

## Comparison of the Effect of Salicylic Acid Chemical Peel Combined with Topical Modified Kligman Formula and Topical Modified Kligman Formula Alone in the Treatment of Melasma

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### ABSTRACT:

#### BACKGROUND:

Many chemicals have been used in the skin peeling for melasma such as trichloacetic acid, Jessner's solution, glycolic acid, lactic acid and salicylic acid which is beta-hydroxy acid used topically in different dermatoses.

#### OBJECTIVE:

To evaluate the efficacy and safety of superficial chemical peel with salicylic acid in combination with topical depigmenting agents in comparison to depigmenting agents alone in treatment of melasma.

#### PATIENTS AND METHODS:

Eighty-eight patients with melasma (45 group-1 and 43 group -2) were selected, mostly of skin type III, IV. Most of them were females recruited in this trial, in particular those who attended outpatient's clinic, Department of Dermatology and Venereology in Sulaimania city from February 2008 to August 2008. Treatment is performed by using a combination of superficial chemical peel with salicylic acid peels of increasing strength from 20% to 30% once every 2 weeks and by application of modified Kligman formula between sessions in group -1, and topical treatment alone in group -2.

#### RESULTS:

Most of the patients had showed a good improvement in their melasma with the use of our treatment with adequate sun protection. The clinical response was much better in epidermal than mixed type and very mild in dermal. The MASI scores significantly decrease after treatment especially in epidermal type while no statistical difference was established among final MASI values of patients with mixed and dermal types ( $p < 0.000$ ) with the result being significantly higher in group -1.

#### CONCLUSION:

Superficial chemical peel with salicylic acid in combination with topical modified Kligman formula for melasma is more effective than topical modified Kligman formula alone. It is easy and cheap.

The results of the epidermal type were better than other types.

**KEYWORDS:** salicylic acid, superficial chemical peel, melasma, topical depigmented agents.

### INTRODUCTION:

Melasma is an acquired irregular brown or sometimes grey-brown hypermelanosis, which affects areas of sun exposure. The condition is seen most commonly on the face of women with skin types IV to VI. Family history was found in most of the cases<sup>(1,2)</sup>.

The two most important causative factors are sunlight and genetic predisposition and the pathogenesis of melasma is not yet fully understood<sup>(3,4)</sup>. Very recently, it has been

suggested that dermal inflammation induced by accumulation of UV irradiation may be associated with activation of fibroblasts, which result in the up-regulation of stem cell factor in melasma dermal skin leading to increased melanogenesis<sup>(5,6)</sup>.

On the basis of Wood's light examination (320-400 nm), melasma can be classified to three types: Epidermal type, dermal type and mixed type<sup>(7)</sup>.

The MASI score (Melasma Area and Severity Index) is an index used to quantify the severity of melasma and changes during therapy. The maximum value of MASI is 48 and means severe hyperpigmentation<sup>(8)</sup>.

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Treatment options of melasma includes: General measures (mostly sunscreen), topical depigmenting agents (like hydroquinone, azelaic acid, Kojic acid, retinoids, corticosteroids), chemical peels (superficial, medium and deep), laser therapy, cryotherapy and dermabrasion.<sup>(9,10)</sup>

Superficial chemical peeling (SCP) involves the application of a peeling agent to the skin, resulting in the destruction of all of the epidermis and sometimes reaching superficial dermis.

Salicylic acid is a beta-hydroxy acid agent, it is one of the superficial peeling agents being used nowadays for the treatment of various facial disorders<sup>(11)</sup>.

It is a lipophilic compound which removes intercellular lipids that are covalently linked to the cornified envelope surrounding cornified epithelioid cells. Due to its anti-hyperplastic effects on the epidermis multiple investigators have used salicylic acid as a peeling agent<sup>(12,13)</sup>.

A variety of formulations of salicylic acid has been used as peeling agents in different concentrations. In general, there are few contraindications of salicylic acid chemical peel and the Side effects of salicylic acid peeling are mild and transient<sup>(14,15)</sup>.

The purpose of the present work is to evaluate the efficacy and safety of superficial chemical peel with salicylic acid in combination with topical depigmenting agents in comparison to depigmenting agents alone in treatment of melasma.

### **PATIENTS AND METHODS:**

This is a comparative therapeutic study was conducted in consultation clinic center, Department of Dermatology and Venereology in Sulaimania city in the period between February and August 2008.

