DIFFERENT THERAPEUTIC MODALITIES FOR TREATMENT OF MELASMA

THESIS
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BY

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AHAs	Alpha-Hyroxy Acids
APPA	(5-[3aminopropyl)-phosphino-oxy]-2-(hydroxymethyl)-4H-1-pyra n4-on)
ASIP	Agouti Signaling Protein
AZA	Azelaic Acid
cAMP	Cyclic Adenosine Monophosphate
DHIA	5,6-Dihydroxyindole-2-Carboxylic Acid
DNA	Deoxyribonucleic Acid
GA	Glycolic Acid
HIV	Human Immunodeficiency Virus
HQ	Hydroquinone
JS	Jessner's Solution
KA	Kojic Acid
LSD	Least Significant Difference
MASI	Melasma Area and Severity Index
MBEH	Monobenzyl Ether of Hydroquinone
MC1R	Melanocortin Receptor 1
MELASQOL	Melasma Quality Of Life Index
Mitf	Microphthalmia -associated transcription factor
MSH	Melanocyte Stimulating Hormone
Nd-YAG	Neodymium-doped yttrium aluminium garnet
NO	Nitrous Oxide

ODA	Octadecene dioic acid
OCPs	Oral Contraceptive Pills
OPT-IPL	Optimal Pulse Technology- Intense Pulse Light
PA	Pyruvic Acid
PAR-2	Protease-Activated Receptor 2
PGE2	Prostaglandin E2
PF	Protective factor
QASAL	Q-switched Alexandrite LASER
RA	Retinoic Acid
Re	Resorcinol
RNA	Ribonucleic Acid
SA	Salicylic Acid
SCP	Superficial Chemical Peeling
SPF	Sun protective factor
SPSS	Statistical Package for Social Sciences
STT	Soybean Trypsin Inhibitor
TCA	Trichloroacetic Acid
TGF	Transforming Growth Factor
TRPs	Tyrosinase Related Enzymes
TxA2	Thromboxane A2
UV	Ultraviolet

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ABSTRACT

Background: Treatment of melasma remains an enigma due to prolonged time to respond as well as the substantial relapse rate. Chemical peels have become a popular modality in the treatment of melasma. Also topical depigmenting agents used for treatment of melasne are widely available.

Objective: To compare the clinical efficiency of chemical peeling using trichloroacetic acid 20% versus Jessner's solution versus the topical use of a mixture of hydroquinone 2% and kojic acid.

Patients and methods: Forty five patients with melasma were randomly assigned into three groups of fifteen patients each. Group A received Jessner's solution peels (4 coats), group B received TCA 20% peels and group C received topical hydroquinone 2% and kojic acid to be used at night for 2 months. Groups A and B were primed with tretinion 0.05% for 2 weeks and peeling sessions were done on weekly basis for 6 weeks. All patients were seen in follow-up period after 16 weeks clinical evaluation using MASI score and photography were recorded before after treatment and also after 16 weeks (follow-up period). Side effects and subjective improvement were noted.

Results: There was an overall decrease in MASI score in all three groups after treatment and after follow-up period but after treatment it was highly significant between groups A and C (P=0.01) and groups B and C (P=0) but not between groups A and B. After the follow-up period, MASI score was highly significant between groups B and C (P=0) and significant between groups A and B and A and C ($P<0.05$).

Conclusion: Chemical peeling using TCA 20% showed better results than Jessner's solution as peeling agent and hydroquinone 2% with kojic acid as a topical agent in the treatment of melasma.

Key Words: Melasma – Chemical peeling – TCA- Jessner's – Hydroquinone-Kojic acid

Introduction and Aim of Work

Normal skin color results from an admixture of several colored pigments: haemoglobin carotenoids and melanins, of which the latter are more important. Melanin pigmentation is a multistep complex process involving both melanocytes and keratinocytes in the epidermal melanin unit ***(Ortonne and Bose,1998).***

Any pigmentary modulation from normally genetically programmed pigmentary control by exogenous (light, chemicals, local infection) or endogenous (hormones, drugs) factors leads to pigmentary abnormality ***(Ortonne and Bose,1998).***

Hyperpigmentation is a darkening of the skin, which typically results from increased melanin. This may occur in the epidermis, dermis, or both Either increased melanin production by existing melanocytes (melanotic hyperpigmentation) or proliferation of active melanocytes (melanocytic hyperpigmentation) is responsible ***(Cayce et al,2004).***

