

Lactic Acid Cream 6% versus 10% Zinc Sulfate Cream as Comparative Study in Treatment of Melasma (Interventional, Single-Blinded, Comparative, Out Patients Study)

*Professor Khalifa E. Sharquie MD; Phd. *Professor Adil A. Noaimi MD;
DDV; FICMS. **Dr. Osama N. Al-Hemiari; MD, FIBMS.

*Department of Dermatology, College of Medicine, University of Baghdad.
Iraqi and Arab Board for Dermatology and Venereology, Baghdad Teaching Hospital,
Medical City, Baghdad, Iraq.

**Department of Dermatology ; Baghdad Teaching Hospital; Medical City, Baghdad, Iraq.

Abstract

Background: Melasma is a major cosmetic problem affecting young people mainly females. There are many modalities of topical therapy but no one was uniformly effective.

Objective: To evaluate the efficacy and safety of 6% lactic acid cream in comparison with 10% zinc sulfate cream in the treatment of melasma.

Patients and Methods: This interventional, single-blinded, comparative, out patients study conducted in the Department of Dermatology, Baghdad Teaching Hospital, Baghdad, Iraq during the period from March 2012 to October 2013. Seventy patients were enrolled but only 47 patients completed the study including both the treatment and follow-up periods. They were divided into 2 groups :

Group A: treated with 6% lactic acid cream once at night for 2 months.

Group B: treated with 10% zinc sulfate cream twice daily for 2 months. Patients were evaluated clinically using Wood's light and modified melasma area and severity index score (MMASI) before and after therapy. Follow up was done regularly every two weeks for two months to assess the improvement and side effects. Also, patients were seen monthly for another 2 months after the end of treatment to see any relapse. All patients were instructed to apply broad spectrum sun screen SPF > 30 before sun exposure for the period of treatment and follow up.

Results : In **Group A:** 22 patients completed the study; their ages ranged from 22-56 (35.95 ± 7.70) years, 4 (18.2%) patients were males and 18 (81.8%) females. The result showed that the average MMASI score before treatment was 17.82 ± 5.57 while after treatment score changed to 10.41 ± 5.17 ; so the reduction was 7.41, this represents a (41.58%) decrease and was statistically significant (p -value < 0.0000002). No important side effects were recorded during the treatment or follow up.

Group B: 25 patients completed the treatment; their ages ranged from 25-50 (34.62 ± 5.53) years, 6 (24.6%) patients were male and 19 (76.0%) were female. The result revealed the mean of MMASI before treatment was 17.76 ± 7.45 while after treatment score became 8.92 ± 4.49 . So the average decrease was 8.84 which represents (49.7%) and it was statistically significant (p -value < 0.000001). No important side effects were recorded during the treatment or follow up. No statistically difference between the two groups (p -value = 0.591).

Conclusion: Both drugs were effective therapeutic modalities for melasma without important side effects and the difference between them was not statistically significant.

Keywords: Melasma, zinc sulfate, lactic acid, topical.

I. Introduction

Melasma is an acquired disorder of hyperpigmentation that affects sun exposed areas of skin, most commonly the face. It is relatively common; most often affects women and is particularly prevalent in women with darker complexions and who live in areas of intensive ultraviolet radiation exposure⁽¹⁾.

It is characterized by brown patches, typically on the malar prominences and forehead. These patches are usually quite sharply demarcated.⁽²⁾

The precise cause of melasma has not been determined. Multiple factors are likely to be involved including: pregnancy, oral contraceptives (OCP), genetics, sun exposure, cosmetic use, thyroid and ovarian dysfunction, nutrition, phototoxic and photoallergic drugs and antiepileptic medications.⁽³⁾

Hypopigmenting topical agents containing hydroquinone, broad-spectrum UV protection and camouflage are considered the current standard of care for treating melasma. Additional therapeutic options include topical retinoic acids (tretinoin),

azelaic acid, microdermabrasion, chemical peeling or electromagnetic devices, such as lasers, all of these modalities were associated with many side effects and high recurrent rates.⁽⁴⁾

