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REVIEW ARTICLE

LASERS FOR ESTHETIC REMOVAL OF GINGIVAL HYPERPIGMENTATION: A SYSTEMATIC REVIEW OF RANDOMIZED CLINICAL TRIALS.

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Abstract

Background: Being a science of beauty, beautiful smile is an integral part of contemporary dental practice. Gingival hyperpigmentation is considered an esthetic problem that needs a patient centered management. Dental operators are attracted to laser benefits not only during surgery but also for postoperative status. This review aimed to assess laser use in esthetic removal of gingival hyperpigmentation in comparison to conventional methods.

Materials and Methods: An electronic database search on PubMed and Cochrane library without date restriction was done and clinical studies in which laser was used for esthetic gingival depigmentation were selected and evaluated. Out of the initial search that yielded 183 studies, 21 were considered potentially relevant for the present review, out of which only 4 were finally selected. They studied the effect of laser on depigmentation, chair time, bleeding index, patient satisfaction and repigmentation.

Results: The analysis of the results shows that the assessed studies are too limited in number beside exhibiting small sample sizes. They are clinically heterogeneous so that a solid evidence based conclusion cannot be reached.

Conclusion: Researchers should be attracted to this research gap. Randomized clinical trials with a larger sample size, different laser parameters and longer follow up are strongly recommended.

Introduction:-

Being a science of beauty, beautiful smile is an integral part of contemporary dental practice. Good smile involves not only teeth shape and color but also the gingival status. Pink gingival color is more favorable than dark one. Melanin hyperpigmentation or darker gingival color can be considered an aesthetic concern rather than a medical problem **(Basha *et al.* 2015)**.

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Dentists should be prepared with the latest evidence based practice for management of such cases. The selection of technique should be based not only on clinical experience and doctor preferences but also on patient preferences **(Thangavelu *et al.* 2012)**. Various methods can be used with varied degrees of success **(Roshna and Nandakumar 2005)**

Gingival hyperpigmentation can be defined as a darker gingival color beyond what is normally expected. The most common cause is racial pigmentation while other causes includes physiologic and/or pathologic factors **(Dummett and Barens 1967)**. Gingival depigmentation is the treatment aiming to remove the melanin hyperpigmentation and it can be done by several techniques including mechanical, surgical, electrosurgical, cryosurgical, free gingival grafts, and lasers **(Cicek and Ertas 2003, Hegde *et al.* 2013, Chandna and Kedige 2015)**. Surgical stripping was the old gold standard but now lasers have gained importance in the past years **(Hegde *et al.* 2013, Basha *et al.* 2015)**.

A critical concern in the management of hyperpigmented gingiva is relapse or gingival repigmentation which can be defined as the reappearance of pigmentation after a period of no clinically hyperpigmentation. Recurrence usually varies according to the used methodology and the length of follow-up **(Hegde *et al.* 2013)**.

The clinical rationale for comparing laser to conventional methods can be simply based upon the need for minimally invasive techniques for achieving a patient relevant outcomes **(Ribeiro *et al.* 2014)**.

Based on this background, the aim of the present systematic review is to evaluate and compare the effects of conventional techniques versus lasers for gingival depigmentation as regards to removal of pigmentation, patient preference and time taken for repigmentation.

Materials and Methods:-

Protocol:-

The methods as well as inclusion/exclusion criteria used in the present study were determined in advance. The current systematic review was performed following the PRISMA guidelines for identification, screening, eligibility, and inclusion **(Moher *et al.* 2010)**. The following focus question was developed: In patient requiring esthetic removal of gingival hyperpigmentation, is laser use recommended over conventional techniques, what is the evidence based recommendation for both patients and operators?

Information Sources:-

The electronic search was performed in two databases, MEDLINE (PubMed) and Cochrane library databases for articles with no date restrictions.

