Efficacy and Safety of Laser-Assisted Drug Delivery compared with Intralesional Triamcinolone Acetonide Monotherapy in the Treatment of Keloids and Hypertrophic Scars: A Single Blind Randomized Controlled Trial*

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ABSTRACT

Background: Keloids and hypertrophic scars are overgrowth of fibrous tissue after damage to the skin. There have been various published treatment modalities for these lesions. Currently, there are still no published studies on the use of laser-assisted drug delivery for hypertrophic scars and keloids in the Philippine setting.

Objective: To determine the efficacy and safety of laser-assisted drug delivery versus intralesional steroid injection alone for the treatment of keloid and hypertrophic scar.

Methods: This was a single center, randomized single-blind controlled study. Participants were randomly assigned into a control group (intralesional steroid injection) or a treatment group (laser-assisted drug delivery). The procedure was done monthly for four sessions. Assessment of lesions using the Vancouver Scar Scale was done at baseline and monthly post-sessions.

Results: A total of 42 participants completed the study, which was divided into two groups of 21 samples each. Results showed that the mean difference in overall skin score from baseline to fourth treatment session was significantly lower in the laser-assisted drug delivery group than the intralesional group (–0.48±0.75 vs. –0.24±0.54, t=2.31, p=0.026). No adverse events were noted throughout the study period.

Conclusion: It is a promising option to use non-ablative fractional CO2 laser-assisted drug delivery as the treatment outcome was comparable to using intralesional steroid injection as monotherapy for keloids and hypertrophic scars.

Keywords: Keloid, Hypertrophic Scar, Laser-Assisted Drug Delivery, Intralesional Steroid Injection

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INTRODUCTION

Wound healing is an intricate and complex series of processes. Phases of wound healing are inflammation, granulation tissue formation, and tissue remodeling, which results in tissue structure integrity. [1] A cutaneous scar results from overgrowth of fibrous tissue after damage to the skin, representing an exuberant healing response.[2] Keloid epidemiology is limited and scattered, with the average keloid incidence estimated only to be 5–10% in African, 0-0.1% in Asian, and <0.1% in other countries. Keloids and hypertrophic scars have equal sex distribution and have the highest incidence in the second to third decade of life.[3] Hypertrophic scars are a common complication of burn injury, with incidence even greater in developing countries. Previous studies have reported diverging incidences of hypertrophic scarring, with incidence rates varying from 40% to 94% following surgery and from 30% to 91% following burns. [4]

The disfiguring appearance of keloids or hypertrophic scars lead to aesthetic, physical concerns, and psychological distress. In a study done by Kassi et al. (2020), Dermatology Life Quality Index (DLQI) was used to assess the Quality of Life (QoL) of black Africans with keloid scars. This study noted a score of 61.66% DLQI among patients with hypertrophic and keloid scars, associated with pain (p=0.046), pruritus (p=0.81) and functional disorders (p=0.29). [5] On the other hand, in the study done by Lu et al. (2021), the Symptom Checklist-90 (SCL-90) results showed that scores on sensitivity to interpersonal relationships, depression and anxiety were higher in the visible scar group than in the invisible scar group or the normal scar group. Depression and anxiety scores were higher in the group with invisible scars than in the normal group, and mental health of female patients was affected more than male patients. Therefore, they recommended further psychological and clinical interventions for patients with keloid and hypertrophic scars.[6]

Intralesional corticosteroid injections, silicone bandages, and local pressure are a few of the commonly utilized treatment regimens for keloid and hypertrophic scars. Ekstein,S. et.al (2021), showed the regression rate of

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keloid using triamcinolone acetonide injection to be 50-100%, while recurrence rate was at 33% to 50% at 1 year and 5-years post-treatment respectively.[7] Other second-line therapy for refractory cases, in turn, includes ablative or non-ablative laser therapy and surgical excision associated with the use of silicone gel (Schuch et al., 2019).[8]

Ablative and non-ablative laser treatments available for keloid treatment were used by Nghi and colleagues in 2019. Fractional CO2 laser at 10,600nm and erbium: YAG with 2,940 nm laser are examples of ablative lasers that cause local tissue destruction by emitting energy that is absorbed by skin water. While non-ablative lasers such as 980-nm diode laser, 1064-nm Nd:YAG laser, and 585 or 595-nm pulsed-dye lasers, target skin chromophores like hemoglobin or melanin and cause selective damage to blood arteries that supply the scar.[9]

With the advancement in laser technology, several studies proved the effectiveness of fractional photothermolysis in scar treatment as monotherapy. Although several researches provide promising data on the use of laser in the treatment of keloids and hypertrophic scars, randomized control trials on the use of non-ablative fractional CO2 laser are still lacking and are warranted to determine its effectivity and efficiency. The fractional CO2 laser was chosen on the basis of a study done by Srivastava et al. (2019), wherein fractional laser showed greater scar improvement than pulsed-dye laser or Q-switched laser.[10] Khansa et al. (2016) reported mixed results of laser-based treatments in different Fitzpatrick skin types, with a higher risk of side effects observed in keloids in skin of color.[11]