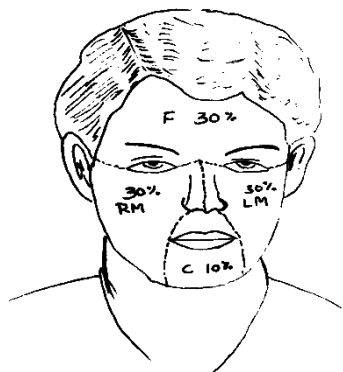
Lactic acid (C₃H₆O₃): is a member of alpha hydroxy acids (AHA), it is colorless or slightly yellow, viscous, hygroscopic organic acid liquid which is odorless, or has a slight but not unpleasant odor and a mildly acidic taste in dilute aqueous solution⁽⁵⁾. Its uses in dermatology include: for treatment of ichthyoids, xerosis, follicular hyperkeratosis, seborrheic keratosis, actinic keratosis, and verrucae vulgaris.⁽⁶⁾ Also, it is used in treatment of recurrent aphthous ulcer in the form of 5% mouth wash⁽⁷⁾, topical 15% lactic acid solution for the treatment of localized type of vitiligo⁽⁸⁾, 10% lactic solution for treatment of pityriasis versicolor⁽⁹⁾, topical 15% lactic acid solution or 12% cream for treating patchy alopecia areata^(10,11) and lactic acid cream 6%, and full strength (92%; PH 3.5) peel used for treatment of melasma^(12,13).

Zinc: is one of the essential trace elements that are required for physiological functions in amount less than 100 mg daily⁽¹⁴⁾. It's used in deodorant and antiperspirants and astringent⁽¹⁵⁾, for treatment of severe herpes simplex infection and previously associated erythema multiforme using zinc sulfate 0.025%-0.05% solution⁽¹⁶⁾, intralesional zinc sulfate 2% for cutaneous leishmaniasis and basal cell carcinoma^(17,18), in photoprotection⁽¹⁹⁾, topical 10% and 2% intralesional zinc sulfate solution in the treatment of viral warts^(20,21), topical 10% zinc sulfate solution, ointment and cream for melasma^(23,24), topical 15% zinc sulfate solution in the treatment of pityriasis versicolor⁽²⁵⁾, topical 10% zinc sulfate solution for superficial fungal infection⁽²⁶⁾, 5% zinc sulfate mouth wash in recurrent aphthous ulcers as treatment and as prophylaxis⁽²⁷⁾, zinc sulfate cream for treatment of psoriasis^(28,29), 5% zinc sulfate solution treatment of rosacea⁽³⁰⁾, 20% topical zinc sulfate solution had both therapeutic and prophylactic role in patients with xeroderma pigmentosa⁽³¹⁾, 25% zinc sulfate solution for actinic keratosis⁽³²⁾, topical 2.5% zinc sulfate cream in combination with 0.05% clobetasol in treatment of chronic hand eczema⁽³³⁾ and lastly topical 15% zinc sulfate solution effective therapeutic and prophylactic action against bad feet odor⁽³⁴⁾.

Melasma Area and Severity Index (MASI)⁽³⁵⁾: In this system the face is divided into 4 areas. Forehead, right malar, left malar and chin that correspond respectively to 30%, 30%, 30% and 10% of the total face area. The melasma in each of these areas was graded on three variables:

1- Percentage of the total area involved on a scale: this was measured by using transparent square paper. By this method the melasma and the total face surface areas were measured accurately by square centimeters, then the percentage of the total melasma area relative to the total area of the face was measured and scoring was done as follow:

| | |
|---|----------------|
| 0 | No involvement |
| 1 | < 10% |
| 2 | 10-29% |
| 3 | 30-49% |
| 4 | 50-69% |
| 5 | 70-89% |
| 6 | >90-100% |



1- **Darkness:** Scoring from 0-4 was assessed according to 4 special color charts

Scale 1=Light brown
 Scale 2=Brown
 Scale 3=Dark brown
 Scale 4=Black



2- Homogeneity: On scale 0(minimal) to 4(maximal).

The MASI score was calculated by the following equation:

$$\text{MASI} = 0.3(\text{DF} + \text{HF})\text{AF} + 0.3(\text{DMR} + \text{HMR})\text{AMR} + 0.3(\text{DML} + \text{HML})\text{AML} + 0.1(\text{DC} + \text{HC})\text{AC}$$

Where D is darkness, H is homogeneity, A is area, F is forehead, MR is right malar, ML is left malar, C is chin and the values 0.3, 0.3, 0.3 and 0.1 stand for respective percentage of the total facial area.

So, the aim of our study is to evaluate the efficacy and safety of 6% lactic acid cream in comparison with 10% zinc sulfate cream in treatment of melasma.

II. Patients And Methods

This is an interventional, single-blinded, comparative, out patients study, carried out in the Department of Dermatology, Baghdad Teaching Hospital, Medical City, Baghdad ,Iraq during the period from March 2012 to October 2013.

