"A COMPARATIVE STUDY OF FRACTIONAL CO2 LASER VERSUS FERULIC ACID SEQUENTIAL (12% & 8%) PEEL IN THE TREATMENT OF NECK ACANTHOSIS NIGRICANS"

BY

DR. AKSHATA YADAV. S, M.B.B.S.

DISSERTATION SUBMITTED TO

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA,

IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF

DOCTOR OF MEDICINE (M.D.)

IN

DERMATOLOGY, VENEREOLOGY AND LEPROSY

UNDER THE GUIDANCE OF

Dr. RAJASHEKAR. T. S.M.B.B.S., M.D.

PROFESSOR AND HEAD OF THE DEPARTMENT

DEPARTMENT OF DERMATOLOGY, VENEREOLOGY AND LEPROSY

SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA, KOLAR,

KARNATAKA – 563101

2025

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH TAMAKA, KOLAR, KARNATAKA

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"A COMPARATIVE STUDY OF FRACTIONAL CO2 LASER VERSUS FERULIC ACID SEQUENTIAL (12% & 8%) PEEL IN THE TREATMENT OF NECK ACANTHOSIS NIGRICANS"** is a bonafide and genuine research work carried out by me under the direct guidance of **Dr. RAJASHEKAR.T. S**, Professor and HOD, Department of Dermatology, Venereology and Leprosy, Sri Devaraj Urs Medical College, Tamaka, Kolar, in partial fulfillment of the requirement for the degree of **M.D. IN DERMATOLOGY, VENEREOLOGY AND LEPROSY.**

DATE: **Signature of candidate**

PLACE: KOLAR **Dr. AKSHATA YADAV S**

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH TAMAKA, KOLAR, KARNATAKA

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **"A COMPARATIVE STUDY OF FRACTIONAL CO2 LASER VERSUS FERULIC ACID SEQUENTIAL (12% & 8%) PEEL IN THE TREATMENT OF NECK ACANTHOSIS NIGRICANS"** is a bonafide and genuine research work done by **Dr. AKSHATA YADAV S** in partial fulfillment of the requirement for the degree of **M.D IN DERMATOLOGY, VENEREOLOGY AND LEPROSY** as per regulations of SRI DEVRAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR.

DATE:

PLACE: KOLAR

SIGNATURE OF GUIDE

DR. RAJASHEKAR T.S, M.D
PROFESSOR AND HOD
DEPARTMENT OF DERMATOLOGY,
VENEREOLOGY AND LEPROSY,
SRI DEVARAJ URS MEDICAL
COLLEGE, TAMAKA, KOLAR

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH TAMAKA, KOLAR, KARNATAKA

ENDORSEMENT BY THE HOD, PRINCIPAL/HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled **"A COMPARATIVE STUDY OF FRACTIONAL CO2 LASER VERSUS FERULIC ACID SEQUENTIAL (12% & 8%) PEEL IN THE TREATMENT OF NECK ACANTHOSIS NIGRICANS"** is a bonafide and genuine research work done by **Dr. AKSHATA YADAV. S** in partial fulfillment of the requirement for the degree of **M.D IN DERMATOLOGY, VENEREOLOGY AND LEPROSY** as per regulations of SRI DEVRAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR.

SIGNATURE OF HOD

Dr. RAJASHEKAR T. S.
PROFESSOR & HEAD,
DEPARTMENT OF DERMATOLOGY
DEVARAJ URS MEDICAL COLLEGE
TAMAKA, KOLAR

DATE:
PLACE: KOLAR

SIGNATURE OF PRINCIPAL

Dr. PRABHAKAR K.
PRINCIPAL
SRI DEVARAJ URS MEDICAL SRI COLLEGE ,TAMAKA, KOLAR

DATE:
PLACE: KOLAR

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION & RESEARCH, TAMAKA, KOLAR, KARNATAKA

ETHICAL COMMITTEE CERTIFICATE

This is to certify that the ethics committee of Sri Devaraj Urs Medical College, Tamaka, Kolar has unanimously approved the dissertation work of Dr. AKSHATA YADAV S, a postgraduate student in the Department of Dermatology, Venereology and Leprosy of Sri Devaraj Urs Medical College entitled **"A COMPARATIVE STUDY OF FRACTIONAL CO2 LASER VERSUS FERULIC ACID SEQUENTIAL (12% & 8%) PEEL IN THE TREATMENT OF NECK ACANTHOSIS NIGRICANS"** to be submitted to **SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA KOLAR.**

SIGNATURE OF MEMBER SECRETARY ETHICAL COMMITTEE

SIGNATURE OF ETHICAL COMMITTEE. PRINCIPAL Dr. PRABHAKAR K. SRI DEVARAJ URS MEDICAL COLLEGE TAMAKA, KOLAR

DATE:
PLACE: KOLAR

DATE:
PLACE: KOLAR

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION & RESEARCH

SRI DEVARAJ URS MEDICAL COLLEGE

Tamaka, Kolar

INSTITUTIONAL ETHICS COMMITTEE

Members

1. **Dr. D.E.Gangadhar Rao, (Chairman)** Prof. & HOD of Zoology, Govt. Women's College, Kolar
2. **Dr. Sujatha.M.P, (Member Secretary),** Prof. Department of Anesthesia, SDUMC
3. Mr. Gopinath Paper Reporter, Samyukth Karnataka
4. Mr. G. K. Varada Reddy Advocate, Kolar
5. Dr. Hariprasad S, Prof. Dept. of Orthopedics, SDUMC
6. Dr. Abhinandana R Asst. Prof. Dept. of Forensic Medicine, SDUMC
7. Dr. Ruth Sneha Chandrakumar Assoc. Prof. Dept. of Psychiatry, SDUMC
8. Dr. Usha G Shenoy, Asst. Prof., Dept. of Allied Health & Basic Sciences SDUAHER
9. Dr. Munilakshmi U Asst. Prof. Dept. of Biochemistry, SDUMC
10. Dr.D.Srinivasan, Assoc. Prof. Dept. of Surgery, SDUMC
11. Dr.Shilpa M D Assoc. Prof. Dept. of Pathology, SDUMC

