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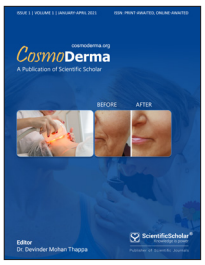

*Original Article*

# Clinical and dermoscopic evaluation of red light emitting diodes with beta-carotene versus red light emitting diodes alone in treatment of photoaging

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## ABSTRACT

**Objectives:** Red light-emitting diodes (LEDs) alter the extracellular matrix and increase fibroblast growth factor which increases the number of fibroblasts. Carotenoids have singlet oxygen quenching properties. The objective of this study was to evaluate combined effect of red light with oral beta-carotene in treating photo-damaged skin.

**Material and Methods:** Enrolled subjects were randomized into two groups, A and B. Group A received two sessions/week for 4 weeks of red light therapy and oral beta-carotene 30 mg/day for 12 weeks and Group B received two sessions/week for 4 weeks of red light therapy alone. Before and after clinical as well as dermoscopic photographs were evaluated. Dermoscopic photoaging scale (DPAS), Physician Global Assessment, and Patient Global Assessment was done at baseline, at end of therapy at 4 weeks and at 12 weeks.

**Results:** The mean DPAS of Group A before the treatment was 22.76 which decreased to 10.08 at the end of follow-up period (12 weeks) and was 19.80 in Group B before the treatment which decreased to 10.84. There was 28.25% reduction in DPAS in Group A at 4 weeks whereas it was 16.18% in Group B. Group A showed 56.12% reduction at week 12, while Group B showed 44.78% reduction. There was statistically significant difference in mean percentage reduction in DPAS between the two groups when compared ($P = 0.001$).

**Conclusion:** Red LED therapy with oral beta-carotene is a better approach for treating photoaging than Red LED therapy alone.

**Keywords:** Photoaging, Dermoscopy, Light emitting diodes, Beta-carotene, Phototherapy

## INTRODUCTION

Photoaging refers to all the skin changes produced by chronic exposure to ultraviolet radiations which fall in the 290–400 nm wavelength spectrum. Cumulative exposure to solar radiation and interplay of various other factors such as genetic predisposition, geographical location, dietary habits, and lifestyle tend to cause complex skin alterations which can result in premature skin aging. Photoaging can manifest in the form of coarse wrinkles, fine lines, pigmentation, lentigines, roughness, rhytides, and telangiectasia which can overlay physiologically aging skin.[1] Apart from being a cosmetic concern, photoaging also poses a great risk of the development of cutaneous carcinomas as ultraviolet radiations also alter signal transduction pathways and cause DNA alterations. Hence, photodamaged skin is more prone to photocarcinogenesis.[2]

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Photoaging is more commonly seen in fairer skin, Fitzpatrick I, II, and III and is less common in darker skin types, Fitzpatrick IV, V, and VI. Males tend to be more prone to photoaging and photo-carcinogenesis due to lack of photo-protective practices, more outdoor work, and decreased innate free radical scavenging activity. Female sex hormones are known to protect against photoaging. There is a greater tendency of wrinkling seen in females after menopause because of decreased estrogen levels.[3]

Light-emitting diode (LED) devices utilizing different wavelengths have many advantages that include rapid wound healing, acne and rosacea treatment, hair restoration, and skin photomodulation. Red LEDs alter the extracellular matrix by increasing matrix metalloproteinase-9 (MMP-9), and decreasing MMP-1, thus increasing procollagen-1. There is also an increase in fibroblast growth factor which increases the number of fibroblasts and histologically a mild inflammatory infiltrate following irradiation is seen. Red LEDs target dermal structures, such as adnexa and fibroblasts as it has the deepest tissue penetration among all the wavelengths in the visible spectrum.[4]

Skin naturally has an array of beneficial antioxidants which include endogenous enzymes such as glutathione (GSH) peroxidase, superoxide dismutase, catalase, and vitamin and minerals involved in biochemical reactions occurring in the body like Vitamin E and Vitamin C. A variety of natural antioxidants are derived from fruit and vegetable components. Non-vitamin plant-derived ingredients like soya also have a protective role. Beta-carotene is one of the provitamins which has a role in preventing and treating acute and chronic alterations produced by photodamage.[5]

Both red LEDs and beta-carotene have been studied extensively as individual modalities for treating photoaging. This study was taken up to evaluate the efficacy of the combination of red LED therapy and beta-carotene supplementation in the treatment of photoaging.

