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Efficacy and Safety of Cauterization by Tricholroacetic Acid in Xanthelasma

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Short title: Timolol VS Timolol & Propranolol in management of periocular eye hemangioma

ABSTRACT

Purpose: The Purpose of this study is to assess the efficacy and tolerability of trichloroacetic acid (TCA) concenteration % 50 the treatment of patients with xanthelasma.

Patients and methods: This clinical trial was conducted to assess the efficacy and tolerability of trichloroacetic acid concentration % 50 the treatment of patients with xanthelasma. The study was carried out on 30 patients attending Mansoura ophthalmic center and suffering from eye lid xanthelasma. The patients were treated with Tricholroacetic acid 50%. Plasma lipid and cholesterol levels were estimated in a lab, Preoperative clinical photography to document the existing eyelid and periorbital anatomy.

Results: Our study results have revealed that the age ranged between 34–56years. The size of the lesion ranged between 3.3–5.7cm2 with mean value 4.61±0.712 cm2. Sites of lesion show that 10(33.3%) were left, 4(13.3%) were right and 16 (53.3%) were bilateral. The Plasma lipid levels of the studied group ranged between 100–144 with mean value 121.17±14.059;22 (73.3%) had normal Plasma lipid levels and 8 (26.7%) had high Plasma lipid levels. The Cholesterol level of the studied group ranged between 174–351with mean value 217.80±51.655; 21(70.0%) had normal Cholesterol level and 9 (30.0%) had high Cholesterol level. Regarding the patient's satisfaction of the studied group, 26 (86.7%) were Satisfied and 4 (13.3%) were Unsatisfied.

Conclusion: TCA 50% administration is an extremely economical method that may be used in ordinary clinical practice, even in a basic care health center, to treat Xanthelasma palpebrarum (XP). It also doesn't require any specific equipment.

Keyword: Xanthelasma palpebrarum, Tricholroacetic Acid.

INTRODUCTION

For cutaneous xanthomas, Xanthelasma palpebrarum (XP) is the most prevalent kind. It's a frequent benign lesion that shows up as a yellowish plaque close to the eyelid's inner canthus. Lesions can be solitary or numerous, nodular, flat and soft, semisolid or calcareous, and are typically spread equally[1].

Xanthelasma Palpebrarum is more common in female (1.1%) than in males (0.3%), with a peak prevalence in the fourth and fifth decades of life. This difference in prevalence may be due to hormonal causes[2].

It's unknown what the precise cause is. On the other hand, xanthelasma appearance has been connected to a number of illnesses, such as hyperlipidaemia, diabetes mellitus, cardiovascular disorders, and thyroid dysfunctions[1,4].

Regarding its relationship to hyperlipidaemia, In around half of the cases with Xanthelasma Palpebrarum, elevated mean cholesterol or low-density lipoprotein cholesterol have been documented. However, individuals with normal triglyceride and cholesterol levels may still experience it[5].

Once it is established, xanthelasma does not go away on its own. It seldom results in functional issues, and the majority of individuals seek medical advice only for cosmetic issues. There are now a variety of therapeutic options, including radiofrequency, laser, ablation carbon dioxide, chemical peeling using trichloroacetic acid or bichloroacetic acid, and surgical excision[6-8].

All of these approaches, however, have drawbacks and side effects, including loss, discolouration, or scarring of the skin, in addition to therapeutic failure resulting in persistent lesions. Thus, there is a dearth of compelling data supporting a single, highly successful XP therapy[9].

PATIENTS AND METHODS

Thirty patients with eye lid xanthelasma who were attending Mansoura Ophthalmic Centre participated in this clinical trial, took place between March 2022 and March 2023. A 50% tricholroacetic acid treatment was given to the patients. included adult individuals with xanthelasma lesions of all genders who were older than 20. The characteristics of the xanthelasma lesions were as follows: a) soft and semisolid; b) sited at the upper or lower eyelid; c) sized between >2mm and <9 mm; and d) numbering: single. Patients with numerous xanthelasma lesions, calcareous xanthelasma lesions, severe dermatochalasis, and skin (eczema) illnesses were excluded. The study was approved by Institutional Research Board (IRB) (MS.22.04.1966), Faculty of Medicine, Mansoura University.