A total of 88 patients with melasma were included, their ages ranged between 18 and 50 years with mean of  $2.39 \pm 0.69$ .

Patients divided into two groups (group-1 + group-2);

1. group -1 (45 cases); treated by salicylic acid lotion as a superficial chemical peel with increasing strength once every two weeks and depigmenting agents between the sessions combined with depigmenting agents.

2. group -2 (43 cases) ; treated by depigmenting agents alone.

Patient's interview:

All patients had melasma for more than one year, with the history of multiple previous therapies for melasma. Each patient has been interviewed and

full history was taken with emphasis on the progress of melasma, previous and present medications for melasma as well as history of contraceptive pills, daily sun exposure history of pregnancy and family history. Not all patients with melasma could be put in the study; they were selected after excluding the following criteria: Pregnancy, History of keloid tendency, History of recurrent herpes simplex, History of systemic retinoid e. g. isotretinoin intake during last six months, History of chemical peeling or any other surgical procedures on the face during last six months, Patients with psychological problems which may lead to non compliance/Patients who could not keep themselves away from sun exposure especially during the course of chemical peeling.

The patients divided into group -1 (45 patients) and group-2 (43 patients) before starting our treatment. The procedure was fully described to each patient including its duration which lasting maximum of 8 weeks in which four peeling sessions will be done once every 2 weeks, also they were informed about the side effects that he or she may face from peeling. All these are made as an informed consent paper and signed by the patient with one of his or her relatives.

Wood's light examination: For each patient in either group, examination of melasma has been done by Wood's light before starting the treatment to detect the type of melasma whether it is epidermal, dermal or mixed.

Photographic assessment: for patients in either group have been taken as a baseline before starting peeling then every 2 weeks, till the last photo has been taken 2 weeks after the last session. All photographs were taken by using a Sony-Digital camera (Model DSC- W55, SONY, 7.2 mega pixels), all patients were photographed in the same place with same distance and fixed illumination.

Skin cleansing and degreasing: After cleaning face with soap and water for removing debris and make-up, cleansing and degreasing are done by using a cotton ball soaked with 25% acetone. The process must be repeated several times.

The method of treatment in the group -1 :

1. Topical depigmenting agent application:

We start by topical bleaching agent with modified Kligman formula (mometasone furoate USP 0.1% w/w, tretinoin 0.025% w/w, and hydroquinone USP 2% w/w (inform of melacare cream) 1 week before starting peeling sessions and continued between peeling sessions at night together with sunscreen at daytime.

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2. Superficial chemical peel by salicylic acid: this procedure had been done every 2 weeks, starting with concentration 20% prepared (by mixing 20gm of salicylic acid powder into absolute ethyl alcohol) in two sessions, followed by another two sessions with 30% salicylic acid (by mixing 30gm of salicylic acid powder into 100 ml of absolute ethyl alcohol). After cleansing and degreasing the face, the patient was lying comfortably on her or his back, nasolabial areas covered by vasaline, after that peeling was done with stick cotton applicator dipped in required solution with smooth strokes to the affected areas. Application was completed within 30 seconds, then termination was done by cleaning face with cold water but without rubbing, as salicylic acid doesn't need neutralization, only cold water was enough. Patients were advised to avoid washing face with soap at least for next 24 hours, with continuous advice to avoid of sun exposure and apply sun screen at daytime after peeling.

Post peeling instructions: Instruction's leaflet which specifies the date for next visit and for the patient's follow up was supplied to all the patients.

The method of treatment in group -2:

The patients in this group is treated by using topical modified Kligman formula (mometasone furoate USP0.1% w/w, tretinoin 0.025% w/w and hydroquinone USP 2% w/w) to melasma area at night and physical sunscreen at daytime for 2 months, with avoidance of any other concomitant therapy for melasma at that time.

Evaluation of the patient and follow up: Follow-up evaluation of patients was done regularly at 2 weeks intervals during peeling sessions, changes in clinical appearance were assessed, MASI score was assessed, and photographs of right, left profiles and full face were taken for each patient to assess the improvement of lesions.

The number of sessions for each patient ranged from 2 to 4 weeks depending on the patient satisfaction and the response of the treatment till the final assessment was made by 2 weeks after the last session.

