

Fractional Carbon Dioxide Laser versus Glycolic Acid Peel in Treatment of Pseudo-Acanthosis Nigricans

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ABSTRACT

Background: Acanthosis nigricans (AN) is a common cutaneous condition that can be a manifestation of systemic disease. AN is characterized by hyperpigmented and hyperkeratotic velvety skin lesions that presents mainly on the flexural sites, for example, the neck, the axillae, and groin.

Objective: The aim of this study was to evaluate the clinical efficacy of fractional carbon dioxide laser versus glycolic acid peel 70% in treatment of pseudo-acanthosis nigricans through assessing changes in degree of area index, severity and texture of lesion.

Patients and methods: Twenty patients with pseudo-acanthosis nigricans were included in this study. They were chosen from the Outpatient Clinic of Dermatology, Andrology & STDs department, Mansoura University Hospitals. All cases were subjected to fractional CO₂ laser on the right side of the neck and glycolic acid peel 70% on the left side of the neck. Each patient was followed up for 3 and half months.

Results: There was statistically significant difference regarding improvement in area index, severity and texture across time subjected to glycolic acid (GA) peeling 70%. There was statistically significant difference regarding improvement in area index, severity and texture across time subjected to fractional CO₂ laser. There was no statistically significant difference when comparing effect of laser and peeling on adult and children. There was no statistically significant difference when comparing effect of laser and peeling on rural and urban cases.

Conclusion: Acanthosis nigricans is a difficult dermatosis to treat, although there are many methods of treatment. Glycolic acid peeling 70% and fractional CO₂ laser are considered effective modalities for AN treatment. However, GA peeling was more effective but statically insignificant.

Keywords: Fractional carbon dioxide laser, Glycolic acid peel, Pseudo-acanthosis nigricans.

INTRODUCTION

Acanthosis nigricans (AN) is a common cutaneous condition that can be a manifestation of systemic disease that is associated with insulin resistance, diabetes mellitus, obesity, internal malignancy, endocrine disorders, and drug reactions⁽¹⁾. Acanthosis nigricans is characterized by symmetrical, hyperpigmented, velvety lesions, which can occur especially in the axilla, groin, neck, antecubital, popliteal fossae, and umbilical region⁽²⁾. These lesions may be skin-colored or brownish and may vary in thickness between 0.1-1 cm⁽³⁾.

Pseudo-acanthosis nigricans is the most frequent form, the term pseudo-acanthosis nigricans was referred to obese individuals who have AN with no underlying endocrinopathies. In these cases, the etiology was attributed to obesity, excessive local friction, and sweat⁽⁴⁾. The severity of AN has a positive correlation with fasting insulin levels⁽⁵⁾. AN is likely the result of high levels of insulin binding to insulin-like growth factor 1 receptors (IGF-1Rs) on keratinocytes and fibroblasts. This leads to a proliferation of both cell types and clinically apparent plaques and papillomatosis⁽⁶⁾.

The treatment of acanthosis nigricans is carried out in particular for cosmetic reasons⁽⁷⁾. For most cases of obesity associated with benign AN; weight loss and lifestyle changes may lead to clinical improvements⁽⁸⁾. Topical medications, such as tretinoin 0.05% and ammonium lactate 12%, are useful in hyperkeratotic

lesions due to their keratolytic effects. Triple-combination depigmentation cream (Kligman's bleaching formula; tretinoin 0.05%, hydroquinone 4% and fluocinolone acetonide 0.01%) nightly with daily sunscreen can also be used safely⁽¹⁾.

Fractional laser improves both the pigmentary and textural changes by removing thin layers of skin with minimal thermal damage leading to dermal wound and new collagen formation, which is the primary mechanism behind the improvement seen after laser resurfacing and the undamaged normal surrounding skin, is a reservoir allowing rapid epidermal repair⁽⁹⁾.

Glycolic acid (GA) peels have anti-inflammatory, keratolytic, and antioxidant effects. GA targets the corneosome by enhancing breakdown and decreasing cohesiveness, causing desquamation. The intensity of peel is determined by the concentration of the acid, the vehicle used to carry it, the amount of acid applied, and the technique used⁽¹⁰⁾.

The aim of this study was to evaluate the clinical efficacy of fractional carbon dioxide laser versus glycolic acid peel 70% in treatment of pseudo-acanthosis nigricans through assessing changes in degree of area index, severity and texture of lesion.

PATIENTS AND METHODS

Twenty patients with pseudo-acanthosis nigricans were included in this study. They were chosen



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from the Outpatient Clinic of Dermatology, Andrology & STDs Department, Mansoura University Hospitals. All cases were subjected to fractional CO₂ laser on the right side of the neck and glycolic acid peel on the left side of the neck.

