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Original Research Article

Expert opinion on the prescription practice of azelaic acid for the management of acne in various age groups in Indian settings

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ABSTRACT

Background: Azelaic acid has been indicated to treat various common dermatoses including acne vulgaris, perioral dermatitis, inflammatory rosacea, melasma, and post-inflammatory hyperpigmentation due to its various modes of action and significant therapeutic efficacy.Considering the scientific advances contributing to the refinement of therapeutic options, it was important for clinicians to stay updated regarding the current treatment standards.

Materials and Methods: This cross-sectional survey employed a multiple-response questionnaire to gather opinions of dermatologists who had experience in treating acne with a special focus on azelaic acid in Indian settings. There was a total of 28 queries and the majority of them were on the management of acne using azelaic acid monotherapy or in conjunction with oral antibiotics.

Results: The survey involved 467 participants, and 35% of them preferred the use of azelaic acid for the management of acne, melasma, and post-inflammatory hyperpigmentation disorders. About 6 to 8 weeks of optimal duration was recommended by 56% of the respondents for treating acne. Azelaic acid with glycolic acid was preferred by 66% of the respondents for acne treatment. Moreover, about 56% of the respondents preferred azelaic acid in combination with oral antibiotics for the treatment of mild-to-moderate papulopustular acne. Approximately 50% and 46% of respondents reported that they occasionally recommend topical azelaic acid as a treatment for keratosis pilaris and lentigo maligna, respectively. About 37% of the respondents preferred a daily dosage of 20% azelaic acid for the effective management of acne, melasma, and post-inflammatory hyperpigmentation.

Conclusion: For the treatment of mild-to-moderate papulopustular acne, the use of azelaic acid in conjunction with other oral antibiotics was advocated. Experts preferred a daily dosage of azelaic acid to achieve better treatment outcomes in patients with acne, melasma, and post-inflammatory hyperpigmentation where they also endorsed for acne management in pregnant women, emphasizing its safety and efficacy.

1. Introduction

Acne affects around 9% of the global population, poses a significant burden on individuals by impairing their physical appearance and self-esteem.[1,2] The multifactorial disease was more prevalent in 85% of adolescents aged between 12 and 25 years. This increased prevalence could primarily be attributed to the role of androgenic hormones during puberty.[2,3] Improper treatments might lead to inflammatory pigmentation and even permanent acne scars. An epidemiological study on Indian patients highlighted that the majority of the patients (73.2%) had acne that persisted into adolescence.[4] In 2009, there were only 9.3% of adult cases reported acne problems as per a South Indian study.[5] This condition has increased in 2019 to

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about 27% of adult acne cases according to another study.[6] Only a few Indian studies have looked at the prevalence and clinical characteristics of adult acne.[7]

Oils can induce comedogenesis and worsen acne by forming an occlusive film on the skin. Additionally, many sunscreens were excessively greasy for individuals with acne, often exacerbating their condition. An Indian-based study noted the occurrence of acneiform outbreaks triggered by facial products in 33% of the participants.[8] Another study found that acne had worsened due to cosmetic reasons in 22% of the patients.[4]

Topical retinoids, azelaic acid, benzoyl peroxide, and combinations of these medications were commonly used as first-line treatments for acne.[9] Oral antibiotics, isotretinoin, or hormone therapy, may be needed for managing resistant or more severe acne forms.[10] Azelaic acid, a nonphenolic substance obtained from the yeast Pityrosporum ovale,[2] inhibits the tyrosinase in melanocytes and mitochondrial oxidoreductases, thereby reducing DNA synthesis in both healthy and dysfunctional melanocytes. It also exhibits bactericidal activity against a variety of gram-positive and gram-negative pathogens. In addition to hyperpigmented skin conditions, azelaic acid was beneficial for comedonal and inflammatory acne.[11,12] Azelaic acid in various topical formulations has been licensed in India for the treatment of inflammatory (papulopustular) rosacea and acne vulgaris. Azelaic acid has been indicated to treat various common dermatoses including acne vulgaris, perioral dermatitis, inflammatory rosacea, melasma, and post-inflammatory hyperpigmentation due to its various modes of action and significant therapeutic efficacy.[13]

Considering the scientific advances contributing to the refinement of therapeutic options, it was important for clinicians to stay updated regarding the current treatment standards.[12] The present survey was intended to gather expert opinions regarding the prescription practice of azelaic acid for the management of acne in various age groups in Indian settings.