Changes in the photoaged skin occur at histological and biochemical levels which require biopsy as a part of the evaluation process which is invasive and undesirable by the patient. Dermoscopy can be used to examine the changes which cannot be seen with the naked eye and patients also tend to readily volunteer for examination as it is non-invasive. Therefore to study the efficacy of treatment modalities dermoscopic photoaging assessment was done.

## MATERIAL AND METHODS

### Participants

Fifty patients consisting of men and women aged 35–65 years, with skin phototype II, III, IV, and V on Fitzpatrick scale and signs of aging II, III, and IV on Glogau scale were enrolled from the outpatient department of a tertiary center after taking the approval from the Institutional Ethics Committee. They were randomized into two groups, A and B comprising of 25 patients each. Group A received two sessions/week for 4 weeks of red light therapy and oral beta-carotene 30 mg/day for 12 weeks and Group B received two sessions/week for 4 weeks of red light therapy alone [Figure 1]. All subjects provided written informed consent to participate in the study.

### Exclusion criteria

The exclusion criteria were: Presence of any active infection or photodermatoses, active rosacea, active inflammatory dermatoses (atopic dermatitis, psoriasis), history of any photosensitizing drug usage, patients on immunosuppressive therapy, and utilization of any kind of topical treatment (e.g., Topical retinoid, azelaic acid creams, and topical steroids) in the previous 1 month, surgical esthetic treatment in the previous 6 months and local injection therapies or cosmetic procedures in the previous 6 months.

### Equipment

The light source was LED (O'melon Omega Led) system containing 283 units (in three panel) that emit red light, with 640 nm wavelength and delivered an irradiance of 0.47 mW/cm$^2$, and fluence of 0.84 J/cm$^2$ [Figure 2]. For dermoscopic assessment of the face AM7515MZT Dino-Lite Edge Videodermoscope (Taiwan) with ×60 magnification in polarized mode was used [Figure 3]. Capsule Oxidon Plus (Micro labs limited) containing 30 mg beta – carotene was given to patients in Group A.

### Procedure

At the beginning of the study, patient with photodamaged skin was enrolled after clinical and baseline assessment. Dermoscopic examination of all the cases was done.