Significance of the Study

Hypertrophic scars and keloids are difficult to treat and require various approaches to therapy. New discoveries and improvements in laser technology provide alternatives in the treatment of hypertrophic scars and keloids in terms of function, symptoms and cosmetic appearance. As of this writing, there are still no published studies on the use of non-ablative fractional CO2 lasers for hypertrophic scars and keloids in the Philippine setting. Hence, this study aims to determine if non-ablative fractional CO2 laser with topical application and intralesional injection of triamcinolone acetonide is superior to intralesional injection of triamcinolone acetonide alone in the treatment of keloid and hypertrophic scar.

RESEARCH QUESTION

Among patients with keloids and hypertrophic scars of less than 2 years duration, is non-ablative fractional CO2 laser with topical application and intralesional injection of triamcinolone acetonide superior in efficacy and safety to intralesional injection of triamcinolone acetonide monotherapy?

OBJECTIVES OF THE STUDY

General Objective:

To determine the efficacy and safety of non-ablative fractional CO2 laser with topical application and intralesional injection of triamcinolone acetonide versus intralesional injection of triamcinolone acetonide alone for the treatment of keloid and hypertrophic scar among patients at the Out-Patient Department of a tertiary government hospital.

Specific Objective

1. To determine and compare the mean Vancouver Scar Scale between patients who received non-ablative fractional CO2 laser followed by topical and intralesional steroid injection and patients who received intralesional steroid injection monotherapy.
2. To determine and compare the difference of mean Vancouver Scar Scale from baseline to fourth treatment session between patients who received non-ablative fractional CO2 laser followed by topical and intralesional steroid injection and patients who received intralesional steroid injection monotherapy.
3. To determine and compare the presence of adverse effects between patients who received non-ablative fractional CO2 laser followed by topical and intralesional steroid injection and patients who received intralesional steroid injection monotherapy.

B. METHODS

This study employed a prospective, single center, single-blind randomized controlled trial design. The protocol was submitted, reviewed and approved by the Technical Review Board and Institutional Ethics Review Board of the institution. Convenience sampling methodology using lesional count was used to recruit participants with keloid and hypertrophic scars at the Out-Patient Department of a tertiary government hospital.

B.1. Selection and Description of Participants

Target Population: The participants were recruited from the patients seen at the Out-Patient Department of a tertiary government hospital.

Inclusion Criteria:

1. Male or female with age >18 years old.
2. Clinical diagnosis of keloid or hypertrophic scar of less than 2-year duration, diagnosed through clinical presentation, diagnosed for the first time at the Out-Patient Department.

Exclusion Criteria:

1. Pregnant or lactating at the time of diagnosis and/or initiation of and during treatment.
2. History of intake of oral retinoids in the past 6 months.
3. Signs of active infection or lesions suspicious of malignancy.
4. History of prior treatment to the keloid or hypertrophic scar, either in a form of topical and/or intralesional modalities of treatment in the past 12 months.

Drop-out Criteria: Participants were considered dropped out if they missed more than 30 days after the previous session and/or used any topical medication other than the ones used during the study period.

Withdrawal Criteria: Participants withdrew from the trial anytime without any implications, especially if participants developed any severe reactions or contraindication to the interventions given.

B.2. Technical Information

Study Outcomes

The primary outcomes of this study were the changes in the Vancouver Scar Scale mean scores from baseline to post-treatment between the control and treatment group. The secondary outcomes were the changes in mean differences from baseline to post-treatment between the control and treatment group and the proportion of participants who experienced adverse events from either group.

