Net Study

# Comparative study of trichloroacetic acid versus glycolic acid chemical peels in the treatment of melasma

*Rashmi Kumari, Devinder Mohan Thappa*

Department of Dermatology and STD, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Pondicherry, India

Address for correspondence:
Dr. Devinder Mohan Thappa, Professor and Head, Department of Dermatology and STD, JIPMER, Pondicherry-605 006, India.
E-mail: dmthappa@gmail.com

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## ABSTRACT

**Background:** Melasma is a common cause of facial hyperpigmentation with significant cosmetic deformity. Many modalities of treatment are available, but none is satisfactory. **Aim:** This study was designed to compare the therapeutic response of melasma in Indian women to glycolic acid (GA 20–35%) versus trichloroacetic acid (TCA 10–20%) for chemical peeling. **Methods:** Forty nonpregnant female patients with a minimum melasma area and severity index (MASI) of 10 were recruited in the study. After a detailed history and clinical examination under natural light, MASI was calculated and color photographs were taken of all the patients. The patients were advised to carry out a prepeel program of daily application of 12% GA cream or 0.1% tretinoin at night for 2 weeks. They were then treated with graded concentrations of 20–35% GA facial peel every 15 days in GA group and 10–20% TCA in the second group. **Results:** Objective response to treatment evaluated by reduction in MASI scoring after 12 weeks was by 79% reduction (from 26.6 to 5.6) in GA group and by 73% reduction in TCA group (from 29.1 to 8.2) but this difference was not significant. Patients with epidermal-type melasma showed a better response to treatment than those with mixed-type melasma ($P < 0.05$). Subjective response, as graded by the patient, showed good or very good response in 75% in GA group and 65% in TCA group. No relation of treatment response to age and duration of melasma could be established in this study. **Conclusions:** A prepeel program of daily application of 12% GA cream at night for 2 weeks, followed by graded increase in GA and TCA concentrations proved to be an equally effective treatment modality for epidermal and mixed melasma. There are hardly any major side effects, and regular use of sunscreens prevents chances of postpeel hyperpigmentation. GA peel is associated with fewer side effects than TCA and has the added advantage of facial rejuvenation.

**Key words:** Melasma, chemical peels, glycolic acid, trichloroacetic acid

## INTRODUCTION

Melasma is a common, acquired, symmetric hypermelanosis, characterized by irregular light to dark brown macules and patches commonly involving the cheeks, forehead, upper lip, nose, and chin.[1] Chemical peeling is an increasingly popular method for treating a myriad of benign skin disorders including melasma. Various combination of topical medications like hydroquinone, tretinoin, topical steroids are also used for melasma but chemical peeling provides more rapid response to topical therapy.[2] Today, a plethora of peeling agents are available. Those most commonly used include phenol, trichloroacetic acid (TCA), alpha hydroxyacids (AHAs), and beta hydroxyacids.

Although both TCA and GA are being used in various centers in India, there have been very few studies comparing these two agents in pigmented patients (Fitzpatrick skin type IV to V) with melasma, using both subjective and objective methods of evaluation (MASI). This prompted us to compare these two easily available agents, TCA and GA. Both are superficial to medium depth peels and are not effective for dermal

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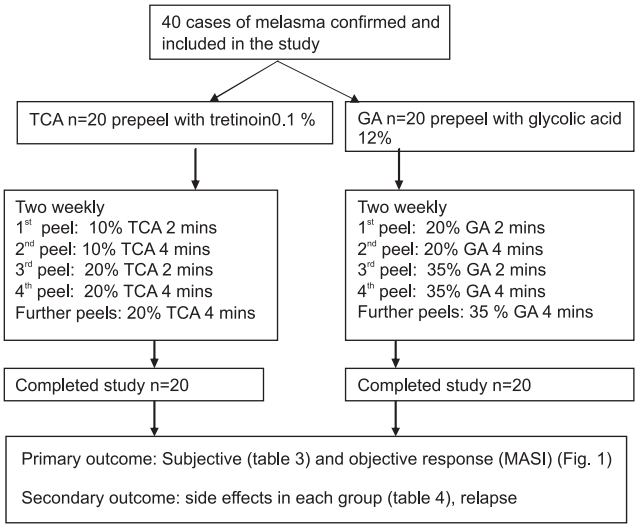
melasma. Hence, cases of dermal melasma were not included in this study. We undertook this study to compare the therapeutic response of melasma in Indian women to graded concentrations of glycolic acid (GA 20–35%) versus trichloroacetic acid (TCA 10–20%) for chemical peeling.