The nature and target of this study were explained for each patient. Formal consent was taken from them before starting the therapy, after full explanation about the nature of the disease, course, the procedure of treatment, follow up, prognosis and the need for pre and post treatment photographs. Also, the ethical approval was given by the Scientific Council of Dermatology and Venereology-Iraqi Board for Medical Specializations.

Inclusion Criteria: Patients clinically presented with different shapes of melasma were included, those using therapy must stop any treatment for 2month prior to the study with use of sun screen SPF > 30.

Exclusion Criteria: Pregnant and lactating females , patients with chronic illness like :liver, kidney, heart, blood dyscrasia, connective tissue diseases and any endocrine disease that interfere with skin pigmentation, patients receiving drugs that interfere with skin pigmentation especially female on hormonal therapy including oral contraceptive pills and immune suppressed patients.

At first visit a detailed history was taken from each patient stressing on the: age, gender, onset and duration of melasma, marital status, use of cosmetics, family history, sun exposure and drug history. Female patients were asked about pre- menstrual flare up, history of pregnancy and use of oral contraceptive pills. The diagnosis was made on clinical bases and Wood's light examination.

Seventy patients with melasma were included in the study, sixty patients were females and 10 patients were males with female to male ratio 6:1.

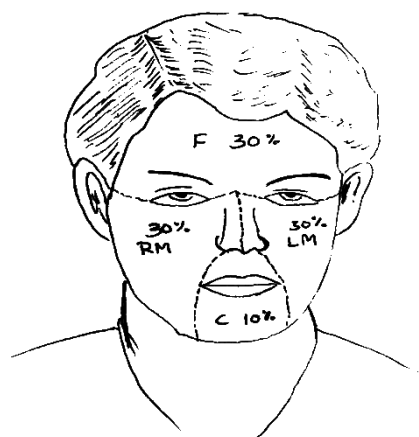
A careful examination of melasma was done as base line and in follow up visits including the following:-

Morphology of melasma : butterfly, mask shape, horse shoe and localized, Wood's light examination was done for all patients was done to assess the depth of pigmentation and response of therapy, color photographs for all patients were performed by using Sony digital camera 14.1 Megapixels in the same place and distance with fixed illumination. Calculation of modified melasma area and severity index(MMASI)score (Sharquie personal communication 2013) was carried out for each patient as follows:-

Modified Melasma Area and Severity Index(MMASI) score: In this system the face is divided into 4 areas. Forehead, right malar, left malar and chin. The melasma in each of these areas was graded on three variables:

1-Percentage of the total area involved on a scale: this was measured by using transparent square paper. By this method the melasma and the total surface areas were measured accurately by square centimeters, then the percentage of the melasma area relative to the total area of the same region was measured and scoring was done as follows:

- 1 <10%
- 2 10-29%
- 3 30-49%
- 4 50-69%
- 5 70-89%
- 6 90-100%



2-Darkness: Scoring from 0-4 was assessed according to 4 special colour charts

Scale 1= Light brown
 Scale 2= Brown
 Scale 3= Dark brown
 Scale 4= Black



3-Homogeneity: on scale 0(minimal) to 4(maximal).

The MMASI score was calculated by the following equation:

$$\text{MMASI} = \text{DF} + \text{HF} + \text{AF} + \text{DMR} + \text{HMR} + \text{AMR} + \text{DML} + \text{HML} + \text{AML} + \text{DC} + \text{HC} + \text{AC}$$

Where D is darkness, H is homogeneity, A is area, F is forehead, MR is right malar, ML is left malar and C is chin.

The patients were divided in two groups: Group A receiving lactic acid cream 6% and **Group B** receiving zinc sulfate cream 10% for 2 months.

Group A: Treatment with 6 % Lactic Acid Cream: Thirty eight patients with melasma were included in this part of the study. They were treated by topical 6% Lactic acid cream. Thirty four (89.5%) were females and 4(10.5%) were males, female to male ratio was **10.75:1**.

Preparation and treatment plan: Concentration of lactic acid solution ($\text{CH}_3\text{CHOH.COOH}$) was 90.08 %, PH= 1.8 made in GAINLAND CHEMICAL COMPANY, U.K.