We collected the following information from every research subject. A-Demographic: age, gender, complaints, metabolic conditions such diabetes mellitus or systemic disorders, history of prior intraocular surgery, etc. B. Past medical history, including family history and the use of medications like aspirin, anticoagulants, or nonsteroidal anti-inflammatory medicines (NSAIDs), which might impair wound healing or predispose a person to xanthelasma. C Ophthalmic examination: Physical examination to determine the state of the skin and to appraise the size, location, and consistency of the xanthelasma lesions.

Investigations: Plasma lipid and cholesterol levels were estimated in the laboratory. Preoperative clinical photography to document the existing eyelid and periorbital anatomy.

Technique: Prior to topical administration of anaesthetic (Emla cream 5%, a solution of 2.5% lidocaine and 2.5% prilocane) on the lesion (13), the border of the skin lesion was marked with a pen. After cleaning the impacted region, petroleum jelly was applied to the surrounding area. then, apply TCA 50% by painting very thin layers in a circular motion over the xanthelasma using an applicator stick, with the most TCA near the lesion's edge. After that, rinse well with water to stop the reaction.

In addition to topical treatment of B-sitosterol, a cream that promotes healing for cosmetically disfiguring scars, for 4-6 weeks, all patients received mixed topical antibiotic/steroid skin creams (betamethasone/fusidic acid) for two weeks.

The lesion was photographed prior to treatment, right after following it, and at every follow-up appointment.

Follow-up:

One week after doing technique

Every 2 weeks up to 3 months (Fig.1).

*some patients need to repeat the technique.

Assessment of the outcome: By skin healing of the lesion.

Fig. 1: show before & after application of TCA and follow up.

Statistical Analysis

Version 20.0 of the IBM SPSS software program was used to feed data into the computer and analyse it (Armonk, NY: IBM Corp). Numbers and percentages were used to describe the qualitative data. The distribution's normality was confirmed using the Kolmogorov-Smirnov test. The terms range (minimum and maximum), mean, and standard deviation were used to characterise quantitative data. The results' significance was assessed at the 5% level.

The tests that were employed were: 1. Chi-square test: Used to compare groups of category variables. 2. Student t-test: To compare two groups under study for normal quantitative variables. 3. Mann Whitney test: To compare two groups under study for abnormally quantitative variables: Kotz S, Vidakovic B, Read CB, Balakrishnan N. The statistics sciences encyclopaedia. Second edition. Wiley-Interscience, Hoboken, N.J., 2006. LA Kirkpatrick, BC Feeney. A basic reference on IBM SPSS statistics in version 20.0. Student ed. Wadsworth, Cengage Learning, Belmont, California, 2013.

RESULTS

Table (1) shows demographic data of the studied group. The age ranged between 34–56 years with mean value 46.30 ± 6.988 years. Male cases were 11 (36.7%) while female cases were 19 (63.3%).

Table 1: Distribution of studied sample according to demographic data.

	Number	**Percent**
Age (years)		
Range	34–56	
Mean ± S.D.	46.30±6.988	
Sex		
Male	11	36.7
Female	19	63.3

Table (2) demonstrates the medical history of the studied group, and it shows that 2 (6.7%) had DM, 6 (20.0%) had HTN and 7 (23.3%) had Hypercholesterolemia. History of drug intake of the studied group show that 2(6.7%) take Anticoagulants, 6 (20.0%) take Aspirin and 7(23.3%) take Nonsteroidal anti-inflammatory drugs (NSAIDs). The history of previous intraocular surgery shows that 3 (10.0%) had History of previous intraocular surgery.

Table 2: Distribution of studied sample according to medical history, history of drug intake, and history of previous intraocular surgery.