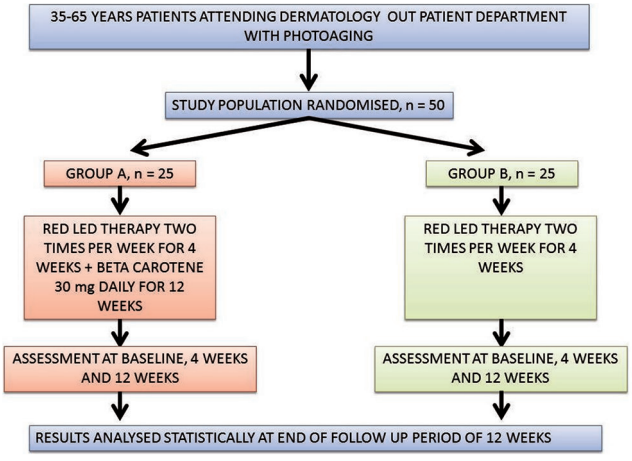


**Figure 1:** Study design flowchart.

**Figure 2:** Light-emitting diode system.

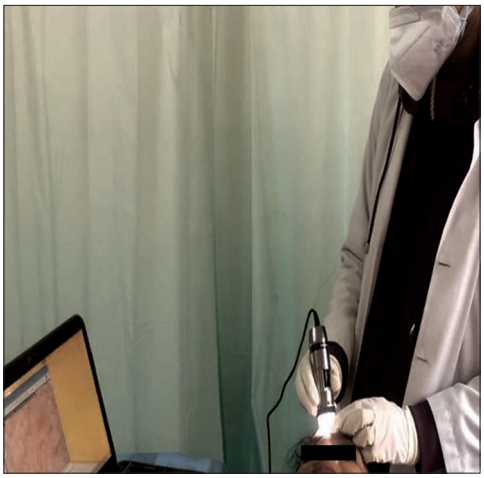

**Figure 3:** Assessment of the face AM7515MZT Dino-Lite Edge Videodermoscope.

Patients were classified according to the Glogau Scale into Group I, Group II, Group III, and Group IV.[6] Physician global assessment (PhGA) was done through a 5-point scale (score ranging from 0 to 4) for seven skin features of photodamage which included global score, fine lines, mottled pigmentation, sallow complexion, tactile roughness, telangiectasia, and coarse wrinkles. Baseline dermoscopic evaluation of the photo-damaged skin was done. Skin was assessed on the basis of Dermoscopic Photoaging Scale (DPAS) consisting of 11 features of photo-damage assessed over four areas of the face (forehead, right cheek, left cheek, and chin). It involved yes (1) or no (0) policy with score ranging from 0 to 11 for one area of face and total score of the face ranging from 0 to 44[7] [Table 1].

After gentle cleansing face was irradiated with red LEDs for a total period of 20 min. Patients were advised to apply sunscreen and emollients over both sides after the procedure. The subjects were instructed to follow photoprotective measures. Sun protection with sunscreen was advised at the start of therapy, during the treatment and in follow-up period. The procedure was done up to 8 times, two sessions/week over a period of 4 weeks. Group A received daily oral beta-carotene 30 mg for 3 months along with red light therapy while Group B received only red light therapy. Assessment was done at baseline, end of red light therapy (4$^{th}$ week) and at 12$^{th}$ week. To assess the clinical response, photographic documentation of all the patients was done with identical camera settings, illumination and from a fixed distance. Frontal, right, and left views for each patient were photographed. PhGA (ranging from 0 to 21), patient global assessment (PGA) (ranging from 0 to 10), and dermoscopic assessment was performed and any adverse events and complications were recorded. In PGA, patients were asked to score the improvement of on a visual analogue scale from 0 to 10 with 0 as no improvement and 10 as the best possible improvement.

**Table 1:** Dermoscopic photoaging scale.[7]

| Criteria | Forehead | Right cheek | Left cheek | Chin |
|---|---|---|---|---|
| Yellowish discoloration | 0/1 | 0/1 | 0/1 | 0/1 |
| White line | 0/1 | 0/1 | 0/1 | 0/1 |
| Lentigo | 0/1 | 0/1 | 0/1 | 0/1 |
| Hypo-hyperpigmented macules | 0/1 | 0/1 | 0/1 | 0/1 |
| Telangiectases | 0/1 | 0/1 | 0/1 | 0/1 |
| Yellowish papules | 0/1 | 0/1 | 0/1 | 0/1 |
| Actinic keratosis | 0/1 | 0/1 | 0/1 | 0/1 |
| Senile comedones | 0/1 | 0/1 | 0/1 | 0/1 |
| Deep wrinkles | 0/1 | 0/1 | 0/1 | 0/1 |
| Superficial wrinkles | 0/1 | 0/1 | 0/1 | 0/1 |
| Criss cross wrinkles | 0/1 | 0/1 | 0/1 | 0/1 |
| Total score | 0-11 | 0-11 | 0-11 | 0-11 |
| | | 0-44 | | |

The data were entered into Microsoft Excel spread sheet and results were analyzed using Statistical Package for the Social Sciences version 21. Mean and standard deviation were calculated for continuous parameters. Quantitative variables were compared using unpaired *t*-test between two groups. Qualitative variables were correlated using Chi-square test and correlation analysis. $P < 0.05$ was considered statistically significant.

## RESULTS

### Patient demographics

Fifty subjects were enrolled and completed the study. Both Group A and B comprised of 25 patients each. There was no significant difference in the demographic data between the two groups [Table 2].