The desired concentration was calculated by following equation:

$$C_1 V_1 = C_2 V_2$$

$$90 * 10 = 6 * X \rightarrow 90 * 10 = 6 * 150$$

C: concentration , V: volume

As the density of lactic acid is 1.2 gm/ml i.e near 1, so the weight is equal to volume. To obtain 6 % lactic acid cream PH=3.2 ,(10 ml) of 90% lactic acid solution had been taken , mixed gently with 140 gm aqua rosa cream , putted in dark closed cup kept at room temperature at hospital.

Six percent lactic acid cream was given to all patients, initially on alternate day over the melasma area for one week in order to minimize or to avoid the possibility of irritation in some patients and to get tolerability, by using the finger tip method with gentle message then daily use over night for two months.

The patient instructed to avoid sun exposure as much as possible during and after treatment, and encourage to use sun screen SPF>30 during day light and repeated every 3 hours .

The patients were seen regularly every 2 weeks for 2 months to assess the response of treatment by calculating Modified MASI, Wood's light examination, taking photos for each patient and recording the side effects if present. All patients were followed up monthly for another 2 months without treatment to record any clinical relapse.

Group B: Treatment with 10% Zinc Sulfate cream: Thirty two patients with melasma were included in this part of the study. They were treated by topical 10% zinc sulfate cream. Twenty six (81.2%) were females and six (18.8%) were males , female to male ratio was 3.4: 1.

Preparation and treatment plan:

Ten percent (W/W) zinc sulfate cream was prepared by dissolving 10 grams of zinc sulfate crystals ($ZnSO_4 \cdot 7H_2O=287.54$ from SDFCL, Mumbai-30,India) in 85 gram of aqua rosa. The crystals dissolved by frequent mixing with aqua rosa liberating water that allowed to dry for about 24 hours and then olive oil was added to make the preparation 100 gram. Olive oil makes the mixture supple.

The patients were instructed to apply the cream over the melasma area twice daily for 2 months by finger tip method with gentle message with application of sun screen with SPF > 30 before sun exposure and repeated every 3 hours.

The patients were examine regularly every 2 weeks for 2 months to assess the response of treatment by performing MMASI, Wood's light examination, taking photos for each patient and recording the side effects if present. All patients were followed up monthly for another 2 months without treatment to record any clinical relapse.

Data were statistically described in terms of range, mean, standard deviation ($\pm SD$), median, mode and frequencies (number of cases) and relative frequencies (percentages). Comparison between first visit and other visits at the same group was done using paired t test. Comparison between groups at each visit was done using independent t test. Comparison between demographic parameters between groups was done using Chi square (X^2) test. A probability value (P value) less than 0.05 was considered significant. All statistical calculations were done using computer statistical programs SPSS ver.20 (Statistical Package for the Social Science; SPSS Inc. Chicago, IL, USA).

III. Results

There were no significant differences for all demographic criteria between the two groups (Table-1).

Group A: Only 22 patients completed the study (both the treatment and follow up), their ages ranged between **22-56 years** with a mean $\pm SD$ of **35.95 \pm 7.70** years, the duration of the disease was range from **0.5-20 years** with a mean $\pm SD$ of **4.53 \pm 4.19**. They were **4(18.2%) males** and **18(81.8%) females** (Table-1). **Thirteen (27.7%)** were married and **9 (19.1%)** were not married. Sun exposure was positive in **20 (90.9%)** patients and negative in **2(9.1%)**, family history of melasma was positive in **9(40.9%)** patients while it was negative in **13 (59.1%)**. **Fourteen (63.6%)** patients use cosmetics while **8 (36.4%)** not use it.

For female patients premenstrual flare up was positive in **6(31.8%)** and negative in **12(68.2%)** patients, association with pregnancy was positive in **7(36.4%)** and negative in **11(63.6%)**. According to Fitzpatrick's classification of skin colure **10 (45.5%)** patients were skin type IV and **12(54.5%)** patients type V. Wood's light examination showed increased contrast in **11(50%)** patients (epidermal type) and mixed in **10(45.45%)** patients (mixed type) and no enhancements (dermal) in **one (4.54%)** patient.

Morphological forms of melasma were as follow: mask like **4(18.2%)** patients, centrofacial **12(54.5%)**, butter fly like **4 (18.2 %)**, horse shoe like **one (4.5 %)** and localized **one (4.5%)** patient.

The response to treatment in this group as follow: In the first visit(as shown in Table-2) mean $\pm SD$ of total MMASI was **17.82 \pm 5.57**, after 1 month of treatment the mean $\pm SD$ was decreased to **14.05 \pm 5.09**, this is statistically significant(P-value < **0.001**), and at 2 month of treatment the mean $\pm SD$ become **10.41 \pm 5.17** (P-value < **0.0001**) and the reduction rate was **41.5%**.