No. DMC/KLR/IEC/25/ 2023-24 **Date: 10/04/2023**

PRIOR PERMISSION TO START OF STUDY

The Institutional Ethics Committee of Sri Devaraj Urs Medical College, Tamaka, Kolar has examined and unanimously approved the synopsis entitled **"A Comparative Study Of Fractional Co2 Laser Versus Ferulic Acid Sequential (12% & 8%) Peel In The Treatment Of Neck Acanthosis Nigricans"** being investigated by **Dr.Akshata Yadav S & Dr.Rajashekar.T.S** in the Department of Dermatology at Sri Devaraj Urs Medical College, Tamaka, Kolar. **Permission is granted by the Ethics Committee to start the study.**

Sujatha.M.P
Member Secretary
Member Secretary
Institutional Ethics Committee
Sri Devaraj Urs Medical College
Tamaka, Kolar.

Chairman
CHAIRMAN
Institutional Ethics Committee
Sri Devaraj Urs Medical College
Tamaka, Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA

COPY RIGHT

DECLARATION BY THE CANDIDATE

I hereby declare that the Sri Devaraj Urs Academy of Higher Education and Research, Tamaka, Kolar, Karnataka shall have the rights to preserve, use and disseminate this dissertation/thesis in print or electronic format for academic /research purpose.

DATE: **Signature of the candidate**

PLACE: KOLAR **Dr. AKSHATA YADAV S**

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION & RESEARCH
TAMAKA, KOLAR, KARNATAKA, INDIA 563103

CERTIFICATE OF PLAGIARISM CHECK

Title of the Thesis/Dissertation	**A COMPARATIVE STUDY OF FRACTIONAL CO2 LASER VERSUS FERULIC ACID SEQUENTIAL (12% & 8%) PEEL IN THE TREATMENT OF NECK ACANTHOSIS NIGRICANS**
Name of the Student	DR AKSHATA YADAV .S
Registration Number	22CD1022
Name of the Supervisor / Guide	DR.RAJASHEKAR.T.S
Department	DERMATOLOGY,VENEREOLOGY, LEPROSY.
Acceptable Maximum Limit (%) of Similarity (PG Dissertation /Ph.D. Thesis)	10 %
Similarity	10%
Software used	TURNITIN
Paper ID	261957683
ORCID ID	0009-0006-2639-9373
Submission Date	12/05/2025

Signature of Student

Signature of Guide/Supervisor

DR. RAJASHEKAR. T.S
Professor & HOD
Dept. OF Dermatology
SDUMC, Tamaka, KOLAR

HOD Signature

DR. RAJASHEKAR. T.S
Professor & HOD
Dept. OF Dermatology
SDUMC, Tamaka, KOLAR

University Librarian,
University Library
Learning Resource Centre
SDUAHER, Tamaka
KOLAR-563103

12/5/2025

PG Coordinator

PG Coordinator
Sri Devaraj Urs Medical College
Tamaka, Kolar-563103

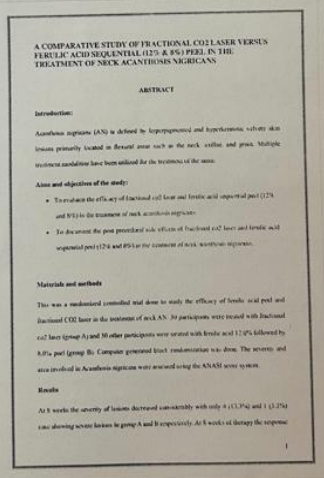
turnitin

Digital Receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	DR.AKSHATA YADAV. S
Assignment title:	PG Dissertation - 2025
Submission title:	A COMPARATIVE STUDY OF FRACTIONAL CO2 LASER VERSUS F...
File name:	12_8_PEEL_IN_THE_TREATMENT_OF_NECK_ACANTHOSIS_NIGRI...
File size:	4.28M
Page count:	78
Word count:	13,565
Character count:	77,359
Submission date:	12-May-2025 09:53AM (UTC+0530)
Submission ID:	2671957683



A COMPARATIVE STUDY OF FRACTIONAL CO2 LASER VERSUS FERULIC ACID SEQUENTIAL (12% & 8%) PEEL IN THE TREATMENT OF NECK ACANTHOSIS NIGRICANS