## METHODS

This study was carried out on 40 nonpregnant women with epidermal and mixed melasma, with a minimum melasma area and severity index (MASI)[7] of 10, visiting the outpatient department of our hospital over 1 year duration from March 2005 to March 2006, after getting due ethical clearance from our institute ethics committee. Patients with a history of herpes, taking oral contraceptive pills, isotretinoin, pregnancy, lactation, history of keloids or hypertrophic scars, concomitant systemic or skin disease and those with unrealistic expectations were excluded from the study. These 40 women were randomized into two groups of 20 patients in each, by computerized generated numbers [Table 1].

To calculate MASI, the face was divided into four regions [forehead (F) 30%; right malar (MR) 30%; left malar (ML) 30%, chin (C) 10%] and each area was given a numerical value (*A*, 0–6). The sum of severity for darkness (*D*, 0–4) and homogeneity (*H*, 0–4) of melasma was multiplied by the numerical value and percentage of each area. These values were then added to obtain MASI by a single-blinded trained dermatologist.

**Table 1: Flow chart representing the methodology of the study**




$$MASI = 0.3(D_F + H_F)A_F + 0.3(D_{MR} + H_{MR})A_{MR} + 0.3(D_{ML} + H_{ML})A_{ML} + 0.1(D_C + H_C)A_{C.}$$

A detailed history was taken and clinical examination was performed under natural light by a team of dermatologists to select cases of epidermal and mixed melasma. In case of any doubt in diagnosis, histopathologic confirmation was done before including the case in this study. The MASI score was calculated and color photographs were taken of all patients under standard conditions in natural light. In a prepeel program, patients were advised to apply topical sunscreen daily [sun protection factor-15 (SPF-15)] and 12% GA cream (in GA group) or 0.1% tretinoin (in TCA group) at night for 2 weeks.

The first group was treated with graded concentrations of GA (20–35%) and second group with TCA (10–20%). For the purpose of peeling, the face was divided into anatomic units – right forehead, left forehead, left cheek, right cheek, nose and glabella, and perioral area. After degreasing, treatment with GA/TCA peel was carried out in the respective group for a period of 20–30 seconds and was left for a definite period of time (first peel: 20% GA/10% TCA for 2 minutes; second peel: 20% GA/10%TCA for 4 minutes; third peel: 35% GA/20% TCA for 2 minutes; fourth peel: 35% GA/20% TCA for 4 minutes, separated by 2-week intervals) on the individual anatomic units, separately and in a preset sequence. The peel was terminated by the dilutional effect of washing with neutralizer sodium bicarbonate in the same sequence as the application in GA group and cold saline/ice in TCA group. At regular intervals, the degree of tolerability to the facial peel and the side effects were recorded before proceeding to the higher concentration. In cases where there was a slow or inadequate response, further treatment with peels was carried out at 2-week intervals.

The primary objective of this study was to assess the degree of improvement in pigmentation objectively using MASI at baseline, 4, 8 and 12 weeks. Color photographs were taken of all patients at baseline and 30 days after the last peel. The patients were advised to apply 2% hydroquinone at night and to continue with topical sunscreen (SPF-15) to maintain the results achieved after the fourth peel.

