Cysteamine – Towards A Novel First Line Treatment for Melasma?

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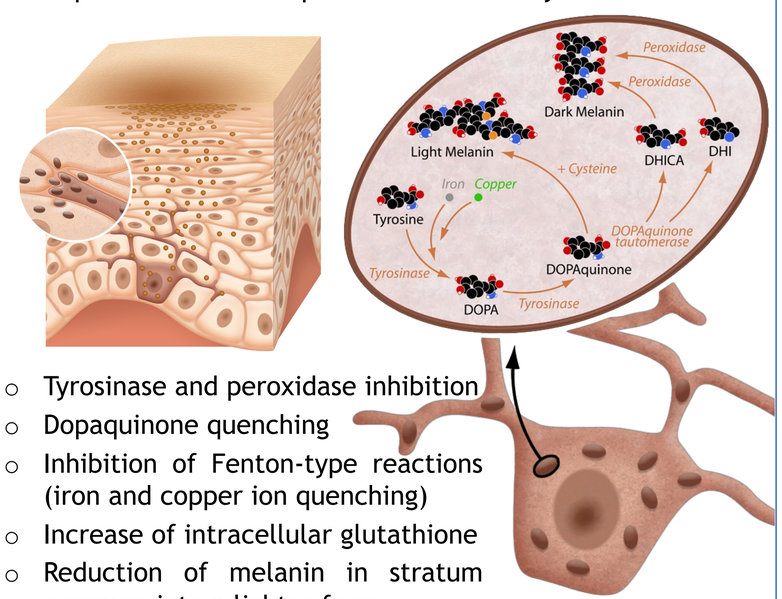
INTRODUCTION

- Cysteamine is the simplest aminothiol physiologically produced in human cells. First shown to have a significant depigmenting activity in 1960's, it was only recently stabilized for use in topical products. Topical cysteamine 5% is shown to be significantly effective for melasma in various clinical trials.
- Kligman's formula remains to date the dermatologists' treatment of choice for melasma, yet side effects and draw-backs are significant: ochronosis, skin atrophy, irritation, photosensitivity and post inflammatory hyperpigmentation.
- Reported to be significantly more potent than hydroquinone in vivo, no comparison have been reported in human.

BACKGROUND

- Cysteamine HCl. was discovered for its physiologic activity in skin pigmentation in 1966 when Chavin investigated the physiology of black goldfishes[(1)].
- In 1968, superior efficacy compared to hydroquinone on mammalian skin was established[(2)], and later its potency was quantified at 80% melanin synthesis reduction in vitro[(3)].
- In 2010 cysteamine was stabilized for use in a topical product
- Cysteamine 5% was reported to be significantly effective for hyperpigmentation in clinical trials [(4,5,6)]:
  - 58% MASI score reduction in melasma patients
  - 67% melanin index reduction in melasma lesions
  - 90% of patients noticed moderate to significant improvements
  - Undesirable effects are non significant
- Product of natural degradation of L-cysteine, cysteamine is biosynthesized during the co-enzyme A metabolism cycle. Well distributed in mammalian tissues, its natural concentration is highest in mother milk. Cysteamine acts as an intrinsic antioxidant. It is an agent with a proven safety profile. Its protective role anti-ionizing-radiation, antitumor, anticarcinogenic and antimutagenic are well recognized[(7)]
- Multiple mechanisms explain the effect of cysteamine[(4)]:



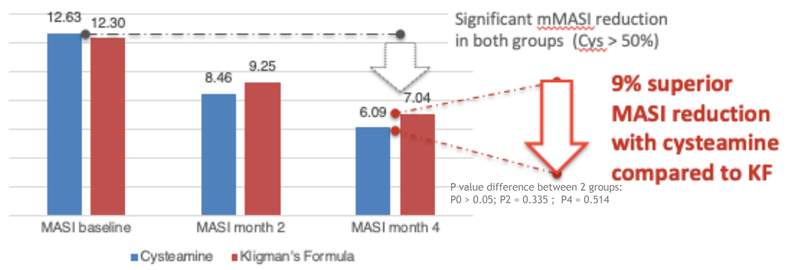
  - Tyrosinase and peroxidase inhibition
  - Dopaquinone quenching
  - Inhibition of Fenton-type reactions (iron and copper ion quenching)
  - Increase of intracellular glutathione
  - Reduction of melanin in stratum corneum into a lighter form

CLINICAL STUDY[(8)]

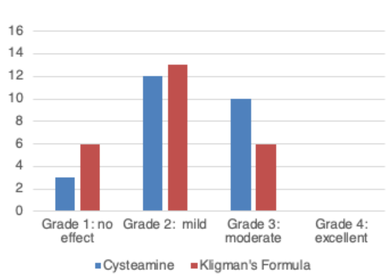
EFFICACY RESULTS

- **mMASI scores were reduced significantly in both groups.**
- **Cysteamine was significantly more effective in reducing the mMASI score at both evaluation points at 8 and 16 week; the difference was statistically significant.**
- **Both Investigator and Patients observed greater improvement with Cysteamine than with Kligman's Formula**