		Number	Percent
Medical history	**DM**	2	6.7
	HTN	6	20.0
	Hypercholesterolemia	7	23.3
History of drug intake	**Anticoagulants**	3	10.0
	Aspirin	6	20.0
	Nonsteroidal anti-inflammatory drugs (NSAIDs)	2	6.7
History of previous intraocula	**No**	27	90.0
	Yes	3	10.0
	Total	30	100

Table (3) shows lesions characteristics of the studied group. The size of the lesion ranged between 3.3–5.7 cm^2 with mean value 4.61±0.712 cm^2 Sites of lesion show that 10 (33.3%) were left, 4 (13.3%) were right and 16 (53.3%) were bilateral. The plasma lipid levels of the studied group ranged between 100–144 with mean value 121.17±14.059; 22 (73.3%) had normal Plasma lipid levels and 8 (26.7%) had high Plasma lipid levels. The cholesterol level of the studied group ranged between 174–351 with mean value 217.80±51.655; 21 (70.0%) had normal cholesterol level and 9 (30.0%) had high cholesterol level.

Table 3: Distribution of studied sample according to lesions characteristics, plasma lipid levels, and cholesterol level.

		Number	Percent
Lesions characteristics	**Size**		
	Range	3.3–5.7	
	Mean±S.D.	4.61±0.712	
	Site		
	Left	10	33.3
	Right	4	13.3
	Bilateral	16	53.3
Plasma lipid levels	**Range**	100–144	
	Mean±S.D.	121.17±14.059	
	Normal	22	73.3
	High	8	26.7
Cholesterol level	**Range**	174–351	
	Mean±S.D.	217.80±51.655	
	Normal	21	21
	High	9	9

Figure (1) illustrates patient's satisfaction of the studied group, and it shows that 26 (86.7%) were Satisfied and 4 (13.3%) were Unsatisfied.

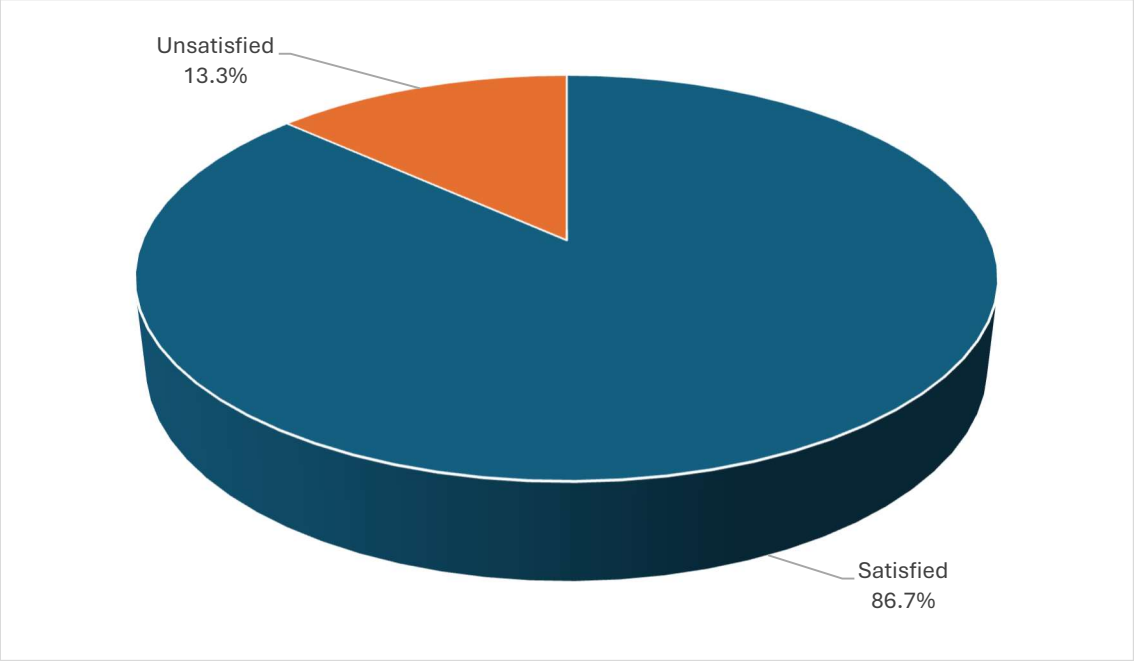

Figure 1: Distribution of studied sample according to patient's satisfaction.

