

Original Research Article

A comparative study of the efficacy of 2% Hydroquinone, 2% Kojic acid and 30% Glycolic peel in the treatment of Facial Melasma and evaluation of melanin content using SIAscopy-A novel objective method of assessment**Dr Meena Makhecha¹, Dr Rohan Nagzarkar², Dr Yasmeen Khatib³, Dr Archana Khade⁴**¹Associate professor, ²Nagzarkar, Registrar, Department of dermatology, Dr. R.N Cooper Municipal General Hospital, Mumbai, Maharashtra, India³Associate Professor, ⁴Assistant Professor, Department of Pathology, Dr. R.N Cooper Municipal General Hospital, Mumbai, Maharashtra, India***Corresponding author**

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Abstract: Melasma is a common acquired cause of hyperpigmentation and is often difficult to treat. Several hypo pigmenting agents like hydroquinone, kojic acid and chemical peels have been used in its treatment with varying results. Spectrophotometric intracutaneous analysis (SIAscopy) is a new noninvasive technique to measure the melanin content of the skin. The objective of the study was to compare the efficacy of hydroquinone 2%, Kojic acid 2% and glycolic acid 30% in the treatment of melasma and to study the effect of the above mentioned treatment modalities on the total melanin content measured by SIAscope. There were 45 patients of facial melasma who were enrolled in the study. Three groups were made each comprising of 15 patients. One group was given daily night application of Hydroquinone (2%), second group was treated by weekly Glycolic acid peel (30%) and third group was given daily night application of Kojic acid (2%). Photographs and SIAscopy readings were taken at base-line, at 15 days & at 30 days interval following treatment. Statistical analysis of the results was done by Analysis of Variance (ANOVA) using software (Epi Info 3.1.1). Hydroquinone (2%) gave the best response followed by Glycolic acid peel (30%) and Kojic acid (2%). The reduction in total melanin content was 13.01% by using hydroquinone (2%), 9.79% by using glycolic acid peel (30%) and only 5.78% on using Kojic acid (2%). The results show that 2% hydroquinone is a better hypo pigmenting agent followed by Glycolic acid peel 30% and Kojic acid 2%. By calculating the exact reduction in total melanin content using a SIAscope an accurate and objective assessment can be made about the response to treatment in cases of melasma.

Keywords: Melasma, hydroquinone, glycolic acid, kojic acid, melanin content, SIAscopy

INTRODUCTION:

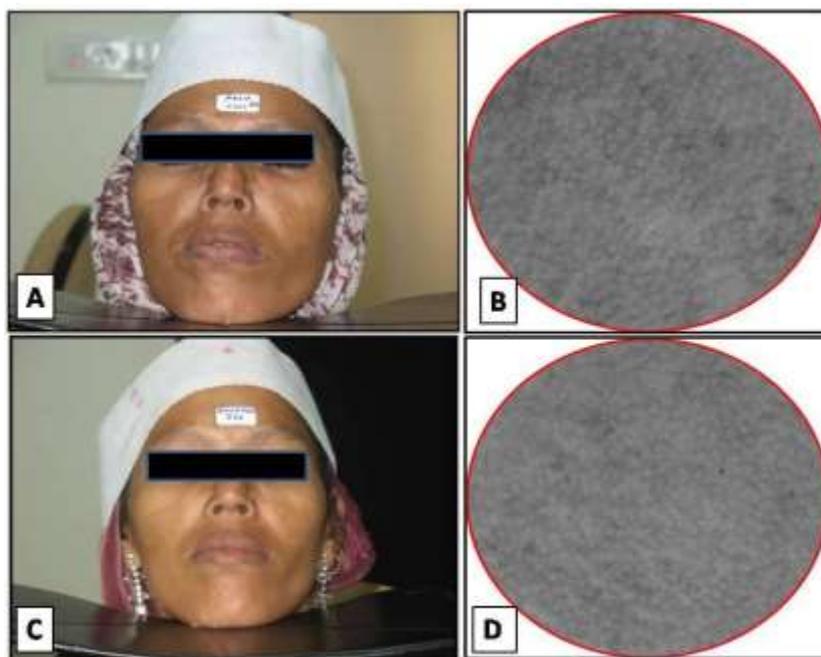
Melasma is one of the most common causes of acquired brown hypermelanosis that occurs exclusively in sun exposed areas particularly involving the cheeks, forehead, upper lip, nose and chin [1, 2]. It is characterized by symmetric, irregular medium to dark brown coloured macules and patches on the face and is found more commonly in women of reproductive age group with Fitzpatrick skin type IV-VI [3]. Genetic predisposition, ultraviolet radiation exposure, hormonal factors such as female sex hormones, thyroid disease, pregnancy and drugs such as phenytoin are the known risk factors. It causes considerable psychosocial impact and prompts affected persons to seek medical advice [3].