Search:-

The researched keywords were: (Black OR pigment OR melanin OR pigmentation OR hyperpigmentation OR pigmented OR dark OR Pigmentary OR pigmentations OR melanin) AND (Lased OR laser OR LLLT) AND (Gingiva OR mucosa OR gingival OR mucosal OR gum).

Selection of studies:-

Titles and abstracts resulted from the search were screened by authors considering the inclusion criteria. Authors decisions about choices and their qualification for further analysis was affirmed after discussion.

Inclusion and exclusion criteria:-

Inclusion criteria:-

- Randomized Clinical trials only
- Laser compared to conventional methods

Exclusion criteria:-

- Pigmentation due to amalgam tattoo, nevus or syndromes
- Case reports
- In vitro and animal studies
- Languages other than English

Assessment of methodological quality:-
The quality of all chosen randomized trials was investigated utilizing The Cochrane Collaboration's tool for evaluating risk of bias **(Higgins *et al.* 2011)**.

According to Cochrane risk of bias tools, each RCT was assigned either; low risk of bias (if it is low for all key domains), high risk of bias (if it is high for one or more of key domains) and unclear risk of bias (if it is unclear for one or more of key domains). Because it was impossible to blind participants or personnel due to nature of intervention and control (i.e. Laser VS surgery), the "BLINDING OF PARTICIPANTS, PERSONNEL" item was not considered.

Results:-

Out of the initial search that yielded 183 studies, 21 were considered potentially relevant for the present study, out of which 4 were finally selected. Figure (1) represents the flow chart for the study. The excluded studies before final inclusion were uncontrolled or without conventional control **(Trelles *et al.* 1993, Hanada *et al.* 1996, Nakamura *et al.* 1999, Ozbayrak *et al.* 2000, Tal *et al.* 2003, Esen *et al.* 2004, Azzeh 2007, Kaya *et al.* 2012, Giannelli *et al.* 2014, Kishore *et al.* 2014, Soliman *et al.* 2014, El Shenawy *et al.* 2015)**, review article **(Karydis *et al.* 2011)**, uncontrolled case reports **(Rosa *et al.* 2007, Bin Cho *et al.* 2010)**, non-randomized trial **(Grover *et al.* 2014)** and the study of Giannelli et at which was a thermographic and fluorescent study for optimizing gingival laser photoablation **(Giannelli *et al.* 2013)**.

The final included studies were four **(Hegde *et al.* 2013, Ribeiro *et al.* 2014, Basha *et al.* 2015, Chandna and Kedige 2015)**. The heterogeneity between trials prevented meta-analysis. Rather, a descriptive analysis of the reported studies was performed. Table (1) represents summary of findings.

Risk of bias within studies:-
The review included 4 studies, 3 studies (**Hegde et al 2013, Ribeiro et al 2014, Basha et al 2015**) used split mouth study design and 1 study **(Chandna and Kedige 2015)** used parallel design. Sex distribution was mentioned in 3 studies **(Hegde et al 2013, Ribeiro et al 2014, Chandna and Kedige 2015)** and not mentioned in 1 study **(Basha et al 2015)**.

For RCT studies, according to Cochrane Risk of Bias Tool, all studies were judged as low risk of bias for incomplete outcome data, selective reporting and other bias. Regarding random sequence generation, 3 **studies (Hegde et al 2013, Ribeiro et al 2014, Basha et al 2015)** were judged as low risk of bias while it was judged as unclear for **Chandna and Kedige 2015** study as it didn't mention type of randomization used. Allocation concealment was unclear for all included studies. Regarding Blinding of outcome assessment, 3 studies **(Hegde et al 2013, Basha et al 2015, Chandna and Kedige 2015)** were judged as unclear as there was no any mention about blinding of the assessor or statistician while it was low risk of bias for **Ribeiro et al 2014** study. All studies were considered overall as unclear risk of bias. Figure (2) represents risk of bias summary: review authors' judgements about each risk of bias item for each included RCT study while Figure (3) represents risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included RCT studies.

