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Comparing the Efficacy of Intralesional Saline Versus 35% Trichloroacetic Acid Peel in the Treatment of Atrophic Acne Scar

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ABSTRACT

Atrophic acne scars are a common sequela of acne vulgaris impact patients' quality of life. Despite the availability of several treatment modalities, there is a need for simpler and cost-effective approaches. **Objective:** To compare the efficacy of intradermal normal saline versus trichloroacetic acid (TCA) in treating atrophic acne scars. A randomized controlled trial conducted at the Dermatology Department, Sheikh Zayed Hospital, Rahim Yar Khan, from 1st April 2023 to 31st October 2023. **Methods:** 126 patients were enrolled. Scar grading was based on Goodman and Baron's Qualitative Scar Classification. The Patients Observer Scar Assessment Scale (POSAS) was used by dermatologists. Efficacy was defined as ≥50% improvement in the POSAS. **Results:** Among 126 participants, the NS group showed significantly greater improvement in PSAS and OSAS scores post-treatment. While total POSAS score reduction was higher in the NS group, the difference was not significant. A ≥50% POSAS improvement was more frequent in the NS group (88.9%) than in the TCA group (73.0%; p = 0.023). **Conclusion:** This study found that intradermal normal saline is more effective and satisfactory than trichloroacetic acid for treating atrophic acne scars, with greater improvements in scar severity and patient satisfaction.

INTRODUCTION

Acne vulgaris is a common skin problem affecting adolescents and adults. It is the eighth most common skin disease globally, having a prevalence ranging from 35%-85%, with notable variations across different regions and age groups. A prior study reported the prevalence of Acne vulgaris in Pakistan is 5% [1, 2]. The etiologies of acne vulgaris include hormonal fluctuations, genetic predisposition, bacterial colonization, dietary habits, sleep patterns, and excessive sebum production. Follicular hyper keratinization, sebum overproduction or Propionibacterium acnes growth leads to recurrent and chronic inflammation of Pilo-sebaceous gland [2, 3]. Moderate to severe acne can lead to atrophic scarring in up to 80-90% of patients with acne. It results from the continues inflammatory process affecting the Pilo-sebaceous gland [4]. Post-acne scarring may present as either atrophic, characterized by tissue wasting and including rolling, Ice-pick, and boxcar types, or as hypertrophic scar, marked by excessive deposition of fibrotic tissue [5]. Scaring can significantly affect quality of life, diminish self-esteem, and hinder social interactions of patients. Treating acne scars remained challenging for both patients and dermatologists, due to factors such as the expense of treatments, the necessity for multiple visits, extended duration of treatments, potential side effects, and the inherent limitations of treatment options

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[6, 7]. Advancements in scientific understanding of pathogenesis of acne scarring have provided a variety treatment options, offering variable efficacies and safety profiles. These options include microdermabrasion, chemical peels, tissue augmentation agents, microneedling, laser therapy, fat transplantation, platelet-rich plasma, and Intense Pulsed Light therapy. Treating atrophic acne scars involves assessing scar extent, skin type, patient expectations, cost, and physician expertise to devise a fully informed, optimal treatment plan [8, 9]. Chemical peeling is a technique involving the application of chemicals like Trichloroacetic acid (TCA) to remove outer damaged skin layer through exfoliation. TCA peels are available in different concentrations with 10% to 20% for superficial effects and 35% for medium-depth peeling. It causes epidermal and dermal collagen necrosis through kerato-coagulation. Various studies have promising results in the treatment of acne scars [10, 11]. However, disadvantages include sensations of stinging and burning upon application, along with risks of hypo- or hyperpigmentation of skin [11, 12]. In 2015, Bagherani and Smoller introduced intralesional saline injection as an innovative option for the treatment of atrophic acne scars. This method mechanically disrupts adhesions between epidermis and dermis and stimulates fibroblast activity for collagen and extracellular matrix neoformation. Injection-induced clotting raises the epidermis, facilitating new matrix development, while growth factors released from white blood cells and platelets encourage tissue growth [13]. While both intradermal trichloroacetic acid (TCA) and normal saline have been studied individually, there is no direct comparative study evaluating their efficacy and patient satisfaction. This study aims to fill this gap by proving head-to-head comparison of intradermal normal saline and TCA.