Tools and Methods

1. Approval from the Institutional Ethics Review Board was obtained prior to conducting the study.
2. Patients diagnosed with keloids and hypertrophic scars seen by the residents at the Out-Patient Department were recruited and endorsed to the investigators.
3. The investigators assessed the eligibility of the participants. Study objectives, procedures, risks, and benefits were explained to the participants.
4. The participants were asked to sign an informed consent form to ensure voluntary participation.
5. Baseline data was obtained from the participants on the first study visit. This data included demographic data (age and sex), type and nature of lesion and location.
6. The participants were endorsed to the assessor other than the primary investigators for baseline assessment of the Vancouver Scar Scale. Baseline photographs were taken. For Vancouver Scar Scale, height was measured with calipers; pliability was by palpation; vascularity was assessed by visual inspection; and pigmentation was scored after blanching using a glass slide and comparing it with the surrounding skin.
7. The participants were given a unique identification number and were assigned to either group A (control group) or group B (treatment group).
8. For the control group, triamcinolone acetonide 40mg/mL solution was injected with a dose of 0.25 mL/cm3 on lesions < 3cm and 0.5 mL/cm3 on lesions > 3cm. Participants were assessed for adverse events following intralesional injection.
9. For the treatment group, participants underwent fractional CO2 laser with the following energy doses depending on the Vancouver Scar Scale score: VSS 0-3 = 15 mJ, 4-6 = 20 mJ, 7-9 = 25 mJ and 10-13 = 30 mJ. Depth was fixed at level 3 and density of 10.
10. Immediately following the fractional CO2 laser, triamcinolone acetonide 40mg/mL was applied on the lesion at a dose of 0.1mL/cm. After which, triamcinolone acetonide 40mg/mL solution was injected with a dose of 0.25 mL/cm3 on lesions < 3cm and 0.5 mL/cm3 on lesions > 3cm. Participants were assessed for adverse events following laser-assisted drug delivery.
11. The participants were asked to follow-up monthly for 4 months. During each study visit, participants were assessed with any adverse events. Lesions were also measured by the assessors using the Vancouver Scar Scale and photographs were taken for documentation. Doses and settings for both control group and treatment group were adjusted based on the Vancouver Scar Scale.

B.3. Statistics

Sample Size Computation

Sample size (*priori*) computation for Analysis of Covariance (ANCOVA) was conducted using G*Power version 3.1.9.4. From the study of Srivastava et al. (2018),

the mean Vancouver Scar Scale (VSS) of the laser-assisted drug delivery group (n_1) was 0.80 (SD=0.50) at 15th-week follow-up. In contrast, the intralesional triamcinolone acetonide group (n_2) had a mean VSS score of 0.25 (SD=0.42) on the 15th week follow-up.[10] These values can be used to estimate an effect size *f* of 0.596 (moderate). With these parameters and with a power of 90%, an effect size *f* of 0.596, and a significance level of 5.00% (two-tailed), a minimum sample size of 32 lesions is necessary. However, the sample size was adjusted to account for a 20% attrition or drop-out rate. Hence, the final sample size for the study was a total of 40 lesions (20 lesions in each treatment arm).

Randomization and Blinding

Lesions were randomly assigned into two groups through block randomization using a Microsoft Excel number generator: Group A (control group: Intralesional injection of triamcinolone acetonide 40mg/mL alone) and Group B (treatment group: Fractional CO2 laser with topical application and intralesional injection of triamcinolone acetonide 40mg/mL).

Randomization was carried out by an assessor not part of the clinical trial. Codes generated were stored in an opaque envelope and accessed at the termination of the study. For all participants who agreed to participate, photography of the affected site (with standardized angle, lighting, and position) and measurements of the vascularity, pigmentation, pliability, and height were done for documentation from baseline to follow-up. In order to protect subjects' anonymity, each subject was assigned with a unique identification code upon enrollment. Their identification codes were used in the summary of results instead of their names or other possible identifiers.

Statistical Analysis

Statistical analyses were conducted using STATA MP – Parallel Edition Statistical Software, Version 18, College Station, TX: StataCorp LP. A significance level (α) of 0.05 was considered statistically significant. Descriptive statistics included mean and standard deviation for normally-distributed, continuous-level data; and, frequency and proportion for nominal data. [19] Between-group comparisons of the demographic and clinical characteristics and baseline efficacy outcomes according to treatment group allocation were conducted using Chi-Square Test of Homogeneity, if the expected frequency per cell is less than 5, for nominal data; Mann-Whitney *U* Test, for ordinal or non-normally-distributed, continuous data; and, independent *t*-test for normally-distributed, continuous data. [19] On the other hand, between-group comparisons (intralesional injection vs. laser-assisted delivery groups) of the skin assessment scores, both overall and indicators (vascularity, pigmentation, pliability, and height), at the different follow-up periods were performed using Analysis of Covariance (ANCOVA). [20] The mean scores were adjusted (adjusted mean) to significant confounders which included the pre-test scores and the respective preceding follow-up scores. [19] The within-group comparisons of the overall skin assessment score and the different indicators from baseline to the different follow-up periods in each treatment group were conducted using Repeated-Measures Analysis of Variance (RM-ANOVA). [19] Afterwards, post-hoc ANOVA using Bonferroni adjustment was performed to identify pairwise comparisons between the baseline and follow-up periods in each treatment group. [19]

C. RESULTS

A total of 42 lesions were included in the study, which were randomly assigned into a control group (intralesional triamcinolone acetonide 40mg/mL alone) or a treatment group (laser-assisted drug delivery) with 21 scar assigned per treatment arm.

