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Original Research Article

Physician perspectives on the use of glycolic acid, salicylic acid, and urea combination in dermatology practice in Indian settings

Manjula S[1]*, Krishna Kumar M[1]

Dept. of Medical Services, Micro Labs Limited, Bangalore, Karnataka, India

Abstract

Background: Keratolytic substances including alpha-hydroxy acids (AHAs), salicylic acid, and urea have long been employed in treating hyperkeratosis and related disorders. Although there were clinical studies available, there was a dearth of studies regarding their clinical practice among clinicians. This study aimed to gather expert opinion regarding the physician's perspective and preference on the use of a combination of glycolic acid, salicylic acid, and urea in managing hyperkeratosis in Indian settings**.**

Materials and Methods: The cross-sectional study used a multiple-response questionnaire comprising 29 questions designed to collect feedback, clinical observations, and experiences from specialists regarding the management of hyperkeratosis by using a combination of glycolic acid, salicylic acid, and urea in routine settings. The questionnaire was structured to capture insights on the frequency of use, perceived efficacy, adverse effects, and preferences for this combination. Data analysis was conducted using descriptive statistics.

Results: The survey involved 559 dermatology specialists, and more than half of them (54.03%) reported 10% as the most commonly prescribed strength of urea for the treatment of hyperkeratosis of the palms and soles. Approximately 63.5% of the participants preferred both glycolic and salicylic acid as keratolytic agents. Majority (74.6%) favored the combination of glycolic acid, salicylic acid, and urea for treating hyperkeratosis on their palms and soles. Almost 51% of the clinicians opined that the glycolic acid (1%), salicylic acid (1%), and urea (5%) combination showed good results, while 47% of them reported it as an excellent monotherapy for the treatment of hyperkeratosis of the palms and soles. Approximately 63% of the participants recommended the use of glycolic acid (1%), salicylic acid (1%), and urea (5%) in combination with topical steroids for the effective management of plaque psoriasis.

Conclusion: The study highlighted a strong preference for treating hyperkeratosis with a combination of glycolic acid (1%), salicylic acid (1%), and urea (5%). Clinicians favored a 10% urea strength and preferred glycolic and salicylic acids as keratolytic agents. The combination of these 3 ingredients emerged as the preferred choice. The combination received positive ratings for hyperkeratosis and was recommended with topical steroids for plaque psoriasis, indicating a consensus on its efficacy.

Keywords: Hyperkeratosis, Glycolic acid, Salicylic acid, Urea, Plague psoriasis

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1. Introduction

The burden of hyperkeratosis is significant, involving a substantial impact on quality of life, coupled with considerable economic costs and management challenges. Clinically, hyperkeratosis presents in various forms including calluses, corns, and more serious disorders like psoriasis, ichthyosis, and acanthosis nigricans. Pathological hyperkeratosis occurs when the concentration of keratin exceeds normal limits, leading to discomfort or pain, and it affects around 20% of the general population, with a higher prevalence among women and the elderly. Hyperkeratotic lesions on the palms and soles are particularly common in dermatological practice, presenting a variety of underlying etiologies that are often clinically indistinguishable.[1-5]

Acanthosis nigricans has a reported prevalence ranging from 7.2% to 74% in various global population-based studies. In India, the prevalence was significant, particularly in urban areas, due to factors like increasing obesity rates and insulin resistance. Psoriasis affects approximately 0.44% to 2.8% of the Indian population, with varying prevalence based on geographic location, genetic predisposition, and

*Corresponding author: Manjula S
Email: drmanjulas@gmail.com

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environmental factors. Globally, ichthyosis vulgaris was estimated to affect about 1 in 250 individuals.[6-8]

Keratolytic substances have long been employed in treating hyperkeratosis and related disorders. These substances, including alpha-hydroxy acids (AHAs), salicylic acid, and urea, help manage excessive keratinization by promoting stratum corneum exfoliation. Formulations containing AHAs, such as glycolic and lactic acids, have been used in clinical practice for decades to treat various skin conditions. Glycolic acid exfoliates the stratum corneum and enhances cellular turnover.[9] The combination of glycolic and salicylic acids, typically in concentrations ranging from 2% to 70%, has been effective in treating acne, ichthyosis, keratosis, warts, psoriasis, and photoaged skin. Salicylic acid, in particular, was renowned for its ability to exfoliate the stratum corneum, making it a versatile keratolytic agent used in conditions like melasma, photodamage, and freckles.[10-13] Urea, another keratolytic agent, acts by hydrating the skin and breaking down the protein structure of keratin, aiding in its removal. It has been identified as an effective therapy for various hyperkeratosis conditions due to emollient, proteolytic, and keratolytic properties.[12,13]

The present study was intended to gather clinicians' perspectives regarding the prescription practice of the combination of glycolic acid, salicylic acid, and urea for the management of hyperkeratosis in Indian settings.

