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Original Research Article

A comparative study of 30% Trichloroacetic acid chemical peel with Q switched Nd-YAG laser 1064nm in the treatment of *Macular amyloidosis*

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ABSTRACT

Background: Macular amyloidosis (MA) is the subtlest of the cutaneous varieties of amyloidosis. In general, the treatment of MA is disappointing. Hence, this study was aimed at comparing the two treatment modalities for the same.
Objective: To compare the efficacy of 30% Trichloroacetic acid (TCA) chemical peel with Q switched Nd-YAG laser 1064nm in the treatment of macular amyloidosis.
Materials and Methods: 50 patients of MA attending our Dermatology outpatient department were enrolled in the study. The study involved application of 30% TCA in 25 patients at an interval of 2 weeks for 10 sittings and Q switched Nd-YAG laser 1064 in 25 patients at an interval of 1 month for 5 sittings. Digital photographs were taken before treatment and then periodically. The response was graded percentage of reduction in pigmentation both by the patient and the observer. The patients were followed up for 5 months post treatment for recurrence.
Results: Both TCA peel and Q switched Nd-Yag laser 1064nm were effective in the treatment of macular amyloidosis. switched Nd-Yag laser 1064nm showed better response compared to TCA peel at the end of the treatment, both by subjective and objective methods and in terms of less number of sittings and fewer side effects. The difference was statistically significant (P <0.05).No permanent side effects were seen in any of the treated patients and the improvement was sustained without any relapse at 5 months except in one patient in the peel group.
Conclusion: Both these treatment modalities are effective and safe in the treatment of MA. Q switched Nd-Yag laser 1064nm was found to be marginally superior to TCA peel.

1. Introduction

Amyloidosis is not a single disease; rather, the term is used to refer to several diseases that share the common feature of abnormal extracellular deposition of amyloid, a fibrillar proteinaceous material, within the tissues.[1] Macular Amyloidosis (MA) most subtle form of primary localised cutaneous amyloidosis(PLCA) and tends to persist unchanged for many years. MA has a characteristic female preponderance[2] with the age of onset ranging between 21 and 50 years.[3] Its etiology is unknown, but many risk factors have been implicated such as UVB, EBV, race, genetic predisposition and atopy. In general, the treatment of PLCA is disappointing. Various modalities such as topical corticosteroids, topical application of 10% DMSO, UVB therapy, etretinate and acitretin therapy have been tried with some success. But the condition seems to relapse after the treatment is stopped. The Q-switched Nd-YAG laser

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(532 nm and 1064 nm) has shown positive response in the reduction of pigmentation in MA.[3] Certain chemical peeling agents like trichloroacetic acid (TCA), salicylic acid, Glycolic and lactic acid have been found to reduce pigmentation in MA. Hence, this study was aimed at comparing the efficacy of 30% TCA chemical peel with Q switched Nd-YAG laser 1064nm in the treatment of MA.

2. Materials and Methods

2.1. Source of data

50 patients of MA attending the Dermatology OPD in Victoria Hospital and Bowring & Lady Curzon Hospital attached to BMC & RI during the period from November 2013 to August 2015.

2.2. Inclusion criteria

1. All male and female patients aged between 18-60 years with MA
2. Treatment naive cases of MA.
3. Old treated cases with treatment free period of one month.

2.3. Exclusion criteria

1. Known immunodeficiency disorders.
2. Patients having keloidal tendency or tendency for post inflammatory hyper pigmentation.
3. Bleeding disorder.
4. Chronic infections/illness.
5. Patients on anti-coagulant therapy.
6. Active skin infection, like Herpes infection and bacterial infection.
7. Pregnancy and lactation.

2.4. Methodology of data collection

The study subjects to be enrolled in the study were requested to give consent to be a part of the study. They were explained about the TCA peels and laser treatment, the cost factor involved, benefits, duration of the treatment, possible side effects and the prognosis of the treatment. A written informed consent was taken. The patients were selected on the basis of signs and symptoms. They were randomly allocated into peel or laser group. Details regarding the age, gender, duration of illness, progression of the disease, habit of scratching or rubbing the area, use of pumice stone/nylon brush, and family history, the exact morphology and distribution of the lesion were recorded.