Figure 1: Participant flow

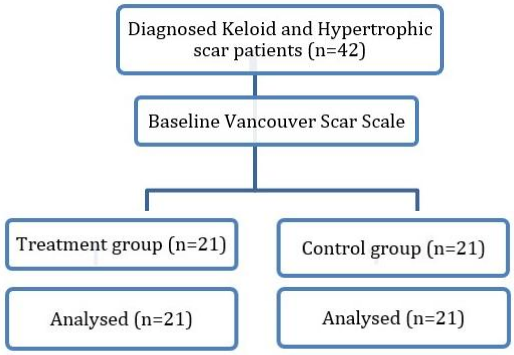


Table 1. Demographic and clinical characteristics of the participants according to their group allocation

Characteristics	Group Allocation (N = 42)			Test Statistic	*p*-value (Two-Tailed)
	Control Group (n = 21)	Treatment Group (n = 21)	Total (N = 42)		
Age (Years; $\bar{x}$, SD)	33.34 (13.33)	26.76 (5.10)	30.00 (10.50)	2.08*	0.044
Sex (*f*, %)				9.72*	0.004
Male	4 (19.05%)	14 (66.67%)	18 (42.86%)		
Female	17 (80.95%)	7 (33.33%)	24 (57.14%)		
Nature of Skin Lesion(*f*, %)				8.86	0.167
Acne	10 (47.62%)	13 (61.90%)	23 (54.76%)		
Post-Surgical	2 (9.52%)	0 (0.00%)	2 (4.76%)		
Trauma	2 (9.52%)	2 (9.52%)	4 (9.52%)		
Varicella	4 (19.05%)	1 (4.76%)	5 (11.90%)		
Tattoo	1 (4.76%)	5 (23.81%)	6 (14.29%)		
Vaccine	1 (4.76%)	0 (0.00%)	1 (2.38%)		
Burns	1 (4.76%)	0 (0.00%)	1 (2.38%)		
Site of Skin Lesion (*f*, %)				9.89	0.248

Chest	7 (33.33%)	5 (23.81%)	12 (28.57%)		
Neck	1 (4.76%)	0 (0.00%)	1 (2.38%)		
Shoulder	3 (14.29%)	8 (38.10%)	11 (26.19%)		
Arm	2 (9.52%)	5 (23.81%)	7 (16.67%)		
Back	3 (14.29%)	3 (14.29%)	6 (14.29%)		
Breast	2 (9.52%)	0 (0.00%)	2 (4.76%)		
Hand	1 (4.76%)	0 (0.00%)	1 (2.38%)		
Knee	1 (4.76%)	0 (0.00%)	1 (2.38%)		
Foot	1 (4.76%)	0 (0.00%)	1 (2.38%)		
Type of Skin Lesion (*f*, %)				1.02	1.000
Hypertrophic Scar	1 (4.76%)	0 (0.00%)	1 (2.38%)		
Keloid	20 (95.24%)	21 (100.00%)	41 (97.62%)		
Note: $\bar{x}$ = Mean, SD = Standard Deviation, *f* = Frequency, % = Percentage					
*Significant at 0.05 †Significant at 0.01					

Clinico-demographic profiles of patients showed a mean age of the subjects was 30.00 years old (SD=10.50), with most being females (57.14%), and had acne scars secondary to acne vulgaris as skin lesions (54.76%). Results also showed that the majority of the subjects had skin lesions in their chest (28.57%) and shoulders (26.19%), and the majority of the participants had keloids (97.62%).

Table 2. Comparison of baseline scar assessment scores using the Vancouver Scar Scale in the control and treatment group

Baseline Scar Assessment	Group Allocation (N = 42)			*t*-Value	*p*-value (Two-Tailed)
	Control Group (n = 21)	Treatment Group (n = 21)	Total (N = 42)		
Overall Baseline Score	6.81 (1.91)	7.57 (1.36)	7.19 (1.69)	–1.49	0.145
Vascularity	1.38 (0.80)	2.00 (0.63)	1.69 (0.78)	–2.77†	0.008
Pigmentation	1.14 (0.48)	1.14 (0.57)	1.14 (0.52)	0.00	1.000
Pliability	2.24 (0.83)	2.90 (0.30)	2.57 (0.70)	–3.46†	0.001
Height	2.05 (0.59)	1.52 (0.51)	1.79 (0.61)	3.07†	0.004
Values are presented as Mean (Standard Deviation)					
*Significant at 0.05 †Significant at 0.01					

The between-group comparisons of the baseline scar assessment scores using the Vancouver Scar Scale between the two groups are illustrated in Table 2. It can be noted that the overall baseline score of the control group and treatment group were 6.81 (SD=1.91) and 7.57 (SD=1.36), respectively, and these values were not significantly different (t=–1.49, p=0.145).

Results also showed that the mean scores of the treatment group in terms of vascularity (2.00±0.63 vs. 1.38±0.80, t=–2.77, p=0.008) and pliability (2.90±0.30 vs. 2.24±0.83, t=–3.46, p=0.001) were significantly higher. In contrast, the mean height (1.52±0.51 vs. 2.05±0.59, t=3.07, p=0.004) in the treatment group was significantly lower compared to the control group.

