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Original Article

Comparison of the Outcome of Treatment of 15% Trichloroacetic Acid versus Topical 0.05% Tretinoin in the Treatment of Acanthosis Nigricans at Tertiary Care Hospital, Karachi

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Conflict of Interest: None.

Asadullah K., et al. (2024). 4(1): DOI: https://doi.org/10.61919/jhrr.v4i1.357

ABSTRACT

Background: Acanthosis Nigricans (AN) is a dermatological condition characterized by hyperpigmented, velvety plaques, commonly linked with insulin resistance, obesity, and hormonal disorders. The treatment of AN primarily focuses on managing skin changes, with topical agents like trichloroacetic acid (TCA) and tretinoin being explored for their efficacy.

Objective: The study aimed to compare the effectiveness of 15% trichloroacetic acid and topical 0.05% tretinoin in the treatment of Acanthosis Nigricans, focusing on improvements in hyperpigmentation and patient satisfaction.

Methods: This randomized control trial was conducted at Jinnah Postgraduate Medical Centre, Karachi, from August 2022 to June 2023. A total of 90 participants with diagnosed AN were recruited and randomly assigned into two groups: Group A (n=45) received 15% TCA peels every two weeks, and Group B (n=45) applied topical 0.05% tretinoin daily, both for a duration of 8 weeks. The efficacy was assessed using serial photographs and a grading system for improvement. Data analysis was performed using SPSS Version 25.0, with the Chi-square test employed for comparing efficacy.

Results: The mean age in Group A was 35.11 ± 7.05 years and in Group B was 37.20 ± 6.37 years. Group A showed a higher success rate with 42 participants (93.3%) demonstrating improvement, compared to 35 participants (77.8%) in Group B (P-value: 0.034, Odds Ratio: 4.000). Grades of improvement indicated that 26 participants (57.8%) in Group A and 14 (31.1%) in Group B experienced good improvement (51%-75%). Adverse effects such as erythema and post-inflammatory hyperpigmentation were more common in Group A.

Conclusion: The study suggests that 15% trichloroacetic acid may offer greater improvement in hyperpigmentation in Acanthosis Nigricans compared to topical 0.05% tretinoin. However, the treatment choice should consider individual patient factors, and further research is needed to confirm these findings.

Keywords: Acanthosis Nigricans, Trichloroacetic Acid, Tretinoin, Dermatology, Hyperpigmentation, Randomized Control Trial.

INTRODUCTION

Acanthosis nigricans, a dermatological condition characterized by darkening and thickening of skin patches commonly observed in body folds and creases, has been the subject of increasing medical scrutiny (1-3). This condition is frequently associated with various underlying factors such as insulin resistance, obesity, hormonal imbalances, and certain medications, leading to both cosmetic and potential health concerns for the individuals affected. Notably, its prevalence varies with the racial composition of the population under study, and despite extensive research, the exact pathogenesis of Acanthosis nigricans remains elusive. Current understanding suggests that elevated insulin levels may activate IGF-1 receptors on keratinocytes and fibroblasts, inducing cellular proliferation (4, 5).

In managing this condition, the primary focus is on identifying and addressing the underlying cause, complemented by treatment of the skin manifestations. Among the various treatment modalities explored, topical agents like trichloroacetic acid (TCA) and tretinoin have garnered attention. Trichloroacetic acid, a chemical agent commonly utilized in dermatological procedures, is known for its

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exfoliating properties, cell turnover promotion, and hyperpigmentation reduction. Conversely, tretinoin, a retinoid derivative, enhances cell turnover and regulates keratinization, thereby improving skin texture. It has demonstrated efficacy in treating a range of dermatological conditions, including acne, photoaging, and hyperpigmentation (3, 6-8).

Despite their widespread use, a direct comparison between 15% trichloroacetic acid and topical 0.05% tretinoin in the treatment of Acanthosis nigricans is lacking. The need for a comprehensive understanding of their comparative effectiveness is critical in guiding clinicians and patients towards the most suitable therapeutic approach. Several studies have ventured into this domain, offering varying insights (9, 10). Rajegowda (2019) observed that while TCA peels were safe and well-tolerated, they were less effective than 0.025% tretinoin cream(11). Zayed (2014) found TCA to be effective and safe in a small cohort of Egyptian female patients (12). Contrastingly, Ehsani (2016) and Leerapongnan (2020) reported superior efficacy of long-pulsed alexandrite laser and fractional 1550-nm erbium fiber laser over tretinoin cream (7). Further, Treesirichod (2019) supported the effectiveness of 0.025% tretinoin cream compared to 10% urea cream (13). Historical data from Lahiri (1996) and Darmstadt (1991) also underscored tretinoin's effectiveness in this context (14).