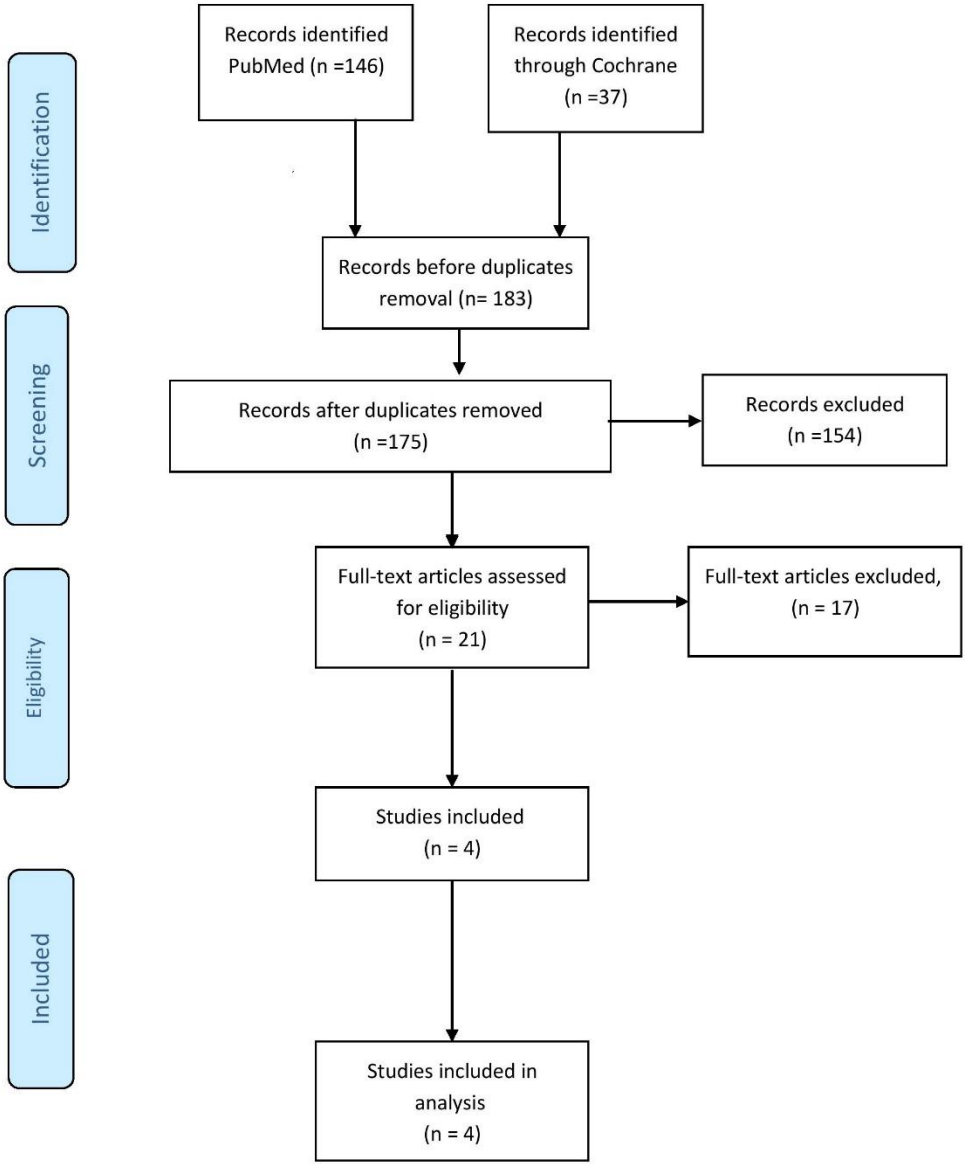

Figure 1:- Prisma flow chart for the study.