Table 3. Comparison of follow-up scar assessment mean scores using the Vancouver Scar Scale in the treatment and control groups

Follow-up Scar Assessment	Group Allocation (N = 42)			*F*-Value	*p*-value (Two-Tailed)
	Control Group (n = 21)	Treatment Group (n = 21)	Total (N = 42)		
Overall 1-Month Follow-up Score	6.76 (0.28)	7.19 (0.28)	6.76 (0.28)	1.19	0.283
Vascularity	1.62 (0.07)	1.67 (0.07)	1.62 (0.07)	0.21	0.651
Pigmentation	1.00 (0.08)	1.14 (0.08)	1.00 (0.08)	1.54	0.222
Pliability	2.33 (0.14)	2.53 (0.14)	2.33 (0.14)	0.90	0.350
Height	1.77 (0.09)	1.90 (0.09)	1.77 (0.09)	0.97	0.331
Overall 2-Month Follow-up Score	6.17 (0.23)	5.40 (0.23)	6.17 (0.23)	5.22	0.028
Vascularity	1.38 (0.09)	1.33 (0.09)	1.38 (0.09)	0.11	0.747
Pigmentation	1.00 (0.09)	0.77 (0.09)	1.00 (0.09)	3.53	0.068
Pliability	2.02 (0.14)	1.84 (0.14)	2.02 (0.14)	0.82	0.371
Height	1.71 (0.09)	1.53 (0.09)	1.71 (0.09)	1.72	0.197
Overall 3-Month Follow-up Score	5.16 (0.18)	4.65 (0.18)	5.16 (0.18)	3.82	0.058
Vascularity	1.27 (0.08)	1.11 (0.08)	1.27 (0.08)	2.07	0.158
Pigmentation	0.86 (0.07)	0.71 (0.07)	0.86 (0.07)	2.02	0.164
Pliability	1.76 (0.09)	1.48 (0.09)	1.76 (0.09)	4.76*	0.035
Height	1.27 (0.09)	1.35 (0.09)	1.27 (0.09)	0.41	0.527
Overall Post-Test Follow-up Score	4.55 (0.13)	4.78 (0.13)	4.55 (0.13)	1.55	0.220
Vascularity	1.10 (0.05)	1.19 (0.05)	1.10 (0.05)	2.11	0.155
Pigmentation	0.79 (0.00)	0.79 (0.00)	0.79 (0.00)	0.00	1.000
Pliability	1.52 (0.07)	1.53 (0.07)	1.53 (0.07)	0.00	0.983
Height	1.16 (0.07)	1.26 (0.07)	1.16 (0.07)	1.15	0.290
Values are presented at Adjusted Mean (Standard Error) after adjustment for the confounding effect of pre-test scores and the respective preceding follow-up scores.					

Table 3 depicts the between-group comparisons of the follow-up skin assessment scores between the two treatment groups. It can be noted that the mean pliability scores using laser-assisted drug delivery was most improved at the third month of follow-up (Adjusted $\bar{x}$ =1.48, SE=0.09) compared to the control group (Adjusted $\bar{x}$ =1.76, SE=0.09). The mean overall mean overall skin assessment, vascularity, pigmentation, and height (p>0.05) were not significantly improved at month 1 and 2 of treatment.

Table 4. Comparison of the mean difference scores in Vancouver Scar Scale of patients in the treatment and control group

Vancouver Scar Scale	Treatment Group Allocation (N = 42)		*t*-statistic	*p*-value (Two-Tailed)
	Intralesional Injection (n = 21)	Laser-Assisted Drug Delivery (n = 21)		
Baseline to 1-Month Follow-up	–0.14 (0.36)	–0.43 (0.60)	1.88	0.068
Vascularity	–0.14 (0.48)	0.00 (0.32)	–1.14	0.260
Pigmentation	–0.10 (0.70)	–0.19 (0.60)	0.47	0.639
Pliability	–0.05 (0.22)	0.14 (0.48)	–1.66	0.105
Height	–0.33 (1.43)	–0.10 (1.18)	–0.59	0.559

Baseline to 2-Month Follow-up	–0.14 (0.36)	–0.76 (0.76)	3.35†	0.002
Vascularity	–0.19 (0.51)	–0.33 (0.66)	0.79	0.437
Pigmentation	–0.43 (0.81)	–0.86 (0.73)	1.80	0.079
Pliability	–0.24 (0.44)	–0.10 (0.44)	–1.06	0.295
Height	–1.05 (1.43)	–1.76 (1.79)	1.43	0.160
Baseline to 3-Month Follow-up	–0.24 (0.54)	–0.76 (0.77)	2.56*	0.014
Vascularity	–0.24 (0.54)	–0.48 (0.75)	1.18	0.244
Pigmentation	–0.57 (0.81)	–1.33 (0.66)	3.34†	0.002
Pliability	–0.67 (0.48)	–0.29 (0.46)	–2.61*	0.013
Height	–1.67 (1.32)	–2.90 (2.00)	2.37*	0.023
Baseline to Post-Test Follow-up	–0.24 (0.54)	–0.48 (0.75)	2.31*	0.026
Vascularity	–0.24 (0.54)	–0.48 (0.75)	1.18	0.244
Pigmentation	–0.67 (0.80)	–1.43 (0.75)	3.20†	0.003
Pliability	–0.81 (0.51)	–0.33 (0.58)	–2.82†	0.007
Height	–2.00 (1.55)	–3.05 (2.09)	1.85	0.072

