

Original Article

To compare the efficacy and safety of trichloroacetic acid peel with topical tretinoin in the treatment of acanthosis nigricans: A randomized controlled study

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Abstract

Background Acanthosis nigricans (AN) is a common pigmentary disorder with several therapeutic modalities to treat. Topical tretinoin is the first drug of choice in the treatment of acanthosis nigricans, however, trichloroacetic acid (TCA) peel has also shown efficacy in the treatment of AN recently.

Objective The study aimed to compare the efficacy & safety of trichloroacetic acid peel versus topical tretinoin in the treatment of acanthosis nigricans.

Material and Methods Fifty patients with acanthosis nigricans were selected and randomly allocated into two groups, where group A was treated with topical tretinoin 0.025% daily and group B with 15% trichloroacetic acid peel once in 15 days. Patients were assessed every fortnight for the improvement for 2 months. The degree of improvement was assessed using a grading system i.e., upto 25% - minimal, 26-50% - moderate, 51-75% - good and >75% - excellent improvement.

Results A total of 41 patients completed the study. At the end of treatment period 47.62% (n=10) patients in group A and 85% (n=17) patients in group B showed moderate improvement and 23.81% (n=5) in group A and 5% (n=1) in group B showed good improvement (p=0.0395). Side effects like erythema, burning sensation were more with topical tretinoin compared to TCA.

Conclusion Topical tretinoin 0.025% cream is more efficacious than 15% TCA. Though TCA is less efficacious, it is safe and well tolerated. Hence 15% TCA peel can be considered as a second line therapy in management of acanthosis nigricans.

Key words

Acanthosis nigricans, tretinoin cream, trichloroacetic acid peel.

Introduction

Acanthosis nigricans (AN) is a common pigmentary disorder affecting large population, clinically characterized by dark, coarse and thickened velvety skin, distributed symmetrically on the neck, the axillae,

antecubital and popliteal fossae, and groin folds. Histopathologically it is characterized by papillomatosis and hyperkeratosis of the skin.^{1,2}

Acanthosis nigricans is common, although exact prevalence depends upon the racial makeup of the population studied.³ Exact pathogenesis is unknown, elevated insulin concentrations result in direct and indirect activation of IGF-1 receptors on keratinocytes and fibroblasts, leading to proliferation.⁴ The dark colour of AN is due to hyperkeratosis rather than a mild

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increase in melanin pigmentation.

Therapeutic approach involves treatment of underlying disease or tumor, cessation/avoidance of the inciting agent in drug-induced AN, use of topical/ oral agents and cosmetic surgery. Commonly used topical agents are tretinoin, salicylic acid, podophyllin, urea, and calcipotriol. Topical tretinoin is the first choice of drug in the treatment of acanthosis nigricans.⁵ Despite several therapeutic modalities, acanthosis nigricans (AN) remains a difficult dermatosis to treat. Recently trichloroacetic acid (TCA), a superficial chemical exfoliative agent has shown efficacy in treating acanthosis nigricans.⁶ Hence this study has been undertaken to know the safety and efficacy of TCA in comparison to topical tretinoin.

Material and Methods

A randomized controlled comparative study was conducted for a period of 12 months between November-2016 to November-2017, at our institute. Patients were enrolled for the study after obtaining written informed consent. Detailed history and clinical examination were carried out and BMI of each patient was calculated. Patients allergic to tretinoin and TCA, pregnant women, and postpartum women upto 1 year were excluded from the study. Patients with AN were graded first based on the standard scale of 0-IV as described by Burkhe et al.⁷ Every consecutive patients with acanthosis nigricans was assigned to Group A for topical tretinoin therapy and group B for TCA peel. The patients in group A were advised to apply topical tretinoin every night as thin film to lesions of acanthosis nigricans in the neck for 2 months. In Group B 15% TCA peel was done every fortnight for 2 months. Regular sunscreen was advised to both groups in the daytime. Patients were assessed every fortnight for the

improvement and side effects using serial photographs for a period of 2 months. The degree of improvement in pigmentation was assessed using grading system i.e., 0-25% - minimal improvement, 26-50% - moderate improvement, 51-75% - good improvement, >75% - excellent improvement. They were also advised to change their lifestyle, reduce weight by regular exercises and also to avoid scrubbing.