2.5. Investigations

Skin biopsy using 4mm skin biopsy punch was done under local anesthesia for histopathological examination to confirm the diagnosis. Then the patients were evaluated for thyroid disorder with thyroid profile, random blood glucose levels in all and with ANA profile in study subjects with suspected connective tissue disorders.

2.5.1. Procedure

The study involved application of 30% TCA peel in 25 patients at an interval of 2 weeks for 10 sittings and Q switched Nd-YAG laser 1064 in 25 patients at an interval of 1 month for 5 sittings. The study subjects were primed with 12% glycolic acid cream at the night for 2 weeks prior and during the treatment interval. And were advised to use regular sunscreen lotions during treatment and the follow up period.

For subjects under peel group, 30% TCA chemical peeling was done once in 2 weeks, where the skin of the affected site was cleansed with 70% alcohol followed by acetone to degrease the skin. Following which 30% TCA was applied with a cotton bud. The appearance of blotchy frosting was taken as the end point following which the TCA was washed off with cold water. Ten such sittings were done with an interval of 2 weeks. Post peel the study subjects were advised to use sunscreens and emollients. And general measures were advised like avoiding scrubbing or any form of friction during or after bathing and avoiding very hot water for bathing.

For study subjects under laser group, Q switched Nd-YAG 1064nm was done once a month with a 3mm probe, frequency ranging from 2-5 Hz and fluency between 3-5 J/cm2. The settings were individualized for each study subjects with increasing fluency for the next sitting. Cooling of the skin was done with ice packs before and after the procedure. Five such sittings were done once month for 5 months.

All study subjects were primed with 12% glycolic acid cream in the night in between the sessions as well, which was started 2 days after the procedure and was asked to 2 days prior to the next sitting. All study subjects were advised strict sun protection. Digital photographs were taken before treatment and then periodically.

2.5.2. Assessment and analysis

At the end of the treatment period the pigmentation was compared with the initial photographs taken and the response was graded as

Excellent for >75%

Good for 50-75%

Fair for 25-49%

Minimal for <25% reduction in pigmentation.

This grading was given both by the patient and the observer. And the average of which was taken. The patients were followed up for 5 months post treatment for recurrence.

2.6. Statistical analysis

Results were analyzed using Chi square test and Fischer exact test.

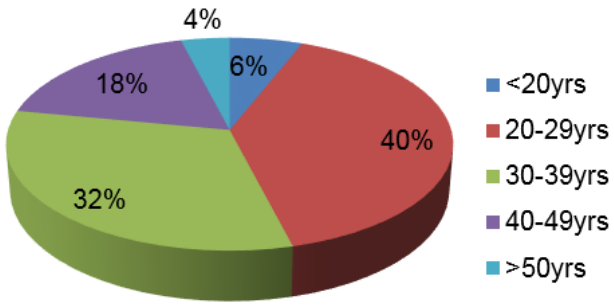
3. Results

The age of the study subjects ranged from 18-52 years, maximum number of patients pooled in the age group 20-29 years in peel group with mean age of 32.12±10.87 years, and 30-39 years in laser group with mean age of 34.96±7.64.(Graph 1)

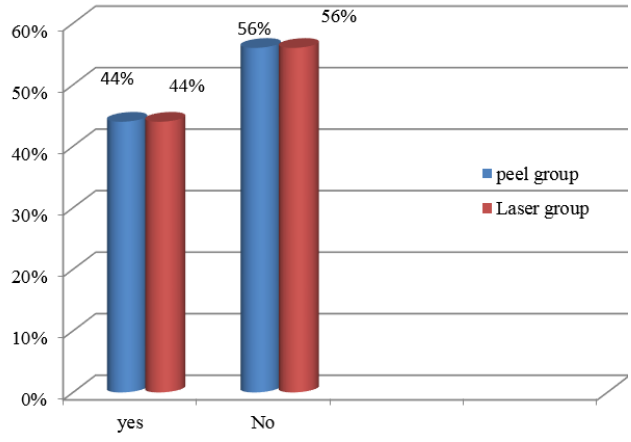
Out of 25 study subjects in peel and laser group, 23(92%) were females and 2(8%) were males in each group.