DISCUSSION

The xanthomata that form around the eyes are called xanthelasma palpebrarum (XP)/xanthelasmata. The upper eyelids and the region surrounding the medial canthus are the most often affected. The most prevalent kind of cutaneous xanthoma, known as XP, often presents in the periorbital area and is symmetrical. For the sufferer, it is a cosmetic and psychological burden[6,10]. Different morphological patterns, including macular, papular, plaque type, and nodular variations, can be seen in XP. Grade I lesions are limited to the upper eyelid; Grade II lesions spread to the medial canthus area; Grade III lesions are observed on both the upper and lower eyelids; and Grade IV lesions are widespread and present on both the medial and lateral sides of the upper and lower eyelids[11].

Numerous techniques, such as electrocautery, cryotherapy, trichloroacetic acid treatment, and surgical excision, have been used to treat XP with varying degrees of success. Every therapy technique has a different amount of drawbacks and adverse effects[12].

Different strengths of TCA are used to treat different XP morphological patterns. Few case reports and pilot studies have shown the effectiveness of TCA in treating XP, despite the fact that it is a relatively cost-effective therapy option[13].

Chlorinated acetic acids, such as mono-, di-, and trichloroacetic acid, are commonly employed as tissue cauterants at high concentrations. They dissolve lipids and precipitate and coagulate proteins as part of their mechanism of action. The concentration of the acid, the method, the application pressure, and the skin preparation all affect the intended outcome on the skin during a chemical peel[14].

The primary side effects of this therapy are ectropion, scarring, hypo- and hyperpigmentation, and the possibility of accidental application to the cornea or conjunctiva, which might cause irritation and scarring[15].

In order to evaluate the effectiveness and tolerability of trichloroacetic acid concentration%50 in the treatment of patients with xanthelasma, this research was conducted on 30 patients who were receiving care at the Mansoura Ophthalmic Centre and had eye lid xanthelasma. The majority of people with xanthelasma palpebrarum are middle-aged and older. The age range, according to the results of our study, was 34–56 years old, with a mean value of 46.30±6.988 years.

In concurrence with Reddy et al.[11] who observed that middle-aged and older persons account for the majority of XP cases, with a peak incidence occurring between 30 and 50 years of age. Additionally, the mean age of the patients in the Karkara et al.[16] research was 45.84 years.

Since xanthelasma palpebrarum is a cosmetic condition and more women seek its treatment, the majority of patients in the current research (63.3%) were female and just 36.7% were male. In a similar vein, women are impacted more frequently than males in the Reddy et al.[11] research. They are observed in individuals with type III hyperlipoproteinemia, familial hypercholesterolaemia, chronic cholestasis, and normal circulating lipid levels[17]. Moreover, Karkara et al.[16] discovered that, with 40 female participants and 10 male participants, that women experience the condition more frequently than men.

According to our findings, the group under study had plasma lipid levels ranging from 100–144, with a mean value of 121.17±14.059. Of them, 22 (73.3%) had normal plasma lipid levels and 8 (26.7%) had excessive plasma lipid levels. The group under study had a mean cholesterol level of 217.80±51.655, ranging from 174–351. Of them, 21 (70.0%) had normal cholesterol and 9 (30.0%) had high cholesterol. This was consistent with the work of Rubinstein et al.[18]. Comparably, 74% of participants in the Karkara et al. [(16)] trial showed a normal serum lipid profile.

Moreover, in keeping with the research conducted by Reddy et al.[11] in which every patient was normolipidemic.

In the research by Mourad et al.[19], 50% of patients had aberrant lipid profiles and 50% had normal lipid profiles. Additionally, those with normal lipid profiles showed much better results than those with aberrant lipid profiles.

It is yet unknown what causes xanthelasma to occur in people with normolipidemia. Therefore, lipid-lowering medication, in conjunction with treatment for any underlying medical conditions, may help people with hyperlipidaemia see a reduction in the size of their plaques[20].