ABSTRACT

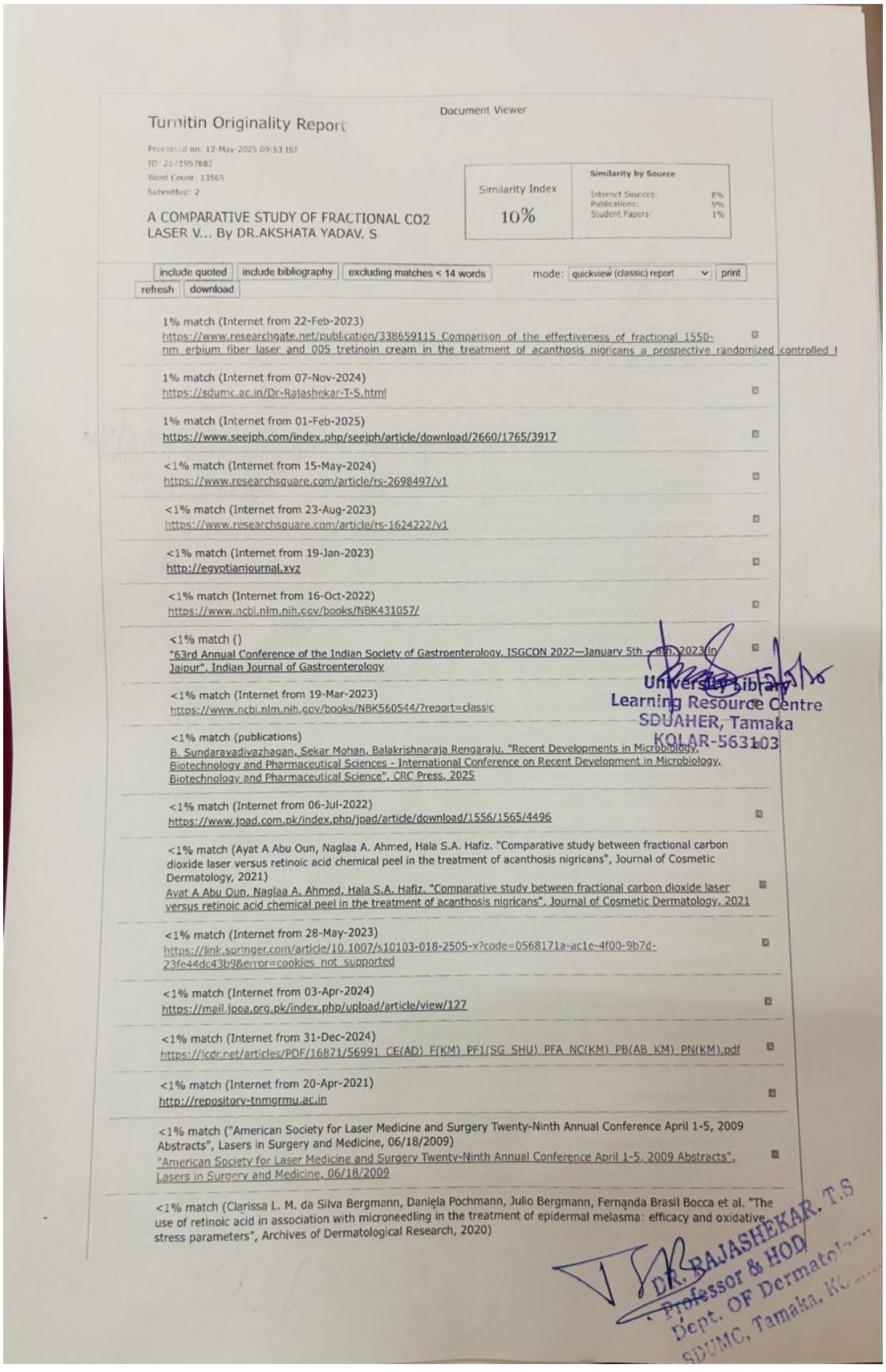
Introduction:

Materials and methods

Results

DR. RAJASHEKAR. T.S
Professor & HOD
Dept. OF Dermatology
SDUMC, Tamaka, KOLAR

University Library
Learning Resource Centre
SDUAHER, Tamaka
KOLAR-563103



Document Viewer

Turnitin Originality Report

Processed on: 12-May-2025 09:53 IST
ID: 2671957683
Word Count: 13565
Submitted: 2

A COMPARATIVE STUDY OF FRACTIONAL CO2 LASER V... By DR.AKSHATA YADAV. S

Similarity Index	Similarity by Source	
10%	Internet Sources:	8%
	Publications:	9%
	Student Papers:	1%

include quoted | include bibliography | excluding matches < 14 words | mode: quickview (classic) report | print | refresh | download

1% match (Internet from 22-Feb-2023)
https://www.researchgate.net/publication/338659115_Comparison_of_the_effectiveness_of_fractional_1550-nm_erbium_fiber_laser_and_005_tretinoin_cream_in_the_treatment_of_acanthosis_nigricans_a_prospective_randomized_controlled_t

1% match (Internet from 07-Nov-2024)
https://sdumc.ac.in/Dr-Rajashekar-T-S.html

1% match (Internet from 01-Feb-2025)
https://www.seejph.com/index.php/seejph/article/download/2660/1765/3917

<1% match (Internet from 15-May-2024)
https://www.researchsquare.com/article/rs-2698497/v1

<1% match (Internet from 23-Aug-2023)
https://www.researchsquare.com/article/rs-1624222/v1

<1% match (Internet from 19-Jan-2023)
http://egyptianjournal.xyz

<1% match (Internet from 16-Oct-2022)
https://www.ncbi.nlm.nih.gov/books/NBK431057/

<1% match ()
"63rd Annual Conference of the Indian Society of Gastroenterology, ISGCON 2022—January 5th – 8th, 2023 in Jaipur", Indian Journal of Gastroenterology

<1% match (Internet from 19-Mar-2023)
https://www.ncbi.nlm.nih.gov/books/NBK560544/?report=classic

<1% match (publications)
B. Sundaravadivazhagan, Sekar Mohan, Balakrishnaraja Rengaraju. "Recent Developments in Microbiology, Biotechnology and Pharmaceutical Sciences - International Conference on Recent Development in Microbiology, Biotechnology and Pharmaceutical Science", CRC Press, 2025

<1% match (Internet from 06-Jul-2022)
https://www.jpad.com.pk/index.php/jpad/article/download/1556/1565/4496

<1% match (Ayat A Abu Oun, Naglaa A. Ahmed, Hala S.A. Hafiz. "Comparative study between fractional carbon dioxide laser versus retinoic acid chemical peel in the treatment of acanthosis nigricans", Journal of Cosmetic Dermatology, 2021)
Ayat A Abu Oun, Naglaa A. Ahmed, Hala S.A. Hafiz. "Comparative study between fractional carbon dioxide laser versus retinoic acid chemical peel in the treatment of acanthosis nigricans", Journal of Cosmetic Dermatology, 2021

<1% match (Internet from 28-May-2023)
https://link.springer.com/article/10.1007/s10103-018-2505-x?code=0568171a-ac1e-4f00-9b7d-23fe44dc43b9&error=cookies_not_supported

<1% match (Internet from 03-Apr-2024)
https://mail.jpoa.org.pk/index.php/upload/article/view/127

<1% match (Internet from 31-Dec-2024)
https://jcdr.net/articles/PDF/16871/56991_CE(AD)_F(KM)_PF1(SG_SHU)_PFA_NC(KM)_PB(AB_KM)_PN(KM).pdf