2. Materials and Methods

We carried out a cross-sectional, multiple-response questionnaire-based study among dermatologists with experience in managing hyperkeratosis in the major Indian cities from June 2023 to December 2023. 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.

2.1. Questionnaire

The questionnaire booklet named HAPPY (Physician Perspectives on the Role of Glycolic acid, Salicylic acid, Urea combination in Dermatology Practice) study was sent to the dermatologists who were interested to participate. The HAPPY study consisted of 29 questions, aimed to gather feedback, clinical observations, and experiences from specialists regarding the routine use of a combination therapy for hyperkeratosis. It was designed to capture insights into the frequency of use, perceived efficacy, adverse effects, and preferences for a combination of glycolic acid, salicylic acid, and urea.

2.2. Participants

An invitation was sent to leading dermatologists in managing hyperkeratosis in the month of March 2023 for participation in this Indian survey. About 559 dermatologists 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 it with peers. A written informed consent was obtained from each dermatologist prior to initiation of the study.

2.3. Statistical methods

The data were analyzed using descriptive statistics. Categorical variables were presented as percentages to provide a clear insight into their distribution. The frequency of occurrence and the corresponding percentage were used to represent the distribution of each variable. To visualize the distribution of the categorical variables, graphs, and pie charts were created using Microsoft Excel 2013 (version 16.0.13901.20400).

3. Results

The survey included 559 clinicians, and 46% reported treating an average of 11 to 12 patients with hyperkeratosis of the palms and soles each month in routine practice. According to 68% of the clinicians, <25 patients are treated for acanthosis nigricans on a monthly average in routine practice. More than half of the respondents (54.03%) reported that the most commonly prescribed strength of urea is 10% for hyperkeratosis of the palms and soles (**Figure 1**).

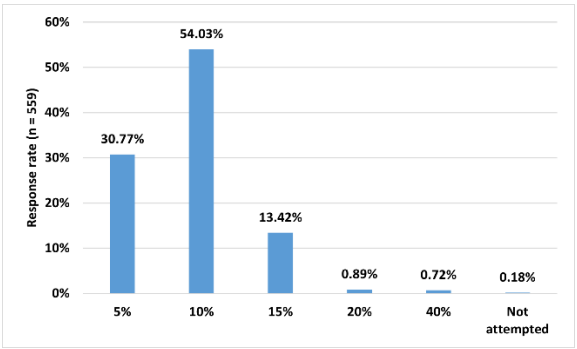

Figure 1: Distribution of response on the most prescribed strength of urea in hyperkeratosis of palms & soles

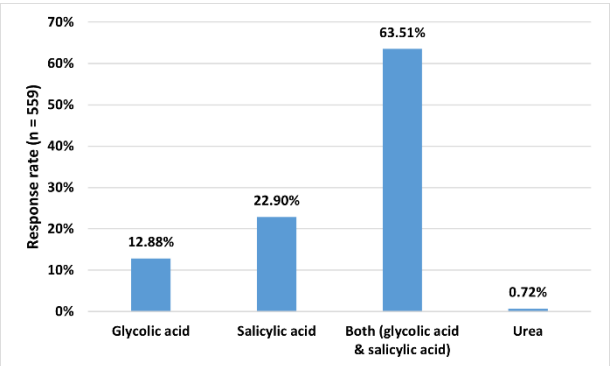

Figure 2: Distribution of response on the preferred keratolytic agent for hyperkeratosis of palms and soles

Almost half of the clinicians (50.98%) stated that <10 patients were treated for ichthyosis vulgaris on average in a month. About 63.51% of the participants preferred both glycolic and salicylic acids as keratolytic agents (**Figure 2**). The majority of the experts (74.6%) preferred a combination of glycolic acid, salicylic acid, and urea to treat hyperkeratosis on the palms and soles (**Table 1**).

Table 1: Distribution of response on the most preferred indications for using glycolic acid, salicylic acid, and urea combination

Indications	Response rate (n = 559)
Hyperkeratosis of palms and soles	74.6%
Acanthosis nigricans	14.31%
Ichthyosis vulgaris	5.55%
All of the above	5.55%

As indicated by 39% of the clinicians, about 11% to 25% of the patients were prescribed a combination of glycolic acid (1%), salicylic acid (1%), and urea (5%) for plaque psoriasis, while 38% reported that fewer than 10% of their patients were prescribed this combination. According to 46%, 44%, and 42% of the clinicians respectively, about 6 to 8 weeks was the recommended duration of therapy with this combination for palmoplantar keratoderma, acanthosis nigricans, and cracked feet. Approximately 43% of the respondents reported that more than 8 weeks was the recommended duration of treatment for plaque psoriasis.