Subjective improvement before and at the completion of the study, the response in each patient was graded as: *no response* if there was no change in MASI score

at the end of three peels; *mild response* if there was less than 25% change; *moderate response* with 25 to <50% decrease in MASI; *good response* if there was 50 to <75% fall in MASI score; *very good response* with more than 75% fall in MASI score. Secondary outcome measures such as the side effects, if any, and cost of the therapy were recorded. A minimum of 6 months of follow up in each case was done to look for relapse, if any. The data obtained were statistically analyzed using SPSS software. Student's paired *t*-test and EPIINFO software were used to calculate significant differences between the parameters.

## RESULTS

There were 40 patients included in the study with 38 females and only 2 males, of age between 18 and 53 years with a mean of 32 ± 6.9 years. Duration of melasma ranged between 1 and 10 years with a mean 4.3 ± 2.5 years. There was no significant precipitating factor observed in relation to occurrence of melasma like relation to pregnancy, history of drugs/oral contraceptive pills, sunlight exposure, etc.

Most cases were of epidermal type (78%) and one-fourth of the cases were of mixed type of melasma (22%). The most common pattern was malar (60%) followed by centrofacial pattern (40%). Total number of peels required in both the groups is as shown in Table 2. Mean of peels required in both groups was 7.13 approximately and was not different in the two groups, GA group (mean 7.0 peels) and TCA (7.3 peels).

Objective response to treatment as studied by fall in MASI scoring after 12 weeks was 79% reduction (from 26.6 to 5.6) in GA group and 73% reduction (from 29.1 to 8.2) in TCA group. The MASI scores at baseline 4, 8, 12 weeks were as shown in Figure 1. There was no significant difference in reduction of MASI scores at the end of six peels after 12 weeks between both the groups ($P > 0.05$). However, TCA peel [Figure 2] showed an initial rapid response compared to GA [Figure 3]. In the TCA group, the patients reported a quicker improvement after two peels but the response was comparable in the two groups at the end of peeling

**Table 2: Number of peels used in the two groups**

| Total number of peels | GA | TCA | Total (%) |
|---|---|---|---|
| Six | 9 | 3 | 12 (30) |
| Seven | 4 | 10 | 14 (35) |
| Eight | 6 | 5 | 11 (27.5) |
| Nine | 1 | 2 | 3 (7.5) |
| Total | 20 | 20 | 40 (100) |