<1% match (Internet from 20-Apr-2021)
http://repository-tnmgrmu.ac.in

<1% match ("American Society for Laser Medicine and Surgery Twenty-Ninth Annual Conference April 1-5, 2009 Abstracts", Lasers in Surgery and Medicine, 06/18/2009)
"American Society for Laser Medicine and Surgery Twenty-Ninth Annual Conference April 1-5, 2009 Abstracts", Lasers in Surgery and Medicine, 06/18/2009

<1% match (Clarissa L. M. da Silva Bergmann, Daniela Pochmann, Julio Bergmann, Fernanda Brasil Bocca et al. "The use of retinoic acid in association with microneedling in the treatment of epidermal melasma: efficacy and oxidative stress parameters", Archives of Dermatological Research, 2020)

University Library
Learning Resource Centre
SDUAHER, Tamaka
KOLAR-563103

DR. RAJASHEKAR. T.S
Professor & HOD
Dept. OF Dermatology
SDUMC, Tamaka, KOLAR

Clarissa L. M. da Silva Bergmann, Daniela Pochmann, Julio Bergmann, Fernanda Brasil Bocca et al. "The use of retinoic acid in association with microneedling in the treatment of epidermal melasma: efficacy and oxidative stress parameters", Archives of Dermatological Research, 2020

<1% match (S.Swamy, Suchetha. "Clinicoepidemiological Study of Acanthosis Nigricans in a Rural Setup and its Correlation with Serum Insulin Levels", Rajiv Gandhi University of Health Sciences (India), 2023)
S.Swamy, Suchetha. "Clinicoepidemiological Study of Acanthosis Nigricans in a Rural Setup and its Correlation with Serum Insulin Levels", Rajiv Gandhi University of Health Sciences (India), 2023

<1% match (Internet from 20-Dec-2022)
https://jlos.uobaghdad.edu.iq/wp-content/uploads/sites/36/2022/05/Fractional-Co2-Laser-Vs-Topical-Estrogen-In-The-Treatment-Of-Vulvovaginal-Atrophy-In-Perimenopausal-Women-...pdf

<1% match (Internet from 01-May-2023)
https://www.biorxiv.org/content/10.1101/663245v1.full

<1% match (Fatma Eldeeb, Reham M. Wahid, Rania Alakad. "Fractional carbon dioxide laser versus trichloroacetic acid peel in the treatment of pseudo-acanthosis nigricans", Journal of Cosmetic Dermatology, 2021)
Fatma Eldeeb, Reham M. Wahid, Rania Alakad. "Fractional carbon dioxide laser versus trichloroacetic acid peel in the treatment of pseudo-acanthosis nigricans", Journal of Cosmetic Dermatology, 2021

<1% match (Internet from 15-Dec-2022)
http://misc.medscape.com

<1% match (Internet from 16-Mar-2022)
https://www.ijhcr.com/index.php/ijhcr/article/download/3547/2462/5342

<1% match ("Textbook of Aging Skin", Springer Nature, 2017)
"Textbook of Aging Skin", Springer Nature, 2017

<1% match ("Dermatology in Public Health Environments", Springer Nature, 2018)
"Dermatology in Public Health Environments", Springer Nature, 2018

<1% match (Darmstadt, Gary L.. "Treatment of Acanthosis Nigricans With Tretinoin", Archives of Dermatology, 1991.)
Darmstadt, Gary L.. "Treatment of Acanthosis Nigricans With Tretinoin", Archives of Dermatology, 1991.

<1% match (David Overbosch, François Peyron, Nicole Picot, Jean-Paul Varichon, Rafaele Dumas, Laurent Chambonneau, Françoise Weber. "Combined Typhoid Fever and Hepatitis A Vaccine: Comparison of Immunogenicity and Safety to Concomitant Monovalent Vaccine over 3 Years", Journal of Travel Medicine, 2006)
David Overbosch, François Peyron, Nicole Picot, Jean-Paul Varichon, Rafaele Dumas, Laurent Chambonneau, Françoise Weber. "Combined Typhoid Fever and Hepatitis A Vaccine: Comparison of Immunogenicity and Safety to Concomitant Monovalent Vaccine over 3 Years", Journal of Travel Medicine, 2006

<1% match (Internet from 19-Apr-2025)
https://jcpsp.pk/article-detail/peffect-of-electrocoagulation-and-direct-pressure-application-on-bleeding-from-liver-bed-during-laparoscopic-cholecystectomyorp

<1% match (AB Chirag, T Sangeetha, SM Darshan. "Impact of Cataract Surgery on Vision-related Quality of Life in Patients with Strabismus: A Quasi-experimental Study", JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH, 2024)
AB Chirag, T Sangeetha, SM Darshan. "Impact of Cataract Surgery on Vision-related Quality of Life in Patients with Strabismus: A Quasi-experimental Study", JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH, 2024

<1% match (Kutlubay, Zekayi, Burhan Engin, Orkhan Bairamov, and Yalçın Tüzün. "Acanthosis nigricans: A fold (intertriginous) dermatosis", Clinics in Dermatology, 2015.)
Kutlubay, Zekayi, Burhan Engin, Orkhan Bairamov, and Yalçın Tüzün. "Acanthosis nigricans: A fold (intertriginous) dermatosis", Clinics in Dermatology, 2015.