In the modern era, the quest of an ideal depigmenting agent started with hydroquinone, the oldest remedy, to the most recent agents like kojic acid, chemical peels, dermabrasion and lasers [4, 5]. Chemical agents like tretinoin, corticosteroids and alpha hydroxyl acids can be used in association with hydroquinone for the treatment of melasma. [3]

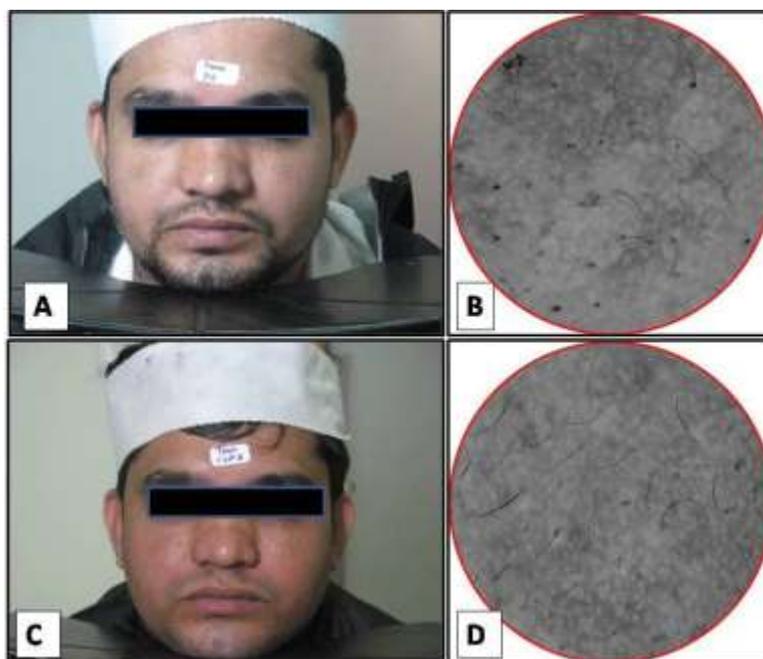
Diagnosis and evaluation of treatment of melasma can be made by clinical examination, photography, woods lamp examination, dermoscopy and confocal microscopy [3]. The severity of melasma can be estimated using colorimetry, mexametry and calculation of melasma area severity index (MASI) [4].

However most of these methods are time consuming and subjective in nature. Spectrophotometric Intracutaneous Analysis (SIA) is a fast, non-invasive and objective method to measure the amount of melanin, haemoglobin and collagen in the layers of the skin [6]. Not many studies have been done to assess

melasma using SIAscopy. Hence the present study was undertaken to compare the efficacy of hydroquinone 2%, Kojic acid 2% and glycolic acid peel 70% in the treatment of melasma and to calculate the fall in total melanin content by using SIAscopy to assess the results in an objective manner.



**Fig 1: A and B shows clinical and SIAscopy pictures before 2% hydroquinone treatment.
Fig 1: C and D shows clinical and SIAscopy pictures after 2% hydroquinone treatment with 13.6% mean reduction in total melanin**



**Fig 2: A and B shows clinical and SIAscopy pictures before 30% glycolic acid treatment.
Fig 2: C and D shows clinical and SIAscopy pictures after 30% glycolic acid treatment with 9.84% mean reduction in total melanin.**