Scoring system: Three independent investigators through the evaluation of serial photography; the clinical response and the rating score were as follows:

- 0% no response
- 1-25% minimal response
- 26-50% mild response
- 51-75% moderate
- Greater than 75% significant

Statistical analysis:

-Statistical package for social science (SPSS) program version 13 was used for statistical analysis  
-Before starting therapy a baseline assessment was done as well as calculation of melasma area severity index (MASI scoring). Statistical analyses were used in all parameters.

-Paired t-test was used to compare the mean of MASI change resulting from treatment.

-P values of less than 0.05 were considered significant.

### RESULTS:

A total of 88 patients: 45 patient in group - 1 (43: 96% females and 2: 4% males) and 43 patient in group -2 (100% females) with melasma included in our study. Their ages ranged between 18 and 50 years with mean of (28.44±60.6) years and 49 (55.7%) of patients were in the second decade of life. They were having Fitzpatrick's skin types III, IV and V. All types of melasma were present among the patients and the duration of facial pathology was for more than one year with multiple previous treatments.

I. Group – 1 (salicylic acid peel + modified Kligman formula) :

Among 45 patients, 23(51.1%) patients completed four sessions, 19(42.2%) patients completed three sessions and, 3(6.7%) patients completed two sessions .

Thirty one (68.8%) patients were married and 14 (31.2%) were unmarried, among married females 27(87%) gave history of pregnancy. Thirty three (73.3%) patient had given family history of melasma, 12(26.7%) had no family history.

Sixteen (35.6%) patients had Fitzpatrick's skin type III, and 29(64.4%) had skin type IV. Ten (22.2%) patients were sunscreen users and 35(77.8%) of them non users. Indoor workers were 38(84.4%) and only 7(15.6%) were outdoor workers

Thirty (66.7%) of patients had epidermal type of melasma based on Wood's light examination, 3 (6.7%) patients had dermal type and 12(26.7%) mixed type. Regarding drug history which is considered as a common cause of melasma, contraceptive pills were used by 28 (62.2%) patients in case group and were not taken by 17 (37.8%) patients.

Side effects: mild erythema associated with slight desquamation which was obvious in most of patients for 2-3 days 3(6.7%) patients suffered from transient postinflammatory hyperpigmentation, in 2 of them hyperpigmentation was around their mouth and 1 infraorbitally especially after peeling with 30%

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concentration and no scarring was recorded in our patients.

Changes in mean of MASI score after session in different types of melasma in group- 1:

In the epidermal type; mean MASI score was  $22.74 \pm 6.6$  before peeling and became  $0.94 \pm 1.5$  after the fourth peeling, so the difference was 21.8 which represents about 97% and was statistically significant ( $p$  value  $< 0.05$ ),

In the mixed type; mean MASI score before peeling was  $26.5 \pm 10.5$ , and became  $12.5 \pm 5.9$  after the fourth peeling. So the difference is 13.2 this represents about 50%  $p$  value is 0.1 ( $> 0.05$  not significant).

In dermal type, mean MASI score before peeling was  $19.33 \pm 4.3$ , then after four sessions of chemical peeling became  $18.50 \pm 3.5$ . So the difference in mean score was 0.8 this represents 4%. The mean difference of group -1 was  $17.53 \pm 1.19$  ( $p$  value  $< 0.001$  statistically significant).

Clinical response of group-1 in different types of melasma and skin types:

In epidermal type Two patients (6.7%) of showed moderate response, and 28(93.4%) showed significant response ( $p$  value  $< 0.05$ ). In mixed type of melasma 4 (33.3%) patients showed mild response, and 8(66.7%) showed moderate response, but patients with dermal type were 3 patients and all of them all (100%) showed minimal response.

In the group -1, ( whose used conjunction of superficial chemical peel with salicylic acid 20%,30% once every 2 weeks and topical modified Kligman formula); Regarding the mean MASI score and skin types, the difference in MASI score was statistically significant in both skin type III and IV ( $p$  -value  $< 0.001$ ). While regarding melasma types the mean difference was  $17.53 \pm 1.19$  which is statistically significant ( $p < 0.001$ ).

So after a total peels a significant decrease in MASI values was established in group – 1.

II. Group -2 ( modified Kligman formula alone ):

Twenty three (53.4%) of the patients were married and 20 (46.6%) were unmarried. Among married females, 17 (39.5%) had given history of previous pregnancy, and 26(60.4%) had not pregnancy. Family history was positive in 24(55.8%) patients and negative in 19(44.2%) patients. History of

contraceptive pill was positive in 33(76.7%), and negative in 10(23.3%).