<1% match (Internet from 30-Oct-2020)
https://theswissbay.ch/pdf/Gentoomen%20Library/Misc/McGrawHill-Cosmetic.Dermatology.Principles.and.Practice.2009.RETAiL.EBook.pdf

<1% match (Internet from 14-May-2024)
https://www.science.gov/topicpages/p/paclitaxel-coated+balloon+catheter.html

<1% match ("Chemical and Physical Procedures", Springer Science and Business Media LLC, 2018)
"Chemical and Physical Procedures", Springer Science and Business Media LLC, 2018

<1% match (Internet from 24-Apr-2016)
http://escholarship.org

<1% match (Internet from 28-Oct-2021)
https://pdfcookie.com/documents/fitzpatricks-dermatology-in-general-medicine-8ed-rv31jxddqe2d

<1% match (Anthony C. Chu, Fernanda Teixeira. "Acquired Disorders of Epidermal Keratinization", Wiley, 2016)
Anthony C. Chu, Fernanda Teixeira. "Acquired Disorders of Epidermal Keratinization", Wiley, 2016

<1% match (Internet from 15-Apr-2023)
https://cms.guncelpediatri.com/Uploads/Article_59945/G%C3%BCncel%20Pediatri-21-52.pdf

<1% match (Internet from 16-Jul-2021)

https://lupinepublishers.com/gastroenterology-hepatology-journal/fulltext/utilization-of-traditional-anticoagulation-for-venous-thromboembolism-in-patients-with-liver-cirrhosis-is-it-safe.ID.000104.php

<1% match (Internet from 09-Sep-2018)
https://tees.openrepository.com/tees/bitstream/10149/620651/2/620651.pdf

A COMPARATIVE STUDY OF FRACTIONAL CO2 LASER VERSUS FERULIC ACID SEQUENTIAL (12% & 8%) PEEL IN THE TREATMENT OF NECK ACANTHOSIS NIGRICANS ABSTRACT Introduction: Acanthosis nigricans (AN) is defined by hyperpigmented and hyperkeratotic velvety skin lesions primarily located in flexural areas such as the neck, axillae, and groin. Multiple treatment modalities have been utilized for the treatment of the same. Aims and objectives of the study: ? To evaluate the efficacy of fractional co2 laser and ferulic acid sequential peel (12% and 8%) in the treatment of neck acanthosis nigricans. ? To document the post procedural side effects of fractional co2 laser and ferulic acid sequential peel (12% and 8%) in the treatment of neck acanthosis nigricans.? Materials and methods This was a randomized controlled trial done to study the efficacy of ferulic acid peel and fractional CO2 laser in the treatment of neck AN. 30 participants were treated with fractional co2 laser (group A) and 30 other participants were treated with ferulic acid 12.0% followed by 8.0% peel (group B). Computer generated block randomization was done. The severity and area involved in Acanthosis nigricans were assessed using the ANASI score system. Results At 8 weeks the severity of lesions decreased considerably with only 4 (13.3%) and 1 (3.3%) case showing severe lesions in group A and B respectively. At 8 weeks of therapy the response was excellent (>75%) in all the subjects in group B and 17 subjects in group A. Rest of the 13 subjects in group A had a marked response (51 – 75%) at 8 weeks of therapy. erythema and post procedure hyperpigmentation was found more among patients in group A who received fractional CO2 laser compared to patients in group B who received Ferulac Peel Classic solution Conclusion After 8 weeks of ferulic acid peel treatment improvement was seen in texture, thickness and pigmentation of acanthosis nigricans. Along with its cost effectives, increased therapeutic effect and better safety profile and lesser side effects, ferulic acid peel is the best option for treatment of acanthosis nigricans. INTRODUCTION Acanthosis nigricans (AN) is a prevalent dermatological disease that may indicate an underlying systemic disease. "AN is defined by hyperpigmented and hyperkeratotic velvety skin lesions primarily located in flexural areas such as the neck, axillae, and groin". Acanthosis nigricans (AN) is a prevalent skin condition with many treatment modalities available. Many topical and systemic drugs, such as oral retinoids, calcipotriol, salicylic acid, and tretinoin, have been used to treat AN. Laser therapy and chemical peels have also been used to treat AN.1 Acanthosis nigricans linked to obesity can be controlled over routine adjustments and mass loss. The treatment of AN is primarily conducted for aesthetic reasons. Numerous therapy techniques are currently available for acanthosis nigricans. Recent use of lasers and chemical peels in the management of AN are being explored.2 Fractional laser enhances both pigmentation and texture by ablation of superficial skin layers with minimal thermal injury, resulting in dermal wounds and subsequent collagen synthesis. This process underlies the observed improvements following laser resurfacing, while the intact surrounding skin serves as a reservoir for expedited epidermal regeneration. Because of its remarkable ability to remove trans-epidermal melanin and ablate superficial skin, fractional carbon dioxide (CO2) laser has become a viable therapeutic option for neck- AN, even though retinoids remain the main treatment option.2 Chemical peels are significant operations in cosmetic or aesthetic practices due to their versatility and cost-effectiveness. Chemical peels exhibit anti-inflammatory, keratolytic, and antioxidant properties. The practice of chemical exfoliation for skin enhancement has been utilized since ancient times.3 The optimal therapy for AN has yet to be determined. To evaluate the relative safety and effectiveness of these several methods in treating acanthosis nigricans, scientific studies are 3 required. Acanthosis nigricans has emerged as a cosmetological problem for both youth and adults in the contemporary period. Studies examining the possibilities of lasers and peels for treating neck AN are scarce. Therefore, The aim of this research project was to evaluate the efficacy of ferulic acid peel and fractional CO2 laser. AIMS AND OBJECTIVES AIM OF THE STUDY: To evaluate the efficacy of fractional co2 laser and ferulic acid sequential peel (12% and 8%) in the treatment of neck acanthosis nigricans.? OBJECTIVES OF THE STUDY: ? To evaluate the efficacy of fractional co2 laser and ferulic acid sequential peel (12% and 8%) in the treatment of neck acanthosis nigricans.? ? To document the post procedural side effects of fractional co2 laser and ferulic acid sequential peel (12% and 8%) in the treatment of neck acanthosis nigricans.? REVIEW OF LITERATURE History: Although Addison may have mistakenly diagnosed an AN case before 1885, the first recorded incidence of AN happened in 1889 in Germany, according to what Unna and Pollitzer said. It was thought that AN was associated with internal cancer by 1909, when there were roughly 50 reported cases., Kahn et al. in 1976 published a significant study that initially elucidated the connection between insulin resistance and anorexia nervosa. The Diabetes Association of America officially acknowledged AN as a risk indicator for the of childhood diabetes in 2000.4 Definition: "Acanthosis nigricans is a velvety, darkening of the skin that usually occurs in intertriginous areas. This hyperpigmentation has poorly defined borders, usually occurs in skin fold areas, such as the back of the neck, axilla, and groin, and may include thickening of the skin".5 Figure 1: Right neck with acanthosis nigricans6 Pathophysiology of Acanthosis Nigricans : Increased growth factor levels and the stimulation of insulin-like growth factor (IGF), which is mediated by insulin on keratinocytes, are likely linked to the pathogenesis of AN. Increased activation of keratinocytes found in the epidermis and fibroblast proliferation appear to be the pathophysiological mechanisms of acanthosis nigricans.7 Research indicates that "insulin or an insulin-like growth factor" enhances epidermal cell proliferation in individuals with benign acanthosis nigricans. There are other mediators that have been discovered, such as the receptor for epidermal growth factor and tyrosine kinase. It is thought that binding to "IGF-1 receptors" causes elevated insulin levels to generate proliferative effects. Notably, "metabolic syndrome" is associated with increased free IGF-1 levels, which in turn promote cell differentiation and proliferation. Acanthosis nigricans has recently seen the identification of both syndromic and inherited variations. It has been discovered that acanthosis nigricans can have both hereditary and syndromic forms. The symptoms of obesity, "craniosynostosis", and "hyperinsulinemia" are similar to those of many other disorders. Two main groups of these conditions are insulin-resistant diseases and "fibroblast growth factor" deficiency. A few other insulin-resistant conditions are "Alström syndrome," "Dunningan syndrome," "Berardinelli-Seip syndrome," "Rabson-Mendenhall syndrome," and "leprechaunism." Severe perspiration or contact could also be an issue. In people with malignant AN, the maximum promoting agent is produced by the tumor units. "Transforming growth factor" and "epidermal growth factor" are two potential candidates, as the two have elevated points in individuals with stomach cancer. Additional data suggest that urine transforming growth factor normalizes following the excision of a mass, subsequently leading to the remission of dermal lesions. The use of drugs such as insulin has been associated, presumably due to the triggering of IGF receptors. Several reports indicate that syndromic patients developed ectopic acanthosis nigricans following skin fixing from an afflicted area. AN is probably induced by stimuli that promote the growth of keratinocytes present in epidermis and "dermal fibroblasts". In the other variants of AN, the likely factor is insulin or an IGF that stimulates