Values are presented as Mean (Standard Deviati *
Significant at 0.05 †
Significant at 0.01

Table 4 depicts the between-group comparisons of the mean differences of the follow-up and baseline skin assessment scores between the treatment groups. Results showed that the mean difference in overall skin score from baseline to post-test was significantly lower in the laser-assisted drug delivery group than the intralesional group (–0.48±0.75 vs. –0.24±0.54, t=2.31, p=0.026). Similarly, it can be noted that the laser-assisted drug delivery group (–1.43±0.75) had a significantly lower (t=3.20, p=0.003) mean difference in pigmentation score compared to the intralesional injection group (–0.67±0.80). It is also interesting to note that the effect size for the between-comparisons yielded partial eta-squared (η2) values of 0.219 for baseline-to-2-month follow-up, 0.141 for baseline-to-3-month follow-up, and 0.118 for baseline-to-post-test comparisons. These values denote that 21.90%, 14.10%, and 11.80% of the differences in mean difference scores at these timeframes were attributed to the administration of the intervention (laser-assisted drug delivery).

Figure 4a. Trend in mean overall scar assessment scores of the control group and experimental group

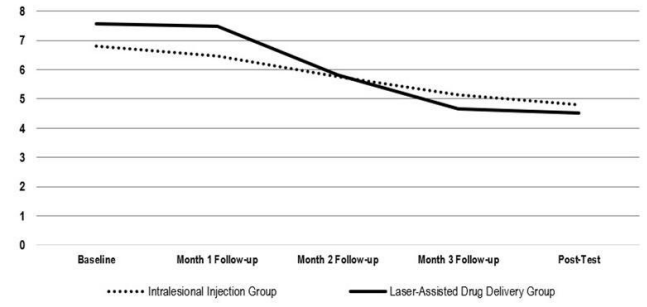


Figure 1. Trend in Mean Overall Scar Assessment Scores of the Intralesional Injection Group (Control) and Laser-Assisted Drug Delivery Group (Experimental)

Figure 4b. Trend in mean scores in vascularity of the control and experimental group

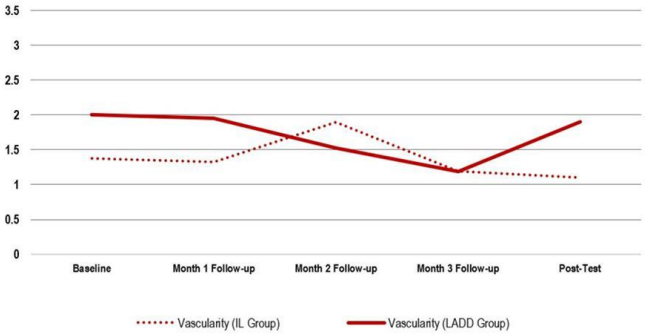


Figure 4c. Trend in mean scores in pigmentation of the control and experimental group

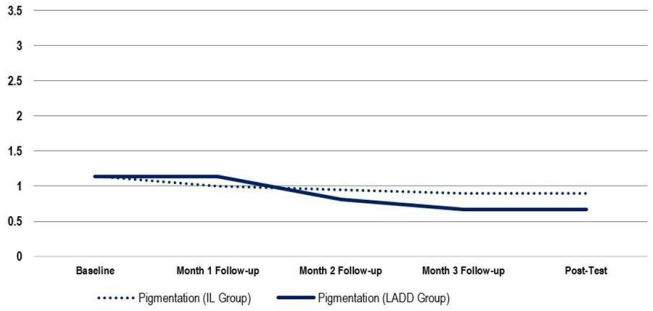


Figure 4d. Trend in mean scores in pliability of the control and experimental group