**Table 2:** Demographic data of participants.

| Demographic Data | Demographic data | Group A (*n*=25) (%) | Group B (*n*=25) (%) | *P*-value |
|---|---|---|---|---|
| Gender | Female | 24 (96) | 24 (96) | 1.000 |
| | Male | 1 (4) | 1 (4) | |
| Age | 35–45 | 2 (8) | 1 (4) | 1.381 |
| | 45–55 | 12 (48) | 16 (64) | |
| | 55–65 | 7 (28) | 5 (20) | |
| | 65–75 | 4 (16) | 3 (12) | |
| Occupation | Housewife | 16 (64) | 10 (40) | 4.689 |
| | Teacher | 3 (12) | 2 (8) | |
| | Nursing staff | 4 (16) | 7 (28) | |
| | Service | 2 (8) | 6 (24) | |
| Marital Status | Married | 25 (100) | 21 (84) | 0.110 |
| | Unmarried | 0 (0) | 4 (16) | |
| Precipitating Factors | Family history | 7 (28) | 9 (36) | 0.762 |
| | Use of cosmetics | 11 (44) | 5 (20) | 0.128 |
| | Use of home remedies/any oil etc | 10 (40) | 7 (28) | 0.551 |
| | Drugs | 11 (44) | 13 (52) | 0.776 |
| | Co morbid illness | 7 (28) | 832) | 7.029 |
| Extent of sun exposure | None or mild | 0 | 0 | 1.786 |
| | Moderate | 14 (56) | 18 (72) | |
| | Severe | 8 (32) | 6 (24) | |
| | Very severe | 3 (12) | 1 (4) | |
| Fitzpatrick Skin Type | III | 17 (68) | 14 (56) | 0.983 |
| | IV | 5 (20) | 8 (32) | |
| | V | 3 (12) | 3 (12) | |
| Glogau Group | I | 0 (0) | 0 (0) | 0.567 |
| | II | 9 (36) | 12 (48) | |
| | III | 16 (64) | 13 (52) | |

### Primary outcome: Dermoscopic photoaging score (DPAS) and PhGA

Three blinded evaluators evaluated the mean DPAS of four areas of face, forehead, right cheek, left cheek, and chin. On baseline dermoscopic examination, most consistent findings were yellowish discoloration, hypohyperpigmented macules, and superficial wrinkles seen in all patients, that is, 50 (100%) of the study cases followed by yellowish papules seen in 48 (96%), deep wrinkles 33 (66%), lentigo 32 (64%), telangiectasia 23 (46%), criss cross wrinkles 12 (24%), and white line 6 (12%) study cases. None of the patients in the study group had senile comedones and actinic keratosis [Figure 4].

The mean DPAS of Group A before the treatment was 22.76 which decreased to 16.2 ($P$ = 0.002) at 4$^{th}$ week and further decreased to 10.08 at the end of follow-up period (12 weeks). Significant reduction in DPAS in comparison to baseline value was noted ($P$ = 0.000). The mean DPAS in Group B before the treatment was 19.80 which decreased to 16.68 ($P$ = 0.000) at 4$^{th}$ week and further decreased to 10.84 at the end of follow-up period (12 weeks). Statistically significant reduction in DPAS in comparison to baseline value was noted ($P$ = 0.004) [Table 3]. Representative before and

**Table 3:** Trends in DPAS with treatment in Group A and B.

| Group | Duration | Mean DPAS | Standard Deviation | *P*-value |
|---|---|---|---|---|
| Group A | Baseline | 22.7600 | 4.711 | - |
| | 4 weeks | 16.2000 | 4.528 | 0.002 |
| | 12 weeks | 10.0800 | 3.785 | 0.000 |
| Group B | Baseline | 19.800 | 3.166 | - |
| | 4 weeks | 16.680 | 3.010 | 0.000 |
| | 12 weeks | 10.840 | 1.772 | 0.004 |

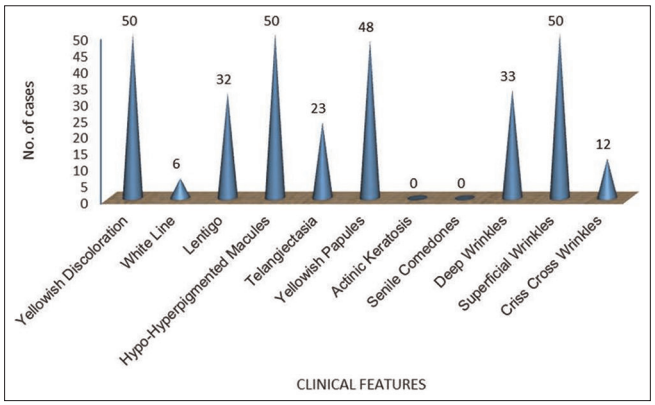


**Figure 4:** Baseline dermoscopic features seen in participants.

after dermoscopic photographs of patients in Group A and Group B are shown in [Figures 5 and 6], respectively.