DR. RAJASHEKAR. T.S
Professor & HOD
Dept. OF Dermatology
SDUMC, Tamaka. KOl

ACKNOWLEDGEMENT

Writing my dissertation work is a great feeling for me because it reflects my entire post-graduation journey and hence, I take this opportunity to thank everyone who helped me complete this genuine novel research in the service to humanity.

I am deeply indebted and grateful to my guide, ***Dr. Rajashekar T.S****, Professor and Head of the Department of Dermatology, Venereology and Leprosy, Sri Devaraj Urs Medical College, for his able guidance, support, timely advice and constant encouragement throughout the period of the study*

I am very grateful to ***Dr. K Hanumanthayya K****, Professor, Department of Dermatology, Venereology and Leprosy, Sri Devaraj Urs Medical College, for his constant advice, support and encouragement during my post-graduation*

And I am thankful to ***Dr.S.B.Murugesh****, Professor of the Department of Dermatology, Venereology and Leprosy, Sri Devaraj Urs Medical College, for sharing his knowledge and wisdom during my post-graduation.*

I thank ***Dr. Suresh Kumar K****, Associate Professor, Department of Dermatology, Venereology and Leprosy, Sri Devaraj Urs Medical College, for his constant advice, guidance, support and encouragement during my post graduation.*

*I would also like to warmly extend my gratitude to****, Dr. Vaishnavi B. V*** *Assistant Professor,* ***Dr. Madhukiran C*** *Assistant Professor****, Dr. Suma K.R,*** *Assistant Professor****, Dr. Pallavi N, Assistant Professor*** *Department of Dermatology, Venereology and Leprosy, Sri Devaraj Urs Medical College, for their constant encouragement.*

Special thanks to my forever support system my husband ***Mr. Abhishek H V****, No words can express the gratitude I feel towards my beloved parents,* ***Mr. Siddappa J S*** *and* ***Mrs. Hemalatha K****, my in - laws* ***Dr Venkatesulu G****,* ***Mrs Jagadambika B K*** *and, I want to thank my. brother* ***S. Abhinandhan Yadav, Dr. Adarshasagar HV*** *and family members whose countless sacrifices and endless love has made me who I am today.*

I am deeply thankful to my Seniors ***Dr.Hussain Kolsawala****,* ***Dr. Shiva Saadhvi, Dr.G. Anjana, Dr.Hariharasubramanian, Dr.Sumedha Tirthani.***

I would also thank my postgraduate colleagues ***Dr. Yeragonda Susmitha, Dr. Samhith Souri, Dr Gunalakshmi K, Dr Jervin chris Rohith*** *for their love, motivation and help. I also thank my senior* ***Dr. Harish Prasanna*** *and my beloved juniors* ***Dr. Swathi Ganesh Shenoy, Dr. Bommaka Sruthi, Dr. M Yashaswini, Dr. Kenkre Namrata Sandeep, Dr. Callista Juneja, , Dr.Sreenidhi, Dr.Zainab Akbani, Dr.Varsha.V, Dr.Yashaswini, Dr.Ramya Priya K, Dr.Sanjana, Dr.Janhvi, Dr.Anapoorna*** *for their endless support.*

I am truly blessed in having the most wonderful friends and would like to thank them for their endless support.

I will be failing my duty if I do not thank all my patients involved in this study, without whose co-operation and patience this study would have been impossible.

Last, but not the least, I would like to express my gratitude to the Almighty for all his blessings.