All patients were subjected to:

- **Full history taking** including name, age, onset, duration of the disease, predisposing factors, possible cause, previous treatments including history of peeling, vitamin A derivatives, history of previous laser therapy, and tendency to scarring or keloid formation.
- **General dermatological examination** for any associated skin diseases and any signs of systemic diseases.
- Disease severity was evaluated by scoring system (Acanthosis Nigricans Area and Severity Index) ⁽¹¹⁾.
- The area were calculated by first finding the total area of the side of the neck by multiplying the length (measured from a point at the junction between the chin and upper neck in full neck extension to a point at the inter-clavicular space) by the width (measured from the point at the junction between the chin and upper neck to a point just below the nape hairline).
- Then the affected area was calculated by multiplying its largest length by its largest width.
- A value was chosen for the severity and texture according to: Acanthosis nigricans area and severity score for assessment of right and left sides of the neck affection ⁽¹¹⁾.
- All patients were photographed with a digital camera (8-megapixel iSight) using identical patient positioning. The photos were taken before starting treatment, at the beginning of every session, and 2 weeks after the last session.
- Before treatment, each patient was asked about his/her goals, concerns and expectations about the treatment to avoid unrealistic expectations. Possible side effects were explained such as pain, erythema and burning
- Sunscreen was strictly used throughout treatment.
- All Patients received topical retinoic acid and whitening agent 10-14 days before each session to decrease post inflammatory hyperpigmentation.
- Follow up visit was done after 2 months of the last session.

Inclusion criteria: Patients who have pseudo-acanthosis nigricans of the neck, with mild to moderate severity were included.

Exclusion criteria: Other causes of acanthosis nigricans were excluded by the following investigations: (Thyroid function test, fasting and post prandial blood sugar and complete blood count). People more prone for post peel and post laser hazards as hyperpigmentation or hypopigmentation as well as scarring and keloidal tendency (were known by full history and examination).

Pregnancy and lactation, systemic diseases as connective tissue disease, diabetes mellitus and skin infection or any other disease which could affect the wound-healing process. Systemic retinoids use within 6 months of study initiation, and/or use of immunosuppressive drugs. Patients who were already treated or undergoing other modes of treatment for acanthosis nigricans a month or less before the study were excluded.

Ethical approval:

Mansoura Faculty of Medicine's Institutional Review Board (IRB) accepted this report (MS.19.04.562). An informed consent was taken from every patient before inclusion of patients into the study. Every care was taken to protect the data's privacy. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Treatment protocol:

Fractional CO₂ laser:

On the right side of neck (laser side) (extending from the midline in front of the neck to the midline of the nape), each patient had three sessions of fractional CO₂ laser (smartxide DOT, fractional hand peice, Deka Co, Italy), with 2-weeks interval. The parameters were low power (10 J), low density (500 μm), short dwell time (500 μs), and double stacking with a single pass on the affected area. Test area was performed first to detect side effects to treatment. Post-operatively, ice packs for cooling were immediately applied after laser sessions, and the patients were advised to apply a topical antibiotic with steroid ointment and emollient after the session.

Glycolic acid (GA) peel: First, skin was degreased with acetone. On left side of neck (extending from the midline in front of the neck to the midline of the nape), the skin had subjected to chemical peeling with GA 70%. Each patient had three sessions with 2 weeks interval. First coat of the peeling was applied and the frosting was observed; if no frosting formed, a second coat was applied. Sodium bicarbonate was applied to neutralize the peeling effect, and emollient was advised for patient for 1 week after peeling ⁽⁹⁾.

Statistical analysis: The collected data were revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Data were presented and suitable analysis was done according to the type of data obtained for each parameter. Shapiro test was done to test the normality of data distribution. Mean, Standard deviation (\pm SD) for parametric numerical data, while Median and range for non-parametric numerical data were used. Student t test was used to assess the statistical significance of the difference between two study group means. A p value is considered significant if ≤ 0.05 at confidence interval 9

RESULTS

A comparative study was carried on 20 patients with pseudo-acanthosis nigricans. All cases were subjected to fractional CO₂ laser on the right side of neck and glycolic acid peel on the left side of neck. 15 cases had 3 sessions, while 5 cases improved after 2 sessions. The mean age of all studied cases was 17.5 ranging from

6 to 39 years. All cases were females. Half of them were children and the other half was adults. Mean BMI was 32.4 kg/m². Most of them were obese (70%), while 30% were non obese. Out of all studied cases, 25% were house wives, 65% were students and 10% were employees. Most of studied cases resided in rural areas (70%), while 30% resided in urban areas (Table 1).

