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Original Article

Comparison of Efficacy and Adverse Effects of 40% Hydrogen Peroxide and 50% Trichloroacetic Acid Preparations in the Treatment of Seborrheic Keratosis in A Tertiary Care Hospital

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ABSTRACT

Objective: To compare the efficacy and adverse effects of 40% Hydrogen Peroxide versus 50% Trichloroacetic Acid in the treatment of seborrheic keratosis in a tertiary care hospital.

Study Design: Quasi-experimental study.

Place and Duration of Study: Department of Dermatology, Combined Military Hospital, Lahore Pakistan, from Oct 2024 to Mar 2025.

Methodology: A total of 192 patients with seborrheic keratosis were enrolled in our study. After randomization, they were divided into two equal groups of 96 patients each. Group-A was treated with 40% Hydrogen Peroxide, and Group-B was treated with 50% Trichloroacetic Acid solution, for a maximum of four sessions at two-week intervals. The Physician's Lesion Assessment score was used to assess therapeutic efficacy. Erythema and other localized skin reactions were also recorded during the four sessions and one month after completion of therapy.

Results: At the follow-up visit, n=33 (34.4%) of patients achieved a PLA score of 0 in Group-A, compared to n=12 (12.5%) of patients in Group-B. A statistically significant difference was observed between the two groups (p=0.001). Group-A had a lower frequency of localized skin reactions, including erythema (4%), burning (2%), crusting (2%), hyperpigmentation (2%), and pruritus (1%). In contrast, Group-B experienced a higher incidence of erythema (68%), burning (78%), and hyperpigmentation (3%).

Conclusion: Treatment with a 40% Hydrogen Peroxide solution is more effective for seborrheic keratosis than 50% Trichloroacetic Acid, while demonstrating a comparatively favorable side-effect profile.

Keywords: Erythema, Hydrogen Peroxide, Keratosis, Seborrheic, Tertiary Care Centers, Trichloroacetic Acid.

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INTRODUCTION

Seborrheic keratosis (SK) is a common benign epidermal tumor arising from keratinocytes. Clinically, seborrheic keratosis presents as discrete, well-demarcated, hyperpigmented lesions and may appear on any cutaneous surface except the mucosa, palms, and soles. Hospital-based studies have reported that seborrheic keratosis constitutes approximately 20%-61.7% of all benign skin tumors evaluated in dermatology outpatient settings.[1] According to Kumar D *et al.*, approximately 42.6% of elderly patients attending dermatology outpatient departments had seborrheic keratosis.[2] SKs are more prevalent among fair-skinned individuals, affecting nearly 30% of Americans.[3]

Although benign, SKs often cause irritation, pruritus, or cosmetic concern, leading many patients to seek removal.[4] Conventional treatment options, such as electrocautery, cryotherapy, or surgical excision, are effective but frequently associated with discomfort, bleeding, and post-procedural scarring. These limitations highlight the need for safe, effective, and non-invasive topical treatment with fewer adverse effects.

Topical agents previously used to treat SK include Trichloroacetic Acid (TCA) solutions (35–50%), urea-based preparations, 1% diclofenac sodium solution, and tazarotene. Hydrogen Peroxide has been approved by the U.S. Food and Drug Administration (FDA) as a topical therapeutic agent for SK treatment. It acts as a chemical cauterant with relatively few side effects.[5]

However, only a limited number of international studies have evaluated the clinical efficacy of Hydrogen Peroxide. In a randomized controlled trial conducted by Agrawal *et al*., 30% Hydrogen Peroxide demonstrated significantly greater clearance of seborrheic keratosis compared with 50% TCA (p=0.017), with no major adverse effects in either

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group, indicating comparable tolerability but potentially enhanced efficacy with Hydrogen Peroxide.[6]

A systematic review of topical treatments has also highlighted Hydrogen Peroxide as one of the most evidence-backed topical agents with very mild and transient skin reactions, and lower risk of post-inflammatory pigmentary changes compared with deeper chemical cautery approaches.[7]

In clinical practice, 40% Hydrogen Peroxide formulations require multiple applications per session and additional follow-up sessions for maximum clearance. All the sessions are well tolerated with common side effects such as stinging and erythema, which usually resolve quickly.[8] To date, no clinical studies have been conducted in Pakistan on this topic, although research on this topic has been published in national journals.

Our study aimed to demonstrate the effectiveness of 40% Hydrogen Peroxide and compare the outcomes with the commonly used 50% TCA solution in treating seborrheic keratosis, with special interest in Asian skin, Fitzpatrick skin type IV – VI. The results of this study will help dermatologists consider more effective and relatively safe treatment options for seborrheic keratosis.