DATE: **SIGNATURE OF CANDIDATE**

PLACE: KOLAR **DR. AKSHATA YADAV S**

LIST OF ABBREVIATIONS

1	ABBREVIATIONS	FULL FORMS
2	AN	Acanthosis Nigricans
3	LASER	Light Amplification by Stimulated Emission of Radiation
4	CO2	Carbon dioxide
5	GPA	Global Photograph Assessment
6	ANASI Score	Acanthosis Nigricans Area And Severity Index
7	VDS	Visual Discomfort scale
8	VAS	Visual Analogue Scale
9	HAIR-AN	Hyperandrogenism, Insulin Resistance, and Acanthosis Nigricans
10	VEGF	Vascular Endothelial Growth Factor
11	IGF	Insulin like growth factor
12	IGF-1	Insulin like growth factor - 1
13	EGF	Epidermal growth Factor
14	FGFR	Fibroblast growth factor receptor
15	SADDAN	Severe achondroplasia with developmental delay‖, and associated anomalies
16	TGF	Transforming growth factor
17	PCOS	Polycystic ovary syndrome
18	GMP	Guanosine monophosphate
19	HOMA-IR	Homeostatic Model Assessment for Insulin Resistance
20	DPP4	Dipeptidyl peptidase-4
21	TZD	Thiazolidinediones

ABSTRACT

Introduction:

Acanthosis nigricans (AN) is defined by hyperpigmented and hyperkeratotic velvety skin lesions primarily located in flexural areas such as the neck, axillae, and groin. Multiple treatment modalities have been utilized for the treatment of the same.

Aims and objectives of the study:

- To evaluate the efficacy of fractional co2 laser and ferulic acid sequential peel (12% and 8%) in the treatment of neck acanthosis nigricans.
- To document the post procedural side effects of fractional co2 laser and ferulic acid sequential peel (12% and 8%) in the treatment of neck acanthosis nigricans.

Materials and methods

This was a randomized controlled trial done to study the efficacy of ferulic acid peel and fractional CO2 laser in the treatment of neck AN. 30 participants were treated with fractional co2 laser (group A) and 30 other participants were treated with ferulic acid 12.0% followed by 8.0% peel (group B). Computer generated block randomization was done. The severity and area involved in Acanthosis nigricans were assessed using the ANASI score system.

Results

At 8 weeks the severity of lesions decreased considerably with only 4 (13.3%) and 1 (3.3%) case showing severe lesions in group A and B respectively. At 8 weeks of therapy the response was excellent (>75%) in all the subjects in group B and 17 subjects in group A. Rest of the 13 subjects in group A had a marked response (51 – 75%) at 8 weeks of therapy.

erythema and post procedure hyperpigmentation was found more among patients in group A who received fractional CO2 laser compared to patients in group B who received Ferulac Peel Classic solution

Conclusion

After 8 weeks of ferulic acid peel treatment improvement was seen in texture, thickness and pigmentation of acanthosis nigricans. Along with its cost effectives, increased therapeutic effect and better safety profile and lesser side effects, ferulic acid peel is the best option for treatment of acanthosis nigricans.

Keywords: Acanthosis nigricans, Fractional CO2 Laser, Ferulic acid peel, ANASI Score.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF GRAPHS

INTRODUCTION

INTRODUCTION

Acanthosis nigricans (AN) is a prevalent dermatological disease that may indicate an underlying systemic disease. ―AN is defined by hyperpigmented and hyperkeratotic velvety skin lesions primarily located in flexural areas such as the neck, axillae, and groin‖. Acanthosis nigricans (AN) is a prevalent skin condition with many treatment modalities available. Many topical and systemic drugs, such as oral retinoids, calcipotriol, salicylic acid, and tretinoin, have been used to treat AN. Laser therapy and chemical peels have also been used to treat AN.[1]

Acanthosis nigricans linked to obesity can be controlled over routine adjustments and mass loss. The treatment of AN is primarily conducted for aesthetic reasons. Numerous therapy techniques are currently available for acanthosis nigricans. Recent use of lasers and chemical peels in the management of AN are being explored.[2]

Fractional laser enhances both pigmentation and texture by ablation of superficial skin layers with minimal thermal injury, resulting in dermal wounds and subsequent collagen synthesis. This process underlies the observed improvements following laser resurfacing, while the intact surrounding skin serves as a reservoir for expedited epidermal regeneration.

Because of its remarkable ability to remove trans-epidermal melanin and ablate superficial skin, fractional carbon dioxide (CO2) laser has become a viable therapeutic option for neck-AN, even though retinoids remain the main treatment option.[2]

Chemical peels are significant operations in cosmetic or aesthetic practices due to their versatility and cost-effectiveness. Chemical peels exhibit anti-inflammatory, keratolytic, and antioxidant properties. The practice of chemical exfoliation for skin enhancement has been utilized since ancient times.[3]

The optimal therapy for AN has yet to be determined. To evaluate the relative safety and effectiveness of these several methods in treating acanthosis nigricans, scientific studies are required. Acanthosis nigricans has emerged as a cosmetological problem for both youth and adults in the contemporary period. Studies examining the possibilities of lasers and peels for treating neck AN are scarce. Therefore, The aim of this research project was to evaluate the efficacy of ferulic acid peel and fractional CO2 laser.

AIMS AND

OBJECTIVES

AIMS AND OBJECTIVES

AIM OF THE STUDY: To evaluate the efficacy of fractional co2 laser and ferulic acid sequential peel (12% and 8%) in the treatment of neck acanthosis nigricans.

OBJECTIVES OF THE STUDY:

- To evaluate the efficacy of fractional co2 laser and ferulic acid sequential peel (12% and 8%) in the treatment of neck acanthosis nigricans.
- To document the post procedural side effects of fractional co2 laser and ferulic acid sequential peel (12% and 8%) in the treatment of neck acanthosis nigricans.