The duration of the disease ranged from 4-20 years, mean duration of illness being 7.84±2.9 years in peel group and 9.92±4.45 in laser group.

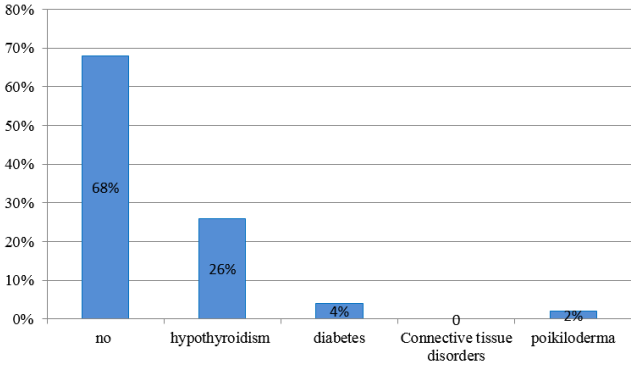
Out of 25 study subjects in peel group and in Laser group, majority of them 14(56%) had exposure to sun and was absent in 11(44%) in each group.(Graph 2)



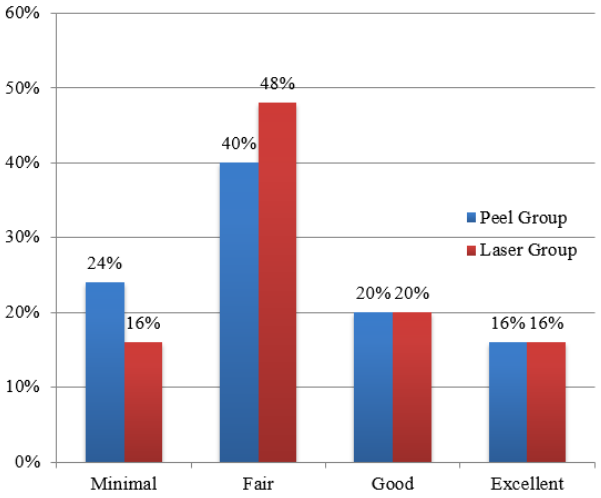
Graph 1: Age distribution



Graph 2: Sun exposure



Graph 3: Associated illness



Graph 4: Comparison of improvement

3.1. Associated pruritus

In peel group 18(72%) of the study subjects gave history of Pruritus, while in laser group 20(80%) had no history of pruritus. Out of 50 study subjects 23(46%) had pruritus.

3.2. Usage of Nylon brush

Out of 25 study subjects in peel group, majority of them 17(68%) had usage of nylon brush while in laser group 19(76%) had used nylon brush .out of 50 study subjects 36(72%) had history of usage of nylon brush.

3.3. Habit of scratching

In peel group 15(60%) of the study subjects gave history of rubbing, while in laser group only 4(16%) had history of rubbing. Out of 50 study subjects 19(38%) had habit of rubbing.

3.4. Family history

In peel group 10(40%) of the study subjects had family history while in laser group only 4(16%) had family history. Out of 50 study subjects 14(28%) had history of similar complaints in the family.