METHODOLOGY

This quasi-experimental study was conducted at the Department of Dermatology, Combined Military Hospital, Lahore, Pakistan, from Oct 2024 to Mar 2025, after obtaining prior approval from the hospital's ethical review board (research review board number 499/ 2024 dated 19 Feb 2024).

Inclusion Criteria: All clinically diagnosed cases of seborrheic keratosis (SK) within the age range of 18-75 years, of either gender, and with Fitzpatrick skin types IV – VI were included.

Exclusion Criteria: Patients with seborrheic keratosis over the eyelids or within 5mm of the orbital margin; a tendency for hypertrophic scar or keloid formation; active infection; or those who were pregnant or lactating were excluded.

The sample size was determined using the WHO sample size calculator with 45% proportion of efficacy achieved with Hydrogen Peroxide as compared to 25% proportion of efficacy with Trichloroacetic Acid (TCA) solution,[9] 80% power of test, and 5% significance level. The estimated sample size came out to be 192 patients.

Non-probability convenient sampling technique was used, and informed consent was obtained from all participants in the study. A total of 192 patients were enrolled and randomly allocated in a 1:1 ratio into two equal groups of 96 patients each using the lottery method, with randomization performed immediately before treatment allocation. Group-A was treated with 40% Hydrogen Peroxide, and Group-B was treated with 50% TCA solution Figure-1.

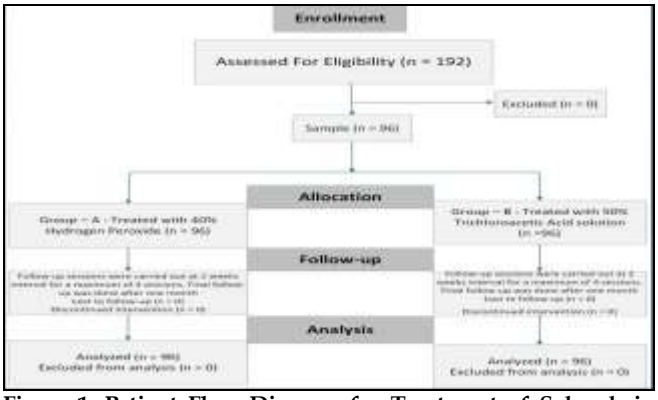

Figure-1: Patient Flow Diagram for Treatment of Seborrheic Keratosis with 40% Hydrogen Peroxide And 50% Trichloroacetic Acid Solution (n=192)

In Group-A, lesions were cleaned with an alcohol swab, and liquid paraffin was applied to the surrounding area. Then, 40% Hydrogen Peroxide was applied with gentle pressure for 20 seconds in a circular motion using a soft cotton-tipped applicator. This procedure was repeated four times with a 60-second interval between applications. The formation of a white layer over the lesions was considered the endpoint. Patients were monitored for 15-20 minutes after treatment for any localized skin reactions (LSRs) Figure-2.

Figure-2: Complete Clearance of Seborrheic Keratosis after application of 40% Hydrogen Peroxide at Follow-up Visit

In Group-B, after similar skin preparations, 50% TCA was applied once using a soft cotton-tipped applicator. After the formation of a white frost over the lesion, it was neutralized, and the patient was monitored for 15-20 minutes for any LSR. Figure-3.

Fig-3: Post-inflammatory Hyperpigmentation Observed after Treatment with 50% Trichloroacetic Acid Solution (TCA)

The Physician's Lesion Assessment (PLA) score was used to assess therapeutic efficacy. It is a four-point scale where: 0 = clear: no visible lesion; 1 = near clear: a visible SK lesion, not raised, with a surface appearance different from the surrounding skin; 2 = thin: a visible SK lesion of thickness <1 mm; 3 = thick: a visible SK lesion of thickness >1 mm. The primary endpoint was complete clearance (score 0 on the PLA scale).[10]

The procedure was repeated for a maximum of four sessions at two-week intervals, and the PLA score was assessed at each visit of the patient. The PLA score was again assessed at the follow-up visit, one month after the cessation of therapy. The efficacy of each chemical agent was defined as the proportion of patients who achieved a PLA score of 0 at the end of treatment.

Erythema and any other localised skin reactions (LSRs) were also recorded during the four treatment sessions and one month after completion of therapy.