2. Materials and Methods

We carried out a cross sectional, multiple-response questionnaire based survey among dermatologists with experience in treating inflammatory skin conditions in the major Indian cities from June 2022 to December 2022.

2.1. Questionnaire

The questionnaire booklet named AZIDERM (Azelaic acid use in Dermatology) study was sent to the dermatologists who were interested to participate. The AZIDERM study consisted of 28 questions, with the majority of them focusing on the use of azelaic acid as monotherapy or in combination with oral antibiotics for the treatment of acne. The study was conducted after receiving approval from Bangalore Ethics, an Independent Ethics Committee which was recognized by the Indian Regulatory Authority, Drug Controller General of India.

2.2. Participants

An invitation was sent to leading dermatologists in managing acne in the month of March 2022 for participation in this Indian survey. About 467 derma experts from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provide necessary data. Dermatologists were requested to complete the questionnaire without discussing with peers. A written informed consent was obtained from each dermatologists prior initiation of the study.

2.3. Statistical methods

Descriptive statistics were employed for data analysis. Percentages were used to represent categorical variables. The frequency and percentage distributions for each variable were displayed as pie charts and bar charts created using Excel 2013 (16.0.13901.20400).

3. Results

The study involved 467 participants and nearly 35% of them indicated the need of azelaic acid for the management of melasma and post-inflammatory hyperpigmentation whereas approximately 27% of the participants preferred azelaic acid for managing acne, acne with pigmentation, melasma, and post-inflammatory hyperpigmentation (Figure 1). According to 50% of the experts, an average of 11-25 patients with melasma visit the clinic monthly. About 53% of the experts indicated that 26-50 patients with acne vulgaris visit their clinic on a monthly basis, while it was around 11-20 patients for post-inflammatory hyperpigmentation according to 49% of the experts.

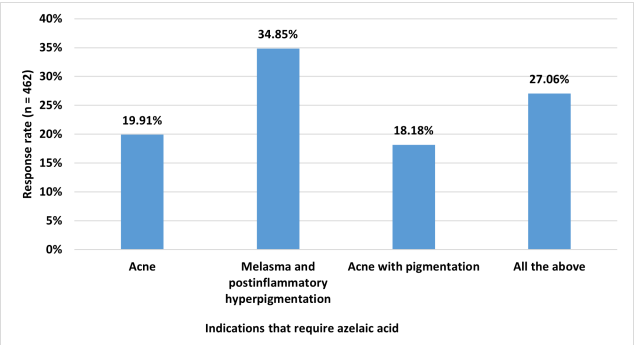

Figure 1: Response to the indications that require azelaic acid

Around 56% of the respondents advocated 6 to 8 weeks as the optimal duration of azelaic acid for treating acne. Approximately 52% of the respondents reported that they

would recommend short-term contact treatment for the first-time use of azelaic acid. Nearly 66% of the respondents preferred the use of glycolic acid in combination with azelaic acid (Figure 2).

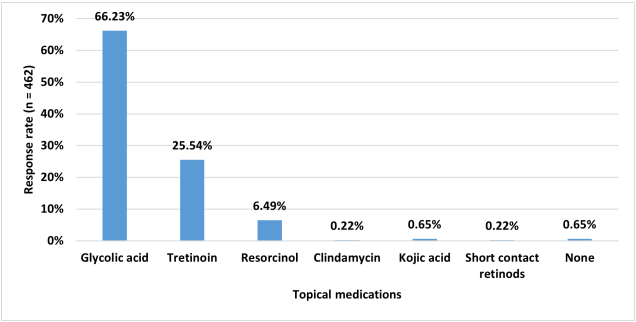

Figure 2: Response to the commonly prescribed topical medication along with azelaic acid

About 56% of the respondents preferred azelaic acid in combination with oral antibiotics for treating mild-to-moderate papulopustular acne (Table 1), and approximately 51% recommended azelaic acid alone for the management of acne in pregnant women. Approximately 64% of the experts opined that they may prescribe the use of moisturizers along with azelaic acid occasionally. About 50% of the participants stated that the prescription practice of azelaic acid might sometimes be influenced by seasonal changes or geographical location. The use of azelaic acid as face wash formulation was commonly preferred by 48% of the respondents (Figure 3).