The mean PhGA in Group A was 14.800 ± 3.582 at baseline and after 4 weeks of treatment, it decreased to 9.9200 ± 3.558 and at the end of follow-up period of 12 weeks, it was 7.0800 ± 3.135. The reduction in the score was statistically significant ($P$ = 0.000). The mean PhGA in Group B was 14.040 ± 2.590 at baseline and after 4 weeks of treatment, it decreased to 10.520 ± 2.293 and at the end of follow up period of 12 weeks, it was 7.040 ± 2.169. The reduction in the score was statistically significant ($P$ = 0.001) [Table 4]. Representative before and after photographs of patients in Group A and Group B are shown in [Figures 7 and 8], respectively.

There was 28.25% reduction in DPAS in Group A at 4 weeks whereas reduction was 16.18 % in Group B. Group A showed 56.12 % reduction at week 12, while Group B showed 44.78 % reduction. There was statistically significant difference in mean percentage reduction in DPAS between the two groups when compared. ($P$ = 0.001) [Figure 9].

### Secondary outcome: PGA

The mean PGA in Group A was 5.125 ± 0.771 after 4 weeks of treatment which increased to 6.25 ± 1.083 at the end of follow-up period (12 weeks). The mean PGA in Group B was 5.000 ± 0.917 after 4 weeks of treatment which increased to 5.542 ± 1.292 at the end of follow-up period (12 weeks).

In Group A, 4 (16%) while in Group B, none of the study cases showed very good improvement (>75% reduction in DPAS). In Group A, 18 (72%) while in Group B, 9 (36%) of the study cases showed good improvement (50–75% reduction in DPAS). Moderate improvement (25–50% reduction in DPAS) was seen in 4 (16%) and 16 (64%) patients, in Groups A and B, respectively. Statistically significant difference in grades of therapeutic improvement was noted between both the groups ($P$ = 0.001). In both the groups, no subject reported dissatisfaction at either 4- or 12-week follow-up [Figure 10].

### Safety outcome: Tolerability and adverse events

Erythema was the only complaint experienced by 2 (4%) cases, one in each Group A and Group B. However, this side effect subsided within 24–48 h period in both the patients.

## DISCUSSION

Photoaging is the process of accelerated skin aging due to chronic solar exposure. Few of the signs are common to both photoaging and photo-protected chronologically aged skin. Photoaging causes significant psychological distress and frustration in the affected individuals due to considerable cosmetic disfigurement and remains a difficult condition to treat. Irradiation with red LEDs targets collagen and reduces the induction of MMP enzymes due to the fact, it can penetrate up to 6 mm of skin. Dietary substances such as beta-carotene, collagen peptides, zinc, and fat-soluble Vitamins D and E also have benefits in preventing and repairing photoaging. Beta-carotene is a plant-derived carotenoid that has a free radical scavenging action. The efficacy of light therapy with concomitant oral beta carotene supplementation has not been