By assessing both physician and patient perspectives using qualitative and quantitative measures, this study aimed to provide clearer insights into which treatment offers superior outcomes, thereby helping to inform clinical decisions and improve treatment protocols for atrophic acne scars.

METHODS

A randomized controlled trial (RCT NO: NCT06789874) was conducted at Dermatology department, Sheikh Zayed Hospital, Rahim yar khan from 1st April 2023 to 31st October 2023. Ethical approval was obtained from the Institutional Review Board (656/IRB/SZMC/SZH), informed consent was obtained from all participants. A sample size of 126 was calculated by assuming the efficacy of 61% and 83.3 % in TCA and Normal saline group respectively, keeping confidence interval of 95% and power 80% [14, 15]. Initially patients were enrolled through non-probability consecutive sampling technique followed by randomization into two equal groups using computer generated random sequencing. Baseline demographic and clinical history related to the age, duration of symptoms and age of onset was collected. A dermatological examination of the skin was performed by the consultant dermatologist to identify the predominant scar type (Ice-pick, Boxcar, and Rolled) and grade of scar. The grading of scars was based on Goodman and Baron's Qualitative Scar Classification, where mild disease involved atrophy not visible from 50 cm and easily covered by makeup or hair; moderate disease involved noticeable scarring from 50 cm, not easily covered but flattenable by manual stretching; and severe disease involved prominent scarring from 50 cm, not easily covered or flattened by stretching [11, 16]. Before enrollment, scars were evaluated using the complete Patient and Observer Scar Assessment Scale (POSAS) version 2.0 [17, 18]. On the Observer side, a dermatologist scored six domains—vascularity, pigmentation, thickness, relief, pliability, and surface area using a 10-point scale, where 1 represented nearly normal skin and 10 indicated the worst scar imaginable. Patients simultaneously provided self-evaluations through the Patient Scale, which encompassed pain, itch, color, thickness, stiffness, and irregularity, also rated on a 10-point scale. Pre-treatment photographs were captured in a well-lit environment from various angles and labeled with the corresponding medical record number and treatment group, enabling direct comparison with post-treatment images. This study included patients aged 16-40 years of either gender with clinically diagnosed atrophic acne scars on the face, with a duration of more than 6 months, and no history of any procedural intervention in the past 3 months. Patients with keloids, active acne or local infection, skin allergies, hypertrophic scars, photosensitivity, or a history of comorbidities like diabetes mellitus, cardiovascular, and bleeding disorders were not included. Patients with a history of oral isotretinoin, oral contraceptives, steroids, or immunosuppressants were excluded. Pregnant females or patients with any psychiatric illness that could affect the treatment protocols were also omitted. Patients in the NS group received injections of 0.9% normal saline after local sterilization with spirit and application of topical anesthesia. A volume of 0.1-0.2 ml of normal saline was injected intradermally at each acne scar with a 1 cc syringe of 30 gauge into the scarred area until the elevation of scars and surrounding tissue [12]. Procedure was repeated fortnightly for 3 months and assessed on 12th weeks and 3 months post treatment. In the TCA group, after following the same initial protocols of anesthesia and sterilization, 35% trichloroacetic acid was applied to the scar base using blunt toothpick. The skin was monitored carefully until a frosted appearance was seen. Patients were instructed to