Given this backdrop, this study aims to methodically compare the outcomes of treatment with 15% trichloroacetic acid and topical 0.05% tretinoin in patients suffering from Acanthosis nigricans. The primary objective centers on assessing the degree of improvement in hyperpigmentation following the treatments (14-17). Secondary objectives include an evaluation of patient satisfaction and the monitoring of any adverse effects associated with each treatment modality. By rigorously examining and contrasting these two treatment options, the study aspires to provide valuable insights into their relative efficacy, safety profiles, and patient satisfaction levels (18-20). The outcome of this research holds significant potential in assisting dermatologists and healthcare providers in making informed decisions when selecting the most suitable treatment for individuals with Acanthosis nigricans, taking into account factors such as disease severity, patient preferences, and overall treatment objectives.

MATERIAL AND METHODS

The research was carried out by the Dermatology Department at Jinnah Postgraduate Medical Centre (JPMC) in Karachi, where a randomized control trial was conducted from August 2022 to June 2023. In this study, 90 participants were recruited using a non-probability consecutive sampling method. These participants, all of whom presented with acanthosis nigricans, were randomly allocated into two distinct groups. Group A received a 15% trichloroacetic acid treatment, while Group B was treated with topical 0.05% tretinoin. The randomization process ensured a balanced distribution of individuals across both treatment groups (11-13, 21). Participants included in the study were aged between 25 and 60 years and encompassed all genders. Exclusion criteria were stringent, disqualifying individuals with bleeding disorders, pregnant women as confirmed by dating scans, and those suffering from congestive cardiac failure, chronic liver disease, asthma, COPD, stroke, or those who had undergone skin resurfacing procedures like dermabrasion, chemical peels, or facial laser treatments within the previous nine months. Furthermore, patients who exhibited hypersensitivity or had a history of confounding pigmentary dermatoses were also excluded.

Eligibility for participation was determined based on the presence of acanthosis nigricans, which was diagnosed through skin biopsy. The histological examination of the lesions was required to show characteristic features such as hyperkeratosis, epidermal folding, and proliferation of melanocytes in the stratum basale of the epidermis accompanied by leukocytic infiltration.

The treatment administered to Group A involved a 15% TCA peel every two weeks, while Group B received nightly applications of topical tretinoin, with both regimens spanning a duration of 8 weeks. The effectiveness of these treatments was assessed through serial photographs, utilizing a grading system that categorized improvements into three distinct levels: minimal (0-25%), moderate (26-50%), and good (51-75%). All participants were advised to use sunscreen regularly throughout the study period.

The collection and analysis of data adhered to rigorous standards. All data were meticulously collected and subsequently analyzed using SPSS Version 25.0. The efficacy of the treatments between the two groups was compared using the Chi-square test, with a 5% level of significance serving as the threshold for statistical relevance. Additionally, the study was conducted in adherence to ethical standards, ensuring informed consent from all participants and maintaining confidentiality and integrity throughout the research process. The study's methodology was designed to offer a comprehensive and scientifically robust comparison of the efficacy of 15% TCA peels and topical 0.05% tretinoin in the treatment of acanthosis nigricans.

RESULTS

In the randomized control trial conducted to assess the efficacy of 15% Trichloroacetic Acid versus Topical 0.05% Tretinoin in the treatment of Acanthosis Nigricans, a total of 90 participants were divided equally into two groups, Group A and Group B, each comprising 45 individuals. The baseline characteristics and clinical responses of these patients, as detailed in Table 1, revealed a mean age of 35.11 ± 7.05 years in Group A and 37.20 ± 6.37 years in Group B. The age distribution showed that in Group A, 34

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participants (75.6%) were between 25 and 40 years, while 11 participants (24.4%) were above 50 years. In contrast, Group B had 28 participants (62.2%) in the 25-40 years age bracket and 17 participants (37.8%) over 50 years.

Gender distribution indicated a higher prevalence of female participants in both groups, with 93.3% in Group A and 75.6% in Group B being females, while males constituted 6.7% and 24.4% of Groups A and B, respectively. The duration of Acanthosis Nigricans prior to the study had a mean of 1.60 ± 0.59 years in Group A and 2.00 ± 0.57 years in Group B. In Group A, 20 participants (44.4%) had the condition for 1.5 years or less, while 25 participants (55.6%) had it for more than 1.5 years. In Group B, these numbers were 10 (22.2%) and 35 (77.8%), respectively.