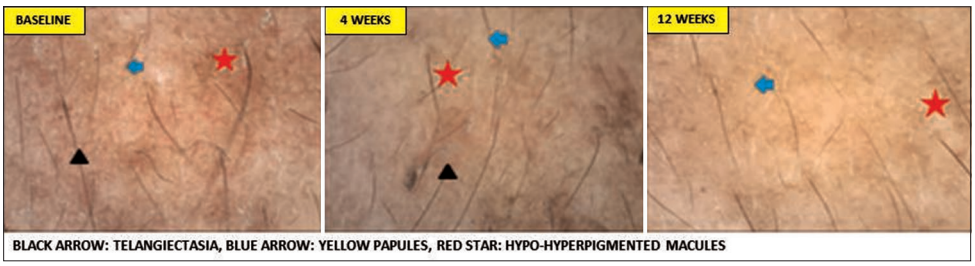


**Figure 5:** Representative before and after dermoscopic photographs of participants in Group A (×60 polarized mode).

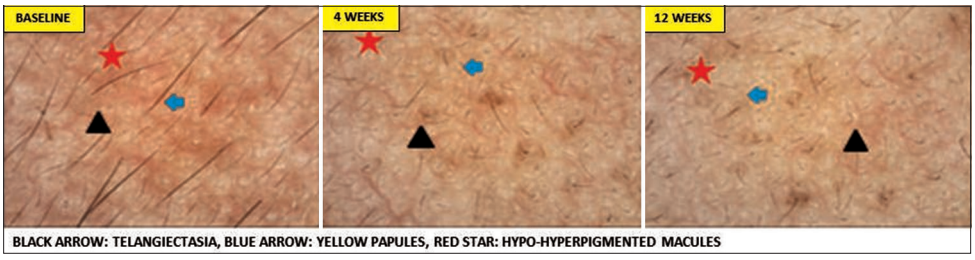


**Figure 6:** Representative before and after dermoscopic photographs of participants in Group B (×60 polarized mode).

**Table 4:** Trends in mean PhGA score with treatment in Group A and Group B.

| Group | Duration | Mean PhGA | Standard Deviation | *P*-value |
|---|---|---|---|---|
| Group A | Baseline | 14.800 | 3.582 | |
| | 4 weeks | 9.9200 | 3.558 | 0.000 |
| | 12 weeks | 7.0800 | 3.135 | 0.000 |
| Group B | Baseline | 14.040 | 2.590 | |
| | 4 weeks | 10.520 | 2.293 | 0.000 |
| | 12 weeks | 7.040 | 2.169 | 0.001 |

PhGA: Physician global assessment

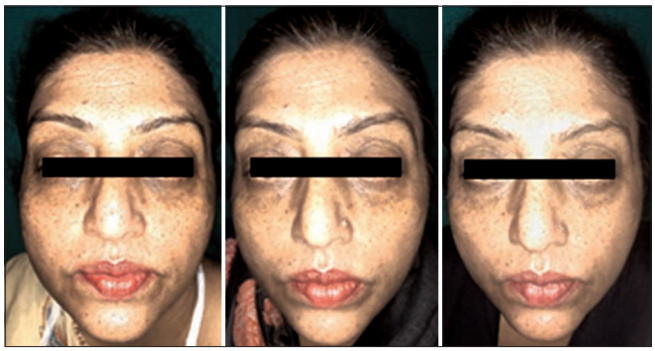

**Figure 7:** Representative before and after dermoscopic photographs of participants in Group A.

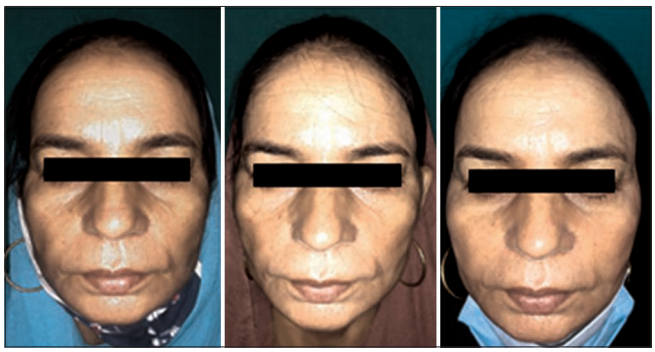

**Figure 8:** Representative before and after photographs of participant in Group B.

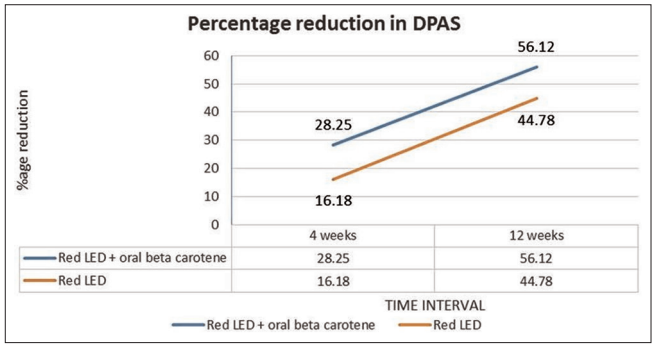


**Figure 9:** Percentage reduction in DPAS in Group A and Group B.

studied earlier. The quantitative assessment of efficacy of this combined modality can be studied through dermoscopic photoaging scale (DPAS).

