South Beach Symposium
clinical + aesthetic dermatology
SBS PART I
THE MEDICAL DERMATOLOGY Summit
WWW.LIVDERM.ORG

Melasma: Clinical and Aesthetic approaches

Amy McMichael, MD
Professor and Chair
Department of Dermatology
Wake Forest Baptist Medical Center
Winston-Salem, NC

1

ETIOLOGY

- Melasma is a common, chronic, and recurring disorder of hyperpigmentation arising from hyperfunctional melanocytes that deposit excessive amounts of melanin in the epidermis and dermis
- Melasma is most common in women, especially during reproductive age
- Occurs on the face and other body areas with high amounts of sun exposure
- Many contributing factors in pathogenesis of this condition: genetics, sun exposure, hormonal effects, pregnancy, and medications.

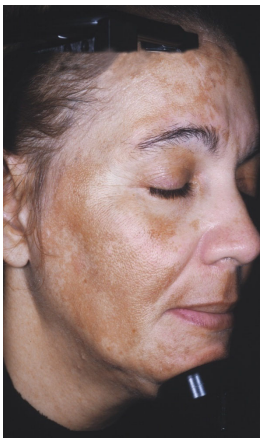
2

HISTOLOGIC TYPES OF MELASMA

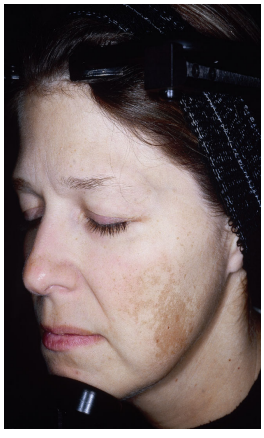
- Epidermal melasma – most common; most treatable form
  - 70% to 94% of cases
  - Hyperpigmented macules of brown color
  - Pigmentation intensified under Wood's light
- Dermal melasma – less common; difficult to treat
  - Hyperpigmented macules of blue-gray color
  - Pigmentation not intensified under Wood's light
  - No treatment to date
- Mixed melasma
- Vascular component of disease

3

CLINICAL PATTERNS OF MELASMA



- Centrofacial (63%)
  - Malar (21%)
- Mandibular (16%)



4

IMPACT ON PATIENT

- Embarrassment
- Social contact may become distressing
- Superstition: Considered bad luck in some cultures
- Treatments may be lengthy, and sun exposure may rapidly reverse all benefits of treatment
- Skin irritation may occur during therapy

5

QUALITY OF LIFE IN PATIENTS WITH MELASMA

BALKRISHNAN R, CAMACHO MS, SALTZBERG, HOUSMAN T, GRUMMER S, FELDMAN S, MCMICHAEL A, CHREN M-BJD 2003

- Study of 102 women, quality of life instrument was administered to melasma patients
- High correlations in quality-of-life domains between the MELQOL and the SKINDEX-16, the DLQI, and skin discoloration evaluation
- Social life, recreation and leisure, and emotional well being are most affected life domains

6

PRINCIPLES OF MELASMA THERAPY

- Protection from sun exposure
- Inhibition of tyrosinase activity
- Removal of melanin
- Destruction or disruption of melanin granules

7

INHIBITION OF TYROSINE

- Hydroquinone (4%)
  - Has been in use for 50 years
  - Can ↑ concentration to 10%, but risk of ochronosis also increases
  - OTC formulations (2%) are relatively ineffective
- Usually involves up to 20 weeks of treatment for results
  - Efficacy plateaus after 4-6 months
- Penetration can be increased through concomitant use with tretinoin
- Arbutin: derivative of hydroquinone
- Licorice Extract, kojic acid

8

DISRUPTION OF MELANIN GRANULES

- Lasers (careful in skin of color patients)
  - Q-switched Ruby
  - Q-switched Alexandrite
  - Q-switched Nd:YAG
  - Newer Lasers
- Used in conjunction with lightening agents (pre/post therapy)