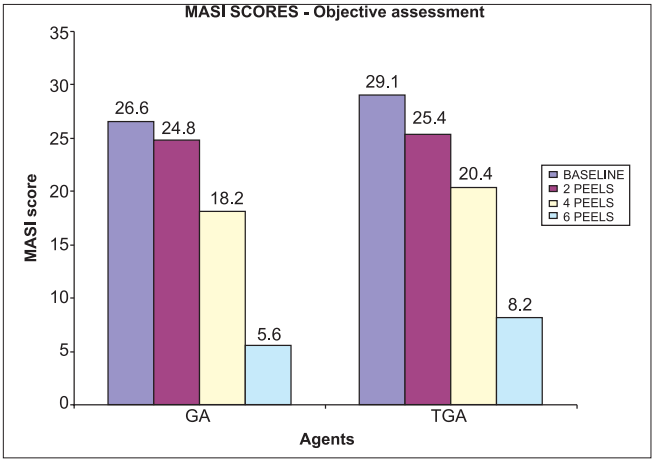



**Figure 1: Objective assessment using MASI scoring with GA and TCA peel**

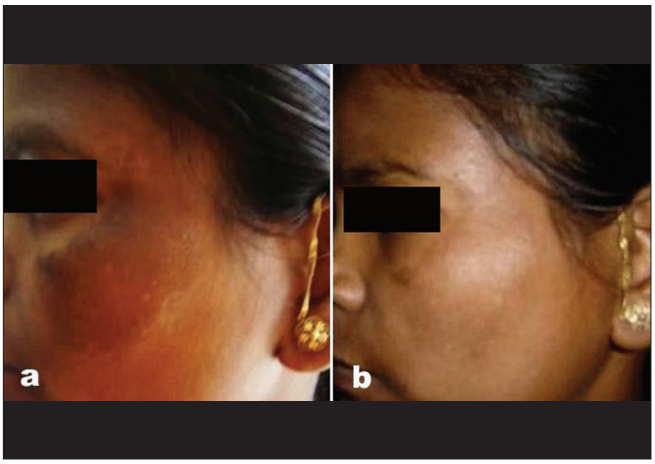



**Figure 2: (a and b) Pre and post treatment photographs after TCA peeling**

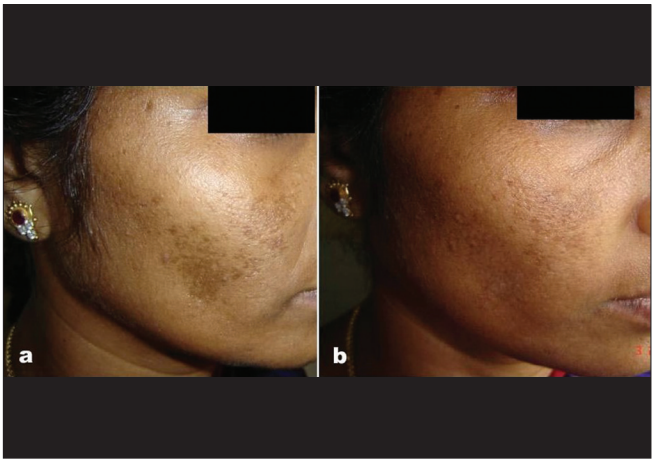



**Figure 3: (a and b) Pre and post treatment photographs after GA peeling**

sessions, with both the groups showing equally efficacious response. Of the 20 cases of melasma which were treated with GA, there was 79% reduction in epidermal melasma (from mean MASI of 25.5 to 5.6) and 48% reduction in mixed melasma cases (from mean MASI 30.2 to 21.8). Also, this difference in response with respect to type of melasma was significant ($P < 0.05$). Comparison of the duration of melasma with the response to treatment gave no significant difference.

Subjective response, as graded by the patient, showed good or very good response in 75% in GA group and 65% in TCA group (statistically insignificant). No relation of treatment response to age or duration of melasma could be established in this study [Table 3].

During the study, the frequency of serious side effects was very low [Table 4]. There was mild burning sensation in 95% of patients in GA group to moderate to severe burning in 75% of patients in the TCA group. Postpeel crackening was reported in 35% of cases in TCA group but in none of the patients in the GA group. Persistent erythema was seen only in one case and peeling was deferred due to side effects on five occasions and done 1 week later till the erythema subsided. There were no side effects of hyperpigmentation in spite of the fact that most patients were of Fitzpatrick skin type IV–VI. There was significant improvement in the texture and glow of skin appreciated by 75% of the patients in GA group, which was not appreciated in TCA group.

Relapse was seen in only two cases after a follow up of 6 months in GA group at the same site. Other patients maintained the results achieved with the regular use of sunscreens after a follow up for more than a year.

**Table 3 Subjective improvement seen in both the groups at the end of peeling sessions**

| Percentage improvement | GA | TCA |
|---|---|---|
| Very good (>75%) | 5 | 3 |
| Good (50–75%) | 10 | 10 |
| Moderate (25–50%) | 2 | 6 |
| Mild (<25%) | 3 | 1 |

**Table 4: Side effects seen after peeling**

| Side effects | GA (%) | TCA |
|---|---|---|
| Mild burning | 95 | 25% ($P < 0.05$) |
| Moderate to severe burning | 5 | 75% |
| Erythema | 15 | 35% (not significant) |
| Postpeel crackening | 0 | 35% ($P < 0.05$) |