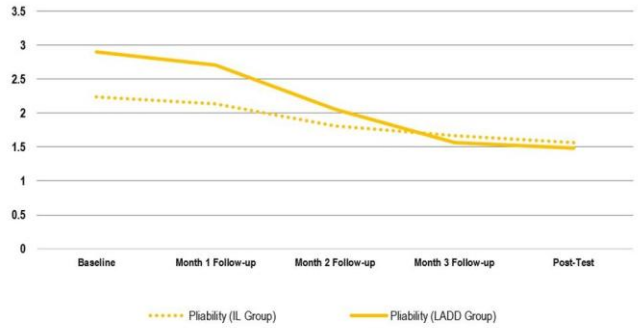
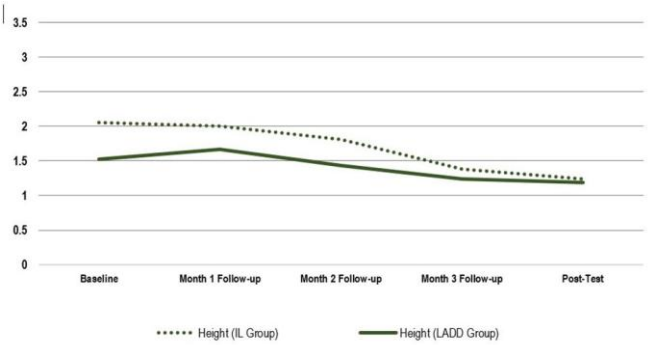


Figure 4e. Trend in mean scores in height of the control and experimental group



The within-group comparisons of the overall skin assessment scores at the different timeframes for each treatment group are presented in Figures 4a, 4b, 4c, 4d, and 4e. For the intralesional injection group, results showed that the mean vascularity, mean pliability, mean height, and mean overall skin assessment scores were significantly different across the five different timeframes (p<0.05). Post-hoc analyses, using Bonferroni adjustment, that the overall mean score was not significantly different between baseline and 1-month follow-up (p=1.000), but it significantly decreased starting 2-month (p=0.032) until 3-month (p=0.001) and post-test (p=0.001) follow-up periods. For the mean pliability scores, results showed that the comparisons of baseline scores were not significantly different with the 1-month (p=1.000) and 2-month (p=0.250) follow-up periods. However, the mean scores at 3-month (p=0.042) and post-test (p=0.010) follow-ups were significantly lower compared to the baseline mean score. Focusing on the height of skin lesions, it can be noted that the mean scores significantly decreased, compared to baseline score, starting 3-month follow-up (p=0.001) until post-test follow-up period (p=0.001). Post-hoc ANOVA analyses of the pairwise comparisons for vascularity and pliability did not show significant differences between the baseline scores and the follow-up scores (p>0.05).

In a different light, results for the laser-assisted drug delivery group showed that the overall skin score and the four indicators or parameters were significantly different across the various timeframes (p<0.05). It is interesting to note that the mean overall skin assessment scores had a downward trend from baseline, which was significantly lower starting 2-month follow-up (p=0.002) until post-test follow-up (p=0.001). Vascularity and pliability scores (p<0.05). were most improved at 2-month follow-up compared to baseline, while scar pigmentation and height (p>0.05) had no statistically significant improvement at two months.

Figure 5a and 5b. Comparison Photos in the Control Group

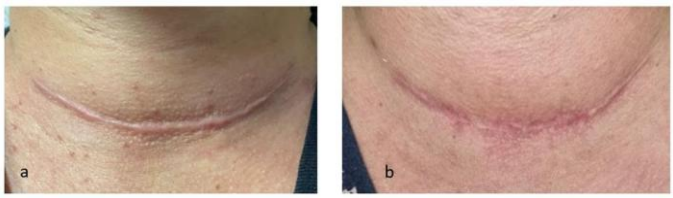


Figure 5a. Hypertrophic scar on the neck post-thyroidectomy, with marked improvement after treatment completion

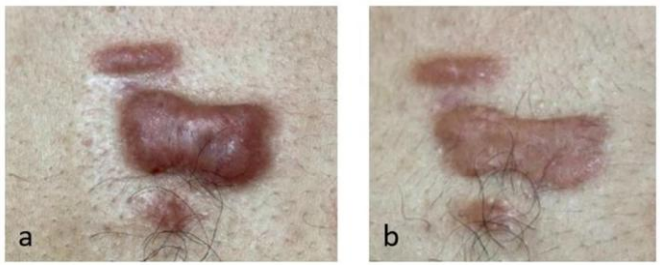


Figure 5b. Keloid on the chest secondary to acne, with noted improvement after 3 treatment sessions

Figure 6a and 6b. Comparison Photos in the Treatment Group

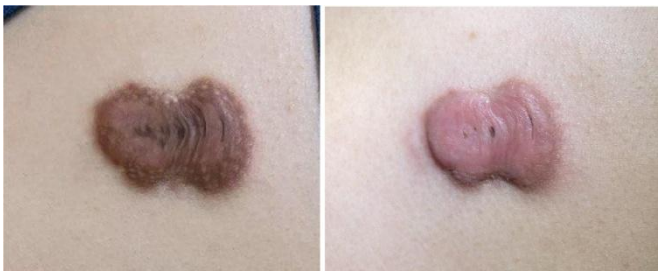


Figure 6a. Keloid on the upper back secondary to varicella, with noted improvement in pigmentation and pliability after treatment completion

