

The comparison between modified kligman formulation versus kligman formulation and intense pulsed light in the treatment of the post-burn hyperpigmentation

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Abstract

Background: Post inflammatory hyperpigmentation (PIH) is a common problem occurs following many dermatologic diseases and medical interventions. Different modalities including topical agents, lasers and intense pulsed light (IPL) are suggested for treatment of the post-burn PIH. In the current study, we evaluated the efficacy of IPL plus modified Kligman cream (MODIFIED KLIGMAN CREAM) versus MODIFIED KLIGMAN CREAM alone in the treatment of the post-burn PIH.

Materials and Methods: This was a randomized, non-blinded clinical trial. A total of 53 patches of post-burn PIP in 14 patients were randomized to receive either two sessions of IPL plus modified Kligman formula or kligman formula for 2 months. The patients were recommended to apply MODIFIED KLIGMAN CREAM cream for 12 h at night.

Results: According to our results, the patients in the MODIFIED KLIGMAN CREAM + IPL group had higher satisfaction as compared with MODIFIED KLIGMAN CREAM alone ($P = 0.000$) (Mann-Whitney test). In addition, according to physician evaluation, the patients in the MODIFIED KLIGMAN CREAM + IPL group had higher satisfaction as compared with MODIFIED KLIGMAN CREAM alone ($P = 0.000$) (Mann-Whitney test). No side effects except a little irritation, erythema and exfoliation due to MODIFIED KLIGMAN CREAM cream were seen in the patients.

Conclusions: The results of our study showed the better efficacy and faster response of the IPL plus modified Kligman formula versus modified Kligman formula in the treatment of the post-burn PIH. To better determine the efficacy of IPL in treatment of the post-burn PIP, more extensive studies as randomized, double-blinded clinical trial are recommended.

Key Words: Burn, hyperpigmentation, intense pulsed light

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Received: 20.08.2014, Accepted: 26.10.2014

Access this article online

Quick Response Code:



Website:

www.advbiores.net

DOI:

10.4103/2277-9175.186997

INTRODUCTION

Post inflammatory hyperpigmentation (PIH) is a common problem that occurs following many dermatologic diseases and medical interventions. Cutaneous infections, allergic reactions, mechanical

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How to cite this article: Siadat AH, Iraj F, Bahrami R, Nilfroushzadeh MA, Asilian A, Shariat S, *et al.* The comparison between modified kligman formulation versus kligman formulation and intense pulsed light in the treatment of the post-burn hyperpigmentation. *Adv Biomed Res* 2016;5:125.

trauma, drug reactions, phototoxic reactions and inflammatory diseases such as lichen planus, lupus erythematosus and atopic dermatitis all may cause this extra deposition of melanin.^[1]

PIH may also occur following application of the electromagnetic devices such as ultrasounds, radiofrequency devices, laser, light emitting diodes, visible light and even microdermabrasion.^[2] The most common causes of the burning are exposure to fire flame or boiling water.^[3-6]

The type and severity of burning are dependent on the depth and extent of the skin involvement. Most of the burn injuries are superficial.^[7] Burn injuries are classified into six groups according to their injury mechanisms including; boiling water burn, contact burning, fire burning, chemical burning, electrical and radiation burning.^[8] Dyspigmentary changes commonly occur following burn injuries. The hypopigmentation occurs because of melanin loss in the basal cell layer and thickening of the skin layers. Hyperpigmentation is due to melanocyte injury.^[9]

Different topical agents including hydroquinone, kojic acid, arbutin, azelaic acid and other medications have been used for treatment of the post-inflammatory hyperpigmentation.^[9]

Wai Sun *et al.* have achieved good clinical response following use of a topical combination of the hydroquinone, steroid and tretinoin for treatment of the post-burn hyperpigmentation in the face area.^[10]

Topical agents used for hyperpigmentation are classified into two groups of the phenolic and non-phenolic. Hydroquinone is a phenolic group agent that is regarded as gold standard treatment for hyperpigmentation in the last 50 years. It blocks tyrosinase enzyme and the conversion of DOPA to melanin. Also, melanin and melanocyte destruction and prevention of the RNA and DNA synthesis are the possible mechanisms of this medication.^[11]

Antioxidants such as vitamin C and penetration enhancing agents such as tretinoin are usually added to hydroquinone for better efficacy.^[9] That is why we used modified Kligman formula that included hydroquinone, vitamin c, tretinoin and triamcinolon in both groups of treatment.

