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Original Article

Topical trichloroacetic acid versus cryotherapy in the treatment of seborrheic keratoses: A prospective study

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Abstract

Background Seborrheic keratoses (SKs) are benign pigmented epidermal skin tumours which causes considerable cosmetic disfigurement. Common techniques for SK removal include cryosurgery, electrosurgery, curettage, surgical excision or chemical peels. However, there is lack of well-controlled clinical studies evaluating the efficacy and safety of these procedures.

Objective To compare the efficacy and safety of topical Trichloroacetic acid (TCA) versus cryotherapy in the treatment of SKs.

Methods In this prospective study, 60 clinically diagnosed cases of SK were enrolled. For each participant, SK lesions were treated with cryotherapy and focal topical TCA upto 65%. The procedure was repeated monthly till desired effect or upto maximum of three sessions. Patients were followed up monthly to evaluate clinical outcome on 3-point scale (>75%-excellent;50-75%-good; <50%- poor response) and patient satisfaction rates assessed. Statistical analysis was done by the chi-square test using SPSS software.

Results Out of 60 patients treated, at the end of 6 months, among the lesions treated with TCA, 91.6 % (55) showed excellent response, 8.3% (5) good response. Among lesions treated with cryotherapy 75% (45) showed excellent response, 25% (15) good response. Polling the patients, 43.3% (26) stated that cryotherapy showed better results, 71.6% (43) felt that TCA was the quickest to heal, 73.3%(44) opined cryosurgery to be most painful.

Conclusion Lesions treated with cryotherapy were painful, with longer healing time, whereas TCA is cost effective with higher efficacy and better patient satisfaction rates. Hence we conclude topical TCA is more efficacious and cost effective than cryotherapy in treatment of SKs.

Key words
Seborrheic keratoses, cryotherapy, trichloroacetic acid.

Introduction

Seborrheic keratoses (SKs) are among most common benign epidermal skin lesions. Patients intend to get treated for various reasons including embarrassment from unsightly nature, pruritus, or desire to look younger.[1] Techniques for SK removal include cryosurgery, electrosurgery, curettage, or surgical excision.[2] A prevalence of 69-100% among adults >50 years is present.[3] Cryosurgery using liquid nitrogen has been the standard and most preferred treatment modality.[4] Flat lesions respond to single 5s and larger lesions require

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30s freeze-thaw cycle (FTC) respectively.[5] Medium depth concentration peels such as trichloroacetic acid (TCA) causes coagulative necrosis with subsequent healing which is used in treatment of SKs.[6] Choice of treatment is based on the number, location, skin pigmentation, thickness, and overall aesthetic considerations.

Material and Methods

Sixty clinically diagnosed cases of seborrheic keratoses, on the basis of history and typical clinical features, fulfilling the inclusion criteria of having multiple seborrheic keratoses at two anatomical sites, age more than 18 years, with no concurrent topical treatment of seborrheic keratoses within the past four weeks were included in the study after clearly explaining the nature of the study, and obtaining written informed consent.

Pregnant and lactating women, patients with clinical lesions suspicious of malignancy [atypical, rapidly growing, or multiple eruptive (i.e., Leser-Trelat sign) SK lesions], keloidal tendency, lesions at difficult to access sites such as periorbital area or within the ears, history of current or prior treatment for the SK lesions in last 6 months were excluded.

The study was conducted over a period of 6 months from May 2019 to October 2019, in outpatient department of Department of Dermatology, at our institute, after obtaining ethical clearance from Institutional Ethical Committee.

Procedure: A thorough demographic and dermatological examination was done to note the Fitzpatrick skin type, degree of actinic damage, current medications, history of scar/ keloidal tendency was assessed. The number, extent, site and type of seborrheic keratoses were diagnosed clinically or with aid of dermatoscope. Required investigations such as skin biopsy and histopathological examination were done in lesions with suspected malignant transformation.

For each participant, SK lesions to be treated were identified at two different anatomical sites. When multiple SKs were present, maximum of 5 with similar characteristics were chosen.

Lesions at one site were treated with cryotherapy using liquid nitrogen in a hand held cryogun and the other site treated with topical trichloroacetic acid. The detailed cutaneous examination was conducted in good light, and appropriate digital photographs were taken. Patients were advised not to use any other treatment for SKs during the study period.