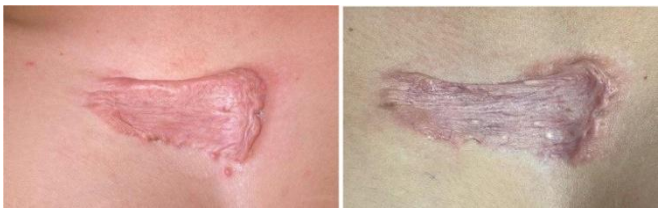


Figure 6b. Keloid on the chest secondary to acne, with noted thinning of lesion after treatment completion

DISCUSSION

Focusing on the treatment group utilizing fractional CO2 laser with topical application and intralesional injection of triamcinolone acetonide 40mg/mL, results of this study showed that the overall skin score was significantly decreased from baseline to post-treatment, with notable differences at 2-month follow-up until the end of all treatment sessions. Results depicted in table 3 showed that there was no statistical difference in the mean overall skin assessment scores between the two groups at post-test follow-up; however upon further analysis, the mean difference in overall skin score from baseline to post-test was significantly lower in the laser-assisted drug delivery group than the intralesional group.

Figure 4 showed the trend in the decrease of the mean overall scar assessment scores for both groups. Both groups showed a downward trend from baseline; however on further analysis, there was a more rapid decrease in the treatment group compared to the control group. There was notable difference in scar appearance after 2 sessions of fractional CO2 laser with topical application and intralesional injection of triamcinolone acetonide, as compared to the later improvement seen in control group after 3 sessions of intralesional injection of triamcinolone acetonide 40mg/mL alone. Adverse events were investigated immediately after every treatment session and on subsequent follow-ups. During the course of the study, no adverse events were noted from both groups. This underscored the efficacy of fractional CO2 laser with topical application and intralesional injection of triamcinolone acetonide 40mg/mL in terms of faster improvement in scar appearance and characteristic.

Similar findings were seen in international publications using ablative fractional CO2 laser. A study by Waibel et al. (2013) provided good evidence on the effectiveness and safety of combination therapy of fractional CO2 laser with topical application of triamcinolone acetonide suspension in the improvement of keloids and hypertrophic scars in terms of texture, hypertrophy and dyschromia, with no complications noted.[22] Another study done by Alexander et al. (2019), showed statistical improvement in height and length of keloids and hypertrophic scars after combination of ablative fractional CO2 laser with intralesional steroid.[14] Srivastava et al. (2018) revealed that among the scar parameters, pigmentation is not completely resolved by any modalities (TAC, verapamil or fractional CO2 laser), as was also seen in this study.[10]

Adverse Event

Results in table 4 also showed there was a decrease in the efficacy of laser-assisted drug delivery overtime as evidenced by the partial eta-squared values of 0.219 for baseline-to-month 2 follow-up, 0.141 for baseline-to-month 3 follow-up, and 0.118 for baseline-to-post-test comparisons. These findings were attributed to the adjustment in the setting of fractional CO2 laser during each visit depending on the Vancouver Scar Scale. As the VSS score decreased, the energy dose of the laser also decreased accordingly. These adjustments were necessary to ensure safety and to prevent any adverse event following treatment.

This study provides novel knowledge on the use of non-ablative fractional CO2 laser with topical application of triamcinolone acetonide suspension in the improvement of keloids and hypertrophic scars. Non-ablative fractional CO2 laser was noted to maintain an intact epidermis while reaching the deeper reticular dermis by increasing the irradiance and using a higher or lower pulse energies depending on the depth of the lesion.

Limitations of the Study

The sample size of this study was limited by the number of sessions, treatment duration, concentration and dose of steroid applied or injected. The treatment sessions were limited to 4 sessions that were 1 month apart. This study was also limited to lesions of less than 2-year duration. Intralesional steroid injection was also limited to 40mg/mL of triamcinolone acetonide, requiring further studies on the effectiveness of lower doses of corticosteroid injections.

CONCLUSION AND RECOMMENDATION

It is a promising option to use non-ablative fractional CO2 laser-assisted drug delivery as the treatment outcome was comparable to using intralesional steroid injection as monotherapy for keloids and hypertrophic scars. No significant difference was seen in the mean overall skin assessment scores from baseline to post-treatment follow-up, however, the mean difference in overall skin score from baseline to fourth treatment session was significantly lower in the laser-assisted drug delivery group than the intralesional group. No adverse events were noted throughout the study period. These findings gave emphasis on the superiority in efficacy and safety of non-ablative fractional CO2 laser as an adjunct to topical application and intralesional steroid injection for the treatment of keloid and hypertrophic scar. Future research and studies are recommended to investigate the effects of other laser machines and lesions with longer duration (>2 years). Long-term follow-up is also suggested to monitor the improvement or possible recurrence of lesions after the end of the study.

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