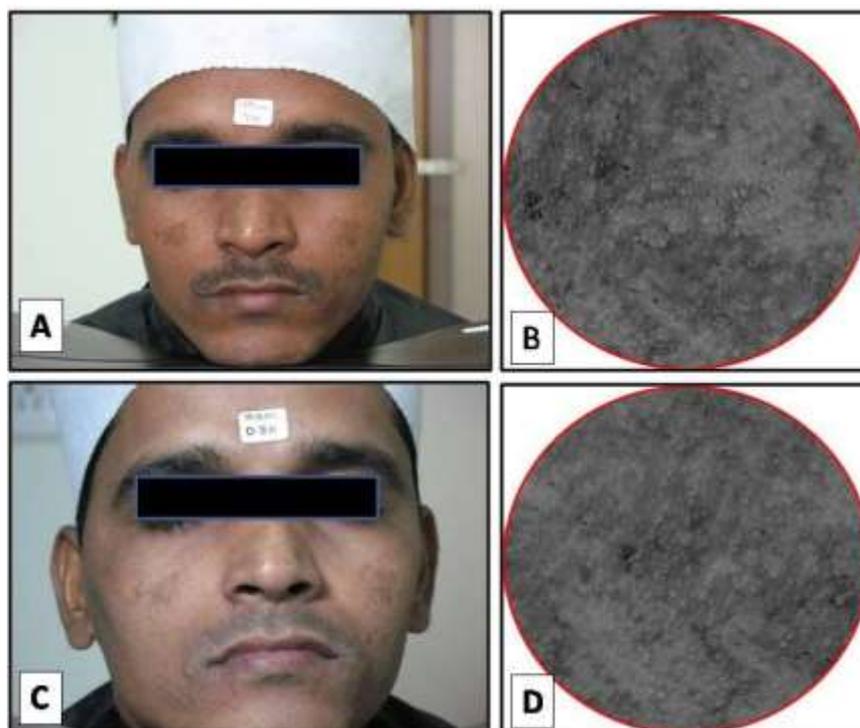


Fig 3: A and B shows clinical and SIAscopy pictures before 2% kojic acid treatment.

Fig 3: C and D shows clinical and SIAscopy pictures after 2% kojic acid treatment with 5.81% mean reduction in total melanin.

MATERIAL AND METHODS:

A prospective randomised single blind study was conducted in the outpatient department of dermatology and venereology of Dr R.N.Cooper Hospital. The study was approved by the Institutes ethics committee. A total of 45 clinically diagnosed cases of melasma of both sexes between the age group of 18yrs to 64yrs who gave their informed written consent were included in the study. A proforma was made to record the age, family history, duration of symptoms, relation to pregnancy, and use of drugs, contraceptives, cosmetics sun exposure and photosensitivity. Patients with actinic damage, on drugs known to cause or aggravate pigmentation, on therapy for other diseases and with known allergy or sensitivity to any of the ingredients present in the formulations used were excluded from the study. Out of 45 patients enrolled for the study, 3 groups A, B and C were made each comprising of 15 patients. Each group had 10 females and 5 males. Each group was studied for 1 month and subjected to 3 different drugs in randomized fashion. Patients diagnosed with melasma were counselled for treatment and explained the importance of regular follow up, expected results and possible complications. Group A patients were advised daily night application of hydroquinone (2%), group B patients were advised daily night application of kojic acid (2%) and group 3 patients were treated with a weekly glycolic acid peel (30%). Patients were advised to avoid sun-exposure and to use topical

sun-screen with sun-protection factor of 26 during the period of treatment. All 3 groups of patients were evaluated at the start of treatment, at 15 days and at 30 days after the treatment. Results were recorded subjectively with the help of visual examination and photographic evaluation and objectively by SIAscopy examination.

SIASCOPY:

Patients were taken for contact SIAscopy and SIAscans were obtained from maximum area of hyperpigmentation. Patients were scanned at three instances at 1st visit, then after 15 days of start of treatment and at end of 1 month. Each time 3 readings were taken and average of 3 was considered. The patients were examined for maximum area of hyperpigmentation on affected area of both the sides (right and left cheek). At first visit maximum area of pigmentation was noted in each patient. The affected area was measured with reference to mid - pupillary and inter - tragal axis. With the help of SIAscope total melanin pigment was measured in the most affected area. In follow up after treatment with 3 different drugs, at the end of 15 days and 1 month again same area was scanned for any reduction in total melanin content using SIAscope and noted.