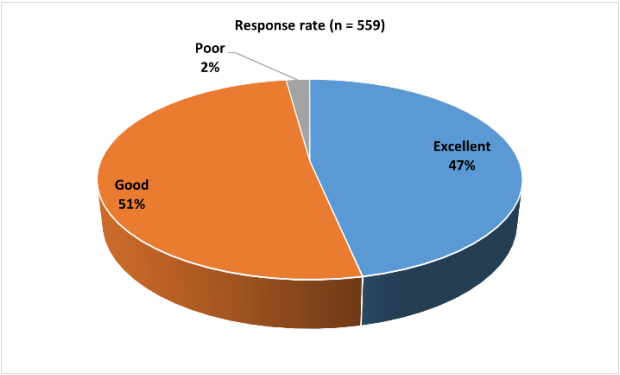

Figure 3: Efficacy of glycolic acid (1%), salicylic acid (1%), and urea (5%) as monotherapy in hyperkeratosis of palms and soles

About 39% of participants sometimes preferred the combination of glycolic acid (1%), salicylic acid (1%), and urea (5%) in lotion formulation, while 35% supported the combination in lotion formulation. According to 40% of the clinicians, 11-20% of patients with keratosis pilaris were recommended this combination. Almost 51% of the clinicians rated the use of glycolic acid (1%), salicylic acid (1%), and urea (5%) as monotherapy as good for hyperkeratosis of the palms and soles, while 47% rated it as excellent (**Figure 3**).

Half of the clinicians (50.63%) responded that they would not recommend the combination of glycolic acid (1%), salicylic acid (1%), and urea (5%) for diabetic foot ulcers, whereas 47% indicated that more studies were required. Around 65% of the participants reported that they would sometimes endorse using two keratolytic agents in the treatment of cracked feet. As reported by 62.79% of the participants, it was recommended to use the combination of glycolic acid (1%), salicylic acid (1%), and urea (5%) with topical steroids for the management of plaque psoriasis (**Table 2**).

Table 2: Distribution of response on the recommended use of glycolic acid 1%, salicylic acid 1%, and urea 5% combination in plaque psoriasis

Therapy	Response rate (n = 559)
Monotherapy	12.52%
Combination therapy with topical steroids	62.79%
Maintenance therapy	23.97%
Never tried	0.18%
Not Attempted	0.54%

About 67% of the clinicians sometimes recommended the combination of glycolic acid (1%), salicylic acid (1%), and urea (5%) for managing ichthyosis vulgaris. Most clinicians (69.05%) believed that patients should be advised sometimes on how to use this combination. About 66% of the clinicians opined that sometimes they suggest occlusion after the application of this combination.

According to 48% of the clinicians, the recommended duration of therapy for this combination in keratosis pilaris was 6 to 8 weeks. Almost 51% of the clinicians did not recommend this topical combination for post-dermatological procedures, while 47% recommended it sometimes. About 63% of clinicians reported that they sometimes alter the prescription of this combination due to seasonal changes or geographical location. Approximately 79% of clinicians preferred prescribing this combination for elderly patients with cracked feet based on skin sensitivity. About 44% of the clinicians recommended using this combination cream with silicone socks, while 37% preferred the cream with an applicator.

A majority (64.76%) of clinicians believed that the combination of salicylic acid and glycolic acid was sometimes effective in the treatment of cracked feet. Approximately 63% of the participants sometimes advised patients that occlusion was required while using the glycolic acid (1%), salicylic acid (1%), and urea (5%) combination. As reported by 52% of clinicians, small-group interactive

sessions were the preferred option for educating patients. According to 47% of clinicians, the primary factor associated with patients' non-adherence to medication was a lack of patient education.

4. Discussion

This study provides valuable insights into physicians' opinions on the effectiveness of a combination of glycolic acid, salicylic acid, and urea for managing hyperkeratosis. It also highlights the synergistic effects of this combination in providing enhanced efficacy in treating hyperkeratosis.[10,14,15] Most respondents favored using 10% urea for treating hyperkeratosis on the palms and soles. Verzì et al. found that using 10% urea in conjunction with topical antifungals can shorten treatment duration and enhance clinical outcomes for various hyperkeratosis conditions.[16] Similarly, Piquero-Casals et al. stated that urea was widely used as a keratolytic agent to treat various dermatological conditions.[17] Furthermore, Schröder indicated that a 10% urea cream shows better results in hyperkeratosis.[18] Urea, typically found in a 10% cream, was commonly utilized to address conditions such as hyperkeratotic skin disorders, while lower concentrations were suitable for treating dry skin. Studies have suggested that applying a nut-sized amount of 10% urea cream three times daily can effectively prevent hyperkeratosis on the palms and soles. These studies emphasized the safety, efficacy, and broad applicability of urea in dermatological therapy, highlighting its minimal side effects.[19-21]

