

# Comparison between Intralesional Triamcinolone and Kligman's Formula in Treatment of Melasma

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Received: 16 Apr. 2014; Received in revised form: 29 Oct. 2014, Accepted: 29 Dec. 2014

**Abstract-** Melasma is a common acquired skin disorder. While different treatments are currently being used, in many cases it is refractory to treatment. According to the effects of topical steroids in decreasing skin pigmentation, we studied the efficacy of this new method for treatment of melasma. A total of 42 women with facial melasma, admitted to the department of dermatology of Hamadan, were enrolled in the study. They were divided randomly into two groups (A and B), group A (case) received subepidermal triamcinolone injections with a dose of 4mg per cc and 5mm intervals until complete blanching of melasma lesions, and group B (control) received Kligman's formula (hydroquinone 5%, tretinoin 0.1%, and dexamethasone 0.1%). At the first visit, we completed the MASI score papers, and we repeated that at weeks 4 and 8 of the study. We followed them for two months, every two weeks. At each visit, side effects and clinical response to treatment were noted. A decrease in MASI was observed in both group ( $11.57 \pm 4.33$  vs  $9.31 \pm 3.75$  at 4th week and vs  $8.01 \pm 3.1$  at 8th week,  $P$ -value  $< 0.001$  in group A, and  $10.46 \pm 5.61$  vs  $9.76 \pm 5.21$  at 4th week and vs  $8.96 \pm 4.96$  at 8th week,  $P$ -value  $< 0.001$  in group B). In comparison between 2 groups, response to treatment was much better in group A than group B ( $P$ -value  $< 0.001$ ). In comparison to topical treatments, based on these findings, triamcinolone microinjection is a new, safe and strong therapeutic method for treatment of melasma.

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*Acta Med Iran* 2016;54(1):67-71.

**Keywords:** Melasma; Triamcinolone; Kligman's formula; Injection

## Introduction

Melasma is an acquired hypermelanosis that usually presents with brown patches and macules in the sun-exposed area of the face such as the forehead, cheeks, lips and nose (1). The lesions are serrated with geographic borders and are usually distributed symmetrically. This condition is particularly common in women in childbearing years (90% of cases in women) who are Hispanic or Asian, African or Middle Eastern and is more common in skin type 4,5 of Fitzpatrick (2,3).

Risk factors for this disease are the following: Ultra Violet (UV) exposure, pregnancy, hormone therapy, thyroid disease, phototoxic drugs and antiepileptic drugs, genetic predisposition. The UV exposure is more important than the others and is believed to be the leading exogenous factor in the development of melasma (4-6).

In all patients with melasma, sunscreen preparations

are indicated because sunlight may be a causative and an aggravating factor (7).

Although the prevalence of melasma in Asian women is not entirely known but has been estimated to be as high as 40% in women and 20% of men (8).

Chloasma and Melasma are used interchangeably, which is hyperpigmentation that often results from pregnancy or imbalance in ovarian hormones (9).

Based on histopathology, there are three types of melasma: Epidermal, with brown color and well-margined border, Dermal, with blue-gray color and fade margin and mixed or indeterminate. In epidermal type, there is hypermelanosis of the basilar layers and in Dermal type, there is epidermal hyperpigmentation and dermal melanophages (1,3).

This condition becomes worse in summer and better in winter (as a significant effect of UV) and has three clinical patterns: Centrifacial, which is the most common, Malar and Mandibular (9).

Melanin deposition is observed in all layers of the

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epidermis, melanophages may be increased too, and epidermal melanocytes are enlarged (3). Some inflammatory mediators such as IL6, IL1a, IL 1b, PGD2, PGE2, PGF2 are suspected in the pathogenesis of melasma too (10).

Pathogenesis of the lesions is not really well understood, several reasons have been suggested and include tyrosine activity, the formation of melanosomes and their transfer in the Keratinocytes and the degree of hyperpigmentation depends on the location of melanin deposition (2,11). Melasma has also been attributed to an elevation of the melanocyte-stimulating hormone, estrogen, and progesterone leading to increased melanogenesis (9).