In our investigation, we discovered that 26 (86.7%) of the patients in the group under review were satisfy, whereas 4 (13.3%) were not. Comparable to the Nahas et al.[21] research, where all patients reported satisfaction with the treatment outcomes with 70% trichloroacetic acid, despite the problems indicated and the results being categorised as excellent, good, and acceptable.

Although the use of TCA in the management of XP has been previously documented, Haque and Ramesh[22] investigated the use of TCA at 50%, 70%, and 100% concentrations in the treatment of EX using chemical peeling. Following therapy, two of the 16 patients experienced hyperpigmentation and three experienced hypopigmentation. For the treatment of lesions less than 3 mm in diameter, they suggested TCA. At larger concentrations, they produced superior effects on papulonodular and flat plaque lesions; however, only 18 patients had 100% TCA treatment, and the length of follow-up was not stated. In their patient group of Indian descent, hypopigmentation was the most prevalent consequence, followed by hyperpigmentation and scarring. Thus, in contrast to Rubin's findings[23], they found that hypopigmentation was unrelated to the TCA concentration. According to what he said, this problem arises when cauterisation is applied so deeply that it alters the hair follicles' melanin.

Similar complication rates were seen in the Nahas et al.[21] study, with 33.4% experiencing hypopigmentation and 12.5% experiencing hyperpigmentation. Compared to white patients (16.6%), hypopigmentation occurred in non-white patients with a much greater incidence (38.8%). Hyperpigmentation was limited to 16.6% of patients who were non-White. Five of the six white patients (83.3%) and six of the eighteen non-white patients (33.3%) thought their cosmetic outcomes were outstanding. According to their findings, white patients will gain more with 70% TCA therapy than non-white patients. Regarding the development of hypertrophic or noticeable scars on the skin, a problem that affected two of their patients.

This was explained by Rubin[23] as a very deep skin wound. Weeks after applying 70% TCA, patches of persistent erythema may occur, which may precede hypertrophy or scar formation. In a study by Haygood et al.[24] on the treatment of xanthelasma

palpebrarum lesions, BCA 100% was applied to 25 lesions. During the follow-up visit after treatment, 16% of patients had minor hypopigmentation at the treated areas. After just one treatment, all eighteen lesions were completely cleared. Over a mean of 64 months, five lesions recurred; these were successfully treated with 100% BCA.

Güngör et al.[25] conducted a research on individuals suffering from xanthelasma. The patients' distinct xanthelasma palpebrarum lesions underwent YAG laser ablation and 70% TCA treatment. According to their findings, the efficacy and complication rates of 70% TCA application and erbium:YAG laser ablation techniques are comparable.

The most often reported TCA adverse effects in the Reddy et al.[11] investigation were scarring, hypopigmentation, and hyperpigmentation.

In the Tahir et al.[26] investigation, pigmentary alterations and scarring were seen, and 75% of the TCA-treated group showed a full response.

No patient in the Mourad et al.[19] trial demonstrated wound infection or scarring, but there was a statistically significant increase in post-therapy hyperpigmentation in patients treated with TCA 50% compared to other groups and an increase in hypopigmentation in patients treated with TCA 70% compared to other groups.

When Nahas et al.[21] used TCA 70% to treat xanthelasma patients, they reported that 33.4% of them experienced hypopigmentation and 12.5% experienced hyperpigmentation. They stated that hypopigmentation is dependent on TCA concentration as it is a consequence of cauterisation that affects the melanin in the hair follicles, and that scar formation was observed in a small number of patients who received TCA 70%.

About the recurrence. The study conducted by Haque and Ramesh[22] revealed that 100% TCA was most efficient in treating papulonodular lesions of XP; however, recurrence rates were not examined.

After using bischloroacetic acid to treat 13 patients, Haygood et al.[24] found that 28% of the patients experienced recurrences.