During the follow up period 2 months without treatment the mean $\pm SD$ of MMASI was decreasing to **10.32 \pm 4.75** compared with first visit it is significant (P-value < **0.0001**) while in comparison with the 3rd visit (after 2 month) it was statistically not significant (P-value was **0.886**).

When the **Darkness (colure)** was considered the response was obvious after 1st visit from **5.68 \pm 1.64** in the first visit to **4.41 \pm 2.51** after 1 month but it was statistically not significant (P-value = **0.229**) and was only statistically significant after 2 month of therapy(P-value = **0.005**). In the follow up period (2 months without treatment) the mean of darkness remain stable although 2 cases of study showed relapse (P-value < **0.0001**) when compared to 1st visit while when compared to 3rd visit it is not significant (P-value = **0.740**).

The **Surface area** in the 1st visit their mean $\pm SD$ was **8.18 \pm 2.75**, it was decreased to **6.59 \pm 2.46** after 1 month of treatment(P-value **0.001**), and continue to decreased after 2 month to **5.50 \pm 2.80** (P-value **0.0001**). At 2 months follow up without treatment it decreased to **5.41 \pm 2.64** (P-value < **0.0001**), when compare it with 3rd visit it is statistically not significant (P-value **0.831**).

Regarding the side effects: 5(20%) patients complain from erythema and mild irritation but they complete the treatment with 2 night apart leave the drug and using only Vaseline and 1 night use the drug.

Group B: Twenty-five patients completed the study, their ages range from **25-50 years** with a mean $\pm SD$ of **34.62 \pm 5.53** years, duration of melasma **0.2-20 years** mean $\pm SD$ of **5.44 \pm 5.84** years. They were **6(24.0%) males** and **19(76.0%) females**, female to male ratio was **3.16:1** (Table -1). **Twelve (48.0%)** females were

married and **13 (52.0%)** were not married. Sun exposure was positive in **23 (92.0%)** patients and negative in **2(8.0%)**, family history of melasma was positive in **9(36.0%)** while it's negative in **16 (64.0%)** patients. **Sixteen (64.0%)** patients use cosmetics while **9 (36.0%)** of them not use it.

For female patients premenstrual flare up was positive in **5(24.0%)** and negative in **14(76.0%)** patients, association with pregnancy was positive in **7(35.0%)** and negative in **13(65.0%)**. According to Fitzpatrick's classification of skin color **1 (4.0%)** was type III, **15 (60.0%)** were type IV and **9 (36.0%)** were type V.

Wood's light examination showed increased contrast in **11(44%)** patients, (epidermal type) and mixed type in **14 (56%)** patients and no dermal type reported in this group.

Morphological forms of melasma were as follows: mask like in **2 (8 %)** patients, centrofacial **8(32%)**, butterfly like in **7 (28.0 %)**, horse shoe like **1(4.0 %)** and localized **7 (28.0%)** patients.

The response of treatment in this group was as follow: In first visit in (Tables-3) mean and SD of total MMASI **17.76 ±7.45**, after 1 month of treatment the mean was decreased to **12.36±4.81**, this is statistically significant(P-value **0.001**), and it continue to decrease mean ±SD was **8.92±4.490** after 2 months of treatment (P-value **<0.0001**), the reduction rate was **49.77%**.

In the follow up period 2 months without treatment mean of MMASI was decreasing to **8.72±4.17** SD compared with first visit it is significant(P-value **<0.0001**) while in comparison with the 3rd visit(after 2 month) it is not significant(P-value was **0.486**).

When the **Darkness (color)** was considered the reduction was from **6.16±2.03** in the first visit to **3.96±1.62** after one month of therapy and it was statistically significant(P-value **0.037**) and was also statistically significant after 2 month of therapy(P-value **0.0008**). In the follow up period (2 months without treatment) the mean of darkness continue to decrease (P-value **< 0.0001**) when compared to 1st visit while when compared to 3rd visit it is not significant (P-value is **0.714**) which is not significant.

Surface area in the 1st visit their mean was **10.88 ± 3.56**, it was decreased to **7.08±2.76** after 1 month of treatment(P-value was **0.010**), and continue to decreased after 2 month to **5.16±2.39** their (P-value was **0.010**), in the 2 month follow up without treatment it decreased to **4.08 ±2.039** (P-value **0.0001**), when compare it with 3rd visit it is statistically significant(P-value **0.03**).