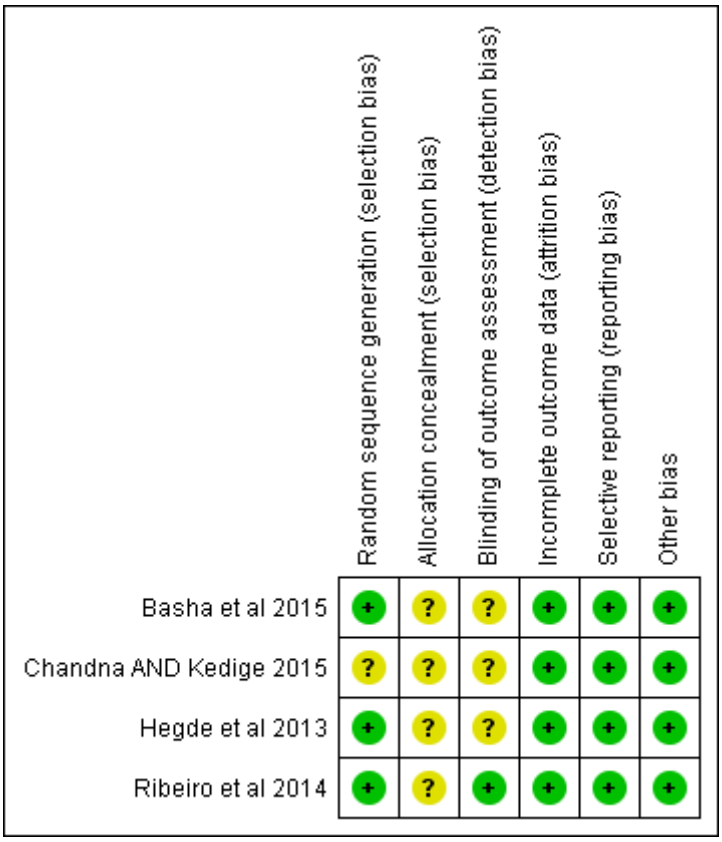

Figure 2:- Risk of bias summary: review authors' judgements about each risk of bias item for each included RCT study.

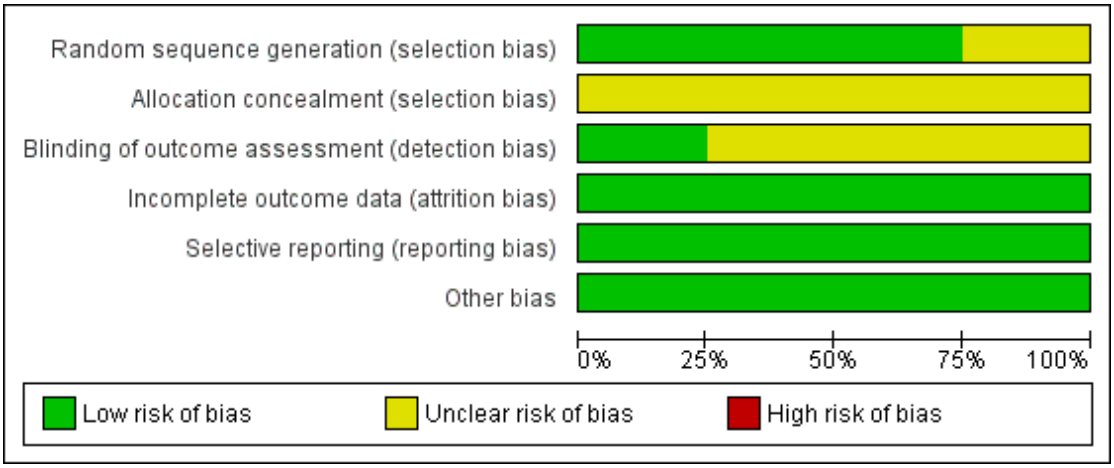

Figure 3:- Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included RCT studies.

Table 1:- Summary of findings table.