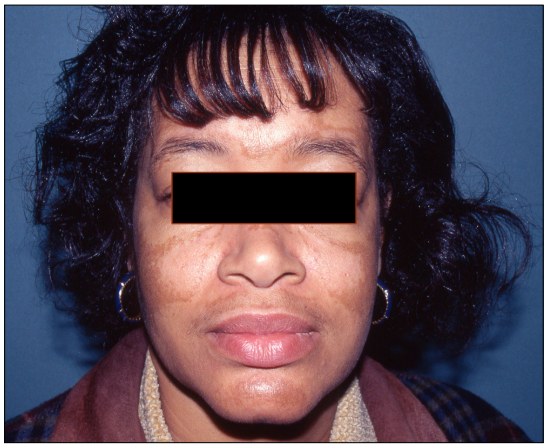
9

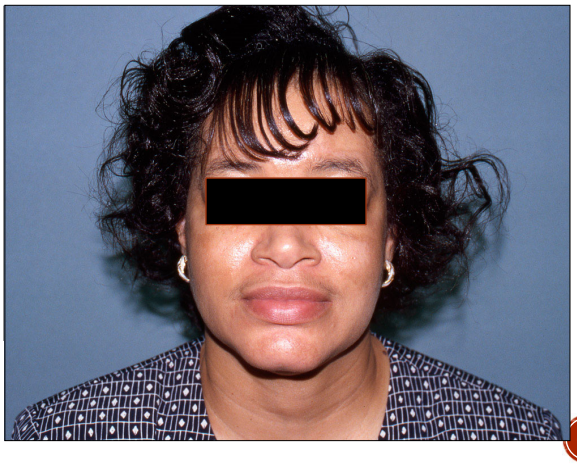
REMOVAL OF MELANIN

- Chemical peels
  - 20 to 35% trichloroacetic acid (TCA) peels
  - Modified TCA peels
  - Jessner's Solution
  - Glycolic acid
  - Salicylic acid
- Microdermabrasion (transient improvement)
- Used in conjunction with lightening agents
- Cryosurgery

10

MELASMA TREATMENT WITH TRIPLE COMBINATION THERAPY

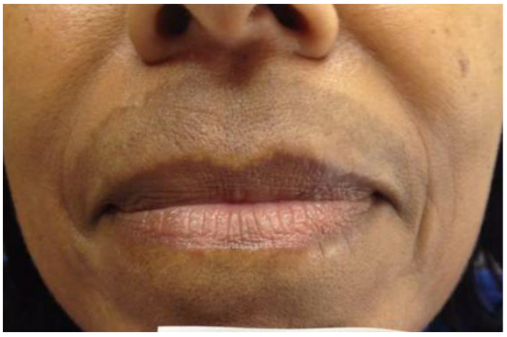


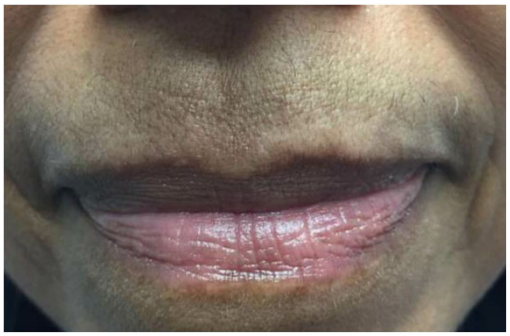


11

PRE AND POST TREATMENT MELASMA

TRIPLE COMBINATION TREATMENT TO HYDROQUINONE

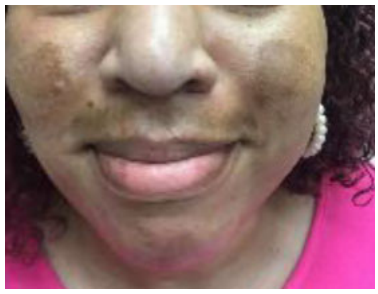




12

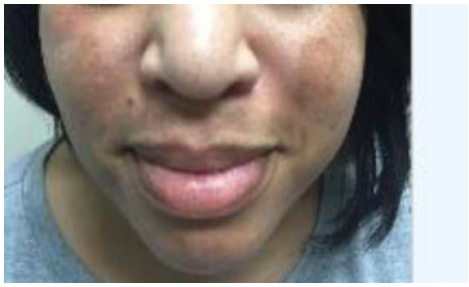
COMBINATION TREATMENTS FOR MELASMA

Baseline



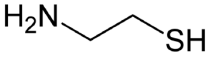
Post triple combination

Post triple combination and topical cysteamine



13

CYSTEAMINE



- Simplest aminothiol physiologically produced in human cells from cysteine
- Used as a non-prescription 15 min contact topical cream
- Interest in cysteamine arose as concerns of hydroquinone toxicity increased

In 1966

Chavin injected Cysteamine into black goldfish skin and observed significant skin depigmentation

Chavin W. et al, 1966, Die Naturwissenschaften 53(16):413-414

THERAPEUTICS — British Journal of Dermatology

Evaluation of the efficacy of cysteamine 5% cream in the treatment of epidermal melasma: a randomized double-blind placebo-controlled trial

P. Mansouri,[1,2] S. Farshi,[1,2] Z. Hashemi[1] and B. Kassaee[3]

[1]Department of Dermatology, Imam Hospital; [2]Skin and Stem Cell Research Center and [3]Deputy of Health Section, Tehran University of Medical Sciences, Tehran, Iran; [4]Exeltis Pharma SA, Geneva, Switzerland

Summary

Correspondence

Accepted for publication

Funding sources

Conflicts of interest

DOI 10.1111/bjd.13424

Background Melasma is a difficult-to-treat hyperpigmentary disorder. While cysteamine is a known potent depigmenting agent, its efficacy in treating melasma has not been tested.

Objective To study the efficacy of cysteamine 5% cream in the treatment of patients with epidermal melasma.

Method In this double-blind randomized study, participating patients (n = 50) received either placebo (n = 25) or cysteamine cream (n = 25). Cysteamine cream or placebo were applied on the lesions once a day at bedtime over 4 months. The efficacy of treatments was determined through Mexameter skin colorimetry, Melasma Area Severity Index (MASI) score, Investigator's Global Assessment (IGA) and patients' questionnaires, all performed at baseline and after 2 and 4 months of treatment.