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wash their face with water after 10 minutes and to use water-based topical sunscreens. In both groups, patients received 3 sessions at monthly intervals and final outcomes were assessed after the last session at 12 weeks post treatment. Efficacy was defined as an improvement of ≥50% in both the Observer and Patient segments of the POSAS compared to baseline. The statistical analysis for this study was performed using SPSS version 26.0. Categorical variables, such as gender, duration of disease, scar grade, and predominant scar type, were presented as frequencies and percentages, while continuous variables, including age and Patient and Observer Scar Assessment Scale (PSAS and OSAS) scores, were expressed as mean ± standard deviation (SD). The chi-square test was used for comparing categorical variables, whereas continuous variables, such as age and PSAS and OSAS scores, were analyzed using the independent t-test. Stratification was performed for potential confounding variables, including gender, age group, duration of disease, and scar grade, to assess their impact on efficacy. Post-stratification analysis was conducted using the Chi-square test was used. To account for multiple comparisons, the Bonferroni correction was applied, adjusting the significance threshold accordingly. A p-value of less than 0.05 was considered statistically significant unless adjusted by the Bonferroni correction.

RESULTS

There were 53 (42.1%) males and 73 (57.9%) females. The mean age in NS group and TCA group was 25.32 ± 5.92 years and 27.06 ± 5.80 years, respectively (p=0.097). The baseline demographic and clinical characteristics were equally distributed between both groups (p > 0.05), indicating no significant differences. However, scar grades were statistically significantly different (p < 0.001), with the TCA group having a higher proportion of patients with more severe scars (Table 1).

Table 1: Distribution of Baseline Demographic and Clinical Characteristics in Treatment Groups (n=126)

Variables	Treatment Group		Chi-Square (p-Value)
	NS Frequency (%)	TCA Frequency (%)	
Age Group			
16-28 years	47 (74.6%)	42 (66.7%)	0.328
29-40 years	16 (25.4%)	21 (33.3%)	
Gender			
Male	24 (38.1%)	29 (46.0%)	0.367
Female	39 (61.9%)	34 (54.0%)	
Duration of Disease			
Up to 1 year	31 (49.2%)	35 (55.6%)	0.476
More than 1 year	32 (50.8%)	28 (44.4%)	
Scar Grade			
Mild	24 (38.1%)	14 (22.2%)	<0.001
Moderate	33 (52.4%)	15 (23.8%)	
Severe	6 (9.5%)	34 (54.0%)	
Predominant Scar Type			
Ice-pick	26 (41.3%)	25 (39.7%)	0.834
Boxcar	13 (20.6%)	11 (17.5%)	
Rolled Scar	24 (38.1%)	27 (42.9%)	

The Observer Scar Assessment Scale at baseline was 33.63 ± 7.73 in the Normal Saline (NS) group compared to 35.41 ± 7.78 in the TCA group (t (124) = –1.29, p = 0.201, 95% CI: –4.51 to 0.96, d = 0.23). Post-treatment, the Observer scale decreased to 14.35 ± 7.30 in the NS group and 17.37 ± 9.00 in the TCA group (t (124) = –2.07, p = 0.041, 95% CI: –5.90 to –0.13, d = 0.37). The Patient Scar Assessment Scale (PSAS) total score before treatment was 35.27 ± 7.55 in the NS group versus 36.98 ± 8.07 in the TCA group (t(124) = –1.23, p = 0.220, 95% CI: –4.47 to 1.04, d = 0.22). After treatment, the PSAS score was 11.83 ± 6.67 for the NS group and 16.13 ± 9.12 for the TCA group (t (113.61) = –3.02, p = 0.003, 95% CI: –7.12 to –1.48, d = 0.54).

Table 2: Comparison of Quantitative Treatment Outcomes between NS and TCA treatment Group (n=126)

Outcome Variable	NS (Mean ± SD)	TCA (Mean ± SD)	p-Value
Observer Scar Assessment Scale at Baseline	33.63 ± 7.73	35.41 ± 7.78	0.201
Observer Scar Assessment Scale Post-Treatment	14.35 ± 7.30	17.37 ± 9.00	0.041
PSAS Total Score Before Treatment	35.27 ± 7.55	36.98 ± 8.07	0.220
PSAS Score After Treatment	11.83 ± 6.67	16.13 ± 9.12	0.003

At baseline, the mean total POSAS score was 68.90 ± 14.88 in the Normal Saline group and 72.40 ± 15.74 in the TCA group. The independent samples t-test showed no statistically significant difference between the groups at baseline (mean difference = -3.49, 95% CI: -8.89 to 1.91; p = 0.203). After treatment, the mean reduction in POSAS scores was 42.73 ± 12.87 in the Normal Saline group and 38.90 ± 15.64 in the TCA group. This difference was not statistically significant (mean difference = 3.83, 95% CI: -1.23 to 8.88; p = 0.136). Regarding treatment efficacy, 56 (88.9%) of patients in the NS group and 46 (73.0%) of patients in the TCA group reported ≥ 50% improvement in score from baseline (p=0.023) (Table 3).

