EFFICACY AND SAFETY OF FRACTIONAL CARBON DIOXIDE LASER FOR TREATMENT OF FACIAL FRECKLES

A thesis
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Abstract

Background: Newly developed lasers produce excellent results with minimal complications compared with traditional treatments for freckles.

Objectives: To assess the efficacy and safety of the fractional CO2 laser in the treatment of freckles.

Patients and Methods: Twenty patients performed a single session of fractional carbon dioxide laser resurfacing then were followed up a month later. Photographs were performed before treatment and a month later at the end of the follow up period. They were examined by three blinded investigators.

Results: After patient assessement, it could be shown that 2 (10%) patients showed grade 1 improvement, while 8 (40%) patients showed grade 2 improvement. Nine (45%) patients showed grade 3 improvement and finally only 1 (5%) patient showed grade 4 improvement.

Conclusion: Fractional ablative carbon dioxide laser resurfacing proved to be effective in the treatment of facial freckles. It is a safe and cheap alternative treatment compared to other lasers.

Keywords:

(Freckles, Ablative fractional CO_2 laser)

CONTENTS.

List Of Abbreviations

µm	**micrometer**
AHAs	**Alpha hydroxy acids**
Cm	**centimeter**
CMN	**congenital melanocytic nevi**
CO2	**Carbon dioxide**
DNA	**Deoxy-ribo-nucleic acid**
Er	**Erbium**
GA	**Glycolic acid**
HQ	**Hydroquinone**
HSV	**Herpes simplex virus**
IPL	**Intense pulsed light**
J	**joule**
KA	**Kojic acid**
kHz	**kilohertz**
KTP	**potassium titanyl phosphate**
LSR	**Laser Skin Resurfacing**
MC1R	**melanocortin 1 receptor**
mm	**millimeter**
ms	**millisecond**
MTZs	**Microscopic Thermal Zones**
Nd:YAG	**neodymium yttrium aluminium garnet**
nm	**nanometer**
PIH	**Postinflammatory hyperpigmentation**
PLDL	**pulsed pigmented lesion dye laser**
QSAL	**Q-switched Alexandrite laser**
QSRL	**Q-switched Ruby laser**
Q-switched	**Quality swithched**
RNA	**ribo-nucleic acid**
TCA	**trichloroacetic acid**
UV	**ultraviolet**
W	**watt**
YSGG	**Yttrium Scandium Gallium Garnet**
µs	**microsecond**

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INTRODUCTION AND AIM OF WORK

Freckles are clusters of concentrated melanin that are most often visible on people with a fair complexion. Freckles do not have an increased number of melanin producing cells. Affection by freckles is genetic and is related to the presence of melanocortin 1 receptor gene variant ***(Plensdorf and Martinez, 2009).***

It is triggered by exposure to sunlight. Ultraviolet B rays activate melanocytes to increase melanin production which can cause freckles to become darker ***(Roshkar and fitzpatrick, 2006).***

Freckles affect mostly face and sun exposed areas.They appear as flat brown or red macules that fade in winter, usually in a fair complexioned patient, but may be present in other skin types ***(Kerry et al., 2006).***

Regular use of sunblocks inhibit their development markedly.There are different lines of treatment of freckles: topical bleaching creams, chemical peeling, cryosurgery (light freeze with liquid nitrogen) and laser freckle removal. But the best evidence is for laser therapy that acts by removal of melanin pigment from freckles by using laser light, e.g.: Q-switched lasers such as the alexandrite laser, the ruby laser and the Nd: YAG laser ***(Geronemus, 2006).***

The gold standard in the industry for non-surgical facial rejuvenation, removal of wrinkles, pigmentation, and general sun damage has been the carbon dioxide (CO_2) laser since the mid 1990s. The traditional CO_2 laser was very effective, however it fell out of favor because it required general anesthesia. It also had a prolonged recovery time. Over the last several years, advances in technology known as fractional resurfacing has made

the CO_2 laser popular again: fractional CO_2 laser treatment is one of the newest laser rejuvenation technologies ***(Tierney et al., 2009).***

