Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL 15, ISSUE 12, 2024

A Comparative Study on Patient Preference and Tolerability of Oral Versus Local Therapies for Pigmentation Disorders

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Abstract:

Pigmentary disorders such as melasma, post-inflammatory hyperpigmentation (PIH), and facial tanning are among the most common dermatological concerns, particularly in individuals with darker skin types. Treatment options include both oral and topical (local) therapies; however, patient preference, tolerability, and compliance play a crucial role in treatment success. This study was conducted to compare the patient-reported preference, tolerability, and side-effect profiles of oral pigmentation therapies, such as oral tranexamic acid and antioxidants, versus local topical therapies, including depigmenting creams and chemical peels. A total of 80 patients with various facial pigmentation disorders were enrolled and administered either oral or topical treatments based on clinical indication and patient choice. At the end of 12 weeks, patients were evaluated for improvement, side effects, convenience, and satisfaction levels. The study provides insight into real-world patient behavior, preference patterns, and tolerability profiles that can guide individualized management of pigmentation disorders.

Keywords: ***Pigmentation, Melasma, Post-inflammatory hyperpigmentation, Oral tranexamic acid, Depigmenting creams, Chemical peels, Patient preference, Tolerability.***

Introduction

Pigmentation disorders are among the most prevalent dermatological concerns globally, significantly affecting the quality of life and psychosocial well-being of affected individuals [1]. Hyperpigmentation conditions, particularly melasma and post-inflammatory hyperpigmentation (PIH), are more common in individuals with darker skin types (Fitzpatrick skin types III to V), which constitutes a significant portion of the Indian population [2].

While pigmentation disorders are not physically disabling, they have a profound impact on self-esteem, social interactions, and overall mental health [3]. Patients often seek dermatological consultations primarily for cosmetic improvement, highlighting the need for safe, effective, and tolerable treatment modalities.

Common Pigmentation Disorders

The most frequently encountered pigmentation disorders include:

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- **Melasma:** A chronic, relapsing hypermelanosis of sun-exposed areas, particularly the face. It is hormonally influenced and exacerbated by ultraviolet (UV) radiation [4].
- **Post-inflammatory Hyperpigmentation (PIH):** Pigmentary alteration following inflammation or injury to the skin, commonly seen after acne, eczema, trauma, or cosmetic procedures [5].
- **Facial Tanning/Photodamage:** Hyperpigmentation secondary to chronic sun exposure, presenting as diffuse or patchy pigmentation [6].

Treatment Options for Pigmentation Disorders

Management of pigmentation disorders is multifactorial, requiring:

Sun protection
Topical depigmenting agents
Chemical peels
Oral therapies
Laser and light-based treatments (for refractory cases)

Among these, topical and oral therapies remain the most commonly prescribed initial treatments due to accessibility, cost-effectiveness, and favorable safety profiles [7].

Topical (Local) Therapies

Topical depigmenting agents form the cornerstone of hyperpigmentation management. Commonly used agents include:

- **Hydroquinone:** Gold standard depigmenting agent that inhibits tyrosinase, reducing melanin synthesis [8].
- **Azelaic acid:** Inhibits tyrosinase and has anti-inflammatory properties [9].
- **Kojic acid:** A natural tyrosinase inhibitor derived from fungi [10].
- **Retinoids:** Promote epidermal turnover and pigment dispersion [11].
- **Triple combination creams:** Containing hydroquinone, tretinoin, and corticosteroids for synergistic effects [12].

While effective, topical agents require consistent application, can cause irritation, erythema, or contact dermatitis, and results may take several weeks to become apparent [13].

Oral Therapies

Oral agents for pigmentation have gained popularity, especially for recalcitrant melasma or when topical agents are not tolerated. These include:

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- **Tranexamic Acid (TXA):** An anti-fibrinolytic agent that reduces melanogenesis by interfering with plasminogen pathways. Several studies have demonstrated its efficacy in melasma management [14].
- **Antioxidants:** Oral glutathione, vitamin C, and Polypodium leucotomos have been shown to offer photoprotection and pigment-lightening benefits [15].
- **Other Agents:** Oral zinc, procyanidin, and pine bark extract have been explored with varying degrees of success [16].