Ten patients (23.3%) had skin type III, 30(64.8%) type IV, 3(7.0%) skin type V. Twenty nine (67.4%) patients were sunscreen user and 14(32.6%) non user. Thirty four (79.1%) patients were indoor, 9 (20.9%) outdoor workers

On Wood's light examination, 17(39.5%) patients had epidermal, 6(14.0%) had dermal and 20 (46.5%) had mixed type.

Changes in mean of MASI score in different types of melasma in group - 2;

In epidermal type mean MASI score before topical treatment was  $20.36 \pm 5.9$ , and became  $7.63 \pm 4.1$  after 8 weeks. The difference in mean score was 12.73 which represents 65% and the response was statistically significant ( $P$  value  $< 0.05$ ).

In the mixed type, the mean MASI score before topical treatment was  $22.51 \pm 5.5$ , and became  $11.06 \pm 3.3$  after fourth topical treatment, so difference in mean score is 11.45 this represents 50% (statistically not significant  $P$  value is 0.1). In the dermal type, mean MASI score was  $19.40 \pm 4.4$  and after 8 weeks of topical treatment became  $18.3 \pm 4.1$ . The difference in mean score was 1.1 which represents only 6% changes (statistically not significant).

So the mean difference in group -2 was  $10.34 \pm 0.83$  which statistically significant, ( $P$  value  $< 0.001$ ).

Clinical response of group -2 in different types of melasma and skin types:

In epidermal type of melasma, 1(5.4%) patients had got no response, 4 (23.5%) showed mild response, 9(52.9%) showed moderate response and 3(17.7%) had significant response. But patients with mixed type of

melasma 12(60%) showed mild response, 7(35%) showed moderate and 1(5%) had got significant response. In dermal type, 4(66.6%) showed no any response, 1(16.7%) minimal, 1(16.7%) had moderate response.

In the group -2, for those patients who had been treated only with topical modified Kligman formula: Regarding the mean MASI score and skin types, The difference was statistically significant in skin type V only. While regarding melasma types the mean difference was  $10.34 \pm 0.83$  which is statistically significant ( $p$  -value  $< 0.001$ ). Side effects; no patient was recorded to have pigmentation in group – 2.

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**Table 1: Changes expressed on MASI score ( mean  $\pm$ SD) after each session in different types of melasma in group-1**

Types of melasma	Mean of MASI score before chemical peel	Mean of MASI score after the first session	Mean of MASI score after the second session	Mean of MASI score after the third session	Mean of MASI score after the forth session
Epidermal	22.74 $\pm$ 6.66	17.48 $\pm$ 6.86	7.15 $\pm$ 4.26	3.24 $\pm$ 1.9	0.94 $\pm$ 1.58
Mixed	26.53 $\pm$ 10.58	23.00 $\pm$ 3.88	15.40 $\pm$ 7.33	13.33 $\pm$ 6.44	12.50 $\pm$ 5.9
Dermal	19.33 $\pm$ 4.39	18.83 $\pm$ 3.8	18.66 $\pm$ 18.00	18.00 $\pm$ 2.6	18.50 $\pm$ 3.5
Total	23.52 $\pm$ 7.88	19.04 $\pm$ 7.7	10.12 $\pm$ 6.68	7.27 $\pm$ 6.65	7.9 $\pm$ 7.75

P value<0.001 (statistically significant < 0.05), mean difference 17.35 $\pm$ 1.19

**Table 2: Changes expressed on MASI score ( mean  $\pm$ SD) after each course in different types of melasma in Group -2**

Types of melasma	Mean of MASI score before topical therapy	Mean of MASI score after 2week 2 weeks	Mean of MASI score after 4 week 4 weeks	Mean of MASI score after 6week 6 weeks	Mean of MASI score after 8week 8 weeks
Epidermal	20.36 $\pm$ 5.9	18.59 $\pm$ 5.6	16.21 $\pm$ 5.8	12.01 $\pm$ 5.05	7.63 $\pm$ 4.1
Mixed	22.51 $\pm$ 5.52	21.38 $\pm$ 5.5	18.82 $\pm$ 5.79	14.36 $\pm$ 5.72	11.06 $\pm$ 3.3
Dermal	19.40 $\pm$ 4.49	19.40 $\pm$ 4.49	19.40 $\pm$ 4.49	19.40 $\pm$ 4.49	18.31 $\pm$ 4.1
Total	21.23 $\pm$ 5.8	20.0 $\pm$ 5.4	17.87 $\pm$ 5.6	14.13 $\pm$ 5.7	10.41 $\pm$ 4.7

