heals through secondary intention. This is a simple technique which doesn't require any sophisticated equipment. It is faster and results in quick healing.<sup>18,19</sup> The disadvantages associated with this technique are bleeding from incision site, post-operative pain and need of surgical pack.<sup>18-20</sup> Scalpel surgery can be combined with bur abrasion to achieve the physiological contour of the gingival. Gingivectomy should be avoided in patients with thin gingival biotypes.

### Gingivectomy with free gingival autograft

Another method of treatment of gingival hyper pigmentation is the use of free autogenous grafts. Free gingival autograft were successfully harvested from palate in a split mouth study design.<sup>1</sup> On one side

recipient bed was prepared by reflecting full thickness flap (along with periostium) and on the contralateral side partial thickness flap was reflected to prepare recipient bed. 4.5 years follow up was successful with no repigmentation except for one case in which partial thickness recipient bed was prepared. The repigmentation in this case was attributed to remaining active melanocytes in the connective tissue layer. Despite favourable results, full thick flap reflection along with bone denudation is associated with the risk of prolonged healing period, attachment loss, significant discomfort and two sites surgery (donor and recipient sites).<sup>21</sup>

### Gingivectomy with acellular dermal matrix

Acellular dermal allograft is a substitute for palatal donor tissue. It is obtained from human cadaver bone. After removal of cellular components, matrix constituents are preserved which are mainly type I Collagen and Elastin. This matrix is acellular and non-immunogenic; and healing occurs by repopulation and revascularization. It has been used successfully for oral soft tissues surgeries including procedures to increase attached gingiva width around implants and natural teeth, root coverage in gingival recession and elimination of melanin pigmentation.

The advantages associated with this technique are predictable results, unlimited quantity, one surgical site and less post-operative discomfort. The disadvantages are increase cost and possibility of graft contraction.<sup>22</sup>

### De-epithelialization Techniques

#### Bur abrasion

Diamond bur in high speed can be used in brushing stroke action with minimal pressure for removal of superficial epithelium. Bur should not be held in one place for longer as it can result in thermal damage and creation of small pits. Although it is a simple method which doesn't require sophisticated instruments, it can cause damage to adjacent teeth, enamel loss, periosteum damage and delayed wound healing if not used with caution.

#### Cryosurgery

Melanocytes are very sensitive to low temperature and cell death occurs at temperature as low as -4 to -7 °C. Cryosurgery technique transfers low temperature to the cells and the resultant physical and chemical changes induced by freezing lead to cell destruction and cell death.<sup>23</sup> Reported advantages of this technique are no need of suturing and surgical pack placement, no bleeding, minimal scar tissue formation, minimal damage to deep and adjacent tissue and no post-operative infection. The disadvantages of this technique are post-operative swelling, difficulty to control depth, expensive cryosurgery instruments and storage of liquid gases.<sup>24</sup> Few studies have used tetrafluoroethane as simple, successful and cost effective substitute of liquid gases.<sup>25,26</sup>

### Laser

Laser is another effective mean for the management of gingival hyper pigmentation. Both heat producing (CO<sub>2</sub> laser, Nd: YAG laser, semiconductor diode laser and argon laser) and non-heat producing lasers (Er: YAG and Er, Cr: YSGG) have been described in the literature for this purpose.<sup>27</sup> Photons are absorbed by water containing cells of the tissues including pigmented cells “melanocytes”. Lasers have the ability to remove a thin layer of epithelium with minimum damage to the underlying bone. Although this modality requires clinician expertise and costly equipment, but at the same time it is associated with no or minimal bleeding, no scar formation and slight post-operative discomfort.<sup>28,29</sup> Laser wounds are sterile and take longer time to heal as compare to scalpel wounds.

### Radiosurgery

Radiosurgery uses a variety of waveforms for making incision including fully rectified filtered form (deep surgical incision), filtered waveform (delicate incision), fully rectified waveform (incision with concurrent coagulation) and the partially rectified waveform (only coagulates). The different waveforms differ in their depth of incision cut and extent of coagulation. This technique uses a bipolar electrode with two parallel wires. One wire produces incision and the other receives radio signals. This setup is believed to reduce the transmission of radio signals to the adjacent tissue, thus minimizing production of undesired lateral heat. This technique works on the principle that melanocytes resides in the basal and suprabasal layers, thus a light touch of electrode is sufficient to remove pigmentation. There is scarce of literature on use of this technique for treatment of gingival hyper pigmentation. However, Sherman<sup>30</sup> has used this technique successfully for the treatment of gingival hyper pigmentation with no recurrence for 6 months. It is also reported that radiosurgery offers minimum pain and discomfort to the patient along with the added benefit of short learning curve for the operator.

### Electro surgery

Electro surgery utilizes current for tissue destruction. This technique involves the application of current to the tissue which results in tissue sloughing. Great care is required as excessive or prolonged contact with tissue results in heat generation and tissue destruction.<sup>24</sup> Contact with alveolar bone can result in bone necrosis too. Beside these issues, it also requires electrocautery equipment.

### Repigmentation

One of the problems associated with majority of the treatment modalities is recurrence of pigmentation. Bergamaschi and colleagues<sup>31</sup> treated melanin pigmentation by gingivectomy. Biopsies were taken at 2, 3, 6, 7, 15, 50, and 180 days and 1.5, 3, and 5 years after the procedure. This was followed by

electron microscopic study which revealed melanocytes in the process of migration and undergoing mitosis 6 and 7 days postoperatively. These cells exhibited, in the 15-day specimens, renewal of their dendritic processes and the four different stages of melanosome development. It was concluded that resection procedures if performed solely for cosmetic purpose, doesn't offer any permanent result. The other modalities (as shown in table-3) including bur abrasion, cryosurgery, laser, autograft and acellular dermal matrix also result in repigmentation on longer follow up.

### CONCLUSION

Melanin induced physiological hyper pigmentation is a cosmetic problem which can also have psychological impact in many patients. The choice of the management option should be tailored according to the individual circumstances, clinician expertise and equipment availability. Patient should be clearly informed about pros and cons of each treatment option available along with recurrence potential of melanin induced gingival hyperpigmentation.

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