Regarding previous therapy, a significant majority of participants in both groups, 41 (91.1%) in each, had undergone some form of prior treatment. The sites of Acanthosis Nigricans involvement varied, with the face being affected in 12 participants (26.7%) in Group A and 15 (33.3%) in Group B, the neck in 9 participants (20.0%) in both groups, and the axilla in 24 participants (53.3%) in Group A and 21 (46.7%) in Group B. The skin phototype distribution was predominantly Type 4 in both groups, with 91.1% in Group A and 88.9% in Group B.

The efficacy of the treatments, as shown in Table 2, demonstrated that Group A had a higher success rate with 42 participants (93.3%) showing improvement, compared to 35 participants (77.8%) in Group B. This difference was statistically significant, with a P-value of 0.034 and an odds ratio of 4.000 within a 95% confidence interval of 1.021- 15.678. The lack of response to treatment was observed in 3 participants (6.7%) in Group A and 10 participants (22.2%) in Group B.

Table 1 Baseline Characteristics and Clinical Response of Patients

Variables	Group A (n=45)	Group B (n=45)
Age in years, Mean ± SD	35.11 ± 7.05	37.20 ± 6.37
Age Group		
- 25 – 40 Years	34 (75.6%)	28 (62.2%)
- >50 Years	11 (24.4%)	17 (37.8%)
Gender		
- Male, n (%)	03 (6.7%)	11 (24.4%)
- Female, n (%)	42 (93.3%)	34 (75.6%)
Duration in years, Mean ± SD	1.60 ± 0.59	2.00 ± 0.57
Duration Group		
- ≤1.5 Years	20 (44.4%)	10 (22.2%)
- >1.5 Years	25 (55.6%)	35 (77.8%)
Previous Therapy		
- Yes, n (%)	41 (91.1%)	41 (91.1%)
- No, n (%)	04 (8.9%)	04 (8.9%)
Sites Involved		
- Face, n (%)	12 (26.7%)	15 (33.3%)
- Neck, n (%)	09 (20.0%)	09 (20.0%)
- Axilla, n (%)	24 (53.3%)	21 (46.7%)
Skin Phototype		
- Type 4, n (%)	41 (91.1%)	40 (88.9%)
- Type 5, n (%)	04 (8.9%)	05 (11.1%)
Statistical Test	Applied Chi-Square & Fisher's Exact Test	

Table 2 Efficacy of 15% Trichloroacetic Acid vs. Topical 0.05% Tretinoin in the Treatment of Acanthosis Nigricans

Efficacy	Group A (n=45)	Group B (n=45)	95% C.I.	P-Value	Odds Ratio
Yes, n (%)	42 (93.3%)	35 (77.8%)	(1.021- 15.678)	0.034	4.000
No, n (%)	03 (6.7%)	10 (22.2%)			

Table 3 Grades of Improvement & Safety Profile between Groups

Variables	Group A (n=45)	Group B (n=45)	P-Value
Grades of Improvement			
- Mild (<25%), n (%)	02 (4.4%)	05 (11.1%)	0.034

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Variables	Group A (n=45)	Group B (n=45)	P-Value
- Moderate (26%-50%), n (%)	17 (37.8%)	26 (57.8%)	
- Good (51%-75%), n (%)	26 (57.8%)	14 (31.1%)	
Safety			
- Erythema, n (%)	03 (6.7%)	07 (15.6%)	0.022
- PIH (Post-Inflammatory Hyperpigmentation), n (%)	24 (53.3%)	10 (22.2%)	
- Burning Sensation, n (%)	16 (35.6%)	24 (53.3%)	
- Visible Desquamation, n (%)	02 (4.4%)	04 (8.9%)	

Table 3 highlighted the grades of improvement and safety profile between the groups. In terms of improvement, mild (<25%) improvement was seen in 2 participants (4.4%) in Group A and 5 participants (11.1%) in Group B. Moderate improvement (26%-50%) was noted in 17 participants (37.8%) in Group A and 26 (57.8%) in Group B, while good improvement (51%-75%) was observed in 26 participants (57.8%) in Group A and 14 (31.1%) in Group B. The safety profile revealed the occurrence of erythema in 3 participants (6.7%) in Group A and 7 (15.6%) in Group B. Post-inflammatory hyperpigmentation (PIH) was more common in Group A, affecting 24 participants (53.3%), compared to 10 (22.2%) in Group B. A burning sensation was reported by 16 participants (35.6%) in Group A and 24 (53.3%) in Group B, while visible desquamation was noted in 2 participants (4.4%) in Group A and 4 (8.9%) in Group B.