## DISCUSSION

Melasma is more common in women of child-bearing age,[3] although men also suffer from the condition and account for 10% of the cases.[4] Melasma affects all races, but is observed more frequently among individuals with skin type IV–VI, especially in women of Hispanic, Caribbean, and Asian origin, who live in areas of intense ultraviolet radiation.[5] There are three clinical patterns – centrofacial, malar, and mandibular – depending upon the area of localization.[1] Histologically, melasma is divided into three types: epidermal, dermal, and mixed.[6] Wood's light causes intensification of pigmentation in epidermal-type melasma, but does not enhance the pigmentation in the dermal type. But this distinction may not be useful in pigmented races. A combination of epidermal and dermal macules is recognized as the mixed type.[7]

Chemical peeling aims at production of controlled chemical burns of epidermis and/or dermis, resulting in exhalation and subsequent resurfacing of the epidermis and remodeling of collagen and elastic fibers with deposition of glycosaminoglycans in dermis. Both the agents used in this study, TCA 10–20% and GA 20–35%, are superficial peels.[8] Superficial peels are defined as those causing injury to the dermis and dermoepidermal interface. Medium depth peels are those that penetrate to the papillary or reticular dermis (35–50% TCA). Deep peels are those that cause destruction into the reticular dermis but have longer healing time and more serious complications. Application of TCA to the skin causes precipitation of proteins and coagulative necrosis of cells in epidermis. In higher concentration, it causes necrosis of collagen in the papillary to upper reticular dermis. Over several days, the necrotic layers sloughs and the skin re-epithelizes from the germinative segments of hair follicles.[8]

The benefits of AHAs have long been recognized.[9] Cleopatra, for example, applied sour milk (contains lactic acid) to her face, while Polynesian women found sugarcane juice (contains GA) to provide them with similar benefits. AHAs decrease corneocyte cohesion leading to sloughing of dead cells and stimulation of new cell growth in the basal cell layer. In higher concentrations, they cause epidermolysis. Products with a small molecular size per volume are more active and penetrate the skin more deeply. GA has the smallest molecular structure, followed by

lactic, pyruvic, malic, tartaric, and citric acids. The bioavailability of AHAs increases as the pH decreases (desirable pH 2.8–4.8), and they are the only peels that are time dependent and can be neutralized easily.[10]

In our study, the average age of patients at the onset of melasma was middle age as reported in other studies from India, but Kimbrough-Green *et al.*[11] reported a much higher age of onset (44 years) in their study of Black patients, whereas in another study in Caucasian patients the age group was comparable with mean of 30 years. The types of melasma in our patients also differed from those studied by Kimbrough-Green *et al.*[11] in Black women and Griffiths *et al.*[12] in Caucasian women. They observed epidermal-type melasma in 43 and 94% of patients, respectively, compared to our figure of 66%. Sanchez *et al.*[6] found centrofacial pattern to be the most common, but in our study and most other studies[13,14] the commonest pattern was malar followed by centrofacial.

In another Indian study carried out by Kalla *et al.*,[15] GA and TCA showed comparable results on subjective scores given by patients [Table 5]. They had not used any scientific scoring system like MASI for comparison. On comparing the results of TCA peels in our study with that done by Kalla *et al.*[15] on 32 patients, there was no significant difference in response to TCA peels [Figure 4], but Kalla *et al.* had used on average only 4.1 peels whereas we used on an average 7.3 peels to achieve the desired results. They found 54% cases having more than 50% response to peeling by both agents as compared to 70% cases in our study. In their study GA (55–70%) had required more number of peels than TCA (10–15%), whereas in our study the response to GA was initially slower but equal number of peels were required in both the groups. Kalla *et al.*[15] observed a more rapid response to TCA than GA in their study. They had found that duration of disease was inversely proportional to response to peeling but our study refutes this fact with similar response to longstanding cases. As with our study the local irritant effects and postpeel crackening were more with TCA than with GA. Relapse and hyperpigmentation were much less in our study. The rate of hyperpigmentation and relapse was higher in the TCA group (25%) than GA group but this was not so in our study where both the groups had minimal postinflammatory pigmentation.