Regarding side effects: only one (0.04%) patient complain from irritation and erythema and continue on study with use of Vaseline.

In (Table-4) the mean ± SD of MMASI in Group A in the 1st visit was **17.82±5.57** and in B was **17.76±7.45**, after 1 month treatment mean and SD of MMASI of group A become **14.05±5.09** while in group B it become **12.36±4.81**. (P-value between 2 groups was **0.252**) which considered non significant. After 2 months of treatment the mean and SD of MMASI in group A become **10.41±5.17** while it become **8.92±4.49** in group B, P-value between 2 groups was **0.301** which also statistically non significant. In follow up period (2 month) the mean and SD of MMASI in group A was **10.32±4.75** and in group B was **8.72±4.17**, P-value between them was **0.231**.

Mean ± SD of total darkness of patients in group A in 1st visit was **5.68±1.64** and in the group B was **6.16±2.03**. After 1 month of treatment it become **4.41±2.15** in group A and **3.96±1.62** in group B, P-value between 2 groups was **0.429**. At the end of 2nd month of treatment it become **3.36±1.64** in group A and **2.92±1.32** in group B, P-value between them was **0.319** which considered non significant. After 2 months follow up without treatment mean and SD of total darkness was **3.45±1.33** in Group A while in Group B it was **2.88±1.23**, P-value was **0.135** which is statistically not significant.

The mean and SD of Total surface area(S.A) in group A was **8.18±2.75** and in B was **10.88±3.56**, after 1 month of treatment mean and SD of SA in group A become **6.59±2.46** while in group B it become **7.08±2.76**. P-value between 2 groups was **0.525** which considered non significant. After 2 month of treatment the mean of SA in group A become **5.50±2.80** while it become **5.16±2.39** in group B, P-value between 2 groups was **0.660** which also non significant. In follow up period (2 month) the mean of total SA in group A was **5.41±2.64** and in group B was **4.08±2.39**, P-value between them was **0.080**.

Table-1: Demographic characteristic of both groups for patients who were complete the study.

| | | Zn S=25 | | L A=22 | | Chi square | P value |
|----------------------------|--------------|---------|-------|--------|-------|--------------|--------------|
| | | N | % | N | % | | |
| Gender | Male | 6 | 24.0% | 4 | 18.2% | 0.237 | 0.627 |
| | Female | 19 | 76.0% | 18 | 81.8% | | |
| Social status | Married | 12 | 48.0% | 13 | 27.7% | 0.578 | 0.447 |
| | Unmarried | 13 | 52.0% | 9 | 19.1% | | |
| Sun exposure | +ve | 23 | 92.0% | 20 | 90.9% | 0.018 | 0.498 |
| | -ve | 2 | 8.0% | 2 | 9.1% | | |
| Family history | +ve | 9 | 36.0% | 9 | 40.9% | 0.119 | 0.730 |
| | -ve | 16 | 64.0% | 13 | 59.1% | | |
| Cosmetic use | +ve | 16 | 64.0% | 14 | 63.6% | 0.001 | 0.979 |
| | -ve | 9 | 36.0% | 8 | 36.4% | | |
| Skin type | III | 1 | 4.0% | 0 | 0 | 2.246 | 0.325 |
| | IV | 15 | 60.0% | 10 | 45.5% | | |
| | V | 9 | 36.0% | 12 | 54.5% | | |
| Morphology of lesion | Mask | 2 | 8% | 4 | 18.2% | 6.538 | 0.088 |
| | Centrofacial | 8 | 32% | 12 | 54.5% | | |
| | Butter fly | 7 | 28.0% | 4 | 18.2% | | |
| | Horse shoe | 7 | 28.0% | 1 | 4.5% | | |
| Premenstrual flare-up | Localized | 1 | 4.0% | 1 | 4.5% | 0.357 | 0.641 |
| | +ve | 5 | 24.0% | 6 | 31.8% | | |
| Association with pregnancy | -ve | 14 | 76.0% | 12 | 68.2% | 0.008 | 0.804 |
| | +ve | 7 | 35.0% | 7 | 36.4% | | |
| Wood's light | -ve | 13 | 65.0% | 11 | 63.6% | 1.864 | 0.394 |
| | Dermal | 0 | 0.0% | 1 | 4.5% | | |
| | Epidermal | 10 | 40.0% | 11 | 50% | | |
| | Mixed | 15 | 60.0% | 10 | 45.5% | | |