Authors and date	Population	Laser type ***Vs*** Control	Outcome
Basha et al 2015	20 patients with 40 bilateral maxillary sites	Nd: YAG laser ***Vs*** Scalpel surgery	Intergroup comparison for time taken, pain, and patient preference was statistically significant in favor of laser. Intragroup comparison for laser and surgical stripping at 6 months for Dummett Oral Pigmentation Index (DOPI), Hedin index, and size of pigmented area was statistically significant. Non-statistical difference in other results.
Hegde et al 2013	35 patients with 140 bilateral sites	CO2 and Er: YAG laser ***Vs*** Scalpel surgery	Thorough removal of pigments, pain reduction, and higher patient preference were associated with Er: YAG laser but more sites showed repigmentation. The CO2 laser was beneficial in terms of complete hemostasis intraoperatively and delaying the rate of repigmentation. Repigmentation was least after the surgical stripping procedure.
Ribeiro et al 2014	11 patients with bilateral anterior maxillary sites	Nd: YAG laser ***Vs*** Scalpel surgery	A statistically lesser chair time was observed in the laser group. A statistically lesser extent of discomfort/pain was in laser group during the first posttherapy week. Non-statistical difference in other results.
Chandna and Kedige 2015	20 patients (10 for each group)	Diode laser ***Vs*** Electro-surgery	A statistically highly significant difference in the pain levels between the two groups 24 h post-operatively in favor of laser group. Despite of lesser mean pain level for the laser group at other times, it was a non-significant difference.

Discussion:-

Lasers can be used as a contemporary alternative to the traditional scalpel in oral soft tissue surgeries because it offers simple manipulation as regards to absence of bleeding, reduced need for local anesthesia and increased patient comfort **(Arnabat-Domínguez *et al.* 2010)**. From that points of view comes the research question, why not to recommend laser over conventional techniques.

Melanin is a word derived from the Greek one ‘‘melas’’ or black **(Hegde *et al.* 2013)**. Melanin hyperpigmentation can affect all races and all ages with no gender predilection **(Eisen 2000)**. Gingival hyperpigmentation is an esthetic problem for many patients, especially if visible when smiling. lasers have been suggested as an alternative to conventional procedures for providing a more patient centered outcome **(Atsawasuwan *et al.* 2000)**. However, up to date, no evidence based recommendation for whether to go for the conventional strategy or replace it with the contemporary lasers.
The trials presented in this review agreed that both techniques are successfully used for the treatment of gingival hyperpigmentation but which one is recommended over the other, an issue that needs further discussion.

Blade surgery for gingival depigmentation is a definite precise and controlled procedure beside being the most economical procedure. Any depigmented areas are appreciated immediately and there is no chance for any residual pigments. On the other hands, this technique required the use of local anesthesia, associated with pain and hemorrhage and required care not to expose the bone or create gingival recession **(Grover *et al.* 2014)**.

Also, periodontal dressing for at least a week is mandatory to guard against food debris, foreign irritants, thermal stimuli and infection **(Gurumoorthy Kaarthikeyan *et al.* , Grover *et al.* 2014)**. The denuded tissues which heal by secondary intention after conventional surgery may promote bleeding after the procedure and is associated with some discomfort and pain for the patient **(Ribeiro *et al.* 2014)**. The denuded connective tissue heals by secondary intention and is associated with pain and late repair **(Roshna and Nandakumar 2005)**.

The expected complicated postoperative period, even if mild, may interfere with patient daily activities and well-being **(Ribeiro *et al.* 2014)**. An experience that should be avoided by the modern patient centered care strategy.

Despite that surgical stripping has been the old gold standard for gingival depigmentation, lasers start to gain prominence in that field **(Coluzzi 2004)**.

Using of lasers for oral soft tissues provides benefits not only to dental operators but also for the patients. Patient-centered outcomes are the main target for researches in the last decade **(Hujoel 2004, Ozcelik *et al.* 2007)**.