Table 1: Response to the recommendation of azelaic acid for mild-to-moderate papulopustular acne

Recommendation of azelaic acid	Response rate (n = 462)
Monotherapy	105 (22.73%)
Combination Therapy with oral antibiotics	260 (56.28%)
Maintenance therapy	97 (21%)

About 57% of the respondents occasionally preferred a minocycline + azelaic acid combination for acne. Minoxidil + tretinoin + azelaic acid combination was preferred by 52% of the respondents occasionally for treating androgenetic alopecia. Azelaic acid monotherapy was preferred by 52% of the respondents for treating truncal acne. For treating hidradenitis suppurativa, oral minocycline or doxycycline with azelaic acid was preferred sometimes by 55% of the experts. About 59% of the participants indicated that sometimes they would prescribe glycolic acid with azelaic acid for treating truncal acne. Around 46% of the respondents indicated that they would prefer topical azelaic acid for lentigo maligna, respectively (Table 2). Approximately 37% of the responders opted for a 20%

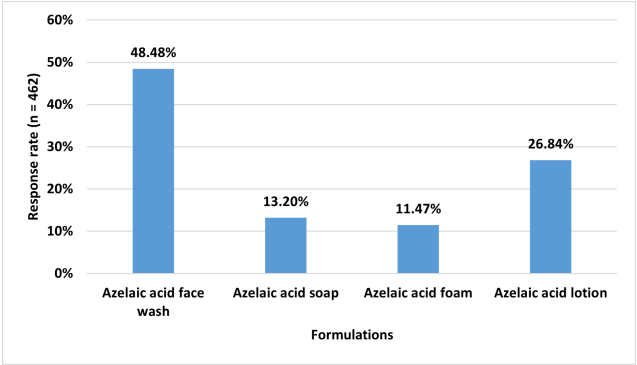

Figure 3: Response to the recommendation of new formulations of azelaic acid

strength of azelaic acid as it was the preferred choice in routine practice.

4. Discussion

The current survey highlighted azelaic acid as the choice of treatment for acne, acne with pigmentation, melasma, and post-inflammatory hyperpigmentation, and the recommended optimal duration of treatment was 6 to 8 weeks. The antibacterial, anti-inflammatory, comedolytic, and anti-tyrosinase activities of azelaic acid make it a suitable therapy for acne vulgaris, post-inflammatory hyperpigmentation and acne rosacea. Studies have indicated that the onset of action for azelaic acid occurs 4 weeks after the treatment initiation, and the drug was equally effective as oral tetracycline in treating acne.[14,15] A comparative study by Sarkar et al. has demonstrated the efficacy of 20% azelaic acid for treating melasma in dark-skinned subjects.[16] Additionally, a pilot trial showed that applying topical azelaic acid gel at 15% twice daily was effective in reducing both acne and post-inflammatory hyperpigmentation.[17] A significant proportion of current survey respondents preferred a daily dosage of 20% azelaic acid for effective management of acne, melasma, and post-inflammatory hyperpigmentation. According to a consensus-based treatment algorithm for Spain, azelaic treatment was recommended for the management of mild-to-moderate papulopustular acne.[18]

The current survey reported azelaic acid in combination with oral antibiotics to be effective for treating mild-to-moderate papulopustular acne. A significant proportion of current respondents occasionally chose a combination of oral antibiotic minocycline with azelaic acid. In an open-label randomized study, it was found that the combination of oral minocycline and topical 20% azelaic acid cream was highly effective in treating mild to moderate acne, and it even reduced recurrences when systemic medication was discontinued.[19] Additionally, a randomized study demonstrated that the combination of topical azelaic acid

Table 2: Response to preference of azelaic acid monotherapy or in combination with other medications for treating various skin diseases