Table-2: Showing the mean and SD of total M MASI, total darkness and total area within Group A for each visit.

| Lactic acid | | Baseline visit | After 1 month | After 2 months | Follow up After 4 months |
|--------------|------|-----------------------|-----------------------|-----------------------|--------------------------|
| | | 1 st visit | 2 nd visit | 3 rd visit | 4 th visit |
| Total MASI | Mean | 17.82 | 14.05 | 10.41 | 10.32 |
| | SD | 5.57 | 5.09 | 5.17 | 4.75 |
| | *P | - | *0.001 | *0.0001 | *0.0001 |
| Darkness | Mean | 5.68 | 4.41 | 3.36 | 3.45 |
| | SD | 1.64 | 2.15 | 1.64 | 1.33 |
| | *P | - | *0.229 | *0.005 | *0.0001 |
| Surface area | Mean | 8.18 | 6.59 | 5.50 | 5.41 |
| | SD | 2.75 | 2.46 | 2.80 | 2.64 |
| | *P | - | *0.0001 | *0.0001 | *0.0001 |

P= P value.

*Paired t test was used. Paired was used to compare baseline visits with other visits.

Table -3: Showing the mean and SD of total MASI, total darkness and total area within Group B for each visit.

| Zinc sulfate | | Baseline visit | After 1 month | After 2 months | Follow up After 4 months |
|--------------|------|-----------------------|-----------------------|-----------------------|--------------------------|
| | | 1 st visit | 2 nd visit | 3 rd visit | 4 th visit |
| Total MASI | Mean | 17.76 | 12.36 | 8.92 | 8.72 |
| | SD | 7.45 | 4.81 | 4.490 | 4.17 |
| | *P | - | *0.001 | *0.0001 | *0.0001 |
| Darkness | Mean | 6.16 | 3.96 | 2.92 | 2.88 |
| | SD | 2.03 | 1.62 | 1.32 | 1.23 |
| | *P | - | *0.037 | *0.008 | *0.0001 |
| Surface area | Mean | 10.88 | 7.08 | 5.16 | 4.08 |
| | SD | 3.56 | 2.76 | 2.39 | 2.39 |
| | *P | - | *0.049 | *0.010 | *0.0001 |

P= P value. *Paired t test was used. Paired was used to compare baseline visits with other visits.

Table -4 : Showing the mean and SD of total MMASI, total darkness and total surface area between groups at each visit.

| | | Baseline visit | | 2 nd visit After 1 month | | 3 rd visit After 2 months | | 4 th visit After 4 months | |
|--------------------|----|----------------|------|--|------|---|------|---|------|
| | | Mean | SD | Mean | SD | Mean | SD | Mean | SD |
| Total MMASI | LA | 17.82 | 5.57 | 14.05 | 5.09 | 10.41 | 5.17 | 10.32 | 4.75 |
| | ZS | 17.76 | 7.45 | 12.36 | 4.81 | 8.92 | 4.49 | 8.72 | 4.17 |
| | *P | 0.976 | | 0.252 | | 0.301 | | 0.231 | |
| Total darkness | LA | 5.68 | 1.64 | 4.41 | 2.15 | 3.36 | 1.64 | 3.45 | 1.33 |
| | ZS | 6.16 | 2.03 | 3.96 | 1.62 | 2.92 | 1.32 | 2.88 | 1.23 |
| | *P | 0.378 | | 0.429 | | 0.319 | | 0.135 | |
| Total surface area | LA | 8.18 | 2.75 | 6.59 | 2.46 | 5.50 | 2.80 | 5.41 | 2.64 |
| | ZS | 10.88 | 3.56 | 7.08 | 2.76 | 5.16 | 2.39 | 4.08 | 2.39 |
| | *P | 0.005 | | 0.525 | | 0.660 | | 0.080 | |

LA= lactic acid Group; ZS= zinc sulfate Group; P= P value *Independent t test was used in comparison between both groups at each visit.



Figure-1: Thirty years old female with melasma for 8 years duration treated by 6% lactic acid cream. **A:** before treatment , **B:** after 2 months of treatment.



Figure- 2: Twenty years old female with melasma for 12 years duration treated by 6% lactic acid cream. **A:** before treatment , **B:** after 2 months of treatment.



Figure -3: Thirty years old female with melasma for 5years duration treated by 10% zinc sulfate cream .
A: before treatment , **B:** after 2 months of treatment.



Figure- 4: Twenty five years old male with history of melasma for 2 years duration treated by 10% zinc sulfate cream. **A:** before treatment , **B:** after 2 months .