Concerning the cosmetic outcomes, some aspects of using lasers may benefit the purpose as precise cutting and control and the application of delicate contact tips during the procedure which enhances trans-operative visualization **(Cobb 2006)**.

One of the advantages of using laser is that patients felt no pain either during or after the treatment without requiring an additional anesthetic injection. Fear of pain during dental surgeries or even the needle used for anesthesia are among the causes of avoiding dental visits. Thanks to lasers that solve a part of that problem **(Matys and Dominiak 2016)** .

The reduced pain in comparison with conventional surgery may be due to the protein coagulum formed on the surface of the wound that acts as a biologic dressing. Sealing of the ends of sensory nerves may be also considered which is not the case in surgical stripping where the nerve endings is left exposed **(Gurumoorthy Kaarthikeyan *et al.* , Hegde *et al.* 2013, Rathod and Mulay 2013, Basha *et al.* 2015)**. A disrupted cell membrane Na^+-K^+ pump with the resulting loss of impulse conduction may be another cause of pain reduction associated with laser use **(Chandna and Kedige 2015)**. The biologic dressing not only reduces pain but also protects the surgical area and provides a better postoperative repair with minimal damage to the tissue **(Ribeiro *et al.* 2014)**.

Patients also appreciated the shorter operating time and minimal bleeding which is not the case in patients treated with the surgical scalpel technique **(Hegde *et al.* 2013, Grover *et al.* 2014)**. The time taken for laser treatment was less than the surgical stripping may be attributed to better visibility due to less bleeding because of the coagulation of blood vessels **(Ko *et al.* 2010, Ribeiro *et al.* 2014, Basha *et al.* 2015)**.

Several studies have compared different lasers with varying results, similar advantages includes a relatively bloodless surgical field, minimal swelling and scarring, reduction of surgical time and less postoperative pain **(Giannelli *et al.* 2014, Kishore *et al.* 2014, Soliman *et al.* 2014, Basha *et al.* 2015)**.

It is the ablative property of laser that makes it possible to be used for gingival depigmentation by targeting the melanin in melanocytes in epithelium which absorbs and converts light energy into heat or what is known as photothermolysis **(Nakamura *et al.* 1999, Coluzzi 2004)**.

A variety of laser systems can be used for gingival depigmentation, including carbon dioxide (CO_2) laser **(Nakamura *et al.* 1999)**, diode laser **(Kaya *et al.* 2012)**, Er:YAG laser **(Kaya *et al.* 2012)**, and Nd:YAG laser **(Atsawasuwan *et al.* 2000)**.
Neodymium–yttrium aluminum garnet (Nd:YAG) laser treatment has been considered as an alternative for gingival hyperpigmention because of rapid healing and minimal bleeding during and after the procedures **(Ko *et al.* 2010)**. Fortunately, Nd:YAG laser is selectively absorbed by hyperpigmented tissues **(Cobb 2006)**.

It is the inherent ability of diode lasers to be absorbed within the chromophores that allows controlled cutting with a limited depth of necrosis or by other words a tissue-specific ablation. The other advantage of diode laser is that its energy is transmitted through water and fortunately it is poorly absorbed in hydroxyapatite **(Convissar 2004)**.

Low-power setting ($\leq$2.5) is recommended during the procedure to avoid discomfort and pain during the post-operative period and for faster healing time. The gated pulsed mode is also recommended to provide the necessary thermal relaxation **(Berk *et al.* 2005, Cercadillo-Ibarguren *et al.* 2010, Kaya *et al.* 2012, Romeo *et al.* 2012, Grover *et al.* 2014)**.

Esthetic gingival depigmentation is considered successful if there is delayed, minimal, or no repigmentation **(Hegde *et al.* 2013)**. According to Bergamaschi *et al*., permanent results are non-achievable **(Bergamaschi *et al.* 1993)**. Recurrence rate may differ not only with the used treatment modalities but also according to the duration of follow-up **(Ribeiro *et al.* 2014)**.