Medications	Skin diseases	Experts' preference	Response rate (n = 462)
Minocycline + azelaic acid	Acne	Yes	20 (4.33%)
		No	179 (38.74%)
		Sometimes	263 (56.93%)
Minoxidil + tretinoin + azelaic acid	Androgenetic alopecia	Yes	16 (3.46%)
		No	208 (45.02%)
		Sometimes	238 (51.52%)
Oral minocycline or doxycycline + azelaic acid	Hidradenitis suppurativa	Yes	12 (2.6%)
		No	195 (42.21%)
		Sometimes	255 (55.19%)
Glycolic acid lotion + azelaic acid	Truncal acne	Yes	45 (9.74%)
		No	146 (31.6%)
		Sometimes	271 (58.66%)
Azelaic acid lotion	Truncal acne	Yes	33 (7.14%)
		No	190 (41.13%)
		Sometimes	239 (51.73%)
Topical azelaic acid	Keratosis pilaris	Yes	16 (3.46%)
		No	229 (49.57%)
		Sometimes	217 (46.97%)
Topical azelaic acid	Lentigo maligna	Yes	3 (0.65%)
		No	247 (53.46%)
		Sometimes	212 (45.89%)

20% and oral minocycline was highly effective for treating various forms of acne.[20] The present survey participants reported the occasional prescription of minoxidil, tretinoin, and azelaic acid for treating androgenetic alopecia. Amirfakhryan et al. denoted that minoxidil and azelaic acid together stimulate hair growth by stimulating the expression of the Sonic hedgehog protein in hair follicles. This study offered insightful information about the function of azelaic acid in the development of hair follicles.[21]

A substantial proportion of current survey experts preferred topical medication in combination with azelaic acid. Kakita and Lowe showed that the combination of azelaic acid 20% cream and glycolic acid 15% or 20% lotion was as effective as hydroquinone 4% cream in treating hyperpigmentation in patients with darker skin tones.[22] Similarly, a randomized controlled study revealed that combining glycolic acid peel with azelaic acid 20% cream was effective in treating melasma in Indian patients. This combination was also found to be comparable to a less potent combination of hydroquinone 2%, tretinoin 0.05%, and fluocinolone 0.01% in triple therapy for melasma management.[23] Majority of the current participants preferred the use of azelaic acid in pregnant women with acne. According to the 2022 expert consensus on the management of acne in India, topical antibiotics can be combined with other topical acne treatments for pregnant women with mild-to-moderate acne. Pregnant and lactating women can be prescribed with antibiotics (such as erythromycin and clindamycin), benzoyl peroxide, azelaic acid, and salicylic acid.[12] As per the consensus-based acne classification system and treatment algorithm for Spain, benzoyl peroxide and azelaic acid can be applied topically during pregnancy.[18]

In the present survey, half of the respondents indicated that the prescription of azelaic acid may need to be adjusted based on seasonal changes or geographical location. In line with this finding, an Indian study conducted by Sardana et al. noted that most acne vulgaris patients experience worsening symptoms during climate changes, particularly in the summer.[24] In another Indian study, 21% of patients reported that seasonal changes had exacerbated their symptoms.[25] Khunger and Kumar found that around 36% of the patients cited summer as a contributing factor for acne.[4]

Considering the increasing challenges posed by acne in both adolescents and adults, the findings from the current survey provide valuable insights for guiding treatment decisions and enhancing patient outcomes. The study also

underscores the importance of medication adherence and the development of personalized treatment plans for effectively managing inflammatory lesions. It was critical to recognize some of the shortcomings of the current survey. Relying on expert judgment in the study introduces the potential for bias, as various perspectives and preferences may have influenced the reported results. It was essential to consider these limitations when interpreting the findings and to conduct further study to validate and expand upon the conclusions.

5. Conclusion

Experts recommend combining azelaic acid with oral antibiotics to treat mild-to-moderate papulopustular acne. Clinicians preferred prescribing daily doses of 20% azelaic acid for a duration of 6 to 8 weeks for the optimal management of acne, melasma, and post-inflammatory hyperpigmentation. Additionally, they suggest the use of topical azelaic acid for acne management in pregnant women, emphasizing its safety and efficacy in this specific group.

6. Source of Funding

None.

7. Conflict of Interest

None.

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