IV. Discussion

Melasma is a major cause of facial hyper melanosis⁽³⁶⁾ that could be induced and triggered by many etiological factors like pregnancy ,oral contraceptive pills, sun and emotional tension⁽³⁾. There are many morphological varieties of melasma like butterfly, mask like, horse shoe and localized and many histopathological types like epidermal, dermal and mixed.^(37,38)

Among the etiopathogenesis of melasma: UV exposure is a major triggering or aggravating factor for melasma development.⁽³⁹⁾

The aim of therapy in treatment of melasma is to reduce the amount of melanin production with or without reduction in number of melanocytes, most of the therapies were difficult and associated with many complications and high relapse rate⁽⁴⁰⁾. There are many varieties of topical therapy : hydroquinone⁽⁴¹⁾, retinoids⁽⁴²⁾, azelaic acid⁽⁴³⁾, kojic acid⁽⁴⁴⁾, ascorbic acid⁽⁴⁵⁾, arbutin/deoxyarbutin:⁽⁴⁶⁾ and tranexamic acid⁽⁴⁷⁾. All of these modalities were associated with many side effects and high recurrent rates.

The present work showed that the reduction rate in MMASI of patients treated with (6%) lactic acid cream was **41.5%** as compared with previous study used 6% lactic acid that showed **53.71%** reduction in the

MASI. ⁽¹³⁾ although, the difference between two studies is not statistically significant and previous study used ordinary MASI score p-value 0.986(Table-5).

The mechanism of action of lactic acid in clearing melasma might be due to epidermal remodeling and accelerated desquamation, which would result in quick pigment dispersion, also lactic acid was shown to inhibit tyrosinase enzyme activity directly, and this effect was not due to the acidity of lactic acid. ⁽⁴⁸⁾

Zinc sulfate cream 10% had been used previously for treatment of melasma^(23,24), the reduction rate in the MASI was **46.41%** while in this study 10% zinc sulfate cream showed **49.77%** reduction rate in MMASI which are very comparable P-value was **0.713**(Table-5). This indicate that MMASI score was almost equivalent to MASI score ,hence , there is no need to use MASI which is complex procedure and advice to use the MMASI which most simpler score.

The mechanism of action of zinc in melasma was unknown but many studies found that :zinc in combination with other micronutrients such as copper, cobalt, nickel, iron, manganese, and calcium has an important role in the process of melanogenesis.⁽⁴⁹⁾ In vitro studies have shown that zinc cations modulate melanogenesis by inhibition of tyrosinase⁽⁵⁰⁾. Other study found that high-dose oral zinc was a potent down-regulator of eumelanin content in murine hair shafts.⁽⁵¹⁾ Also, it seems that zinc is effective in treatment of melasma via its roles as anti-inflammatory, anti-oxidant, peeling, sun-screening and healing agent. ⁽²⁴⁾

In this study both 6% lactic acid cream and 10% zinc sulfate cream are safe therapy as they have no side effect that produced by other types of topical modalities for melasma like skin atrophy, telangiectasias and acne rosacea that produced by steroid .⁽⁵²⁾ Ochronosis that produced by hydroquinone not reported in any patients in both groups .

In this study, even after stopping the medication MMASI was remained stable or continue to decrease in both group except in 2 patients treated with lactic acid whose their MMASI were elevated but their elevation not affect the mean of total reduction in MMASI P-value 0.0001.

The reduction rate in MMASI of lactic acid group was **41.5%** while in zinc sulfate group was **49.7%** but there was no statistically difference between them P-value was **0.301**.

Table -5 : Percent reduction rate of total MASI for both groups and its comparison with other studies.

| Treatment type | Studies | MASI before therapy | MASI after therapy | *Percent reduction rate | Paired t test | P value between groups |
|----------------------|-------------------------------|---------------------|--------------------|-------------------------|-----------------|------------------------|
| Zinc cream 10% | Present study MMASI | 17.76 | 8.92 | 49.77% | 0.000001 | 0.713 |
| | Sharquei etal ⁽²³⁾ | 9.45 | 5.26 | 46.41% | 0.0005 | |
| Lactic acid cream 6% | Present study MMASI | 17.82 | 10.41 | 41.58% | 0.000002 | 0.986 |
| | Sharquei etal ⁽¹³⁾ | 11.45 | 5.3 | 53.71% | 0.0005 | |

*Percent Reduction = (A-B)/A*100, A is an initial value, B is a final value.

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