Table (1): Sociodemographic data among studied cases

		Cases (N=20)	
Age (years)	Median, range	17.5	6-39
Children	N, %	10	50%
Adult	N, %	10	50%
Females	N, %	20	100%
BMI (kg/m ²)	Mean ± SD	32.4	±5.9
Non obese (BMI<30kg/m ²)	N, %	12	30%
Obese (BMI≥30kg/m ²)	N, %	28	70%
Occupation	House wife	5	25%
	Student	13	65%
	Employee	2	10%
Residence	Rural	14	70%
	Urban	6	30%

BMI: Body Mass Index

Mean hemoglobin was 11.6 g/dL, mean RBG was 87.1 mg/dL, median TSH was 2, ranging from 0.8 to 4.9 mU/L. Median HOMA-IR was 1, ranging from 0.5 to 3. About baseline clinical data, there were no statistically significant difference when comparing between right and left sides (p > 0.05) for area index, severity and texture. Area index ranged from 30 to 49% in 20% and 30%, while it ranged from 50 to 69% in 25% and 20%, and ranged from 70 to 100% in 55% and 50% on right and left sides respectively. Moderate severity was found in 25% and 40%, while severe lesions were found in 75% and 60% on right and left sides respectively. As regards the texture, it was mild in 5% and 5%, moderate in 15% and 25% and extremely coarse in 80% and 70% on right and left sides respectively (Table 2).

Table (2): Laboratory and clinical data among studied cases

		Cases (N=20)				
HGB (g/dL)	Mean ± SD	11.6		± 0.9		
RBC (X10 ⁶ /L)	Mean ± SD	4.5		± 0.4		
WBC (X10 ⁹ /L)	Mean ± SD	7.5		± 1.4		
Platelet (X10 ⁹ /L)	Mean ± SD	283.2		± 43.4		
RBG (mg/dL)	Mean ± SD	87.1		± 9.8		
TSH (mU/L)	Median, range	2		0.1		
HOMA-IR	Median, range	1		0.08		
Baseline clinical data		Right side		Left side		
		N	%	N	%	
Area index	30-49%	4	20%	6	30%	P=0.838
	50-69%	5	25%	4	20%	
	70-100%	11	55%	10	50%	
Severity	Moderate	5	25%	8	40%	P=0.311
	Severe	15	75%	12	60%	
Texture	Mild	1	5%	1	5%	P=0.842
	Moderate	3	15%	5	25%	
	Extremely coarse	16	80%	14	70%	

HGB: Hemoglobin, RBG: Random Blood Glucose, TSH: Thyroid stimulating hormone, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance.

Although, peeling on left side showed higher percentage improvement in area index, severity and texture but with no statistically significantly difference compared to CO₂ laser on right side (Table 3).

Table (3): Comparison of improvement between right side of neck treated with laser and left side of neck treated by peeling in patients with Pseudo-acanthosis Nigricans

	Cases N=20				P
	Right side		Left side		
	Mean	±SD	Mean	±SD	
Area index improvement (%)	63.8	±17.3	71.3	±11.4	0.114
Severity improvement (%)	67.9	±15.1	70.4	±6.3	0.499
Texture improvement (%)	86.7	±19.9	90	±19	0.592

Percentage improvement was calculated from baseline.



Figure (1): (A) Left side before treatment. (B) Left side after GA peel. (C) Right side before treatment. (D) Right side after fractional laser.

DISCUSSION

A comparative study was carried on 20 patients with pseudo-acanthosis nigricans. Thirty patients were assessed for illegibility, 10 were excluded and 20 cases were allocated for the study. All cases were subjected to fractional CO₂ laser on the right side of neck and glycolic acid peel on the left side of neck. Each patient had 3 sessions every two weeks and follow up for recurrence after 2 months of last session. 15 cases had 3 sessions, while 5 cases improved after 2 sessions.

All cases were females and mean age was 17.5 ranging from 6 to 39 years. Female preponderance was reported by *Zaki et al.*⁽⁹⁾, *Eldeeb et al.*⁽¹³⁾ and *Leerapongnan et al.*⁽¹²⁾ studies. Conversely, *Thomas et al.*⁽¹⁴⁾ study has shown that AN is more prevalent in the male population [55 were male (55%) and the rest 45 were female (45%)].