The study was approved by the Ethical Committee of Mandya Institute of Medical Sciences (MIMS), Mandya, Karnataka. The data was entered and analyzed using statistical tests like chi-square test and proportions.

Results

In our study, patients with acanthosis nigricans were randomized into two groups of 25 each. In group A, out of 25 patients, 23 were female and 2 were male. In group B, 21 were female and 4 were male. M:F :: 1:7.3.

During the study period, 4 patients from group A and 5 patients from group B did not come for follow up. So, 21 patients in group A and 20 patients in group B were analysed at the end of study period.

According to Burkhe et al.⁷ grading of neck involvement, out of 50 patients, 5 patients had grade IV (**Figure 1a**), 33 patients had grade III (**Figure 1b**), 11 patients had grade II (**Figure 1c**) and only 1 patient had grade I involvement in the neck.

Among group A patients, 6 patients showed mild improvement (<25%), 10 patients showed moderate improvement (26-50%) (**Figure 2a & 2b**), 5 showed good improvement (51-75%) (**Figure 3a & 3b**), & none of them showed >75% improvement in pigmentation.



Figure 1a



Figure 1b



Figure 1c

Burke's grading of acanthosis nigricans involving neck. 1a-Grade IV, 1b- Grade III, 1c- Grade II



Figure 2a



Figure 2b

Moderate improvement (26-50%) with tretinoin 0.025% cream



Figure 3a

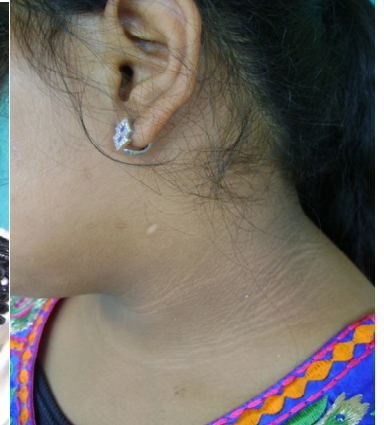


Figure 3b

Good improvement (51-75%) with tretinoin 0.025% cream



Figure 4a



Figure 4b

Good improvement (51-75%) with TCA peel



Figure 5

Persistent erythema with topical tretinoin



Figure 6

Visible desquamation with topical tretinoin

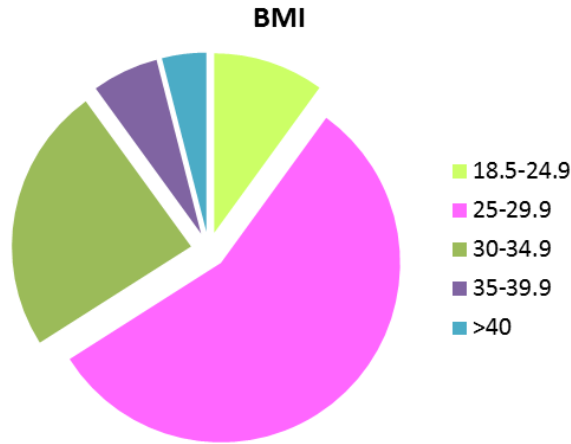


Figure 7 Body mass index and acanthosis nigricans

TABLE 1

Grade of improvement	Group A	Group B
Upto 25%	6(28.57%)	2(10%)
26-50%	10(47.62%)	17(85%)
51-75%	5(23.81%)	1(5%)

TABLE 2

Safety profile	Group A	Group B
Erythema	11	5
Burning sensation	13	8
Visible desquamation	4	2
Post inflammatory hyperpigmentation	2	1
Secondary infection	0	1

Among group B patients, 2 patients showed mild improvement (<25%), 17 patients showed moderate (26-50%), 1 patient showed good improvement (51-75%) (**Figure 4a & 4b**), & none had >75% improvement in pigmentation. (**Table 1**). The chi-square statistics is 6.4609 and the p value is 0.0395. the result is statistically significant at p value <0.05.