Most of the current survey participants preferred both glycolic and salicylic acids as keratolytic agents. In line with this, Kessler et al. found that both acids significantly reduced acne lesions, but glycolic acid showed slightly better results in terms of reducing skin and inflammatory lesions. They preferred glycolic acid due to its effectiveness in treating multiple types of skin lesions and its efficacy as a keratolytic agent.[22] Suzan Obagi indicated that keratolytics act as exfoliating agents based on their ability to disrupt adhesions between keratinocytes. Glycolic acid and salicylic acid were the most commonly used keratolytic peeling solutions.[23] Akamine et al. found that salicylic acid significantly improves scaling, erythema, induration, and investigator global assessment compared to baseline.[24] Similarly, Berardesca et al. reported that glycolic acid significantly reduces hyperkeratosis and erythema.[25]

The survey respondents also underscored the combination of glycolic acid, salicylic acid, and urea as the preferred choice to treat hyperkeratosis of palms and soles. Similarly, Jacobi et al. demonstrated that the synergistic effects of combining keratolytic agents such as glycolic acid and salicylic acid with urea provide enhanced therapeutic outcomes for patients with hyperkeratosis, particularly on the palms and soles.[26] Studies have shown the efficacy of combination treatments for hyperkeratosis and found that topical keratolytic treatment products containing a mix of glycolic acid, salicylic acid, and urea showed superior results in reducing keratin buildup and improving skin texture compared to single-agent treatments.[21,27]

The present survey has also highlighted the use of glycolic acid (1%) salicylic acid (1%) and urea (5%) as monotherapy for managing hyperkeratosis of palms and soles. In line with this, several studies have indicated that low concentrations of glycolic acid effectively treat hyperkeratotic conditions without significant irritation, making it suitable for sensitive areas like the palms and soles. Urea enhances skin hydration and promotes desquamation, effectively reducing hyperkeratotic skin conditions. Urea at concentrations of 5-10% significantly reduces the thickness of hyperkeratotic skin lesions by increasing water content and softening the stratum corneum. Combining AHAs and beta hydroxy acids with moisturizing agents like urea enhances the overall efficacy in treating hyperkeratosis. The study noted reduced irritation and improved keratolytic action. Another clinical trial indicated a significant reduction in hyperkeratotic lesions when using salicylic acid in combination with other keratolytic agents.[10,22,28,29]

The majority of the current experts recommended the use of the combination of glycolic acid (1%), salicylic acid (1%), and urea (5%) in conjunction with topical steroids for treating plaque psoriasis. Studies have indicated that combining salicylic acid with topical steroids enhances psoriasis treatment outcomes by more effectively reducing plaque thickness and scaling compared to using steroids alone. This combination therapy can be considered a first-line treatment for thick, scaly plaques. Salicylic acid is a valuable adjunct in psoriasis treatment, as it helps reduce scaling and softens lesions, thereby improving the efficacy of steroids by enhancing their penetration. It was particularly useful for application on areas with a thick stratum corneum, such as the palms, soles, and scalp, and can also be used on the trunk.[30.31]

The current survey results may assist clinicians in clinical decision-making and enhancing patient care by considering the preferences and prescription practices of a combination of glycolic acid (1%), salicylic acid (1%), and urea (5%) in Indian settings. The major strengths of the survey are the larger sample size and the utilization of a well-designed and validated questionnaire to collect data from clinicians. However, it is important to acknowledge certain limitations of the study. The results may be biased due to reliance on expert opinion, with diverse perspectives and preferences among clinicians influencing the outcomes. Additionally, the survey may not fully account for emerging evidence or evolving trends in the management of hyperkeratosis. One significant limitation of the present study was the lack of extensive literature directly addressing the combination of glycolic acid, salicylic acid, and urea for hyperkeratosis of the palms and soles. It was essential to keep these limitations in mind when interpreting the findings. To

address these limitations, it was recommended to conduct prospective trials or real-world observational studies to validate the survey results and provide a more comprehensive understanding of optimal treatment approaches.

5. Conclusion

The study highlighted a significant preference for using the combination of glycolic acid (1%), salicylic acid (1%), and urea (5%) for managing hyperkeratosis. This combination was also recommended with topical steroids for treating plaque psoriasis. Clinicians preferred a 10% urea strength for hyperkeratosis of the palms and soles and favored glycolic and salicylic acids as keratolytic agents.

6. Source of Funding

None

7. Conflict of Interest

None

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