A Comparative Study to Assess the Safety and Efficacy Of 12% Glycolic Acid V/S 10% Azelaic Acid in the Treatment of Post Acne Hyperpigmentation

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Abstract - Background: Acne vulgaris is the most common condition encountered in dermatologic practice. Recent literature suggests racial and ethnic difference in the sequelae of acne complications with post acne hyperpigmentation topping the list. Therapeutic goals include promoting degradation of melanosomes and inhibiting their formation. Thus it is a challenge to treat patients of darker skin and find an agent to reduce hyperpigmentation without causing undesirable lightening of surrounding normal skin. A right balance of topical and repetitive superficial resurfacing procedures must be undertaken in addition to ultraviolet protection measures.

Objectives: To compare the safety and efficacy of 10% azelaic acid v/s 12% glycolic acid in the treatment of post acne hyperpigmentation.

Materials and Methods: A prospective study including 30 patients with post acne hyperpigmentation attending OPD at Fr Muller Medical College between September 2014 to March 2015 were included. Ethical clearance was obtained prior to commencement of study. Collected data was analysed by frequency, percentage and chi square test.

Conclusions: Hyperpigmentation reaction is thought to be a default pathophysiological response of dark skin to cutaneous injury. For patients the lingering effects of PIH is more disturbing than the actual acne itself, hence adjunctive treatment like microdermabrasion or chemical peels can address this issue and cosmetically give better results.

Index Terms: post inflammatory hyperpigmentation, azelaic acid, glycolic acid

I. INTRODUCTION

Disorders of hyperpigmentation are a challenge to treat especially in patients with darker skin, considering the propensity to hyperpigment, post any inflammation. The challenge is therefore to find an agent to reduce the hyperpigmentation without causing undesirable lightening of surrounding normal skin. Acne even in mild form can have a lasting effect on the mental health of the patient causing anxiety & depression. Lately literature has begun to recognize that race and ethnicity play a vital part in the successful management of acne vulgaris, however current evidence suggests that key differences exist in relation to post acne sequelae. PIH results from overproduction of melanin or an irregular dispersion of pigment after cutaneous inflammation. When limited to the epidermis there is an increase in the production and transfer of melanin to surrounding keratinocytes, the rise in melanin activity being stimulated by the release of cytokines, pro inflammatory mediators and reactive oxygen species. A study done by Gavneet pruthi and Nandita babu using a quality of life measure for patients with skin disease developed by Chren et al., showed that physical discomfort and anger were the major causes of distress among young adults with acne thus the study confirmed that acne not only hampered the physical but the psychosocial frame of mind of the patient.

II. MATERIALS AND METHODS

This prospective study was conducted in the Out-patient Department of Dermatology, Venereology and Leprosy, Fr. Muller Medical College Hospital, Mangalore during September 2014 to March 2015. Ethical clearance for the study was obtained from the institutional review board. Data was collected from 30 patients with Post acne hyperpigmentation. Patient with history of acne vulgaris, ages 18 and above, both sexes and willing to participate were included in the study. Exclusion criteria included patients with active lesions, patients not willing to be part of the study, patients who are pregnant and patients with h/o previous keloid.

III. TREATMENT REGIMEN

All patients who fulfilled the selection criteria were allocated alternately into groups A and B. Group A patients received 10% Azelaic acid and group B received 12% Glycolic acid, and were advised to apply topically once daily at night and wash their face the next morning. All patients were advised to apply broad spectrum sunscreens with a minimum SPF of 15. Pre treatment evaluation was done with detailed history, examination and colour photographs. Response to treatment was evaluated at weeks 4, 8 and 12. At each visit, clinical response to treatment and efficacy was assessed using the 8 point scale suggested by Grimes et al (Table 1) and data was analysed by frequency, percentage and chi square test.