Side effects like erythema (**Figure 5**), visible desquamation (**Figure 6**), burning sensation were more with topical tretinoin than TCA peel. Hence, TCA peel is better in terms of safety compared to topical tretinoin 0.025% (**Table 2**).

Body mass index of each patient was calculated prior to treatment, out of 50 patients, 30 patients were overweight (BMI: 25-29.9), 17 patients were obese and 3 patients had normal BMI

(**Figure 7**). Patients were advised about the change in the life style.

Discussion

Acanthosis nigricans (AN) is a mucocutaneous eruption that is characterized by hyperpigmented papillomatous thickening with a velvety texture. AN was classified by Curth into four simple types, benign, malignant, drug induced & syndromic/ pseudo.⁸ It usually affects the flexural areas with a symmetrical distribution, but unilateral AN does not show a pattern similar to the other variants of AN.⁹ The term AN was originally proposed by Unna, but the first case was described in the year 1891 by Pollitzer and Janovsky. AN can be classified into 8 variants, including the benign, obesity-associated, syndromic, malignant, acral, unilateral, medication-induced and mixed-type.¹⁰ AN is commonly associated with obesity and insulin resistance which helps in early diagnosis of related systemic disorders including type 2 diabetes, metabolic syndrome, and polycystic ovary syndrome. Acanthosis nigricans is graded on a standard scale of 0-4 as described by Burke et al.⁷

True pathogenesis of AN is more complex. Higher insulin levels in obese patients activates IGF-1 receptors.^{11,12} The predilection areas of AN, such as neck and axilla suggests perspiration and/ or friction as necessary cofactors.^{13,14}

AN is a difficult dermatosis to treat. Identifying the underlying systemic cause (malignancy, metabolic disorders) is utmost important factor in management. Many therapeutic modalities were available for the treatment of AN. Weight loss and exercise have shown to increase insulin sensitivity and reduce insulin levels causing improvement in obesity associated AN.¹⁵ Warning flags that should trigger a careful

evaluation for malignancy in patients presenting with acanthosis nigricans include unintentional weight loss and rapid onset of extensive AN.¹⁶ Mucosal involvement is more common in patients who have AN in association with a malignancy, as are tripe palms, florid cutaneous papillomatosis, and the sign of Leser-Trélat.¹⁶ Though the goal of therapy is to correct the underlying disease process, improvement of the skin appearance is often the patient's primary concern.

Topical retinoid is considered first-line treatment in all forms of AN, especially for unilateral nevoid AN.⁵ In our study topical tretinoin 0.025% has shown better efficacy than 15% TCA. Lahiri and Malakar in their study have reported that intermittent tretinoin application is needed to maintain improved status.¹⁷ Adverse effects like erythema, desquamation and burning sensation were more with topical tretinoin, so it was less accepted by the patients.

Trichloroacetic acid (TCA) is a superficial chemical exfoliating agent causing destruction of the epidermis with subsequent repair and rejuvenation. TCA (15%) is caustic and causes coagulation of skin proteins leading to frosting. Precipitation of proteins leads to necrosis and destruction of epidermis, followed by inflammation and activation of wound repair mechanisms. This leads to re-epithelialization and replacement with smoother skin. The advantages of TCA are that it is a stable product, hence systemic absorption and peel depth correlate with the intensity of frost and endpoint is easy to judge.⁶ In our study 90% of patients showed moderate to good improvement with 15% TCA comparable to the study by Zayed et al. Side effects with TCA peel were less compared to topical tretinoin.

No randomized controlled studies exist for any treatment of AN. Limitations of our study is

short duration which is inadequate to assess the relapses. Larger multi-centric randomized controlled trials with longer follow-up are required to confirm our results.

Conclusion

Despite the several modalities of treatment, acanthosis nigricans remains a difficult dermatosis to treat. Underlying systemic problem needs to be corrected in management of AN. Topical tretinoin 0.025% being the first line agent, found to be more efficacious than TCA peel. However, Trichloroacetic acid (TCA) peel being the superficial chemical exfoliating agent with better patient compliance; is safe and can be considered as a second line therapy in the management of acanthosis nigricans.

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