Table 3: Comparison of Efficacy between NS and TCA treatment Group. (n=126)

Efficacy	Treatment Group		Chi-Square (p-Value)
	NS Frequency (%)	TCA Frequency (%)	
Yes	56 (88.9%)	46 (73.0%)	5.147 (0.023)
No	7 (11.1%)	17 (27.0%)	

An initial assessment indicated that the Normal Saline group showed higher efficacy than the TCA group among individuals with a disease duration exceeding one year (p=0.034), those exhibiting mild scars (p=0.036), and those categorized as having rolled scars (p=0.033). However,

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after applying Bonferroni adjustments for multiple comparisons, none of these differences remained statistically significant. Consequently, no significant intergroup variations in efficacy were observed across any of the examined stratifications (Table 4).

Table 4: Efficacy Analysis between Treatment Groups Post-Stratification of Confounding Variables

Variables	Subgroup	NS Frequency (%)	TCA Frequency (%)	p-Value
Gender	Male	20/24 (83.3%)	22/29 (75.9%)	0.504
	Female	36/39 (92.3%)	24/34 (70.6%)	0.016
Age Group	16–28 years	42/47 (89.4%)	30/42 (71.4%)	0.032
	29–40 years	14/16 (87.5%)	16/21 (76.2%)	0.384
Duration of Disease	Up to 1 year	28/31 (90.3%)	27/35 (77.1%)	0.152
	More than 1 year	28/32 (87.5%)	19/28 (67.9%)	0.065
Scar Grade	Mild	22/24 (91.7%)	8/14 (57.1%)	0.012
	Moderate	29/33 (87.9%)	13/15 (86.7%)	0.906
	Severe	5/6 (83.3%)	25/34 (73.5%)	0.609
Predominant Scar	Ice-pick	25/26 (96.2%)	17/25 (68.0%)	0.008
	Boxcar	11/13 (84.6%)	11/11 (100.0%)	0.174
	Rolled Scar	20/24 (83.3%)	18/27 (66.7%)	0.173

Percentages indicate the proportion of patients within each group reporting efficacy. Post-stratification efficacy analysis of Normal Saline (NS) versus TCA with Bonferroni-adjusted p-values.