PHOTOGRAPHY:

Colour photographs of face were taken at base-line and during treatment at 15 days and at 1 month.

Statistical Analysis-

We applied Analysis of Variance (ANOVA) for statistical analysis using software (Epi Info 3.1.1). A significance level of > 0.05 indicated statistically significant differences among the mean difference after 30 days of treatment with three different drugs. Also > 0.05 significance level meant a 95 percent certainty that the differences among the means are meaningful and not the result of random chance.

Observations and result:

We had enrolled 45 patients for melasma study which included 30 females (66.66%) and 15 males (33.33%). Majority of the patients were in the age group of 21yrs – 30yrs (40.1%) and 31yrs – 40yrs (33.33%). Majority (84.44%) of patients had no significant symptoms and thus sought advice only for cosmetic purpose. Only some of the patients had itching and burning (15.54%) and photo aggravation was noted in 35 (77.77%) of cases. Duration of hyperpigmentation

in majority of them (75.54%) was 0-2 yrs. Only 15 (33.33%) patients had history of long standing facial application of cosmetics that could have contributed to the pigmentation. Family history of similar lesions was noted in only 10 (22.22%) patients and 35 patients (77.77%) had no family history.

Out of 45 patients enrolled for the study, 3 groups were made each comprising of 15 patients. Each group had 10 females and 5 males. Each group was studied for 1 month and subjected to 3 different drugs in randomized fashion.

- One group for hydroquinone (2%)
- One group for weekly glycolic acid peel (30%)
- One group for kojic acid (2%).

Baseline reading for total melanin content was taken using SIAscope and then the treatment was started. In our study, results were recorded objectively with the help of SIAscope and subjectively through visual examination and photographic evaluation.(Table-1).

Table 1: Comparative evaluation of hydroquinone, glycolic acid peel and kojic acid

Treatment used	SIAscopy	Visual and Photographic evaluation
Hydroquinone 2%	13.01 % (mean % reduction in total melanin content)	10 out of 15 showed improvement (66.66 %)
Glycolic acid peel 30%	9.79 % (mean % reduction in total melanin content)	8 out of 15 showed improvement (53.33 %)
Kojic acid 2%	5.78 % (mean % reduction in total melanin content)	6 out of 15 showed improvement (40.00 %)

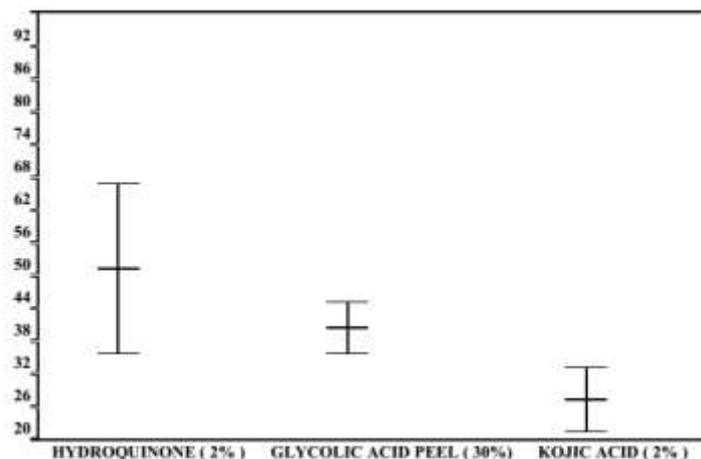
We found that among the three groups, patients who were on treatment with hydroquinone (2%) had marked reduction in total melanin content (13.01%) with 66.66% cases showing improvement. Those who were on weekly glycolic acid peel (30%) ranked second in order with 9.8% reduction in melanin and 53.33%, patients showing response. Patients on

KOJIC ACID (2%) showed only 5.78% reduction in total melanin content and only 40% showed improvement.