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 25.Qualitative variables, including gender, efficacy, and localized skin reactions, were presented as frequencies and percentages. Both groups were compared for efficacy and side effects using the Chi-square test, with a *p*-value ≤0.05 considered statistically significant.

RESULTS

A total of 192 patients were enrolled in the study, of whom 153(79.7%) were male and 39(20.3%) were female. Most patients were in the 41-75-year age group. In Group-A, 96 patients were treated with 40% Hydrogen Peroxide, and 33(34.4%) patients achieved a PLA score of 0 at the follow-up visit, whereas only 12(12.5%) patients achieved a PLA score of 0 at the follow-up visit, after treatment with 50% Trichloroacetic Acid solution (TCA) in Group-B. (Table-I)

A statistically significant difference (p=0.001) was observed when the results of 40% Hydrogen Peroxide (H2O2) and 50% TCA were compared (Table-II)

Localized skin reactions (LSRs) observed in Group-A patients treated with 40% Hydrogen Peroxide were erythema in 4(4%) patients, burning in 2(2%) patients, crusting in 2(2%) patients,

Table-I: Comparative Distribution of Physician's Lesion Assessment (PLA) Scores at Successive Hospital Visits Among Patients Treated with 40% Hydrogen Peroxide Group-A and 50% Trichloroacetic Acid Solution Group-B (n=96 each)

Physician's Lesion Assessment (PLA) Score	Hospital Visit									
	1st		2nd		3rd		4th		Follow- up	
	Group-A, n(%)	Group-B, n(%)	Group-A, n(%)	Group-B, n(%)	Group-A, n(%)	Group-B, n(%)	Group-A, n(%)	Group-B, n(%)	Group-A, n(%)	Group-B, n(%)
3	28(29.2%)	35(36.4%)	24(25.0%)	22(22.9%)	6(6.2%)	13(13.5%)	0(0%)	0(0%)	0(0%)	0(0%)
2	46(47.9%)	56(58.3%)	46(47.9%)	59(61.4%)	48(50.0%)	40(41.7%)	31(32.3%)	25(26.0%)	16(16.7%)	16(16.7%)
1	22(22.9%)	5(5.2%)	25(26.0%)	15(15.6%)	38(39.6%)	40(41.7%)	42(43.7%)	64(66.7%)	47(48.9%)	68(70.8%)
0	0(0%)	0(0%)	1(1.1%)	0(0%)	4(4.2%)	3(3.1%)	23(23.9%)	7(7.3%)	33(34.4%)	12(12.5%)
Total	96(100%)	96(100%)	96(100%)	96(100%)	96(100%)	96(100%)	96(100%)	96(100%)	96(100%)	96(100%)

Table-II Comparison of Physician's Lesion Assessment (PLA) Scores At Follow-Up Visit Between Patients Treated With 40% Hydrogen Peroxide versus 50% Trichloroacetic Acid Solution (n=96 each)

Treatment	Physician's Lesion Assessment (PLA) Score At the Follow-Up Visit n(%)				*p*-value
	3	2	1	0	
40% Hydrogen Peroxide	0(0%)	16(16.7%)	47(48.9%)	33(34.4%)	0.001
50% Trichloroacetic Acid Solution	0(0%)	16(16.7%)	68(70.8%)	12(12.5%)	

hyperpigmentation in 2(2%) patients, and pruritus in 1 (1%) patient. In contrast, LSRs observed in Group-B patients treated with 50% TCA included erythema in 65 (68%) patients, burning in 75 (78%) patients, and hyperpigmentation in 3 (3%) patients.

DISCUSSION

The findings of the study advocate for Hydrogen peroxide as being more effective and therapeutically compliant medication for the treatment of Seborrheic Keratosis. Various therapeutic modalities have been used in the management of seborrheic keratosis (SK), including chemical agents such as Hydrogen Peroxide and Trichloroacetic Acid solution (TCA).[10] Hydrogen Peroxide is postulated to act through the generation of reactive oxygen species, resulting in lipid peroxidation and oxidative injury to keratinocytes, ultimately leading to lesion destruction.[11] Hydrogen Peroxide carries a lower risk of post-treatment hypo- or hyperpigmentation compared with other treatment options, as it is less cytotoxic to melanocytes and promotes melanocyte viability.[12]

In a study conducted by Leskelä *et al*., seborrheic keratosis was found to be more common in males (p<0.05),[13] supporting the findings of our study, in which seborrheic keratosis was observed in 153(79.7%) male and 39(20.3%) female patients, within the study population. Seborrheic keratosis can occur at any age; however, its incidence increases with advancing age. The most commonly affected age group in our study population was 66-70 years, comprising n=75(39.1%) patients. Of these, 68 were male, and 7 were female, and the association between age group and gender distribution was statistically significant (p=0.001). These findings were consistent with the study conducted by Noushin *et al*., which also reported a higher frequency of seborrheic keratosis in the elderly population.[5] The age-related increase supports the degenerative and cumulative environmental exposure theories implicated in the pathogenesis of SK.