There are two methods of treatment: local and systemic, in local treatment hypopigmenting agents are used. Hypopigmenting agents include phenolic and nonphenolic derivatives. Phenolic agents include hydroquinone and hydroquinone containing preparations. Nonphenolic agents include tretinoin and azelaic acid and etc. Some of other local treatments include: steroids, kojic acid, glycolic acid, combination therapy and laser therapy, in systemic therapy oral administration of vitamin C or/and vitamin E, intravenous injection of vitamin C and glutathione are available (4,12).

Combination therapy is better, the well-known combination therapy in the world is Kligman's formula that was recommended at 1975 and includes: hydroquinone5%, tretinoin 0.1%, and dexamethasone 0.1% (2).

## Materials and Methods

The current study was an open-label randomized control trial. A total of 42 women with facial melasma who referred to Hamadan Farshchian Hospital, department of dermatology as outpatients in 2013 were recruited to the study. Risks, benefits and all probable side effects were completely explained; informed consent sheet was completed by patients. All the patients had Fitzpatrick's skin types 2 to 3.

The period of this study was two months. The age range was 25 to 40 years. Exclusion criteria were:

Pregnancy, autoimmune disease, autoimmune

disorders, males, women who received hormone replacement therapy, for example, oral contraceptive, the coexistence of atrophy and telangiectasia of the skin at the site of melasma.

At the first visit, the patients were divided randomly into two groups, using a table of random numbers: group A received subepidermal triamcinolone microinjection as the intervention group and group B received Kligman's formula as the control group. The patients were advised to use a broad spectrum of sunscreen for protection from UV.

At the first visit, we completed the MASI score papers that represent the objective assessment of melasma and we repeated that at weeks 4 and 8 of the study. At each visit, clinical response to treatment and efficacy was assessed using the MASI score. The severity of the melasma in each of the four regions (forehead, right malar region, left the malar region and chin) was assessed based on three variables: Percentage of the total area involved (A), darkness (D), and homogeneity (H) (13).

The subepidermal injection was performed with an insulin syringe, with a dose of 4mg per cc, and 5mm intervals, until complete blanching of melasma lesions and was repeated 30 days later. Group B applied Kligman's formula (hydroquinone5%, tretinoin 0.1%, and dexamethasone 0.1%), every night for two months on melasma lesions.

The patients were followed for two months and visited every two weeks.

## Results

A total of 42 women with facial melasma were evaluated in this study. After statistical evaluation, the following results were obtained:

The age range was 25 to 40. The average age was  $30.23 \pm 4.4$  years in the group A and  $32.42 \pm 4.98$  years in the group B, with no significant differences between them.

With the use of Repeated Measure Analysis test, a decrease in MASI was observed in both groups ( $11.57 \pm 4.33$  vs  $9.31 \pm 3.75$  at 4th week and vs  $8.01 \pm 3.1$  at 8th week,  $P < 0.001$  in group A, and  $10.46 \pm 5.61$  vs  $9.76 \pm 5.21$  at 4th week and vs  $8.96 \pm 4.96$  at 8th week,  $P < 0.001$  in group B) (Table 1).

Table 1. MASI in the consecutive measurements in Group A and B

Group A	Min	Max	Mean	S.d	Group B	Min	Max	Mean	S.d
MASI1	3.8	21.7	11.57	4.33	MASI1	2.4	21.6	10.46	5.61
MASI2	2.1	18.1	9.31	3.75	MASI2	2	19	9.76	5.21
MASI3	1.8	16.2	8.01	3.10	MASI3	1.8	18	8.96	4.96
Age	25	39	30.23	4.40	Age	25	40	32.42	4.98

In comparison between two groups, significant differences were observed between two groups, and group A (case) had a much better response than group B ( $P < 0.001$ ) (Figure 1).

(Figure 1). Improvement in the clinical melasma area severity index (MASI), showing a more beneficial effect in the group A compared with the group B.