Hyperpigmentation is a common disorder of the skin, particularly in brown-skinned patients ***(Cayce et al,2004).*** Hyperpigmentation disorders include a multitude of forms. They are typically divided into three large categories: dermal, epidermal, or mixed, depending on the site of abnormality. The location of the increased melanin affects treatment options **(*Cayce et al,2004*).** Epidermal involvement appears as brown discoloration, dermal as

blue-gray, and mixed epidermal and dermal as brown-gray ***(Pandya and Guevara,2000).***

A variety of skin diseases could be presented by dermal hyper pigmentation like melasma ***(Gupta et al,2006)***, post inflammatory, drug induced ***(Dereure,2001),*** Mycosis Fungoides ***(Kikuchi et al,1996),*** Nevus Of Ota , Nevus Of Ito, Incontinentia pigmenti, macular amyloidosis ***(Cayce et al,2004),*** hyperthyroidism, Addison's disease ***(Banba et al,1999)*** and others.

Melasma or cloasma or mask of pregnancy is a common disorder of macular hyperpigmentation which involves mostly sun-exposed areas of the face and neck. Those most affected are women. Multiple factors have been postulated in the etiology and pathogenesis of melasma including race, pregnancy, oral contraceptives, genetics, sun exposure and cosmetics. Many cases also showed the development of melasma without any of these predisposing factors. It was even seen in men ***(Kauch and Zachian,1999) .***

Several therapeutic modalities either alone or in combination protocols had been studied like combination of Q-switched alexandrite laser or the pigmented lesion dye laser, and at the same session 15-25% trichloroactic acid (TCA) with or without Jessner's solution were used for the chemical peeling ***(Ga-YoungLee et al,2002).*** Q-switched ruby laser and Q-switched Nd-YAG ***(Ogata,1997),*** chemical peeling solutions using alpha-hydroxy acid ***(Briden,2004),*** lactic acid and Jessner's solution ***(Sharquie et al,2006)***.

Although melama has been studied, its pathogenesis remains largely unknown and its treatment is still met with difficulty ***(Victor et al,2004)***

Aim of the work

The aim of the work is directed to compare the efficacy of chemical peeling and topical hypopigmenting agents as different therapeutic modalities for melasma and to compare efficacy of different types of chemical peeling.

MELASMA

Definition

Facial hyperpigmentation is a broad term usually reflecting an increased amount of melanin either within the epidermis, the dermis, or both. Many factors might be responsible for facial hyperpigmentation and the increased pigment might be a local phenomenon or a manifestation of a generalized disorder. In addition, the hyperpigmentation might be acquired, congenital, or inherited ***(Jimbow and Minamitsuji,2001)*** .

Melasma is derived from the Greek word melas, meaning black. It is also referred to as chloasma and mask of pregnancy. It is defined as a light to dark brown and ashen gray-brown on occasions, irregular hypermelanosis of the face and neck, ***(Perez-Bernal et al,2000)*** . Although melasma is the most common cause of facial pigmentation, there are many other forms such as ashy dermatosis, Riehl's melanosis, poikiloderma of Civatte, erythrosis peribuccale of Brock, and drug-induced and postinflammatory hyperpigmentation ***(Katsambas and Antoniou,1995 and Schwartz,2004)*** .

Epidemiologic data

The true incidence of melasma is unknown. The over-the-counter dispense of bleaching agents contributes to the limitation of valid incidence study results. The disease affects predominantly women, with men comprising only 10% of all cases. All racial groups are affected. but melasma is most prevalent in darker-complexioned individuals (skin types IV-VI) **(Table 1)**. East Asian and Southeast

Asian origin who live in areas of intense ultraviolet (UV) radiation. Melasma and postinflammatory hyperpigmentation are quite common among black patients, cited as the third most common reason for seeking private practice dermatology care ***(Grimes,1995).***

Table 1: Fitzpatrick's classification of sun-reactive skin types

Skin type	Reaction to Moderate sun exposure*	Skin Color
Melanocompromised		
I	Burn, no tan	Pale white
II	Burn, minimal tan	Pale white
III	Burn, then tan well	White
Melonocompetent		
IV	Tan, no burn	Light brown
V	Tan, no burn	Brown
VI	Tan, no burn	Dark brown

*Thirty minutes unprotected sun exposure i.e. without sunscreen, in peak season (spring or summer)

(Fitzpatrick and Ortonne, 2003)