Treatment protocol: For all subjects, lesions at one site were treated with cryotherapy using liquid nitrogen in a hand held cryogun to ensure that the freezing stayed within the confines of lesion for approximately 12 seconds of FTC.[3]

Topical TCA at 10-65%, depending on the thickness of lesion, was applied to a focal pigmented area with the tip of sharpened wooden toothpick after cleaning the area with alcohol while protecting the surrounding normal skin with vaseline. The excess TCA was blotted using gauze pad. Focal application of TCA produced evenly frosted spots which indicated the end point.[7] Patients were instructed to apply an antibiotic ointment two times daily for 5-7 days at both treatment sites. The focal TCA peel and cryotherapy were performed every month for 3 months or until the desired response was achieved depending on the reduction in size and pigmentation of the lesion.

Outcome evaluation: The patients were evaluated clinically and by comparing with

baseline clinical photographic records at each treatment session for resolution of treated SKs, their size and any immediate or late adverse effects, if any. Any adverse reactions at both sites were recorded as well. Serial digital photographs were taken both before, during each session and after the follow up period. The dimensions of the lesions were measured using a paper scale/ dermoscope at the initial visit, end of sessions and after the 3 month follow up period. Results were assessed based on the percentage improvement in lesions on a 3- point grading scale in terms of reduction in size and pigmentation with the help of baseline photographs as follows:

- >75% improvement - excellent response;
- 50–75% improvement - good response;
- <50% improvement - poor response.

After completion of treatment period, the patients were also followed up every month for three months.

Statistical analysis*:* Data was analyzed with the help of the SPSS version 20 software. Data were expressed as mean±SD for quantitative variables, and number and percentage for qualitative ones. Chi-square test and T-test were used wherever appropriate. The P-values <0.05 was considered significant.

Results

Sixty patients with SKs were enrolled in the study. The age of the patients ranged from 30-89 years, with mean age of 60.45 years. Majority of the patients were aged between 60 to 69 years (36.6%). There were 34 males and 26 females with ratio of 1.3:1. The total duration of SKs varied from minimum of 1 month to maximum of 20 years. All patients belonged to Fitzpatrick's skin type IV and V. The various socio-demographic characteristics and distribution of SKs has been depicted in **Table 1**.

Most common associated co-morbidities were hypertension seen in 38.3% patients and diabetes mellitus in 28.3% patients. Lesions were asymptomatic in majority with itching present only among 19 patients (31.7%). Family history was positive among 9 patients (11.4%). Most common associated benign pigmentary cutaneous lesions were Idiopathic guttate hypomelanosis (IGH) seen in 36 patients (60%) which was statistically significant ($p<0.05$). Other cutaneous disorders present among the subjects were scalp psoriasis, ashy dermatosis, acrodermatitis continua of Hallopeau, palmoplantar psoriasis, senile purpura in one patient each and eczema was present in 4 patients. History of chronic sun exposure was present among 31 patients (51.6%).

Comparing baseline images and post treatment images, it was concluded that excellent improvement was seen among 55 patients

Table 1 Socio-demographic parameters and distribution of SK lesions.

Demographic parameters	*Frequency*	*Percentage*
Sex		
Male	34	56.6
Female	26	43.3
Age group distribution		
30-39	3	5
40-49	4	6.6
50-59	17	28.3
60-69	22	36.6
70-79	12	20
80-89	2	3.3
Duration of lesions		
≤ 1 year	22	36.6
2-5 years	19	31.6
6-10 years	12	20
11-15 years	5	8.3
16-20 years	2	3.3
Site of distribution of lesions		
Lower limb	16	26.7
Upper limb	6	15.0
Upper limb and lower limbs	28	46.7
Trunk	7	11.7

Figure 1 Excellent improvement following A) cryotherapy after 3 sessions and B) Topical TCA after 1 session.