Fig. 1: Beforeand after photographs of TCA peel

Fig. 2: Beforeand after photographs of TCA peel

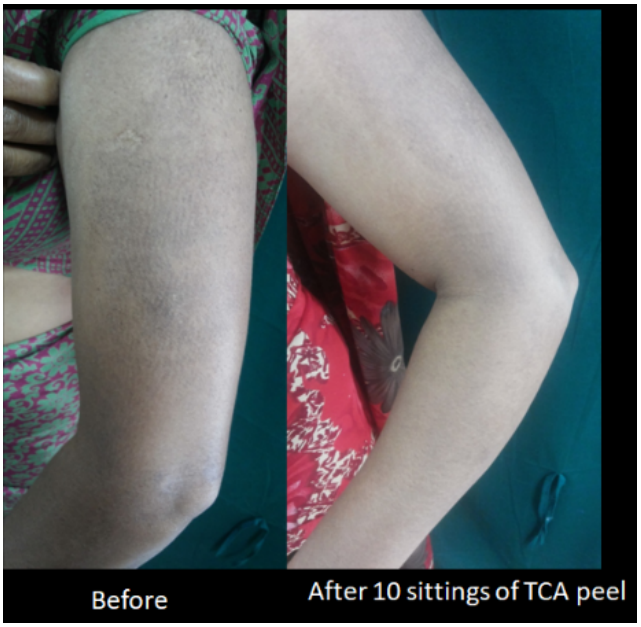


Fig. 3: Before and afterphotographs of TCA peel

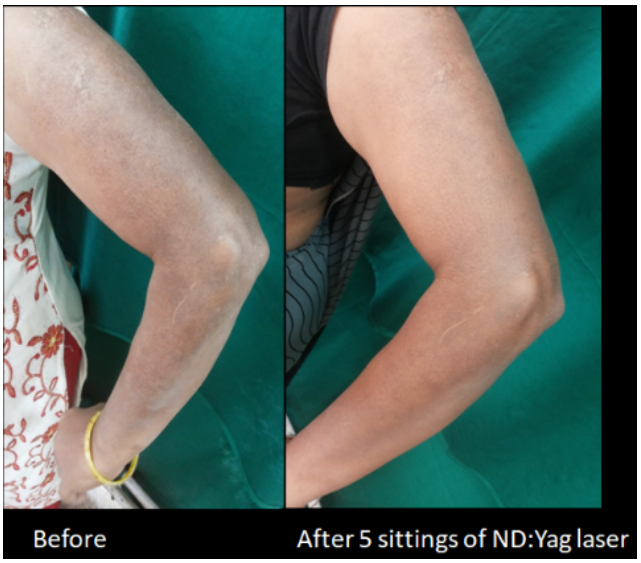


Fig. 4: Beforeand after photographs of Nd:Yag laser

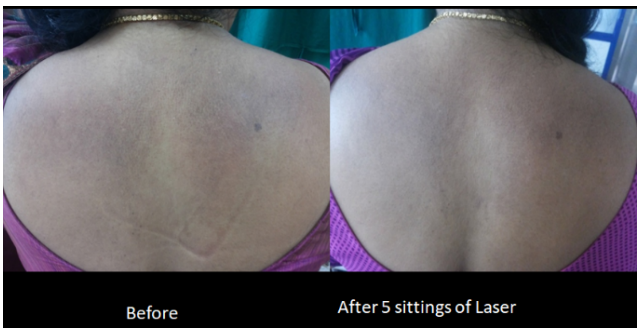


Fig. 5: Beforeand after photographs of Nd:Yag laser

Table 1:

Results	Peel Group 10 sittings		Laser Group 5 sittings		Total	
	No	%	No	%	No	%
Minimal	6	24.0	4	16.0	10	20.0
Fair	10	40.0	12	48.0	22	44.0
Good	5	20.0	5	20.0	10	20.0
Excellent	4	16.0	4	16.0	8	16.0
Total	25	100.0	25	100.0	50	100.0

X^2=0.08, df =1, p<0.05

3.5. Associated Illness

Majority 17 (68%) of the study subjects in each group had no associated illness. Hypothyroidism was seen in 7(28%) and 6(24%), diabetes in none and 2(8%) in peel and laser group respectively, poikiloderma was seen in 1(4%) of the study subjects.(Graph 3)

Majority of the study subjects had skin type 4 in 27(54%), followed by type 3 in 15(30%) and type 5 in 6(12%).