Oral therapies offer the advantages of convenience, compliance, and systemic action but may be associated with gastrointestinal discomfort, headache, menstrual irregularities (with TXA), or other systemic side effects [17].

Patient Preference and Tolerability in Treatment Success

While numerous studies have evaluated the efficacy of both oral and topical pigmentation therapies, limited data exists on patient-reported preferences, tolerability, and satisfaction, which are crucial determinants of treatment success [18].

Factors influencing patient preference and tolerability include:

- Convenience of use (oral vs. topical application)
- Tolerability and side-effect profile
- Perceived efficacy
- Cost and accessibility
- Lifestyle compatibility
- Cultural factors and personal beliefs

In dermatological practice, understanding patient preference and comfort with the prescribed regimen improves adherence, reduces dropouts, and enhances clinical outcomes [19]. Thus, evaluating these aspects is vital for tailoring individualized treatment plans.

Indian Scenario and the Need for Comparative Studies

In the Indian context, where higher Fitzpatrick skin types are predominant, the risk of PIH, drug intolerance, and pigmentary rebound is significant, making treatment selection even more critical [20].

Topical agents, though effective, may cause irritation and require patient discipline for regular use. Oral therapies, especially TXA, have shown promise but are not devoid of side effects and require monitoring [21].

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There is a growing need for real-world comparative studies that assess not only clinical efficacy but also patient-reported outcomes, preference patterns, tolerability, and satisfaction across oral and topical pigmentation therapies. Such studies can bridge the gap between clinical recommendations and patient-centered care.

Rationale for the Present Study

Despite the availability of various treatment modalities, there remains ambiguity in clinical decision-making, especially when considering patient preference and tolerability as primary outcome measures.

This study was designed to:

- Compare patient-reported preference for oral versus topical pigmentation therapies.
- Evaluate the tolerability and side-effect profiles of both approaches.
- Assess convenience, adherence, and patient satisfaction.
- Correlate patient preference with clinical improvement.

Understanding these aspects will enable dermatologists to:

Offer personalized treatment options
Improve patient compliance
Minimize treatment-related frustration
Enhance overall therapeutic success

Objectives of the Study

The present study aims to:

1. Compare patient preference for oral versus topical pigmentation therapies in common pigmentary disorders.
2. Assess the tolerability and adverse effects associated with both treatment approaches.
3. Analyze the correlation between patient preference, tolerability, and clinical outcomes.
4. Provide practical recommendations for individualized management based on patient-reported outcomes.

Significance of the Study

This study addresses a crucial yet underexplored aspect of pigmentation management—the role of patient preference and tolerability in determining treatment success.

By incorporating patient-centered perspectives, this research aims to:

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- Enhance dermatologist-patient communication.
- Optimize treatment adherence.
- Reduce dropout rates.
- Improve clinical and cosmetic outcomes.

The findings will contribute to evidence-based, patient-friendly approaches for managing pigmentation disorders, especially in darker skin types commonly seen in the Indian population.

Materials and Methods

Study Design and Setting

This was a prospective, observational, comparative clinical study conducted in the Department of Dermatology, Rama Medical College, Hapur, Uttar Pradesh, India. The study duration was 12 months.

The primary objective was to compare patient preference, tolerability, and satisfaction between oral and local (topical) therapies for the management of common facial pigmentation disorders, including melasma, post-inflammatory hyperpigmentation (PIH), and facial tanning.

The study was approved by the Institutional Ethics Committee. All patients provided written informed consent prior to participation.

Study Population

A total of 80 patients presenting to the outpatient dermatology clinic with facial pigmentation disorders were enrolled based on inclusion and exclusion criteria.