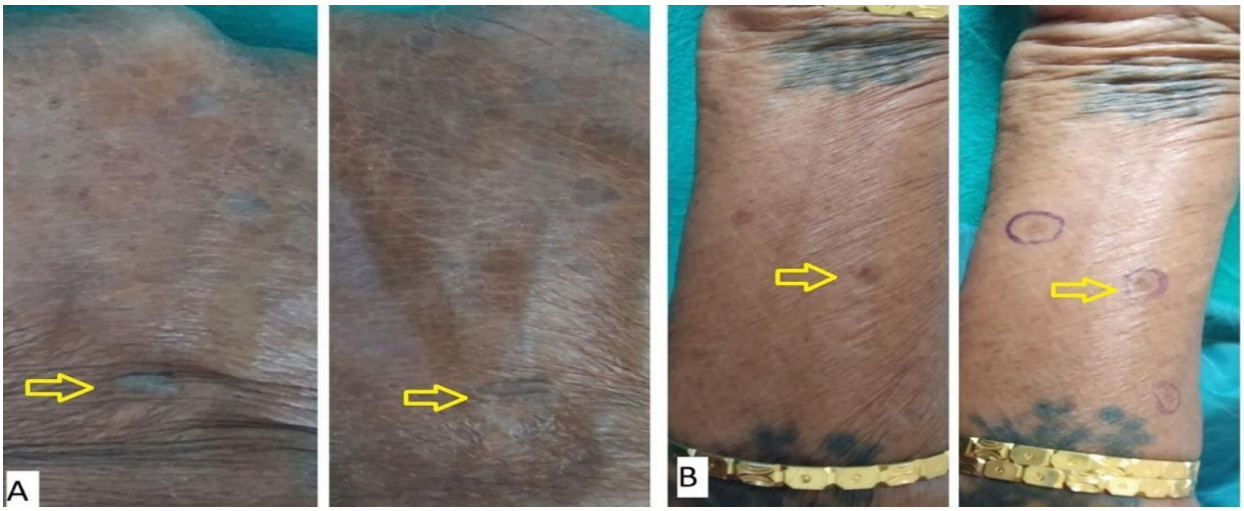
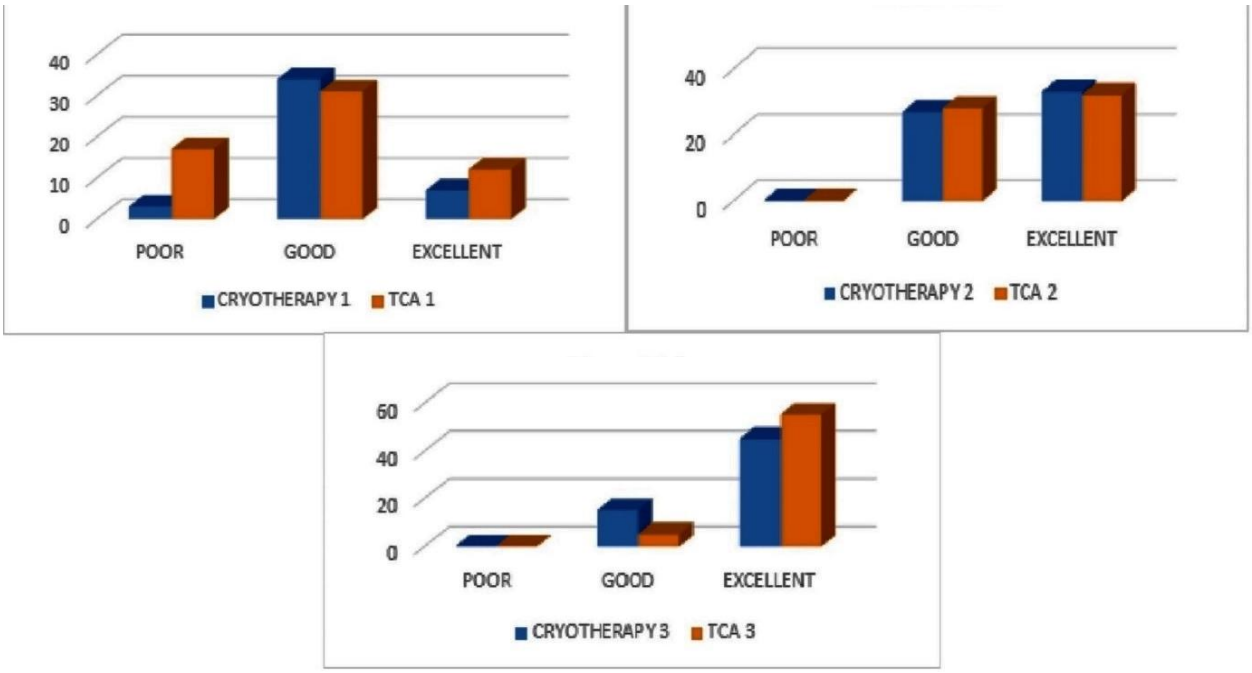


Figure 2 A) Good response following TCA after first session B) poor response following cryotherapy after first session.

(91.6%) treated with topical TCA and 45 patients (75%) treated with cryotherapy **(Figure 1).** This difference was statistically significant with p=0.014.

Good improvement was seen among 5 patients (8.3%) treated with topical TCA and 15 patients (25%) treated with cryotherapy (p=0.014) **(Figure 2)**. The grades of improvement following each session with TCA and cryotherapy has been depicted in **Graph-I**.