In our study it was observed that 40% of peel group had fair response to treatment, 24% minimal response, 20% with good response and 16% with excellent response with 10 sittings of treatment with 30% TCA peel, while 48% had fair response, 20% with good response and 16% with minimal & excellent response with 5 sittings of Q switched Nd Yag laser 1064 (Table no 1 and Graph 4) The observed results were statistically significant (p<0.05). Out of 25 study subjects in peel group maximum improvement in pigmentation was seen around sitting 8-9 accounting for 10.40±3.20% followed by sitting 9-10 accounting for 10.00±3.54%. Out of 25 study subjects in laser group maximum improvement in pigmentation was seen around sitting 4-5 accounting for 19.61 ± 6.32% followed by sitting 3-4 accounting for 18.00±6.29%.(Figures 1, 2, 3, 4 and 5)

On follow up out of 25 study subjects in each group, no recurrence was seen in 19 (76%) of peel group and 22(88%) of laser group, improvement in pigmentation in 5(20%) and 3(12%), recurrence in 1(4%) and none in peel group and laser group respectively.

In our study post inflammatory hyperpigmentation was seen in 2(8%) followed by excessive peeling in 3(12%) of study subjects in peel group whereas none of the patients had any complications in laser group which was significant statistically (P=0.05). Post inflammatory hyperpigmentation was managed with depigmenting agent and sunscreens. And excessive peeling of skin was managed with emollients.

4. Discussion

Virchow, in 1854, introduced the term “amyloid”. He believed that the substance resembled starch or cellulose because, like starch, it turned blue when stained with iodine followed by dilute sulfuric acid.[4] In dermatology, Gutmann first described amyloidosis in the skin and named it amyloidosis localis cutis nodularis et disseminata in 1927. Macular form of cutaneous amyloidosis was first described by Palitz and Peck in 1952.[5] This skin disorder is rare in the West but has a high incidence in Southeast Asia and some South American countries and its treatment remains unsatisfactory.[6]

In general, MA and LA occur more frequently in individuals with skin phototypes III and IV.[7] According to a study done by Rasi et al. in Iran on MA, ninety-three patients were female and seven were males. The patients were aged between 16 and 76 years, with 81% being in the age range 21–50 years. The mean age of the patients was 36.25±1.19 years; 36.9±1.22 years and 26.71±3.41 years for the female and male patients, respectively. There was a significant difference between the sex and age distribution of the male and female patients (P = 0.027).[2]

Another study done by Badhlish et al. there was a characteristic female preponderance (88%) with a female to male ratio of 7.3:1, with a mean age of onset of MA being earlier in females. Upper back was involved in 80% of patients and sun-exposed sites were involved in 64% cases. Incidence of MA was high in patients with skin photo type III. Role of friction was inconclusive.[3]

Most authors believe that localized trauma in the form of continuous friction, scratching or manipulation on taking bath or skin cleansing with the use of various gloves, sponges, brushes, plant stalks or leaves plays a role in the genesis of amyloid due to mechanical damage to keratinocytes or their apoptosis. It has been proposed that basal layer keratinocytes die due to apoptosis or release keratin bodies to the dermis, where they are lined with antikeratin (AK) antibodies. Upon being phagocytosed by macrophages, they are believed to take active part in the formation of AK, transforming proteins with previously α structure into β pattern proteins.[8] The disease has been described by various terms such as friction melanosis, friction amyloidosis, macular amyloidosis and towel melanosis.[9] Rasi et al. found no association between MA and friction but postulated the role of female hormones in the disease genesis because of its predominant occurrence in young age females.[2] In India, similar cases have been reported from South India, following the use of nylon or plastic brushes, pumice stones, nylon wire sponges or coconut fiber to scrub the skin.[10]

The precursor protein involved has not been fully characterized; however, the amyloid of macular and lichenoid variants of PLCA is thought to be keratinocyte derived.[11] This has been supported by ultrastructural studies demonstrating transitional forms between viable keratinocytes and amyloid, as well as by positive reactions with monoclonal antibodies directed against keratins of basal keratinocytes.[12]

TCA is a chemical cauterant the application of which to the skin causes protein denaturation, so called keratocoagulation, resulting in a readily observed white frost. The degree of tissue penetration and ensuing injury by a TCA solution is dependent on several factors, including strength of TCA used, skin preparation and anatomic site. Selection of appropriate strength TCA is critical when performing a peel. TCA in strengths of 10–20% results in a very light superficial peel not penetrating below the stratum granulosum; a strength of 25–35% results in a light superficial peel with penetration encompassing the full thickness of the epidermis; 40–50% results in a medium-depth peel injury to the papillary dermis; and finally, greater than 50% results in injury extending to the reticular dermis. Unfortunately the use of TCA concentrations above 35% TCA can produce unpredictable results including scarring.