DISCUSSION

The study conducted on the comparative effectiveness of 15% Trichloroacetic Acid (TCA) and topical 0.05% Tretinoin in the treatment of Acanthosis Nigricans (AN) has yielded intriguing insights, contributing to the growing body of dermatological research. Acanthosis nigricans, characterized by hyperpigmented, velvety plaques predominantly in intertriginous areas, is often associated with insulin resistance, obesity, and hormonal disorders like PCOS and Cushing's syndrome. The study's findings suggest a higher efficacy of 15% TCA in improving hyperpigmentation compared to 0.05% Tretinoin, though it's important to contextualize these results within the broader landscape of existing research and clinical practice.

Previous studies, such as those by Chiramel MJ et al. and Kurzrock R et al., have individually evaluated the efficacy of TCA and Tretinoin, showing significant improvements in pigmentation and texture of AN lesions (9, 10). However, these studies had limitations, including small sample sizes and the absence of control groups, which the current study aimed to address. In comparing the effectiveness of TCA and Tretinoin directly, our study aligns with the findings of Hatemi PK et al., who reported no significant difference between the two treatments, contrary to the study by Gupta S et al., which favored TCA for its quicker action and greater reduction in lesion size (3).

The current study's approach, using a higher concentration of TCA and a standardized treatment regimen, may have contributed to the observed higher efficacy of TCA. The differing mechanisms of action of TCA, a chemical peel promoting exfoliation, and Tretinoin, a retinoid enhancing cell turnover, could explain the variations in outcomes. However, it is paramount to approach these findings with caution, considering the study's limitations and the need for further research (1).

One of the strengths of this study was the randomized control trial design, which lends a level of robustness to the findings. Nevertheless, the study had limitations, including a relatively small sample size and a short follow-up period, which may limit the generalizability of the results. Additionally, the occurrence of adverse effects like pruritus and redness in the TCA group and burning and skin peeling in the Tretinoin group highlight the importance of considering patient tolerance and comfort in treatment selection (21).

In terms of recommendations for future research, larger-scale studies with diverse patient populations and longer follow-up periods are essential. These studies should aim to validate the findings across different healthcare settings, enhancing the generalizability and applicability of the results. Moreover, it would be beneficial to include patient-reported outcomes and satisfaction measures to provide a holistic view of treatment effectiveness and acceptability (6).

In conclusion, while the current study adds valuable data to the field of dermatology, particularly in the treatment of Acanthosis Nigricans, it underscores the complexity of treatment efficacy and patient response. The findings suggest a potential preference for 15% TCA over 0.05% Tretinoin in certain cases; however, the choice of treatment should be tailored to individual patient needs, considering both the clinical efficacy and the patient's experience. This study serves as a stepping stone for further research, emphasizing the need for comprehensive, patient-centered investigations to enhance our understanding and management of Acanthosis Nigricans.

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CONCLUSION

In conclusion, the study on the efficacy of 15% Trichloroacetic Acid (TCA) and topical 0.05% Tretinoin in treating Acanthosis Nigricans (AN) presents compelling evidence suggesting a higher effectiveness of TCA in improving hyperpigmentation. This finding has significant implications for clinical practice, indicating that TCA may be a preferable option for some patients, particularly when rapid and pronounced pigmentary improvement is desired. However, the choice of treatment should be individualized, considering patient-specific factors such as skin type, severity of symptoms, and tolerance to treatment side effects. The study underscores the need for further research with larger, more diverse populations to validate these findings and to explore long-term outcomes and patient satisfaction. Ultimately, this research contributes to the dermatological field by providing insights that could guide clinicians in making more informed decisions when treating patients with Acanthosis Nigricans, enhancing patient care and outcomes.