We applied Analysis of Variance (ANOVA) statistical method using software (Epi Info 3.1.1) and following output was generated :

Table 2: Statistical output showing better results with hydroquinone than glycolic acid and kojic acid

Source	Df	SS	MS	F	P-value
Treatments	2	20176.453	10088.226	56.4238	-0.0000
Error	87	15555.048	178.794		
Total	89	35731.501			



A significance level of > 0.05 indicated statistically significant differences among the mean difference after 30 days of treatment with three different drugs. Also > 0.05 significance level meant a 95 percent certainty that the differences among the means are meaningful and not the result of random chance

DISCUSSION:

Melasma is characterized by dark brown blotchy pigmented spots on the face and is the single largest cause of facial pigmentation. It causes considerable distress in affected persons and is difficult to treat [4]. A great deal is known about the biology and biochemistry of melanin synthesis but an acceptable means of reducing excessive melanisation is not at hand.

Hydroquinone Kojic acid and glycolic acid peels are all used in the treatment of Melasma with varying results. Of the topical treatments, hydroquinone is the most widely used and the most effective. When used at a concentration of 2% it is as effective as at higher concentrations (4 to 6%) and presents lower rates of side effects [7-11]. Apart from being a tyrosinase inhibitor it is believed to have additional actions such as degradation of melanosome, destruction of melanocytes and inhibition of DNA and RNA synthesis. These additional actions make it a better hypo pigmenting agent than Kojic acid and Glycolic acid. Its efficacy is improved when used with other agent's like tretinoin and topical steroids. Kojic acid has been demonstrated to cause depigmentation and suppression of melanogenesis. It is fungal metabolite derived from *Aspergillus*, *Acinobacter* and *Penicillium* species. It is an inhibitor of tyrosinase, the pivotal, rate-limiting enzyme in the process of melanin synthesis. With its depigmenting potential, autooxidising and antibiotic properties as well as minimal side effects, Kojic acid has become a novel 'skin brightening' agent [12].

Glycolic acid is an alpha hydroxyl acid that is used as a peeling agent in concentration of 50 to 60% at

a higher concentration; keratinocytes get totally detached resulting in "epidermolysis". Its effect on melanocyte is decreased melanin production by direct inhibition of tyrosinase. Pigmentation is also reduced because the hyper proliferative epidermal keratinocyte carry lesser melanin [13].

We found that among the three groups, patients who were on treatment with hydroquinone (2%) had marked reduction in total melanin content. Those who were on weekly glycolic acid peel (30%) ranked second in order, and patients on kojic acid (2%) also showed reduction in total melanin content but not to that extent. There have been studies comparing the efficiency of different hypo pigmenting agents. Garcia Fulton, Lim JT and Macedo *et al.*; compared the efficacy of glycolic acid peel 30% and hydroquinone 2% or kojic acid 2% for the treatment of melasma and found better results with hydroquinone treatment which was similar to our study [14-16]. Monteiro *et al.*; also found better results with hydroquinone as compared to Kojic acid with vitamin C in treatment of facial Melasma [7]. Their assessment was by calculating MASI index while we used reduction of total melanin content by SIAscopy. Study was carried out to assess the efficacy of 2% hydroquinone cream as compared to 30% glycolic acid peel. Pigmentation was measured objectively using a mexameter [17]. Hydroquinone treatment had a significant effect in reducing skin pigmentation compared with glycolic acid peel. Sarkar *et al.*; found a better response with 30% glycolic peel than a mixture of hydroquinone 4% tretinoin 0.05% and hydrocortisone acetate [3].

SIAscopy is a method of probing the skin with both visible and infrared light to return information regarding the composition, concentration and position of various chromophore within a horizontal plane. In particular the quantity of collagen within the papillary dermis, vasculature of the skin, distribution and quantity of melanin especially relative to the dermo-

epidermal junction can be assessed in a rapid non-invasive manner. Studies have shown the usefulness of this approach in the assessment of pigmented and other skin lesions [18].

There are only few studies in which SIAscope has been used to assess the severity and response to treatment in melasma. Barysch MJ *et al.*; have used SIAscope to study the melasma patients treated with non ablative fractionated photothermolysis by using reduction in total melanin content as an indicator of response to treatment as was done in the present study [19].

CONCLUSION:

The study recommends the use of SIAscope to diagnose dermatological diseases with respect to changes in total melanin, haemoglobin and collagen content. It is a very objective way of judging the response to treatment. Hydroquinone is still the most effective drug compared to glycolic acid and kojic acid. Glycolic acid also gives fairly good results.

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