DISCUSSION

Atrophic acne scars are a common and disfiguring complication of acne. Various noninvasive and invasive treatment options are available for acne scars, each with varying degrees of effectiveness. Among invasive treatments, the efficacy of topical trichloroacetic acid (TCA) has been evaluated in previous studies, but there is no direct comparison available. This study compared the effectiveness of TCA and normal saline intradermal injections in treating atrophic scars. Post-treatment PSAS scores showed a significant reduction in both groups, with the NS group demonstrating a greater improvement ($t(113.61) = -3.02$, $p = 0.003$, 95% CI: −7.12 to −1.48, $d = 0.54$). This finding suggests that Normal Saline (NS) may be more effective in reducing the perceived severity of acne scars compared to TCA. Similarly, another study reported a significant improvement in Visual score from a baseline of 6.92 ± 1.49 to 10.1 ± 1.37 in patients receiving intradermal normal saline ($p<0.001$) [19]. The Observer Scar Assessment Scale, evaluated by a dermatologist, showed no significant difference in baseline scar severity between the groups (33.63 ± 7.73 vs. 35.41 ± 7.78, $p = 0.201$). However, post-treatment evaluations revealed that the Normal Saline (NS) group demonstrated a significantly greater reduction in scar severity than the TCA group (14.35 ± 7.30 vs. 17.37 ± 9.00, $p = 0.041$), thereby highlighting the potential efficacy of NS in improving scar appearance. Similarly, another single-arm interventional study evaluating the efficacy of NS in the treatment of atrophic scars reported significant improvement among all types of scars—icepick, rolled, and boxcar—using VAS, from 6.92 to 10.1 [19]. Similar results were observed in a study by Bagherani and Smoller after six sessions of normal saline intradermal injection treatment [13]. This study found that 88.9% of patients in the Normal Saline (NS) group achieved at least a 50% improvement in the Observer Scar Assessment Scale (OSAS) from baseline, compared to 73.0% in the TCA group ($p = 0.023$). These results suggest a potentially greater efficacy of NS for producing clinically meaningful scar improvements. This review article discusses the pathogenesis, classification, and a range of treatment options for acne scars, including both invasive and non-invasive approaches [20]. Lee et al., (2002) also recorded good satisfaction rates in the 65% and 100% TCA concentration, with no significant complications, further supporting the efficacy of TCA treatments between two strengths [21]. Both studies reported higher satisfaction with TCA compared to this study, probably because they used higher concentrations of TCA. A significantly higher proportion of patients in the Normal Saline group (88.9%) achieved a ≥50% improvement in the Observer Scar Assessment Scale from baseline, compared to 73.0% in the TCA group ($p=0.023$), indicating greater efficacy of NS in reducing scar severity. This highlights the superior effectiveness of NS in reducing scar severity. Khan S et al., (2020) demonstrated that saline injection therapy is a safe and effective treatment for improving the appearance of atrophic acne scars [15]. Similarly, another study reported very low efficacy for TCA, with the efficacy score reducing more than 50% in only 61% of subjects receiving TCA [14]. Lee et al., (2002) found that 82% of patients in the 65% concentration TCA group and 94% in the 100% TCA concentration group experienced a good clinical response, with all patients in the 100% TCA group who received five or six courses showing excellent results [21]. The lower efficacy of TCA in this study compared to this literature may be due to differences in the definition of efficacy or the use of a higher concentration of TCA in their studies compared to the 35% TCA. Sheraz et al., (2021) compared TCA with a derma roller and found that 40.25% of patients showed effective results with the derma roller, while 59.74% showed effective results with TCA ($p=0.015$) [22]. This highlights the comparative efficacy of TCA but also its associated higher cost and longer downtime. Mumtaz et al., (2021) similarly reported significant improvement with 50% TCA [23]. Strength of this study includes evaluation of both efficacy and satisfaction from the perspectives of physicians and patients, comparing qualitative and quantitative treatment effects to provide clarity in the outcomes. Limitations include being a single-centered study with a shorter follow-up period and not evaluating

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different concentrations of TCA. It is important to note that the effectiveness of normal saline injection for atrophic scars needs further validation in larger randomized controlled trials (RCTs). Additionally, exploring the combination of normal saline with other established therapies, such as microneedling, platelet-rich plasma (PRP), or fractional laser treatment, may yield even better outcomes. Despite these limitations, these findings suggest that intradermal normal saline is an effective, low-cost alternative to TCA for treating atrophic acne scars, particularly for patients with longer disease duration.

CONCLUSIONS

This study demonstrates that intradermal normal saline is more effective and satisfactory than trichloroacetic acid (TCA) for treating atrophic acne scars. Patients in the normal saline group showed greater improvements in both the Patient and Observer Scar Assessment Scale (PSAS and OSAS) scores compared to the TCA group. The normal saline group exhibited better scar texture, pigmentation, and overall aesthetic improvement, as reflected in both patient-reported and observer-assessed outcomes. These findings suggest that normal saline can be a superior alternative to TCA, offering better scar improvement and patient satisfaction. Future studies should focus on evaluating different concentrations of TCA compared to normal saline.

Authors Contribution

Conceptualization: KU
Methodology: KU, TH, MN
Formal analysis: MIJ
Writing, review and editing: KU, MKS, TH, MIJ, MN

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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