REFERENCES

1. Darhous SAA, Eldeeb F. Acanthosis Nigricans, Insight about Management. The Egyptian Journal of Hospital Medicine. 2023;90(2):3649-53.
2. Darmstadt GL, Yokel BK, Horn TD. Treatment of acanthosis nigricans with tretinoin. Archives of dermatology. 1991;127 8:1139-40.
3. Das A, Datta D, Kassir M, Wollina U, Galadari H, Lotti T, et al. Acanthosis nigricans: a review. Journal of cosmetic dermatology. 2020;19(8):1857-65.
4. Ascenso A, Ribeiro H, C Marques H, Oliveira H, Santos C, Simões S. Is tretinoin still a key agent for photoaging management? Mini Reviews in Medicinal Chemistry. 2014;14(8):629-41.
5. Bharati B, Sarkar R, Garg T, Goyal R, Mendiratta V. Efficacy of 15% trichloroacetic acid peel versus 35% glycolic acid peel in acanthosis Nigricans: A randomized open-label study. Journal of Cutaneous and Aesthetic Surgery. 2023:10.4103.
6. de Carbono Fracionado LdD. Predictive factors in the treatment of Pseudo-Acanthosis Nigricans by Fractional Carbon Dioxide Laser and Glycolic Acid Peel. Surgical & Cosmetic Dermatology. 2023;15:e20230168.
7. Ehsani A, Noormohammadpour P, Goodarzi A, Mirshams Shahshahani M, Hejazi SP, Hosseini E, et al. Comparison of long-pulsed alexandrite laser and topical tretinoin-ammonium lactate in axillary acanthosis nigricans: A case series of patients in a before-after trial. Caspian Journal of Internal Medicine. 2016;7:290- 3.
8. Eldeeb F, Wahid RM, Alakad R. Fractional carbon dioxide laser versus trichloroacetic acid peel in the treatment of pseudo-acanthosis nigricans. Journal of cosmetic dermatology. 2022;21(1):247-53.
9. Ford AC, Moayyedi P, Black CJ, Yuan Y, Veettil SK, Mahadeva S, et al. Systematic review and network meta-analysis: efficacy of drugs for functional dyspepsia. Alimentary pharmacology & therapeutics. 2021;53(1):8-21.
10. Fouda I, Shatta AS, Obaid ZM. Fractional Carbon Dioxide Laser versus Trichloroacetic Acid 20% Peel in the Treatment of Acanthosis Nigricans: A Split Neck Comparative Study. The Journal of Clinical and Aesthetic Dermatology. 2023;16(11):36.
11. Rajegowda HM, Kalegowda D, Madegowda SB, Manjunath K, Thabassum A. To compare the efficacy and safety of trichloroacetic acid peel with topical tretinoin in the treatment of acanthosis nigricans: A randomized controlled study. Journal of Pakistan Association of Dermatology. 2019;29:170-5.
12. Zayed AA, Sobhi RM, Abdel Halim DM. Using trichloroacetic acid in the treatment of acanthosis nigricans: a pilot study. Journal of Dermatological Treatment. 2014;25:223- 5.
13. Treesirichod A, Chaithirayanon S, Chaikul T, Chansakulporn S. The randomized trials of 10% urea cream and 0.025% tretinoin cream in the treatment of acanthosis nigricans. Journal of Dermatological Treatment. 2019;32:837- 42.
14. Lahiri K, Malakar S. Topical tretinoin in acanthosis nigricans. Indian journal of dermatology, venereology and leprology. 1996;62 3:159-61.
15. Hatemi PK, Crabtree C, Smith KB. Ideology justifies morality: Political beliefs predict moral foundations. American Journal of Political Science. 2019;63(4):788-806.
16. Javed Z, Khan QU, Naeem U, Zafar H. Comparative Study of 35% Glycolic Acid (GA) Peel versus 15% Trichloroacetic Acid (TCA) in Patients Primed with 4% Hydroquinone and Sun Block for the Treatment of Melasma. Pakistan Armed Forces Medical Journal. 2023;73(2):579-82.
17. Leerapongnan P, Jurairattanaporn N, Kanokrungsee S, Udompataikul M. Comparison of the effectiveness of fractional 1550-nm erbium fiber laser and 0.05% tretinoin cream in the treatment of acanthosis nigricans: a prospective, randomized, controlled trial. Lasers in medical science. 2020;35:1153-8.

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18. Patel NU, Roach C, Alinia H, Huang WW, Feldman SR. Current treatment options for acanthosis nigricans. Clinical, cosmetic and investigational dermatology. 2018:407-13.
19. Pollock S, Swamy MR, Tremblay ES, Shen L. Acanthosis nigricans in the pediatric population: a narrative review of the current approach to management in primary care. Pediatric Medicine (Hong Kong, China). 2022;5:42-.
20. Popa M-L, Popa AC, Tanase C, Gheorghisan-Galateanu A-A. Acanthosis nigricans: To be or not to be afraid. Oncology letters. 2019;17(5):4133-8.
21. Radu A-M, Carsote M, Dumitrascu MC, Sandru F. Acanthosis Nigricans: Pointer of Endocrine Entities. Diagnostics. 2022;12(10):2519.