Many studies reported recurrence after laser depigmentations **(Bergamaschi *et al.* 1993, Nakamura *et al.* 1999, Esen *et al.* 2004, Rosa *et al.* 2007, Kaur *et al.* 2010)** while others reported no repigmentation **(Atsawasuwan *et al.* 2000, Tal *et al.* 2003, Azzeh 2007)**. Grover et al. reported that no statistical significance was seen in the comparison of conventional and laser techniques in terms of repigmentation **(Grover *et al.* 2014)**.

It was noted that repigmentation appeared in the papillary areas and marginal gingiva which may be due to difficulty in treating these areas with lasers because of lying near tooth structure and the risk of thermal damage which recommends lower energy dose with inadequate depth of penetration of the laser beam, incomplete depigmentation, and faster recurrence **(Hegde *et al.* 2013)**

To avoid recurrence, the gingival tissue should be entirely cleared of melanin to avoid recurrence by melanocytes migration **(Sharon *et al.* 2000)**. Also, patient race, environmental exposure exposure and smoking may play a role in repigmentation **(Ünsal *et al.* 2001, Sridharan *et al.* 2011)**.

Interestingly, another aspect that may affect repigmentation is the number of performed laser sessions. All the studies that used multiple sessions for laser ablation reported no recurrence **(Tal *et al.* 2003, Azzeh 2007, Kaya *et al.* 2012)**.

Also, repigmentation was more common in the maxillary arch in comparison to the mandibular arch which may be due to more exposure to environmental factors during smiling and speech, factors that are not related to the technique used **(Hegde *et al.* 2013)**.

Laser biomodulation may be a double-edged weapon as while accelerating healing, melanocytes from adjacent areas migrate faster, leading to faster repigmentation **(Hegde *et al.* 2013)**

Laser application requires that the operators are trained about safe and effective use of lasers **(Ribeiro *et al.* 2014)**. The surgical stripping gives the benefits of tactile sensation beside no risk of thermal damage to the underlying structures **(Hegde *et al.* 2013)**

It is important to mention that care should be taken not to injure the gingival margin and interdental papilla during ablation of pigmented gingival tissue in these delicate areas. Also, higher doses can cause like delayed wound healing promoted by severe coagulation or pain caused by uncontrolled carbonization **(Ribeiro *et al.* 2014)**.

Laser requires more advanced technology and armamentarium and it causes higher financial costs than more economical scalpel technique **(Ribeiro *et al.* 2014)**. The patients' perceptions of costs and benefits balance interfere in the decision about choosing laser or scalpel surgical therapy.

The advantages of lasers over conventional surgical procedures are: bloodless field, reduced bacteremia and mechanical trauma, minimal post-operative swelling and scarring and minimal post-operative pain. On the other hand, loss of tactile sensation and expensive and sophisticated equipment that needs special training and precautions are considered disadvantages **(Chandna and Kedige 2015)**.

Conclusion:-

The found clinical studies are not only too limited in number but also exhibit small sample sizes, besides being clinically heterogeneous so that a solid conclusion cannot be reached. Researchers should pay attention to this interesting field to work upon. Each kind of laser application should pull attention of researchers in oral and maxillofacial field to close obvious, yet important, research gaps of lack of enough randomized clinical trials that can be relied upon to get a standard evidence based clinical practice.

Within the limitations of this review, it can be concluded that lasers can be used as a safer and effective treatment modality to provide optimal esthetics and enhanced comfort with lesser pain to the patients during the treatment for

gingival hyperpigmentation. However, surgical stripping is a cost-effective procedure for achieving gingival depigmentation. Higher patient preference and pain reduction favor laser depigmentation, but more sites showed repigmentation. The lower cost of surgical stripping and the lower rate for repigmentation favor the old technique. Further studies with a larger study samples and a longer follow-up period would be desirable with special concern on multiple laser sessions to reach a solid evidence based conclusion regarding which technique is better keeping in mind the effect on repigmentation.

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