After the follow up, patient satisfaction rates were assessed among all patients, better results were attributed to cryotherapy by 26 (43.3%) patients, and to TCA by 24 (40%) patients. Rest 10 patients (16.6%) were equivocal of both modalities in terms of efficacy. Forty-three patients (71.6%) opined that TCA was the quickest to heal, but 14 of 60 (23.3%) felt that cryosurgery had quicker healing. The rest found no difference between both (0.05%). Treatment was comparatively painful with cryotherapy among 44 patients (73.3%), whereas only 6 patients (10%) found TCA to be more painful. 10 patients (16.6%) were unable to give conclusive opinion of pain with both techniques **(Table 2)**.



Graph 1 Grade of improvement among the two modalities of treatment following first, second and third session.

Table 2 Patient Satisfaction Rates at the end of follow up.

Parameters	*Cryotherapy (N=60)*	*TCA (N=60)*
Best result	26 (43.3)	24 (40%)
Most painful	44 (73.3)	6 (10)
Healed quickest`	14 (23.3)	43 (71.6)

Table 3 Various side effects observed for each treatment modality.

Most common side effects observed	*TCA (n= 60)*	*Cryotherapy (n=60)*
Mild pain	6 (10%)	44 (73.3%)
Burning sensation/ stinging	15 (25%)	25 (41.6%)
Pigmentary changes	none	6 (10%)

The most common side effects noted were local skin reactions characterised by mild pain, stinging or burning sensation which was most commonly associated with cryotherapy **(Table 3)**. One patient with scalp psoriasis was withdrawn from the study after first session as he developed koebnerization at the sites treated with both modalities. Post inflammatory hypopigmentation following cryotherapy was seen in 6 patients (10%) which was transient and healed in 2-3 weeks **(Figure 3)**.

Figure 3 Transient post inflammatory hypo-pigmentation following cryotherapy resolved in 3-4 weeks.

No permanent side effects were seen in any of the patients. After the follow up period, no recurrence was found at sites treated with both modalities, response achieved was sustained and no long term pigmentary changes or scarring was seen at both treatment sites.

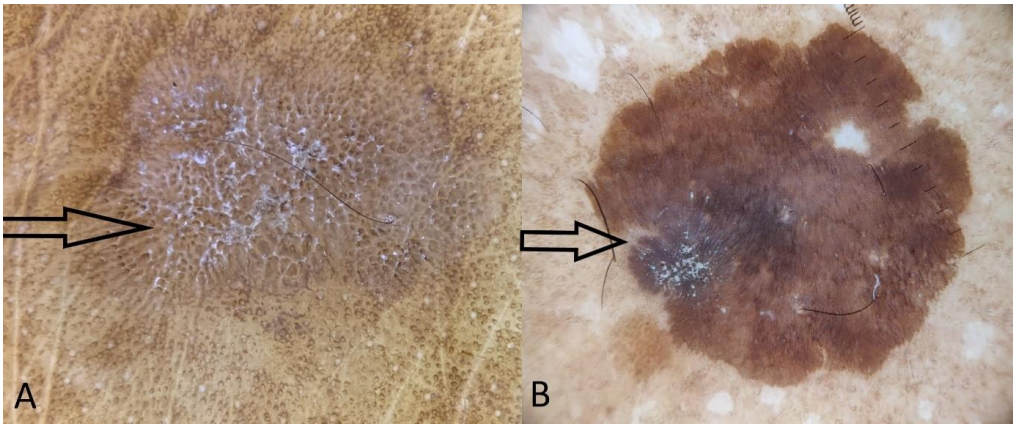


Figure 4 A) Fissures and ridges on dermoscopy in common SK.
B) moth eaten border and sharp demarcation on dermoscopy.

Table 4 Frequencies and distribution based on dermoscopic criteria of SK in clinical variants.

Dermoscopic finding	*Common SK (N= 19)*	*Flat SK (N=11)*
Comedo like opening	15 (79%)	0
Fissures and ridges	9 (47%)	0
Milia like cysts	4 (21%)	4 (36%)
Moth eaten border	5 (26%)	1 (9%)
Hairpin blood vessels	0	3 (91%)
Sharp demarcation	15 (79%)	10 (91%)

The dermoscopic findings recorded in various clinical variants of SK have been summarized in **Table 4**. Of the 30 patients, common SKs constituted 19 patients (63.3%) and flat SKs in 11 patients (36.6%). Overall the most common findings were sharp demarcation in 25 patients (83.3%), followed by comedo like openings in15 patients (79%), fissures and ridges in 9 (47%), milia like cysts in 8 (26.6%), moth eaten border in 6 (20%) and hairpin blood vessels in 3 (10%) patients **(Figure 4)**.