A Study done by Sacchidanand et al. included 40 patients of frictional melanosis of the forearm, Group A was treated with TCA-15% peel and Group B with glycolic acid (GA-50%) peel. Four peels were done one every 15 days. Clinical photographs were taken to assess the response. Response to therapy was evaluated by both objective and subjective methods. The patients were followed up for 3 months after the last peel to note any relapse. Both TCA and GA peels were effective in frictional melanosis. TCA showed better response compared to GA at the end of the treatment, both by subjective and objective methods. However, this difference was not statistically significant ($P > 0.05$). Though TCA was found to be marginally superior to GA.[13]

Another study done by Nandhini et al. for treatment of MA using TCA peel included a total of 25 patients with clinical diagnosis of MA. TCA peel was done at an interval of 6 weeks between sessions. First session was done with 10% TCA and further sessions with 20% TCA. Clinical response to treatment after each session was graded according to quarentile grading and any adverse effects were noted. Clinical improvement was more than 51% in 50% of patients after 3 sessions. Mean improvement scores increased proportionately with each session. Side effects included burning sensation during the procedure, peeling for almost 2 weeks and hyperpigmentation/ hypopigmentation.[14]

The fundamental principle behind laser treatment of cutaneous pigment and tattoos is selective destruction of undesired pigment with minimal collateral damage. This destruction is achieved by the delivery of energy at the absorptive wavelength of the selected chromophore. The exposure time must also be limited so that the heat generated by the laser–tissue interaction is confined to the target. The target chromophore of pigmented lesions is the melanosome. Q-switched lasers produce pulses in the nanosecond range. These high peak power lasers deliver light with a pulse width shorter than the approximately 1-ms thermal relaxation time of the melanosomes or the tattoo ink particles.

Q-switched lasers used for the treatment of superficial pigmented lesions include the 532-nm frequency-doubled Q-switched Nd:YAG, the 694-nm ruby, and the 755-nm alexandrite lasers. Strong absorption of light at these wavelengths by melanin makes these lasers an excellent treatment modality for superficial pigmented lesions. The Q-switched 694-nm ruby, 755-nm alexandrite and 1064-nm Nd:YAG lasers are useful for treating deeper pigmented lesions such as nevus of Ota and tattoos. The Q switched1064 nm laser should be used when treating patients with darker skin, because it reduces the risk of epidermal injury and pigmentary alteration.

A prospective, controlled, clinical trial study done by Ostovari et al. included twenty subjects with clinical diagnosis and pathology confirmation of MA treated with Q-switched Nd:YAG laser: 532 nm in a part of their plaques and with 1064 nm in another part of their plaques. Assessment of efficiency was done by colorimetric scores based on Mexameter measurement and also digital photographs before laser therapy and 8 weeks after treatment. Mexameter-based data analysis showed that the two lasers are effective in reducing the degree of MA patches pigmentation, and 532 nm is meaningfully more effective than 1064 nm in this matter. Photograph-based analysis showed that 90% of cases treated by 532 nm had good or very good response, and for the 1064 nm treated patches, 60% of cases had the good or very good response.[15] Hence this study was aimed at comparing these two modalities of treatment.

5. Conclusion

TCA peel is an easily available peeling agent, cost effective and an office based procedure which has been tried in various other pigmentary dermatosis and has shown good results and hence can be tried in the treatment of MA. Though it has its own disadvantages like post inflammatory hyperpigmentation, burning sensation and excessive peeling which has to be kept in mind and has to be managed effectively.

Similarly Q switched Nd:YAG 1064nm has also shown promising results in the treatment of various hyperpigmentary dermatosis with relatively lesser side effects. Hence these two modalities of treatment were tried and thus concluded laser as a better treatment option as there

was ealier outcome with lesser sittings and minimal side effects.

6. Conflicts of Interest

None.

7. Source of Funding

None.

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