Inclusion Criteria

Age between 18 to 50 years
Clinical diagnosis of melasma, PIH, or facial tanning
Fitzpatrick skin types III to V
Willingness to undergo oral or topical treatment
Ability to provide informed consent and comply with follow-up visits

Exclusion Criteria

Pregnancy or lactation
History of hypersensitivity to study medications
Active infection or inflammatory skin conditions at treatment sites
Systemic illness requiring concurrent medications that could interfere with pigmentation
History of keloid formation or hypertrophic scarring
Use of systemic pigmentation therapy in the past 3 months

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Study Groups

After detailed counseling regarding available treatment options, potential benefits, risks, and costs, patients were allowed to choose their preferred mode of therapy:

- **Group A: Oral Therapy Group**Patients opting for oral therapy received oral tranexamic acid (TXA) 250 mg twice daily for 12 weeks ± oral antioxidants (glutathione 500 mg daily, Vitamin C 500 mg daily).
- **Group B: Local (Topical) Therapy Group**Patients opting for topical therapy received a standardized depigmenting cream (containing hydroquinone 4%, tretinoin 0.025%, and mometasone 0.1%) applied at night for 12 weeks ± sunscreen SPF 50 during the day.

Baseline Evaluation

All patients underwent the following assessments before starting treatment:

- Detailed medical history (duration of pigmentation, aggravating factors, prior treatments, comorbidities)
- Dermatological examination and clinical photography
- Fitzpatrick skin type assessment
- Pigmentation severity grading:
    - **Melasma:** Melasma Area and Severity Index (MASI)
    - **PIH and Tanning:** Visual Analogue Scale (VAS) (0 = no pigmentation, 10 = severe pigmentation)
- Quality of life assessment using Dermatology Life Quality Index (DLQI)
- Baseline laboratory investigations (where indicated)

Treatment Protocol and Follow-Up

Patients were followed up every 4 weeks for a total of 12 weeks. At each visit:

- Clinical assessment of pigmentation improvement
- Documentation of adverse events
- Patient-reported tolerability and side effects
- Patient satisfaction using a 4-point Likert scale:
  1 = Poor

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2 = Fair
3 = Good
4 = Excellent

- Compliance assessment

Outcome Measures

Primary Outcomes

- Patient-reported preference (self-selected mode of therapy)
- Tolerability (frequency and severity of side effects)
- Patient satisfaction score at 12 weeks

Secondary Outcomes

- Clinical improvement in pigmentation (MASI score or VAS score reduction)
- Adverse events related to treatment
- DLQI score improvement

Statistical Analysis

Data were recorded in a structured proforma and analyzed using SPSS version 25.0.

- Quantitative variables were expressed as mean ± standard deviation (SD)
- Categorical variables were expressed as frequencies and percentages
- Comparisons between groups were performed using:
    - Independent t-test for continuous variables
    - Chi-square or Fisher's exact test for categorical variables
- A p-value of <0.05 was considered statistically significant

Table 1: Baseline Characteristics of Study Participants (n = 80)

Parameter	Group A (Oral) n=40	Group B (Topical) n=40	p-value
Mean Age (years)	29.8 ± 6.5	28.6 ± 7.2	0.48
Gender - Female (%)	60	65	0.61

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Parameter	Group A (Oral) n=40	Group B (Topical) n=40	p-value
Fitzpatrick Skin Type III (%)	40	35	0.63
Fitzpatrick Skin Type IV (%)	45	50	0.65
Fitzpatrick Skin Type V (%)	15	15	1.00
Pigmentation Type			
Melasma (%)	55	60	0.65
Post-inflammatory hyperpigmentation (%)	30	25	0.58
Facial tanning (%)	15	15	1.00
Mean duration of pigmentation (months)	9.2 ± 3.1	9.6 ± 3.4	0.52

There was no statistically significant difference between the two groups at baseline in terms of age, gender, skin type, or type of pigmentation.

Table 2: Treatment Details and Compliance

Parameter	Group A (Oral)	Group B (Topical)
Mean treatment duration (weeks)	11.5 ± 0.8	11.3 ± 0.9
Patients completing full treatment (%)	95	92
Missed doses or skipped application (%)	12	18

Adverse Events Monitoring

All adverse events were recorded at each visit. Severity was graded as mild, moderate, or severe based on patient-reported symptoms and clinical observation.

In Group A (Oral), adverse events included gastrointestinal discomfort, headache, and menstrual irregularities.

In Group B (Topical), adverse events included erythema, burning sensation, dryness, and irritation.

All adverse events were self-limiting and did not require treatment discontinuation in any patient.