IV. RESULTS

In the present study out of the 15 cases in each group, 3 male patients (23.07%) and 12 female patients (76.92%) received azelaic acid (AA) 10% and 3 male (20%) and 12 female (80%) received glycolic acid (GA) 12% cream. An overall female
The preponderance was noticed, male to female ratio being 1:4:1. Upon tabulation of the results, it was found that patients in both the groups were matched according to age and sex. The mean age of patients receiving AA was 26.69 yrs and 24.40 yrs for patients receiving GA. The distribution of the various clinical patterns among the two regimens was uniform statistically. A positive history of photodamage was equally predominant in both groups AA being 18.8% and GA being 60%. Most of the patients had a minimum duration of 5-6 years of acne concomitantly (56.3%, 60%) (AA,GA). Although most patients had no prior history of drug intake (75%, 73.3%) (AA,GA), a significant number: 65.2%, 73.35 (AA,GA) did apply topical anti-acne medications. We observed that 81.3%, 86.7% of patients (AA,GA) did not take any treatment for their post acne hyperpigmentation. The efficacy of each depigmenting agent was found to be statistically highly significant. In patients who received AA there was a significant decrease in visible hyperpigmentation from week 0 to week 12 \( (P \leq 0.001) \), moreover the change was visible in the first four weeks and then gradually decreased over the next eight weeks (0-4 wks: 2.38-1.88) and (0-12 wks: 2.38-1.47). In patients who received GA there was no significant change in the first four weeks (mean: 2.93-2.33), but changes began to show in the eighth week (mean: 2.93-1.87) and by 12 weeks (mean: 2.93-1.69) a visible decline was seen. So at the end of the 12 week treatment regimen, both the agents were equally efficacious in the respective groups, with 10% Azelaic acid showing a much quicker response with a stable plateau of improvement as compared to 12% Glycolic acid showing a more consistent decline in hyperpigmentation over 12 weeks. Side effects such as erythema and burning sensation were noted in one patient with Glycolic acid and post treatment hypopigmentation was observed in one patient using Azelaic acid.

V. DISCUSSION

Post inflammatory hyper pigmentation (PIH) is an acquired condition in which increased skin pigmentation occurs as a consequence of cutaneous inflammation, it can be seen in any age or gender, most commonly seen in Fitzpatrick type 3-6, typically develops at the site of preceding inflammation. \(^5\) Sun exposure reverses the positive effects of any topical agent, hence sun protection being the prime objective to arrest the process of hyperpigmentation. \(^6\) Pigmentary disorders can cause emotional distress and can pose a negative impact on a patient's health related quality of life and skin lightening agents work to break melanin production degradation cycle. A right balance of topical and repetitive superficial resurfacing procedures must be undertaken in addition to ultraviolet protection measures.\(^7\) Chemical substances, exfoliants, alpha hydroxyl acids stimulate cell renewal, facilitates the removal of melanized keratinocyte leading to melanin pigment loss. \(^8\) α-Hydroxy acids (AHAs) are a group of nontoxic organic acids and include glycolic acid, lactic acid, malic acid, tartaric acid, and citric acid. The most commonly used AHAs are glycolic and lactic acids. Lower concentrations diminish corneocyte cohesion which reduces stratum corneum thickness. At higher concentrations, these same acids cause epidermolyisis. \(^9\) Clinical studies have shown that AHAs used in glycolic acid peels and topical preparations can help repair and reverse changes such as fine wrinkling, coarse texture, and the overall severity of sun damage.\(^10-11\) Burns et al. reported a rapid and better improvement of PIH with the use of GA peels. GA has been used in combination with azelaic acid, tretinoin ascorbic acid thus enhancing depth of penetration while decreasing toxicity and morbidity of deeper peels.\(^1\) A study conducted by Perricone et al. to test the anti-inflammatory and photoprotective effect of glycolic acid found that GA provides SPF of approximately 2.4 and accelerates resolution of erythema. The data obtained supports the hypothesis that glycolic acid acts as an antioxidant.\(^12\) Azelaic acid (AA/ASA) is a naturally occurring saturated 9 carbon dicarboxylic acid. It possesses anti-tyrosinase activity, inexpensive and is more soluble to be incorporated in base creams than dicarboxylic acids\(^13\) Passi et al. manipulated the donor electron groups and demonstrated that AZA competitively inhibits tyrosinase – the key enzyme of melanogenesis. \(^13\) Under controlled conditions, twice daily topical application of 20% AZA cream (over a 3-month period) appeared more effective (64%) than placebo (36%) in reducing comedonal, papular and pustular lesions in mild-to-moderate acne. After treatment for 6 months, topical 20% AZA cream applied twice daily was of comparable efficacy to topical 0.05% tretinoin cream, topical 5% benzoyl peroxide gel, topical 2% erythromycin cream, and oral tetracycline 0.5-1.0 g/day in comedonal and mild-to-moderate (80%) and moderate-to-severe (60%) inflammatory types of acne.\(^14-19\) Allergic reaction most commonly encountered is a local type of irritant, erythematous lesion that appears mild and transient. Other associated symptoms were burning, itching, stinging, but they generally subsided after 2-4 weeks of therapy. Azelaic acid has in vitro antimycotic properties anti-acne, antimicrobial, keratinization normalizing properties, a favorable safety profile, is not teratogenic, is not associated with systemic adverse events or photodynamic reactions and does not induce resistance in \(P. acnes\). The results of this study showed that 10% azelaic acid and 12% glycolic acid are both equally efficacious topical depigmenting agents, however azelaic acid proved more beneficial in acne grades 1 and 2 and glycolic acid proved to be efficacious in grade 3 acne and above and the side effects associated with the two agents were not significant.
IMAGES:

Table 1

<table>
<thead>
<tr>
<th>Grade</th>
<th>Overall Disease Severity</th>
<th>Pigmentary Intensity of Hyperpigmented Lesions</th>
<th>Area of Hyperpigmented Lesions</th>
<th>Degree of Hypopigmentation</th>
<th>Erythema, Burning, Peeling, Dryness</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal</td>
<td>None (normal)</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>Present, but &lt; mild</td>
<td>Trace (mild and localized)</td>
<td>Trace (1%-10% of face)</td>
<td>Trace (slight and localized)</td>
<td>Trace</td>
</tr>
<tr>
<td>2</td>
<td>Mild (slightly noticeable)</td>
<td>Mild (mild and diffuse)</td>
<td>Mild (11%-25% of face)</td>
<td>Mild (slight and diffuse)</td>
<td>Mild</td>
</tr>
<tr>
<td>3</td>
<td>Between mild and moderate</td>
<td>Moderate (moderate and diffuse)</td>
<td>Moderate (28%-40% of face)</td>
<td>Moderate (noticeable and diffuse)</td>
<td>Moderate</td>
</tr>
<tr>
<td>4</td>
<td>Moderate (noticeable)</td>
<td>Marked (moderate and dense)</td>
<td>Marked (41%-50% of face)</td>
<td>Marked (noticeable and dense)</td>
<td>Marked</td>
</tr>
<tr>
<td>5</td>
<td>Between moderate and marked</td>
<td>Severe (prominent and dense)</td>
<td>Severe (&gt;50% of face)</td>
<td>Severe (complete lack of melanin pigmentation)</td>
<td>Severe</td>
</tr>
<tr>
<td>6</td>
<td>Marked (distinctive)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>7</td>
<td>Between marked and severe</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>8</td>
<td>Severe (very distinctive)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

GRAPH 1:
DISTRIBUTION OF PATIENTS AT BASELINE. MOST OF THE PATIENTS BELONGED TO GRADE 3 AND 4 (TABLE 1)
GRAPH 2: ASSESSED AT WEEK 4. MOST OF THE PATIENTS OF AA GROUP WERE IN GRADE 1 AND 2

GRAPH 3: ASSESSED AT WEEK 8. PATIENTS OF GA GROUP ARE CONCENTRATED IN GRADE 1 AND 2
GRAPH 4:
ASSESSED AT WEEK 12. ALL THE PATIENTS ARE CONCENTRATED IN GRADE 1

FIGURE 1A; GRADE 1 PRE TREATMENT

FIGURE 1 B, GRADE 1 PRE TREATMENT
FIGURE 8A, GRADE 4 POST TREATMENT

FIGURE 8B, GRADE 4 POST TREATMENT

FIGURE 9A, PRE TREATMENT

FIGURE 9B, POST TREATMENT HYPOPIGMENTATION
REFERENCES


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