Results At baseline, the mean differences between pigmented and normal skin (calculated by Mexameter) were 75·2 ± 17 and 68·9 ± 11 in the cysteamine and placebo groups, respectively. After 2 and 4 months of application of cysteamine and placebo cream, the mean differences were 19·7 ± 14·4 and 34·2 ± 16 in the cysteamine group, and 43·8 ± 23·4 and 60·7 ± 27·3 in the placebo group, respectively. Statistically significant differences were found between the group outcomes at both points ($P = 0·001$ and $P < 0·001$). At the end of the treatment, the MASI scores were significantly lower in the cysteamine group vs. placebo (7·7 ± 5·5 vs. 11·6 ± 7·9, $P = 0·02$). The IGA and patients' viewpoints indicated significant efficacy of cysteamine cream vs. placebo.

Conclusions Cysteamine cream showed significant efficacy in the treatment of melasma.

What's already known about this topic?

- Melasma is an acquired hyperpigmentary disease that is hard to treat.
- Cysteamine is known to be a depigmenting agent, but has not been studied as the treatment of melasma.

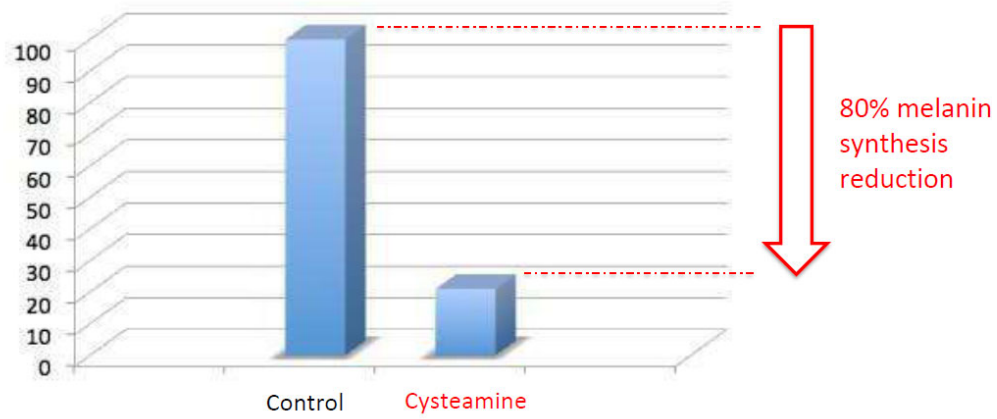
What does this study add?

- Cysteamine showed greater efficacy than placebo in the treatment of melasma, at both 2 and 4 months.
- Cysteamine showed significant efficacy both by Investigator's Global Assessment and patients' viewpoints.

14

In 2000s

interests for Cysteamine resumed as HQ toxicity emerged



In vitro study on the depigmenting effect of Cysteamine resulted in **80% reduction of melanin synthesis in B16 melanocytes**

Qui L. et al, J. Invest Dermatol. 2000 Jan;114(1):21-7

15

15

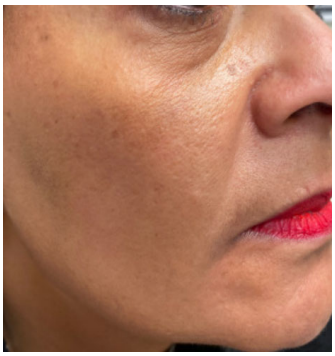
FOR RESISTANT MELASMA, CONSIDER TRANEXAMIC ACID

- Oral tranexamic acid (TA) is a synthetic derivative of the amino acid lysine that works as a anti-fibrinolytic agent
- TA works via the inhibition of ultraviolet-induced plasmin activity in keratinocytes
- TA competitively inhibiting the activation of plasminogen activator (PA) through reversible interactions with its lysine-binding sites inhibiting PA from converting plasminogen to plasmin
- Typical dose is 250 mg twice daily
- Duration of treatment varies among studies (3-9 months)
- **Screen out patients with history of: thromboembolism, stroke, heart disease**
- Few side effects noted in most studies: mild GI upset, palpitations, oligomenorrhea, urticarial rash
- Can use topical tranexamic acid

Lee HC, et al. JAAD 2016;75: 385-392
Zhang L et al. Biomed Res Int. 2018; 1683414

16

TRIPLE COMBINATION AND TRANEXAMIC ACID



17

17

MELASMA THERAPEUTIC LADDER

- Sunscreen, sunscreen, sunscreen (prefer inorganic, tinted)
- Hydroquinone 4% or triple combination bleaching agents
- Cysteamine topical
- Topical tranexamic acid, topical Vitamin C, microdermabrasion, chemical peels
- Micro-needling with PRP
- Oral tranexamic acid
- Rarely use >4% concentration hydroquinone
- 5 minutes in the sun will undo all your work

18

18