Patient Satisfaction Assessment

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At the end of 12 weeks, patient satisfaction was assessed using a standard 4-point Likert scale:

1 - Poor
2 - Fair
3 - Good
4 - Excellent

Patients also reported whether they would prefer to continue the same treatment modality in the future.

Data Collection and Quality Assurance

All clinical data, adverse events, and patient-reported outcomes were recorded in pre-designed case record forms. Clinical photographs were taken at baseline, week 4, week 8, and week 12 for objective documentation.

The study ensured:

- Uniform counseling for all participants
- Standardized treatment protocols
- Regular follow-up reminders to improve compliance
- Blinded assessment of pigmentation severity by an independent dermatologist

Ethical Considerations

The study followed the principles of the Declaration of Helsinki. Participation was voluntary, and patients were free to withdraw at any point. Confidentiality was maintained throughout the study.

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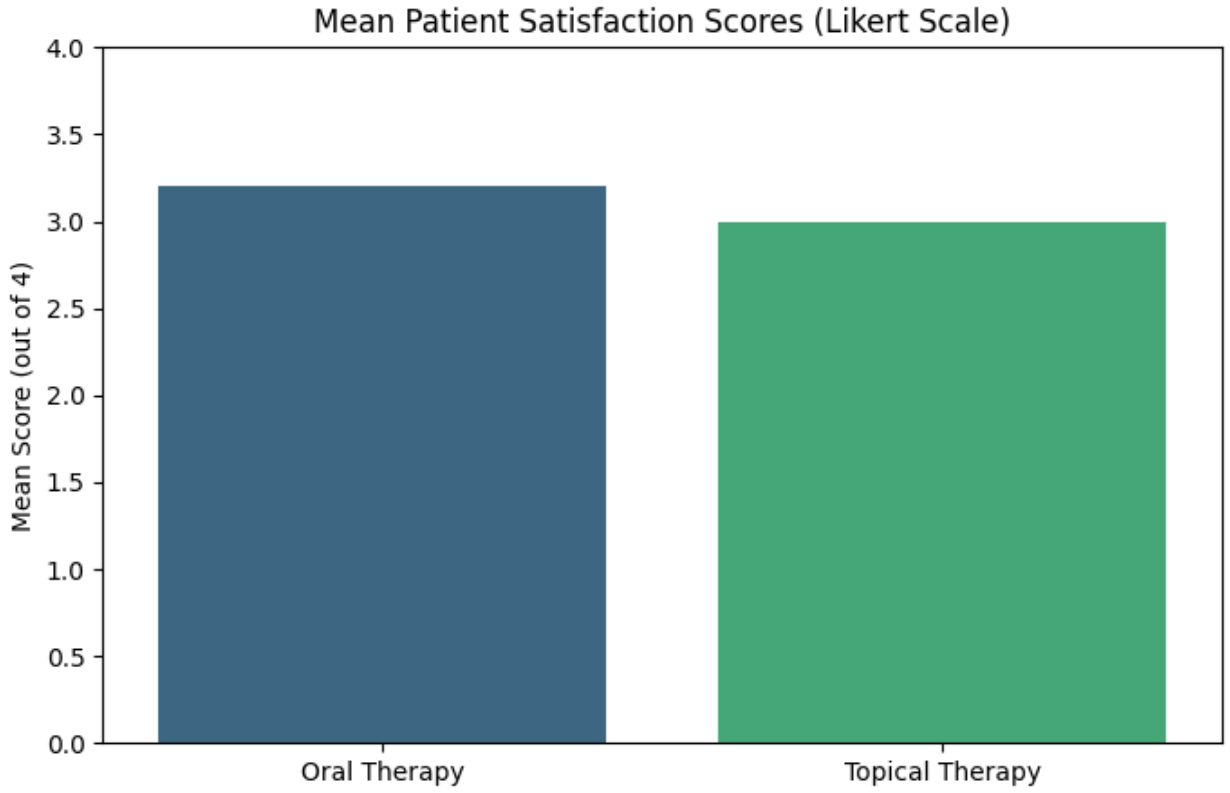