Mean BMI was 32.4 kg/m², most of them were obese (70%), while 30% were non obese. **This finding is going with Leerapongnan et al.**⁽¹²⁾ who found that the mean body mass index was 29.88 ± 5.17 kg/m². Body mass index is an important confounding factor in the association of Acanthosis Nigricans with type 2 diabetes mellitus, which is why it is said that

“Acanthosis nigricans is not a skin disease per se but a cutaneous sign of an underlying condition or disease⁽¹⁵⁾.”

Regarding HOMA-IR, the current study demonstrated that, median HOMA-IR was 1 ranging from 0.5 to 3. HOMA-IR is a widely used and validated tool for quantifying IR in clinical and epidemiological studies on the association of AN and among children and young adults⁽¹⁷⁾. *Álvarez-Villalobos et al.*⁽¹⁸⁾ study showed that homeostatic model assessment-IR values were significantly higher in AN group than in control group (3.71 versus 2.5) in cases with fasting plasma glucose below 100 mg/dL. A relationship between AN and IR has been described⁽¹⁷⁾. The role of AN as a precursor to IR and/or obesity should also be considered⁽¹⁸⁾. AN screening may help to identify coexisting comorbidities related to adiposity or patients at high risk⁽¹⁹⁾.

Baseline clinical data were similar when comparing between right and left sides (p > 0.05) for area index, severity and texture. Area index ranged from 30 to 49% in 20% and 30%, while it ranged from 50 to 69% in 25% and 20%, and ranged from 70 to 100% in 55% and 50% on right and left sides respectively (p:

0.838). Moderate severity was found in 25% and 40%, while severe lesions were found in 75% and 60% on right and left sides respectively (p : 0.311). Texture was mild in 5% and 5%, moderate in 15% and 25% and extremely coarse in 80% and 70% on right and left sides respectively (p : 0.842). This comes in accordance with **Zaki et al.**⁽⁹⁾ study who demonstrated that all patients had similar, however not identical, degree of severity for both sides (right and left) before treatment (P value = 0.99).

There was overall improvement in area index, severity and texture across time subjected to CO₂ laser ($p < 0.001$). This finding is in agreement with **Eldeeb et al.**⁽¹³⁾ study who reported that the use of fractional CO₂ laser resulted in marked improvement of both the texture and pigmentation of AN. In contrast to the current findings, **Zaki et al.**⁽⁹⁾ study demonstrated that the mean severity of the lesion did not improve after using CO₂ laser on the right side of the neck, where the mean Acanthosis Nigricans Area and Severity Index (ANASI) at the start of the study was 23.50 ± 8.85 , and after the laser treatment sessions, it became 19.10 ± 7.62 , (P value = 0.1) which showed no statistical improvement. The discrepancies among the current study and the previously mentioned studies may be due to good patient preparation and selection and different laser machine.

There was overall improvement in area index, severity and texture across time subjected to GA peeling ($p < 0.001$). In agreement with our result, **Zaki et al.**⁽⁹⁾ reported that the mean severity of the lesion at the start of the study, according to ANASI was 23.55 ± 8.68 , and after the GA treatment sessions on the left side of the neck, it was 13.50 ± 8.33 . The improvement was statistically significant. (P value = 0.001). Additionally, **Ichiyama et al.**⁽²¹⁾ study showed the usefulness of GA peeling for the Japanese familial AN patients with the skin type IV. GA Peeling showed higher percentage improvement in area index, severity and texture when compared to CO₂ laser (mean=71.3 versus 63.8), (mean=70.4 versus 67.9) and (mean=90 versus 86.7) although did not reach significant level ($p > 0.05$). In contrast to the current findings, **Zaki et al.**⁽⁹⁾ reported that, the clinical improvement on the side treated by glycolic acid peel was 43% when compared to 19% improvement on the laser side and there was statistical difference between both sides ($P=0.008$). Additionally, a higher statistically significant improvement was found in the AN lesions treated with CO₂ laser compared to TCA peels in **Eldeeb et al.**⁽¹³⁾ study ($p < 0.001$). This could be attributed to different peeling, laser parameters, and longer treatment duration in their study (four sessions).

CONCLUSION

Acanthosis nigricans is a difficult dermatosis to treat, although there are many methods of treatment. Glycolic acid peeling 70% and fractional CO₂ laser are considered effective modalities for AN treatment.

However, GA peeling was more effective but statically insignificant.

RECOMMENDATION

Good patient preparation and education is an important factor for any cosmetic procedure. GA peeling and fractional CO₂ laser are good options for treatment of AN. GA is considered easy and cheap method for treatment of AN. Fractional CO₂ laser is a promising method for treatment. Further studies are needed to be done to assess efficacy of laser on AN with different parameters and different laser machines.

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