Many other studies[6,9] that have used GA in various concentrations in similar skin type patients have shown variable results as shown in Table 6. But there have been very few studies focusing on the efficacy of these two commonly available agents in a scientific manner in South Indian patients who are mostly dark skinned and hence comparison is difficult. Previous studies have shown significant clinical improvement of melasma pigmentation following 70 or 50% GA facial peel after two consecutive peels 1 month apart.[13,14] Grover and Reddu[16] had in their experience with GA (10–30%) in various cases received a similar response, that is, above 60% in more than 90% of cases. Sarkar *et al.*[2] had compared the efficacy of 20% GA with Kligman's formula in 20 cases of epidermal melasma and had seen a significant reduction (>80%) in MASI scores with GA when compared to plain Kligman's regime. The response is not as high in our study as that of Javaheri *et al.*,[9] while comparing the MASI scores of GA group but subjective response was comparable. We compared the MASI scores in the GA group with respect to type of melasma (epidermal versus mixed) with that of the GA peeling scores obtained in the study of Javaheri *et al.* [Table 7]. It showed significant differences in response

**Table 5: Comparing the response in the TCA group of our study with that of Kalla *et al.*[15]**

| Subjective improvement | Kalla *et al.* | Our study |
|---|---|---|
| >75% | 9 | 3 |
| 50–75% | 11 | 10 |
| 25–50% | 8 | 6 |
| <25% | 4 | 1 |
| Total | 32 | 20 |

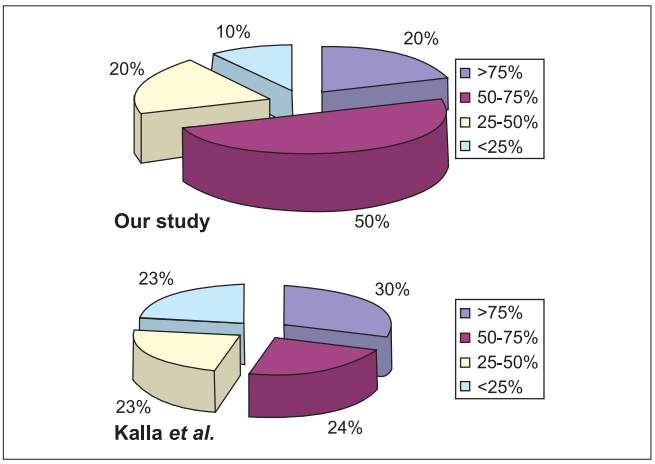



**Figure 4: Comparison of subjective scores of patient response of our study with that of Kalla *et al.***

**Table 6: Comparison of our study with various other studies of chemical peeling using GA**

| | Our study | Javaheri *et al.*[9] | Kalla *et al.*[15] | Grover *et al.*[16] | Sarkar *et al.*[2] |
|---|---|---|---|---|---|
| Percentage of GA and interval | 20–35% and 2 weeks | 50% and 4 weeks | 55–70% and 2 weeks | 10–30% and 2 weeks | 30–40% and 3 weeks |
| No. of cases and average no. of peels | 20 cases and seven peels | 23 cases and three peels | 68 cases and seven peels | 15 cases and eight peels | 20 cases and six peels |
| Response | >50% in 70% patients | >50% in 60% patients | >50% in 54% patients | >60% in 90% patients | >80% excellent |
| Reduction in MASI scores | 79% | 47% | NA | NA | MASI 46%, 80% |