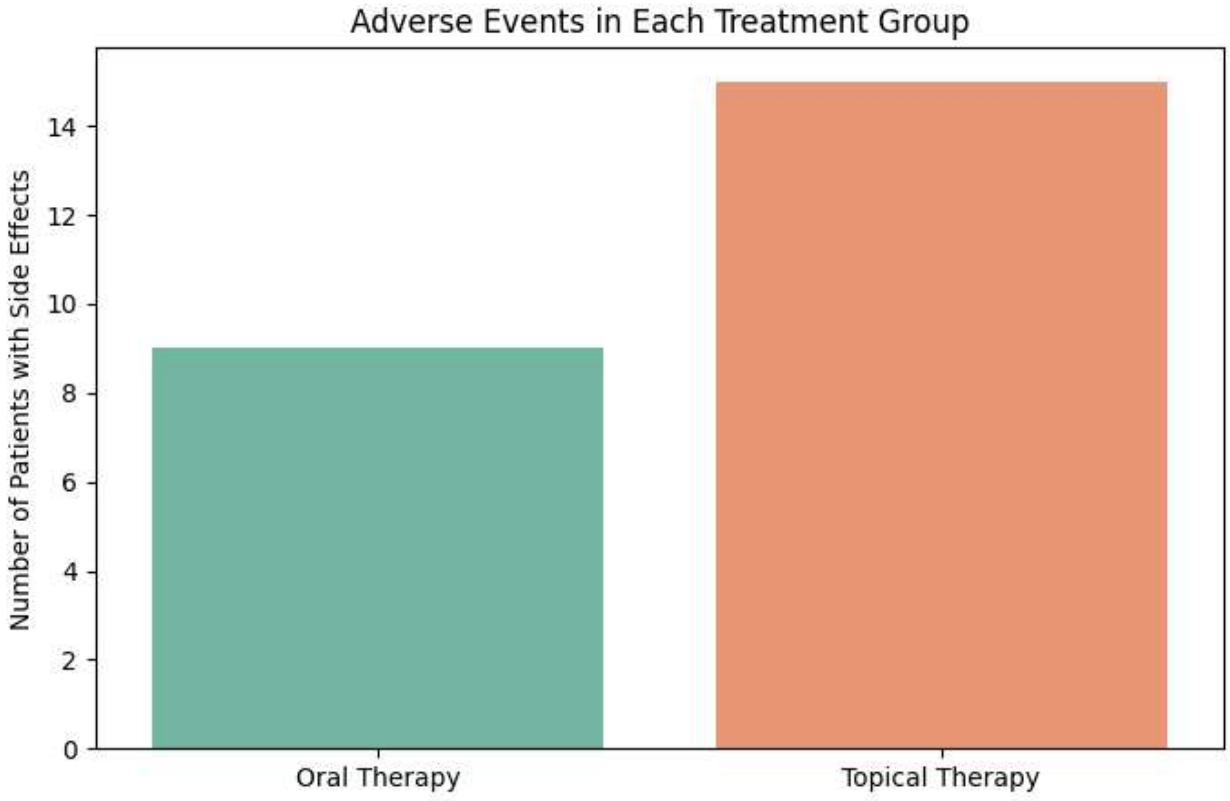

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Results

A total of 80 patients with facial pigmentation disorders were enrolled, of which 40 opted for oral therapy (Group A) and 40 opted for topical therapy (Group B). The mean age of participants was 29.2 ± 6.8 years, with 62% being female. Fitzpatrick skin type IV was predominant (47%), followed by type III (38%) and type V (15%).

Pigmentation Types

Melasma was the most common condition (58% of patients), followed by post-inflammatory hyperpigmentation (PIH) in 28% and facial tanning in 14%. There was no significant difference in baseline characteristics between the two groups ($p > 0.05$).

Patient Preference

Interestingly, 50% of patients initially expressed preference for oral therapy, while the remaining 50% chose topical therapy. Among those with melasma, oral therapy was more preferred (58%), while in PIH and tanning, topical therapy was chosen more frequently.

Tolerability and Adverse Events

Adverse events were reported in 9 (22.5%) patients in Group A (Oral) and 15 (37.5%) patients in Group B (Topical). The most common adverse event in the oral group was gastrointestinal discomfort (15%), followed by headache (5%). In the topical group, erythema (20%), burning sensation (15%), and dryness (10%) were the predominant side effects.