At a mean follow-up of 14.3 months, Cannon et al.[27] identified a full success rate of 70% in the group of patients who were examined in the clinic at least three months following their last TCA medication. After a mean follow-up of 31.8 months, as determined by telephone interview, this percentage fell to 33%. Just 17 patients in this group expressed worry about the look of their lesions and asked to be referred for additional discussion of potential treatment options, despite the high rates of recurrence and persistence. They found no correlation between the number of eyelids involved or the number of TCA treatments and the rate of recurrence or persistence of the lesions. An additional 14 patients felt that the TCA treatment had only partially succeeded in either reducing the colour or the size of the lesions, and these patients were not concerned by their appearance. Eleven patients in the recurrent group had just one TCA therapy, whereas 17 individuals received two. Among the patients with chronic lesions, a similar pattern was observed: 5 ⁄ 9 individuals only received one therapy.

According to Nahas et al.'s[21] study, which used 70% TCA for XP, 45.8% of patients had great results, 33.3% had good results, and 25% had recurrences after six months. The study also found that EX recurs often regardless of therapy. Small xanthelasmas, which are best treated with 70% TCA, have higher recurrence rates. Since 70% TCA is the standard therapy for minor EX lesions, the high recurrence incidence may be attributable to more instances treated than to the treatment itself. Severe effects like palpebral ectropion or deforming scars were not seen. They did, however, experience two instances of mild relief change.

A few investigations have demonstrated that TCA is nearly as effective as lasers[28].

For the excision of xanthelasma, laser therapies are well-liked and well-respected, and the outcomes appear to be good[7].

Raulin et al.[29] found that in 23 patients, the CO2 laser therapy had a 13% recurrence rate 10 months later. Moreover, palpable hypopigmentation accounted for 13% of complications, with lesser rates of hyperpigmentation (4%).

The laser offers good haemostasis and outcomes, but its drawbacks include high cost, equipment maintenance, and the need for specialised training to utilise it. TCA is affordable, readily available, and the operation may be done as an outpatient. On the other hand, surgical care necessitates a group of medical professionals and hospital costs. Furthermore, not every plaque can be taken out in a single day, and a two-month waiting time is required before trying a new strategy[3]. For every lesion, surgical xanthelasma excision takes at least 20 minutes. Applying TCA, on the other hand, takes five to ten minutes since each lesion needs to be treated until a frost occurs, which takes just one minute[21].

Only two participants experienced recurrence in the Mourad et al.[19] trial. Abnormalities in both individuals' lipid profiles might contribute to recurrence. However, recurrence rates were greater when lesions included deeper layers. One possible issue with TCA application is that not enough TCA may be used to prevent significant scarring and harm to the surrounding normal skin. On the other hand, applying thin layers of TCA to the lesion with a wooden applicator that has a pointed tip minimises TCA leaking and accidental administration to healthy skin or the eyes. The preservation of skin tissue is one benefit of TCA.

This research's limited sample size is one of its limitations, but it also has the drawback of being a single centre study. Nevertheless, a good number of lesions were treated, and the results were consistent in every lesion.

CONCLUSION

According to our study, TCA 50% administration is an extremely economical method that may be used in ordinary clinical practice, even in a basic care health centre, to treat XP. It also doesn't require any specific equipment.

The therapy is inexpensive and easy to use, but it takes several administrations to get the desired effects. In light of the fact that this study lacked a control group, we would advise doing a bigger, controlled investigation to corroborate the results, which appear to indicate that TCA therapy yields positive outcomes.

Also, in order to examine the long-term effectiveness of each modality, side effects, and relapse, we advise conducting multi-center randomised comparative trials with bigger sample sizes and longer follow-up periods.

Ethical approval

- The Mansoura University faculty of medicine's medical research ethics committee reviewed and approved the study protocol.
- After confidentiality was guaranteed, each study participant provided written informed permission.
- Every potential negative impact of the intervention was controlled.

Participants in the research are able to withdraw from it at any moment and without consequence.

- Throughout the whole study, personal privacy and confidentiality were upheld.
- The information gathered was not put to any other use.

Authors contribution

All authors are equally contributed.

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Data Availability: The authors declare that all data supporting the findings of this study are available within the article and its supplementary information file.

Competing interests: The authors declare no competing interests.

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Conflict of interest statement

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