The fractional CO_2 laser is a mico-ablative laser, meaning that it drills a microscopic zone within the skin. The skin is vaporized and allows for collagen to stimulate and fill in the column that was created. Between these microscopic zones, there are columns of intact skin that was not affected by the laser. These untreated areas allow for faster recovery and healing compared to the traditional CO_2 laser. This means that patients can return back to work in a matter of a few days as opposed to weeks. In addition, the fractional technology makes the CO_2 laser a lot safer as well. It is characterized by having less than a week downtime without significant sloughing, crusting and oozing. Most patients feel like they have had a sunburn and most resume normal activity in about 4 to 5 days. After the first few days, there may be some residual redness but patients can resume normal activity and the redness can be covered with a makeup ***(Tierney et al., 2011).***

Nowadays, fractional CO_2 laser is used in skin rejuvenation, treatment of wrinkles, scars and in pigmentation disorders. To the best of our knowledge, based on a thorough search of literature, no clinical studies assessing fractional CO_2 laser in the treatment of freckles could be retreived.

Aim of work:

This study was designed to assess the efficacy and safety of the fractional CO_2 laser in the treatment of facial freckles.

FRECKLES

I. Definition:

An acquired benign pale-brown, macular lesion, usually less than three millimeters in diameter with a poorly defined lateral margin, which appears and darkens more commonly on light-exposed skin sites during periods of ultraviolet (UV) rays exposure ***(Bastiaens et al., 2001).***

II. Clinical features:

At any age, simple freckles are not associated with other skin conditions and are commoner in individuals who are red or fair-haired and fair-skinned (figure 1). Lesions appear as light or dark brown macules over sun exposed areas such as the face, hands and neck. The lesions fade during the winter months ***(Newton Bishop, 2010).***

Simple freckles are absolutely harmless. They are not cancerous and generally do not become cancerous ***(Newton Bishop, 2010).***

Rare concerns about freckles may arise when they are associated with other diseases, like:

1. **Xeroderma pigmentosum:** which is a recessive chromosomal disorder where there is a failure of DNA repair after sun exposure. Clinically, it is characterized by presence of freckles

at all sun exposed areas, and hyperpigmented plaques and nodules that may develop into squamous cell carcinoma and basal cell carcinoma ***(McLean and Gallagher, 1995).***

2. **Neurofibromatosis:** the freckles and café-au-lait spots of neurofibromatosis are distinguished as they are commonly on the trunk and axilla, and other features of neurofibromatosis may be present, such as hypopigmented macules, skin nodules, and sometimes nerve compression symptoms such as convulsions ***(McLean and Gallagher,1995).***

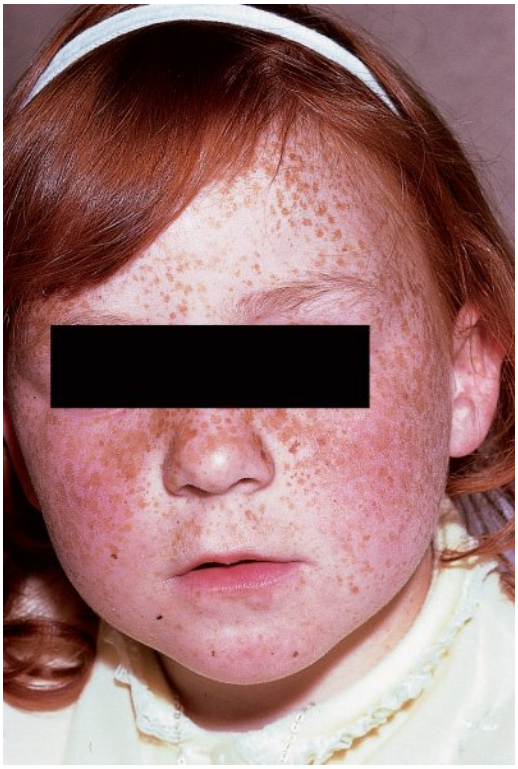

Figure (1): Freckles in a child with red hair: freckles are indicative of fair skin vulnerable to sunburn *(Newton Bishop, 2010).*

III. Differential diagnosis:

Lentigens are macular hyperpigmented skin lesions that persist throughout the year, which are commonly due to sun exposure or rarely as a part of a multisystem disorder. They can be easily confused clinically with freckles. However, the lentigen can be differentiated by the fact that it persists in the absence of UV stimulation, and histologically it has a linear increase of melanocytes at the dermo–epidermal junction, while the freckles histopathology shows an increased amount of pigment and melanophages and increased size of melanocytes without increase in number. The two entities coexist in the same individual and the risk factors for both are generally the same ***(Newton Bishop, 2010).***

Freckles may be also confused with the following more serious conditions:

(1) Lentigo maligna ("malignant freckle"): This is an uncommon superficial skin cancer that generally occurs on the faces of older adults due to sun exposure. This condition may, if untreated, develop into a more aggressive malignant variety called lentigo maligna melanoma. Skin biopsy can help diagnose lentigo maligna ***(Rajpar and Marsden, 2006).***

(2) Melanoma: A malignant tumour arising from the epidermal melanocyte occurring more commonly in Australia, New Zealand, North America and Europe where skin is very fair. Melanoma is predominantly a cancer of white-skinned people,

which gave the first clue that sun exposure is causal. In comparison with benign (non-cancerous) freckles, melanomas tend to be larger, darker, and have more irregular color and shape variations. It may occur alone or on top of a previous nevus ***(Gandini et al., 2005).***

IV. Pathology:

Light microscopy examination of freckles shows an increased amount of pigment and melanophages and increased size of melanocytes. The keratinocytes often display atypical features such as enlarged nuclei, giant size, or fibrillar degeneration. Homogenization of the papillary dermis can be seen. The activation of melanocytes is usually confirmed electron microscopically, and pathological features such as large amounts of lipid droplets and lysosome-melanosome complexes within the melanocytes are usually seen. The Langerhans cells are mostly normal, whereas the keratinocytes show cytolytic changes, fibrillar degeneration, and vacuolization. It arises as a result of temporary overproduction of melanin by a normal quantity of melanocytes due to stimulation by UV radiation. It has been claimed that the melanocortin 1 receptor gene (MC1R) is the major freckle gene, and that *MC1R* gene variants are required for the development of freckles, but it is still unclear what mechanism underlies this. It has been even speculated that the signal for increased transfer of pigment from the melanocyte might come from the keratinocyte ***(Bastiaens et al., 2001).***

V. Treatment:

Freckles are considered an aesthetic nuisance to some patients, particularly in the western culture. Different therapeutic modalities, including topical skin lighteners, cryotherapy, chemical peels, and more recently pigment-specific lasers and light sources, have been tried to remove these freckles, with acceptable clinical success ***(Rashid et al., 2002).***

A) Topical skin lighteners:

Topical agents include phenols (hydroquinone), retinoids (tretinoin), azelaic acid, kojic acid and glycolic acid.

1-Hydroquinone:

Hydroquinone (HQ) 2%–4% has been widely used for freckles therapy. It inhibits the conversion of dopa to melanin by inhibiting the activity of tyrosinase. Moreover, it has been proposed that it may interfere with DNA and RNA synthesis, degrade melanosomes, and destroy melanocytes ***(Mahé et al., 2005).***

There are rare case reports of allergic contact dermatitis to HQ, however, irritant reactions are more common. So it is recommended that patients test HQ on a hidden area, e.g the upper inner arm, prior to use on areas that are especially visible, such as the face. Other side effects include: post-inflammatory hyperpigmentation, nail bleaching and rarely, ochronosis-like pigmentation ***(Mahé et al., 2005).***

2-Retinoids:

Topical tretinoin 0.05%–0.1% reduces pigmentation by inhibiting tyrosinase transcription, as well as by interrupting melanin synthesis. While tretinoin may be effective in reducing freckles, it typically takes at least 24 weeks to see clinical improvement. It may also increase pigmentation secondary to irritation and may cause erythema and peeling. Other retinoids including adapalene, tazarotene and topical isotretinoin can be also used in treatment ***(Barrientos et al., 2001).***

3- Azelaic Acid:

Azelaic acid 15%–20%, a C9 dicarboxylic acid, is a reversible inhibitor of tyrosinase and may also have both cytotoxic and antiproliferative effects on melanocytes. In a randomized, double-blind study, azelaic acid was shown to be as effective as HQ 4% but without its side effects. The combination of azelaic acid with 0.05% tretinoin or 15%–20% glycolic acid may produce earlier, more pronounced skin lightening. Adverse effects include pruritus, mild erythema, scaling, and burning ***(Halder and Richards, 2004).***

4- Kojic Acid:

Kojic acid (KA) 2% is produced by the fungus *Aspergilline oryzae* and is a tyrosinase inhibitor. It is generally equivalent to other therapies but may be more irritating. In one double-blind study, KA 2% combined with HQ 2% was shown to be superior to glycolic acid (GA) 10% and HQ 2%. Another double-blind study