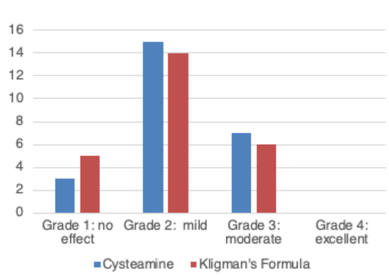
Mean MASI Scores in Melasma Patients
Comparison of Cysteamine and Modified Kligman's Formula



Investigator's Global Assessment at 4 mths
Cysteamine vs. modified Kligman's Formula



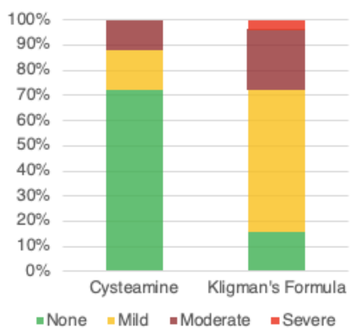
Patient's viewpoint at 4 mths
Cysteamine vs. modified Kligman's Formula



TOLERABILITY RESULTS

- **Cysteamine was significantly better tolerated by patients than modified Kligman's formula.**

Irritation score for patients at 4 mths
Cysteamine vs. modified Kligman's Formula



Cysteamine : low level of undesirable effects (28% irritation)

vs.

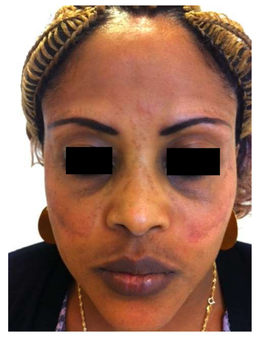
Kligman's formula : very high level of undesirable effects (84% irriation)

METHODS & MATERIALS

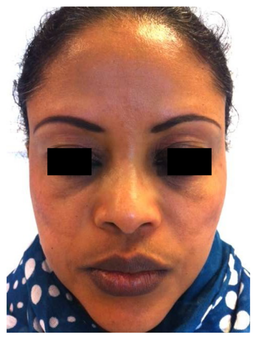
- Trial design: 50 patients; pragmatic; single-blind; randomized
- Evalutation at week 0, 8 and 16: modified MASI score determination; IGA (investigator global assessment); Patient questionnaire
- Groups: 25 patients treated with modified Kligman's formula (HQ 4%, retinoic acid 0.05%, beta-methazone 0.01%; once daily, evening, leave-on); 25 patients treated with Cyspera® cysteamine 5% (once daily, evening, 15 min. exposure). Moisturinsing once daily & sunscreen throughout the day for both groups
- Inclusion criteria: Epidermal melasma ageing more than 6 months; Female; Age 20 and 50 years; Patients not receiving any medication for at least 2 months.
- Exclusion Criteria: Any corticosteroids treatment 3 months before study; pregnancy and breastfeeding; oral contraceptive pills; endocrine diseases

CASES STUDIES

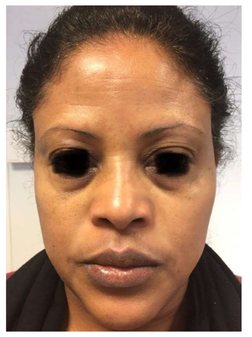
- Sporadic cases are now being reported indicating that melasma patients who are resistant to Kligman's formula can show a significant therapeutic response to cysteamine.



Patient under Kligman's formula treatment (Pigmanorm cream) for the past 3 years

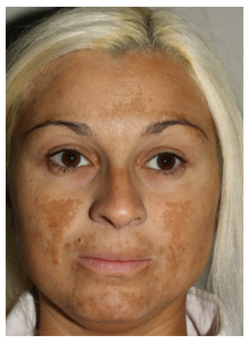


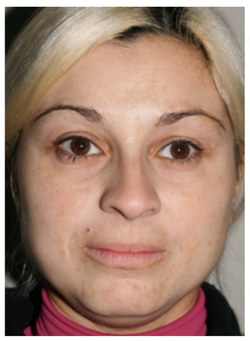
Discontinuation of Pigmanorm and treatment with Cysteamine for 4 months



continued Cysteamine use twice weekly as maintenance therapy for the past 5 years.

- This first case shows a patient with phototype V who had used Kligmans formula for 4 consecutive years with partial response and signs of skin atrophy due to this treatment that had a full therapeutic response to Cyspera (5% cysteamine cream).[(9)]





Patient treated after multiple cycles of modified Kligman's Formula.

Results are a 8 weeks combination protocol[(10)]

- In-office procedures: Full face micro-dermabrasion, 5% hydroquinone peel-off mask and Cysteamine
- Intensive phase of Cysteamine + azelaic
- Maintenance phase of cysteamine

- This second case showed that Cyspera (5% cysteamine cream) was an extremely effective, well accepted, complication-free depigmenting formulation particularly considering that both cases have been previously treated with multiple modified KF cycles.[(10)]

CONCLUSION

- Cysteamine is at least as effective as the Kligman's formula.
- Sporadic cases shows its efficacy in Kligman's formula resistant patients.
- Cysteamine is a safe molecule with anti-mutagenic, anti-carcinogenic and anti-melanoma activities.
- The high efficacy of cysteamine as well as its high safety profile in contrast to Kligman's formula makes it a very promising alternative for the treatment of melasma.
- A first option for the treatment of melasma?

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