Different modalities including topical agents, lasers and intense pulsed light (IPL) are suggested for treatment of the post-burn PIH. There is only one study that evaluated efficacy of IPL in the treatment of the post-burn hyperpigmentation as a non-controlled

case series. Over 78% of the patients showed more than 50% clinical clearance and nearly 32% of the patients were able to achieve more than 75% clearing with one patient had 100% clearing.^[10]

In the current study we evaluated the efficacy of IPL plus modified Kligman formula (MODIFIED KLIGMAN CREAM) versus modified kligman formula alone in the treatment of the post-burn PIH.

MATERIALS AND METHODS

This was a randomized, non-blinded clinical trial that was performed in Isfahan University of Medical Sciences and Skin Diseases and Leishmaniasis Research Center clinics in 2013-2014 (Research no: 391067) The ethical committee clearance and informed consent was achieved. All of the selected patients had history of burning with its resulting PIP. All of the selected patients were female and only patients who were older than 5 years old were recruited. The lesions were randomized to receive MODIFIED KLIGMAN CREAM or IPL + MODIFIED KLIGMAN CREAM using simple randomization method.

Exclusion criteria included history of sensitivity to any MODIFIED KLIGMAN CREAM components, pregnancy, lactation, and aggravation of the lesion after MODIFIED KLIGMAN CREAM or IPL treatment, history of skin cancer or connective tissue disorder and non-compliance of the patients for treatment.

The interval between burning and PIP should be at least 3 months. A total of 53 patches of PIP were selected in the 14 patients. If there were two similar patches with the same color and same location, each of them were randomized to receive modified Kligman's cream (MODIFIED KLIGMAN CREAM) or MODIFIED KLIGMAN CREAM + IPL and if not, half part of the patch was treated with MODIFIED KLIGMAN CREAM and other part was treated with or MODIFIED KLIGMAN CREAM + IPL.

The MODIFIED KLIGMAN CREAM was provided by pharmacist and included the combination of 5% hydroquinone, 3% of vitamin C, 0.025% of tretinoin, and 0.01% of triamcinolon in the cold cream base.

The patients were recommended to apply a small amount of MODIFIED KLIGMAN CREAM their lesions at night (for 12 h) as all of the patch would be covered with a thin layer of the cream and to apply sun screen cream with SPF of 55, three times a day.

For IPL, Smooth Cool Device (Jeisys company), and cut-off filter of 590 nm or 640 nm (according to skin

type) with contact cooling temperature of -5° of centigrade was used. All of the patched were treated with MODIFIED KLIGMAN CREAM 2 weeks earlier and then IPL treatment was applied.

The energy, pulse delay, pulse width and pulse time in different skin types were used as Jeisys company instruction as following [Table 1].

After IPL treatment the patients recommended to apply ice pack for at least 10 min and to cover area with zinc oxide paste and to start MODIFIED KLIGMAN CREAM from the following day.

The IPL treatment was used at monthly interval for maximum of two sessions and the patients were examined at the end of 2 month for comparison of the treatment. The degree of improvement by percent was rated by patient and intervening physician by the comparison of the baseline and final color as rated by the patient and comparison of the photographs. All of the data were recorded in questionnaires and the collected data were analyzed using SPSS ver. 13 and statistical tests including *t*-test and Ki-square

RESULTS

All of the selected cases were female. The mean age of patients in the MODIFIED KLIGMAN CREAM MODIFIED KLIGMAN CREAM group was 35.68 ± 5.14 years and 34.04 ± 6.09 years in the MODIFIED KLIGMAN CREAM MODIFIED KLIGMAN CREAM plus IPL group. There was no

significant difference regarding age of the patients and time of burning between the two groups ($P = 0.306$).

In our selected cases, the causes of the post-burn PIP were, fire: 36%, contact burn: 32%, laser: 18%, boiling water: 14%

Also, in our selected cases, the location of the post-burn PIP were, upper extremity: 49%, face: 37.3%, trunk: 5.9%, and lower extremity: 7.8%.

The comparison between the patients satisfaction in the two groups are shown in Table 1. According to our results, the patients in the MODIFIED KLIGMAN CREAM + IPL group had higher satisfaction as compared with MODIFIED KLIGMAN CREAM alone ($P = 0.000$) (Mann–Whitney test).