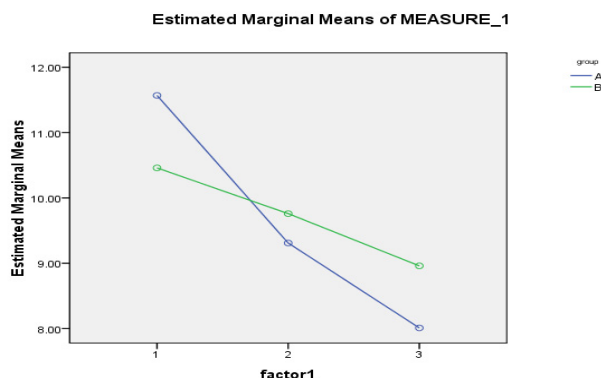


Figure 1. Comparison of response to treatment between group A and B

Some patients complained of painful injection but were reassured when we explained them the probable benefit of the method.

In continuation of the study, none of the patients had significant adverse effects, one patient had minimal skin atrophy improved in follow-up for two months.

One patient had mild telangiectasia resolved after one session of PDL laser.

In this study, injection of triamcinolone subepidermal had significantly greater efficacy than Kligman's formula.

## Discussion

The current study was the first study that demonstrated the effect of triamcinolone in the treatment of melasma lesions, and response to treatment was excellent. Despite the strict criterion, present results were excellent. Moreover, another advantage of this study was the simplicity of our method because in other methods the patients must use a topical cream such as (Kligman's formula or kojic acid preparations) for several months, but in our method, only two sessions of injection had excellent results.

Melasma is a well-known disease, but its treatment is still a problem. Despite the variety of treatments available, most patients experience at best only partial improvement.

Melasma has a psychological effect on affected patients and can reduce the quality of life (14). In one study social interactions and emotional well-being were

adversely affected by this condition (15). Then, more researchers about the nature of this disease and its treatment are necessary.

Making the right decision to choose the best treatment is important, but none of the available treatments has complete satisfactory results.

The goal of treatment is removing the involved area and returning to skin color to previous normal color with at least complications (9). A treatment for melasma is based on preventing the production of melanin, inhibiting the transfer of melanosome (16).

Many topical treatments such as hydroquinone, steroids, retinoids, azelaic acid, kojic acid, glycolic acid and combination therapy are available. In monotherapy, hydroquinone is the most popular treatment, but it is cytotoxic and has side effects such as irritant and allergic contact dermatitis, nail discoloration, exogenous ochronosis, and leukoderma (4,17).

Kligman's formula is a well-known combination therapy but is associated with complications such as dryness, scaling, pruritus, burning, erythema, atrophy and telangiectasia and achieving successful results depends on diligent, long-term treatment by patients who are carefully instructed in the method of use (18,19).

Another new method for treatment of melasma is a laser, although lasers have demonstrated significant efficacy in the treatment of a variety of hyperpigmentation disorders, their precise efficacy in melasma is still questionable (14).

Skin hypopigmentation is common after applying

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topical steroids and usually the normal skin color returns after stopping them (19,20). The true mechanism for skin hypopigmentation after topical steroids is not well defined yet, and it is assumed that steroids interference with the synthesis of melanin in smaller melanocytes (21).

Triamcinolone injection is a treatment for different dermatosis: acne, alopecia areata, hypertrophic scars, and keloids (22).

In injection, our goal was to deliver an adequate amount of drug directly to the target site of the skin as a mesotherapy (10).

Some inflammatory mediators such as IL6, IL1a, IL1b, PGD2, PGE2, and PGF2 are suspected in the pathogenesis of melasma, so inhibition of these mediators by nonselective suppressor function of corticosteroids can be the explanation for the effect of triamcinolone in our study (10,23). In our opinion, melasma is a chronic mild inflammatory disease because of its excellent response to triamcinolone and the role of inflammatory mediators in its pathogenesis as mentioned above. Another mechanism for an explanation of triamcinolone effect in melasma is probably interference of steroids with the synthesis of melanin in smaller melanocytes.

We performed this study to assess the safety and efficacy of this new method. Based on our findings, subepidermal injection of triamcinolone is a rapid and safe method for treatment of melasma with no significant side effect ( because, in our study, we used very dilute triamcinolone (4mg per cc) , and often the side effects are due to use of non-diluted triamcinolone).

Finally further studies are necessary to evaluate this treatment, doses, and the frequency of injections, in our opinion, those patients who didn't answer to treatment, with repeated injections or the use of more concentrated doses of triamcinolone would improve.

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