P value<0.001 (statistically significant < 0.05), mean difference 10.34 $\pm$ 0.83



A

B

**Figure 1: A 28 years old female with skin type IV had epidermal type of melasma: a: Before treatment, B after 3 session, chemical peel combined with topical depigmenting agent.**



**Figure 2: A 25 years old female with epidermal type of melasma: a: Before treatment, B After 2 session chemical peel combined with topical depigmenting agent.**

**DISCUSSION :**

Superficial and medium-depth chemical peels are recommended for the treatment of melasma, mainly in fair-skinned individuals. People with higher skin phototype are usually resistant to therapy and therapeutic results are unsatisfactory<sup>(16)</sup>, however our patient's skin type was mostly type IV and we obtained good response.

The group-1 was treated with 20% and 30% salicylic acid peels and a topical regimen of a modified Kligman formula, but the group -2 received the topical regimen alone, after a total of four peels or 8 week of treatment a significant decrease in MASI values was established in both groups ( $p < 0,001$ ).

Chemical peels act by increasing the penetration of medical therapy, not only by peeling off the pigment<sup>(16)</sup>, this was confirmed in the study conducted by Sarkar R et al<sup>(17)</sup> in two groups of Indian patients, the same result has been obtained in our study in which the women in group- 1 who received the salicylic acid peel showed a statistically significant trend toward a more rapid and greater improvement ( $p < 0,001$ ), thus the effect of our peeling with salicylic acid increased the efficacy of topical treatment..

Most of the melasma patients were females, this is a natural phenomenon because of the female hormonal activity during pregnancy together with the use of contraceptive pills was reported to exacerbate melasma<sup>(4)</sup>. The study includes 2 males only since they were less commonly complain and unreliable for post peeling instructions.

According to previous reports, the family history of melasma patients suggests the importance of

genetic factors, pregnancy and sun exposure in the pathogenesis of this condition<sup>(18)</sup>. In the present study, 33 (73.3%) of patients gave family history of melasma among group -1 and 24(55.8%) among group -2. And among married females, 27(87%) gave history of previous pregnancy in group-1 and 17 (39.5%) in group-2. Contraceptive pills were used by 28(62.2%) patients in group-1 and by 33 (76.7%) in group - 2. Indoor workers are appeared to be 38(84.4%) and only 7(15.6%) patients were outdoor workers in group -1, in addition 34(79.1%) patients were indoor workers, in group -2and 9 (20.9%) outdoor workers. These indicate that causes like contraceptive pills, genetic (family history) and pregnancy have had important role in developing melasma in this study.

In current study, Almost all of the patients in group - 1 tolerated the procedure of salicylic acid peeling but they are experienced some burning irritation, occasional stinging and pain just after application of salicylic acid peel which disappear immediately after face washing with water, also there was slight desquamation two to three days after peeling, mostly over cheeks, especially with application of 30% salicylic acid lotion which was efficiently controlled with twice application of fucicort cream for a day or two and dryness was managed with local application of emulsifying ointment. Erythema was not severe as salicylic acid has anti-inflammatory and anesthetic properties, this is also observed in previous studies<sup>(11,19)</sup>.

Post inflammatory hyperpigmentation appeared in three patients of Fitzpatrick's skin type IV after

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application of 30% salicylic acid lotion two of them around their mouth and one infra-orbitally, the result of the premature desquamation of the epidermis in these regions are due to the active contraction of the muscles during speaking and eating<sup>(16)</sup>.

Superficial chemical peel with salicylic acid (20% and 30%) in combination with topical modified Kligman formula is more effective than topical treatment alone, especially for epidermal type but less effective in mixed and with no result in dermal type. It is easily performed and cheap. Side effects with

salicylic acid was few like slight erythema, desquamation, and crusting, no scarring was recorded.

### CONCLUSION:

Superficial chemical peel with salicylic acid in combination with topical modified Kligman formula for melasma is more effective than topical modified Kligman formula alone. It is easy and cheap.

The results of the epidermal type were better than other types.

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