About therapeutic efficacy, complete lesion clearance was not achieved after the first session of 40% Hydrogen Peroxide in our study. This contrasts with reports of higher early clearance rates using 30% Hydrogen Peroxide by Suvarna *et al*.[14] The observed discrepancy may be due to differences in lesion characteristics, patient populations, and treatment protocols. Factors, including the thickness of lesions, anatomical distribution, techniques of application, and timing of follow-up, may have influenced the response to treatment.

In the present study, complete lesion clearance (PLA score 0) was achieved in 34% of patients treated with 40% $H2O_2$ at the end of all treatment sessions, compared to only 12% of patients attaining a PLA score 0 after treatment with 50% TCA solution. These findings are comparable to those reported by Salecha *et al*.,[9] where 45% of patients attained a PLA score of 0 following completion of therapy. Overall, our results indicate a superior therapeutic response with 40% H_2O_2 compared to 50% TCA.

Similarly, Agrawal *et al*., reported superior efficacy of 30% Hydrogen Peroxide over 50% TCA, demonstrating complete lesion clearance in 41.8% of patients in the Hydrogen Peroxide group versus 23.8% in the TCA group.[6] Although the absolute clearance rates in our study were slightly lower, the overall trend remains comparable, supporting the greater effectiveness of Hydrogen Peroxide-based therapy over TCA.

Notably, larger multicenter trials have reported higher clearance rates at longer follow-up intervals in a study conducted by Funkhouser *et al*.[15] The comparatively lower clearance rate observed in our study may be due to the shorter follow-up duration (90 days versus longer assessment periods in other trials), which may have underestimated delayed therapeutic responses.

While our findings suggest greater efficacy of Hydrogen Peroxide over TCA, the available literature is not entirely consistent. In contrast to the present study, study conducted by Mosbeh *et al*., and Abd-Elshakour *et al*., have demonstrated greater effectiveness with cryotherapy and TCA compared to Hydrogen Peroxide in the treatment of seborrheic keratosis.[16,17] This variability may be due to differences in study design, concentration of chemical agents used, and number of treatment sessions. Such variation underscores the need for individualized treatment selection based on lesion morphology, patient preference, skin type, and risk of adverse effects.

In addition to efficacy, safety remains a key consideration in selecting any treatment modality. Traditional treatment options such as cryotherapy, electrocautery, and curettage are frequently associated with adverse effects, including erythema, pain, blistering, scarring, and post-procedure hypo- or hyperpigmentation.[18] In contrast, patients treated with 40% Hydrogen Peroxide in our study experienced minimal localized reactions, with erythema observed

in only 4% of cases. This incidence is lower than that reported in several previous clinical trials.[19], suggesting good tolerability in our study population. Conversely, 50% TCA was associated with a relatively higher frequency of erythema (68%) and burning sensation (78%), findings that are consistent with previously reported literature.[20]

Collectively, the study suggests that 40% Hydrogen Peroxide provides a more favorable balance between efficacy and safety compared to 50% TCA in the treatment of seborrheic keratosis. The reduced incidence of adverse effects, particularly pigmentary complications, makes Hydrogen Peroxide a promising therapeutic option, especially in populations with darker skin types where post-inflammatory hyperpigmentation is a significant concern. However, further large-scale, randomized controlled trials with longer follow-up durations are recommended to validate these results. The findings of this study will lay the groundwork for further research on this topic, especially in the Pakistani population.

LIMITATIONS OF STUDY

The limitations of our study include a small sample size, a short follow-up period of only 30 days, a narrow focus on patients with Fitzpatrick skin types IV-VI, and the evaluation of only one concentration (40%) of Hydrogen Peroxide, whereas various concentrations are available in the market. The use of convenience sampling may limit the generalizability of the findings and introduce selection and observer bias.

CONCLUSION

The findings of our study indicate that 40% Hydrogen Peroxide is a more effective treatment for seborrheic keratosis compared to 50% Trichloroacetic Acid, with a relatively favorable side effect profile.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SZ & SZ: Data acquisition, data analysis, critical review, approval of the final version to be published.

AR & AK: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

HM & NM: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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