NA: Not applicable

**Table 7: Comparing the response to peeling in the GA group in our study with that of Javaheri *et al.***

| Type of melasma | Our study | | | Javaheri *et al.*[9] | | |
|---|---|---|---|---|---|---|
| | Before | After | Reduction | Before | After | Reduction |
| Epidermal (significant) | 25.5 | 5.6 | 20.7 (79%) | 20.3 | 10.8 | 9.5 (46.7%) |
| Mixed (not significant) | 30.2 | 21.8 | 8.4 | 26.8 | 19.5 | 7.3 |

to epidermal melasma [Figure 5] with a better response, but in mixed melasma cases both the studies had a similar response to GA. In a recent study[17] from Pakistan, chemical peeling was done in group A (GA 50%) and group B (TCA 20%) with 25 patients in each group. The mean score of response calculated for both the groups revealed better overall clinical response in TCA group than in GA group but this difference was statistically insignificant ($P > 0.05$). In another study, 1% tretinoin peel versus 70% GA at weekly intervals was carried out in 10 patients in a split-face trial. A significant decrease in the modified MASI from baseline to 12 weeks was observed on both facial sides ($P < 0.001$). Nevertheless, there was no statistically significant difference between the right and left sides. The study concluded that serial 1% tretinoin peel is as effective a therapy for melasma as chemical peeling with 70% GA.[18]

Limitation of our study included the observer bias in the subjective scoring. To eliminate this, MASI scoring was done by a single-blinded independent person but split-face analysis was not attempted by us. This is a small series of patients treated with chemical peeling at our center to see the response to chemical peeling to both TCA and GA.

Postinflammatory hyperpigmentation has been reported to be the most common side effect with GA facial peels[14] but in our study the frequency of all side effects was much lower as compared to that of

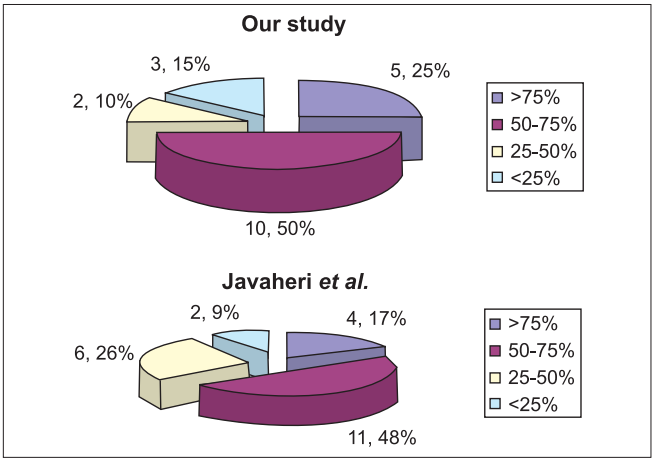



**Figure 5: Comparison of objective scores of patient response to GA of our study with that of Javaheri *et al.***

other studies.[2] This may have been due to the graded concentration method of acids use and strict adherence to photoprotection. The fewer side effects that occurred like mild erythema and burning sensation were mostly well tolerable. No patient developed herpes, vesiculation or keloids post peels as was reported in other studies. Regular use of sunscreens helped in maintaining the result of the peels on follow up. Postpeel crackening effect that occurred only with TCA and not with GA makes it beneficial for patients to continue outdoor activities and office work in GA group.[19] In TCA group, many patients took leave from there work to avoid facing their colleagues but in GA group patients were not embarrassed in any way and the glow due to facial rejuvenation made them look

appreciably younger. Hence, the higher cost of GA compensates by the less number of leaves patient may henceforth require during the procedure.

## CONCLUSIONS

A prepeel program of daily application of 12% GA cream at night for 2 weeks, followed by graded increase in GA and TCA concentrations of facial peel for a duration of 2–4 minutes once every 2 weeks for three consecutive months proved to be an equally effective treatment modality without any major side effects. The beneficial results achieved can be maintained with topical application of sunscreen SPF-15 and 2% hydroquinone. Regular use of sunscreens prevents the chances of postpeel hyperpigmentation. GA peel is associated with fewer side effects than TCA and has the added advantage of facial rejuvenation and patients can continue to go for work.

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