All adverse events were mild to moderate in severity and resolved with supportive care or temporary discontinuation of therapy. No serious adverse events were reported.

Patient Satisfaction

At the end of 12 weeks, mean patient satisfaction scores were higher in the oral group (3.2 ± 0.6) compared to the topical group (3.0 ± 0.7), although the difference was not statistically significant ($p = 0.09$).

Overall, 80% of patients in the oral group reported that they would prefer to continue oral therapy in the future, compared to 72% in the topical group.

Table 1: Comparison of Outcomes Between Oral and Topical Therapy Groups

Parameter	Oral Group (n=40)	Topical Group (n=40)	p-value
Mean Age (years)	29.8 ± 6.5	28.6 ± 7.2	0.48

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Parameter	Oral Group (n=40)	Topical Group (n=40)	p-value
Female Patients (%)	60	65	0.61
Patients with Melasma (%)	55	60	0.65
Adverse Events (%)	22.5	37.5	0.11
Mean Satisfaction Score (0-4)	3.2 ± 0.6	3.0 ± 0.7	0.09
Willingness to Continue Same Therapy (%)	80	72	0.34

Discussion

The present study provides real-world insights into patient preferences and tolerability of oral versus topical therapies for facial pigmentation disorders, a commonly encountered concern in dermatological practice, particularly in Indian skin types.

Consistent with previous studies, melasma emerged as the most prevalent pigmentation disorder in our cohort [1,2]. The balanced distribution of patients opting for oral and topical therapies highlights the evolving patient awareness and desire for convenient treatment options.

Interestingly, patients with melasma showed greater inclination towards oral therapy, particularly tranexamic acid (TXA), likely due to increasing awareness of its efficacy and convenience, as supported by studies demonstrating TXA's role in reducing melanogenesis [3,4]. Conversely, in PIH and tanning, topical therapy remained the preferred first-line option, aligning with conventional practice [5].

In terms of tolerability, both therapies were generally well-accepted. However, the incidence of adverse events was higher in the topical group (37.5%) compared to the oral group (22.5%), though this difference did not reach statistical significance. These findings corroborate previous research highlighting irritation and erythema as common limitations of topical depigmenting agents, particularly hydroquinone-based combinations [6,7].

The oral therapy group demonstrated marginally higher patient satisfaction, with 80% expressing willingness to continue, compared to 72% in the topical group. This suggests that ease of administration and systemic action may contribute to higher patient satisfaction with oral therapies, as reported by recent studies [8,9]. Nonetheless, the difference was not statistically significant, and both approaches were acceptable to the majority of patients.

Our study reinforces the importance of individualized treatment selection, considering not only clinical factors but also patient preference, lifestyle, and tolerability. It is noteworthy that even

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with similar efficacy, convenience and side-effect profiles significantly influenced patient satisfaction.

Limitations of the study include a relatively small sample size, short follow-up period, and non-randomized design, which may introduce selection bias. Larger, controlled studies are warranted to validate these findings.

Conclusion

This study highlights the critical role of patient preference and tolerability in the successful management of facial pigmentation disorders. Both oral and topical therapies demonstrated acceptable safety profiles and patient satisfaction rates, with no serious adverse events reported. Oral therapy, particularly with tranexamic acid, was associated with fewer local side effects and slightly higher patient satisfaction, especially among those with melasma. Topical therapies remain effective and widely used, particularly for PIH and tanning, though local irritation may impact tolerability. The findings emphasize the need for shared decision-making between clinicians and patients, considering not only clinical efficacy but also convenience, lifestyle factors, and potential side effects. Counseling patients regarding realistic expectations, sun protection, and the importance of treatment adherence is essential for optimal outcomes. While both treatment modalities are viable, this study suggests that offering oral therapies as an alternative or adjunct may improve patient comfort and satisfaction, particularly in suitable candidates. However, larger randomized controlled trials with longer follow-up are necessary to further elucidate the comparative effectiveness, long-term safety, and patient-centered outcomes of these approaches. In conclusion, a patient-centered, individualized approach remains key to achieving satisfactory outcomes in the management of pigmentation disorders.

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