Discussion

Seborrheic Keratoses (SKs) are one of the most common benign epidermal tumours typically presenting as well-demarcated, slightly elevated patches or plaques that range in colour from flesh-toned to grey, brown, or black.[8] Multiple eruptive SKs is known as the Leser-Trélat-syndrome indicates paraneoplasia with underlying internal malignancy.[9] No definitive cause for SK has been confirmed. Some factors implicated in its pathogenesis include sunlight, genetic mutations, viruses, such as human papillomavirus.[10,11] In our study, history of chronic sun exposure was seen in 51.6 % of patients and hence multifactorial causation holds good in pathogenesis of SKs.

Dermoscopy is a reliable method of distinguishing these lesions from malignant and other pigmented lesions. The classic criteria – milia-like cysts and comedo-like openings –are most common. Other findings include fissures and ridges, hairpin blood vessels, sharp demarcation, motheaten borders, and 'fat fingers'.[12,13]

Our findings on dermoscopy were similar to other studies by Rajesh et al[14] and Nayak et al[15] with common type of SK having findings of comedo like openings (79%) as the characteristic dermoscopic finding **(Table 4)**.

Physical modalities include cryosurgery, curettage, shave or surgical excision, electrosurgery, ablative and non-ablative lasers, intense pulsed light (IPL) have been used yet none of them with uniform guidelines to treat and much depending on the expertise of the treating physician.

TCA has been used in varying concentrations alone or in combination with other chemical peels in treatment of SKs.

In a study by Khater et al, a combination of 50% TCA and 70% Glycolic acid peel was used,[16] focal TCA 65% was used to treat benign pigmented skin lesions by Chun et al.[7]

In our study, 55 patients (91.6%) showed excellent improvement which is greater than in studies conducted by Chun et al, where 19 of 23 (83%) patients with seborrheic keratosis showed a good clinical response (50-70% improvement),[7] with focal TCA application, and Khater et al where there was a 50% excellent (>70% improvement), 40% good (50-70% improvement) and 10% fair (30–50% improvement) cure of seborrheic keratosis lesions from face focally treated by mix of TCA 50% and Glycolic acid 70%.[16]

In a study by Herron et al, after one treatment with cryosurgery, all nine SKs responded with edema, blister formation, crusting and erosion with complete re-epithelialization at 1 month. No evidence of scar formation, hypopigmentation, or recurrence was seen on biopsy at 6 months,[4] whereas in our study only 7 patients (11.6%) showed excellent improvement with single session whereas others required a minimum of 2-3 sessions. This difference may be due to the duration and number of FTCs.

In our study, 26 patients (43.3%) preferred cryotherapy over TCA focal application whereas in study by Wood et al, at greater than 12 months, 11 of 18 preferred cryotherapy (61%) over curettage.[3] This difference may be because of the invasiveness of curettage compared to cryotherapy.

Long term complications were not observed in both the modalities of treatment except for pain in 44 patients (73.3%) which was significant in the lesions treated with cryotherapy and transient hypopigmentation which resolved within 3-4 weeks with no residual pigmentary change. This may be because all patients belonged to Fitzpatrick's skin type IV and V and risk of post inflammatory hypopigmentation is high among this population. This finding was similar to study by Herron et al,[4] where none of the patients treated with cryotherapy had any scarring or pigmentary changes. TCA was safe compared to cryotherapy and had fewer side effects with better patient compliance. This finding was similar to study by Chun et al where no complications were associated with focal TCA application.[7] This was because varying concentrations based on thickness of the lesions was used and with focal application which reduces the risk of complications.

Advantages: Since it was a comparative study patient satisfaction rates among both the modalities of treatment could be assessed and the rest of the lesions were treated with the modality that had most optimal result individualized to patients.

Limitations: The response to treatment may vary according the site, thickness and distribution of lesions. Patient satisfaction rates may be influenced according to the age of the patient and degree of improvement desired.

Conclusion

Although both treatment modalities achieved good results, TCA focal peel was better than cryotherapy with better patient satisfaction rates and quick healing time. TCA is easily accessible as cryotherapy may not be available at all centres. Since there are no standardized guidelines for treatment of SKs new modalities are being tried, yet the search for an ideal

treatment suitable among all age group populations still persists and further comparative studies among different modalities in different populations are required for framing standardized therapies.

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