The risk of wrinkling and pigmentary changes increases as such with age. People in their sixties are 12 times more prone to wrinkling, and subjects in their seventies are 56 times at a higher risk compared to the younger group. It is believed that pigmentary changes are more evident clinical signs of photoaging in Asians and that wrinkling is late compared to Caucasian subjects of a similar age.[8] However, we found that both wrinkling and pigmentary changes were a prominent feature of cutaneous photodamage in our patients and were seen at an early age of 35 years.

Intrinsic aging affects both genders equally while photoaging is seen more in males owing to greater duration of exposure to the sun. Females have increased skin thickness, moisture retention, and decreased skin wrinkling because of the protective effect of estrogen.[3] In our study, most of the patients were female, 48 (96%). This does not reflect the true epidemiology as female attendance for cosmetic issues is more. This fact is consistent with the previous studies where more female patients were enrolled.[9,10]

Occupation holds significance in regards to the degree of sun exposure. In a study conducted by Green *et al.*, it was found that individuals who had outdoor occupations had 60% raised odds of higher grades of photoaging.[11] This was not consistent with our study as housewives who do not have much photo exposure constituted a majority i.e. 26 (52%) of our patients.

The role of cosmetics and intake of certain drugs such as photosensitizing substances have also been considered as risk factors for photoaging. Use of cosmetics and oil application was reported in 17 (34%) in the form of over-the-counter fairness cream, cold cream, bleaching creams, foundations, etc. These products when used for a long duration can lead to serious complications like epidermal thinning, atrophy, and can also make the skin photosensitive.[12]

History of intake of systemic drugs was reported in 10 (20%) study cases. The most common type was ayurvedic and homeopathic medication followed by thyroxine, antihypertensives, and other medications like analgesics.

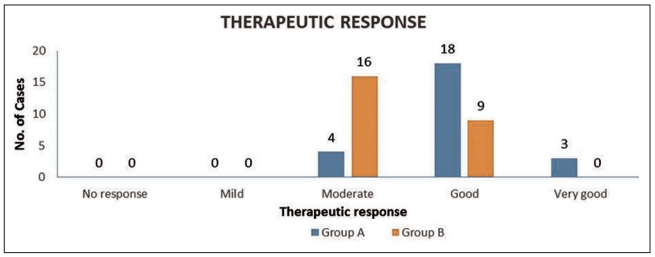


**Figure 10:** Therapeutic response in Group A and Group B.

It was found that hypothyroidism was the most common associated comorbidity. It was seen in five patients (three in Group A and two in Group B). There are studies that correlate the presence of subclinical hypothyroidism with increasing age. A study conducted by Bocheva *et al*. emphasizes that hypothyroid state could be a risk factor for increased oxidative skin damage in chronically photo-exposed skin due to oxidative stress. Lipid peroxidation is one of the main steps through which photo-oxidative stress helps in causing photocarcinogenesis and photoaging.[13]

Both groups showed significant reduction in DPAS at 4th and 12th week follow-up suggesting decrease in signs of photodamage. Majority of the patients reported improvement in skin smoothness, firmness, and complexion with softening of fine lines in both the groups. Tolerance of treatment was good in both the groups. However, there was 28.25% reduction in DPAS in Group A and 16.18% in Group B at 4 weeks. Group A showed 56.12% reduction and Group B showed 44.78% reduction at 12 weeks. While both the groups showed improvement, on comparing the two groups, it was seen that addition of oral beta-carotene in Group A along with red light therapy resulted in significant superior results than what was seen in Group B (red light therapy alone). Therefore, we suggest that combination red light therapy with oral beta-carotene is better, convenient, and effective approach than red light therapy alone in the treatment of photoaging.

Limitations of the study included small sample size. There is a possibility of observer's bias as DPAS is a subjective assessment tool. A longer follow-up period could have allowed for assessment of the longevity of all the outcomes.

## CONCLUSION

Our results suggest that red LED therapy with concomitant oral beta-carotene is effective in treatment of photoaging without significant adverse effects.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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