In addition, according to physician evaluation, the patients in the MODIFIED KLIGMAN CREAM + IPL group had higher satisfaction as compared with MODIFIED KLIGMAN CREAM alone ($P = 0.000$) (Mann-Whitney test) [Tables 2 and 3].

No side effect except a little irritation, erythema and exfoliation due to MODIFIED KLIGMAN CREAM cream was seen in the patients in the both groups.

DISCUSSION

Intense pulse light is light sources that emit non-coherent light with wave lengths of the 500–1200 nanometer and pulses with different duration and different energies.^[12] In the current study, we used cut-off filter of 590 nm.

In the only study that evaluated the efficacy of IPL for treatment of the post-burn PIH, 19 Chinese patients with post burn hyperpigmentation were treated by IPL. Their age ranged from 8 to 51 years with a mean age of 29.4 ± 11.6 years. The cutoff filters of 550, 570, and

Table 1: Laser parameters by the skin type

	Skin type I-II	Skin type III	Skin type IV	Skin type V
Pulse time	2 ms	2 ms	2 ms	3 ms
Pulse width	2 ms-3 ms	3 ms-5 ms	2 ms-6 ms	2 ms-2 ms-6 ms
Pulse delay	10 ms	20 ms	30 ms	10 ms-30 ms
Energy	17J-19J	21J-25J	19J-23J	16J-20J

Table 2: Hyperpigmentation improvement as rated by patients in the MODIFIED KLIGMAN CREAM and MODIFIED KLIGMAN CREAM+IPL group

Type of treatment	No improvement	1-25% improvement	26-50% improvement	51-75% improvement	76-99% improvement	100% improvement	Total
Modified Kligman Cream alone	0 (0%)	10 (34.5%)	10 (34.5%)	9 (31.5%)	0 (0%)	0 (0%)	29 (100%)
Modified Kligman Cream+IPL	0 (0%)	0 (0%)	7 (29.2%)	7 (29.2%)	8 (33.3%)	2 (8.3%)	24 (100%)

$P=0.000$ Mann–Whitney test. PIL: Intense pulsed light

Table 3: Hyperpigmentation improvement as rated by physicians in the MODIFIED KLIGMAN CREAM (modified kligman cream) and MODIFIED KLIGMAN CREAM+IPL group

Type of treatment	No improvement	1-25% improvement	26-50% improvement	51-75% improvement	76-99% improvement	100% improvement	Total
Modified Kligman Cream alone	0 (0%)	4 (13.8%)	16 (55.2%)	9 (31%)	0 (0%)	0 (0%)	29 (100%)
Modified Kligman Cream+IPL	0 (0%)	0 (0%)	5 (20.8%)	12 (50%)	5 (20.8%)	2 (8.3%)	24 (100%)

$P=0.000$ Mann–Whitney test. PIL: Intense pulsed light

590 nm were used for 3-7 treatments at intervals of 3-4 weeks. Patients were treated with an energy fluence of 28-46 J/cm², pulse width of 1.7-4 milliseconds, double pulse mode, and a delay of 15-40 milliseconds. Over 78% of the patients showed more than 50% clinical clearance and nearly 32% of the patients were able to achieve more than 75% clearing. Although two patients had no clinical response, one patient had 100% clearing. Three patients developed blisters and one patient had erythema that all resolved within 1 week without leaving permanent marks.^[10] However, in this study, in contrary of the current study, no bleaching agent was used. In addition, in the current study, we used control group to better determine the efficacy of the IPL treatment.

In the only study that used IPL treatment for post-burn PIP, no other medication was used along the treatment. In the current study, we used both the MODIFIED KLIGMAN CREAM and IPL so we expected better response with fewer treatment sessions. The results of our study showed the better efficacy and faster response of the IPL plus modified Kligman formula versus modified Kligman formula in the treatment of the post-burn PIH.

In addition, no side effect was observed in the two groups. To better determine the efficacy of IPL in treatment of the post-burn PIP, more extensive studies as randomized, double-blinded clinical trial are recommended.

Limitation: No limitation except IPL cost was in this study.

ACKNOWLEDGEMENT

We appreciate the SDLRC personnel for their help to perform this research.

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Source of Support: Isfahan University of Medical Sciences
Conflict of Interest: None declared.