REVIEW OF

LITERATURE

REVIEW OF LITERATURE

History:

Although Addison may have mistakenly diagnosed an AN case before 1885, the first recorded incidence of AN happened in 1889 in Germany, according to what Unna and Pollitzer said. It was thought that AN was associated with internal cancer by 1909, when there were roughly 50 reported cases., Kahn et al. in 1976 published a significant study that initially elucidated the connection between insulin resistance and anorexia nervosa. The Diabetes Association of America officially acknowledged AN as a risk indicator for the of childhood diabetes in 2000.[4]

Definition:

―Acanthosis nigricans is a velvety, darkening of the skin that usually occurs in intertriginous areas. This hyperpigmentation has poorly defined borders, usually occurs in skin fold areas, such as the back of the neck, axilla, and groin, and may include thickening of the skin‖.[5]

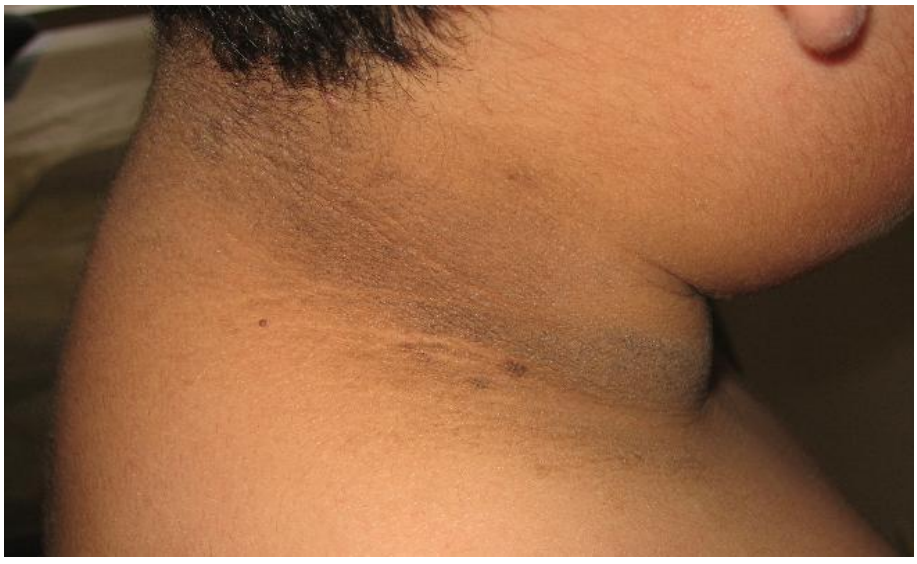


Figure 1: Right neck with acanthosis nigricans[6]

Pathophysiology of Acanthosis Nigricans :

Increased growth factor levels and the stimulation of insulin-like growth factor (IGF), which is mediated by insulin on keratinocytes, are likely linked to the pathogenesis of AN. Increased activation of keratinocytes found in the epidermis and fibroblast proliferation appear to be the pathophysiological mechanisms of acanthosis nigricans.[7]

Research indicates that ―insulin or an insulin-like growth factor‖ enhances epidermal cell proliferation in individuals with benign acanthosis nigricans. There are other mediators that have been discovered, such as the receptor for epidermal growth factor and tyrosine kinase. It is thought that binding to ―IGF-1 receptors‖ causes elevated insulin levels to generate proliferative effects. Notably, ―metabolic syndrome‖ is associated with increased free IGF-1 levels, which in turn promote cell differentiation and proliferation.

Acanthosis nigricans has recently seen the identification of both syndromic and inherited variations. It has been discovered that acanthosis nigricans can have both hereditary and syndromic forms. The symptoms of obesity, ―craniosynostosis‖, and ―hyperinsulinemia‖ are similar to those of many other disorders. Two main groups of these conditions are insulin-resistant diseases and ―fibroblast growth factor‖ deficiency.

A few other insulin-resistant conditions are "Alström syndrome," "Dunningan syndrome," "Berardinelli-Seip syndrome," "Rabson-Mendenhall syndrome," and "leprechaunism." Severe perspiration or contact could also be an issue.

In people with malignant AN, the maximum promoting agent is produced by the tumor units. ―Transforming growth factor‖ and ―epidermal growth factor‖ are two potential candidates, as the two have elevated points in individuals with stomach cancer. Additional data suggest that

urine transforming growth factor normalizes following the excision of a mass, subsequently leading to the remission of dermal lesions.

The use of drugs such as insulin has been associated, presumably due to the triggering of IGF receptors. Several reports indicate that syndromic patients developed ectopic acanthosis nigricans following skin fixing from an afflicted area.

AN is probably induced by stimuli that promote the growth of keratinocytes present in epidermis and ―dermal fibroblasts‖.

In the other variants of AN, the likely factor is insulin or an IGF that stimulates epidermal cell proliferation; other suggested intermediaries include various ―tyrosine kinase‖ receptors, such as the EGF receptor or the FGF receptor.[8]

At high dosages, insulin may have significant proliferative effects through its high-affinity binding to IGF-1 receptors. Additionally, hyperinsulinemic obese people may have elevated free IGF-1 levels, which enhances cell proliferation and differentiation.[9]

FGF abnormalities including initiating mutations in ―FGFR2 (Beare-Stevenson syndrome)‖ & ―FGFR3 (Crouzon syndrome with associated anomalies, thanatophoric dysplasia, severe achondroplasia with developmental delay‖, and associated anomalies [SADDAN]). In the familial instances of AN without further syndromic manifestations have been associated with FGFR mutations.[10,11]

Moisture or rubbing can also contribute, as indicated by the preference of AN for body wrinkles.

In cases of malignant acanthosis nigricans (AN), the suspected trigger is a biochemical substance either secreted directly by the tumor or produced as a physiological response to its presence. One likely candidate is transforming growth factor-alpha (TGF-α), which shares a

similar molecular structure with epidermal growth factor (EGF). Research has identified both TGF-α and EGF within gastric cancer cells, while epidermal growth factor receptor (EGFR) expression has been observed in the skin cells affected by AN lesions. Notably, after surgical removal of the tumour, levels of TGF-α in both urine and serum tend to return to normal, a change that correlates with a subsequent reduction or regression of the associated skin manifestations.[12]

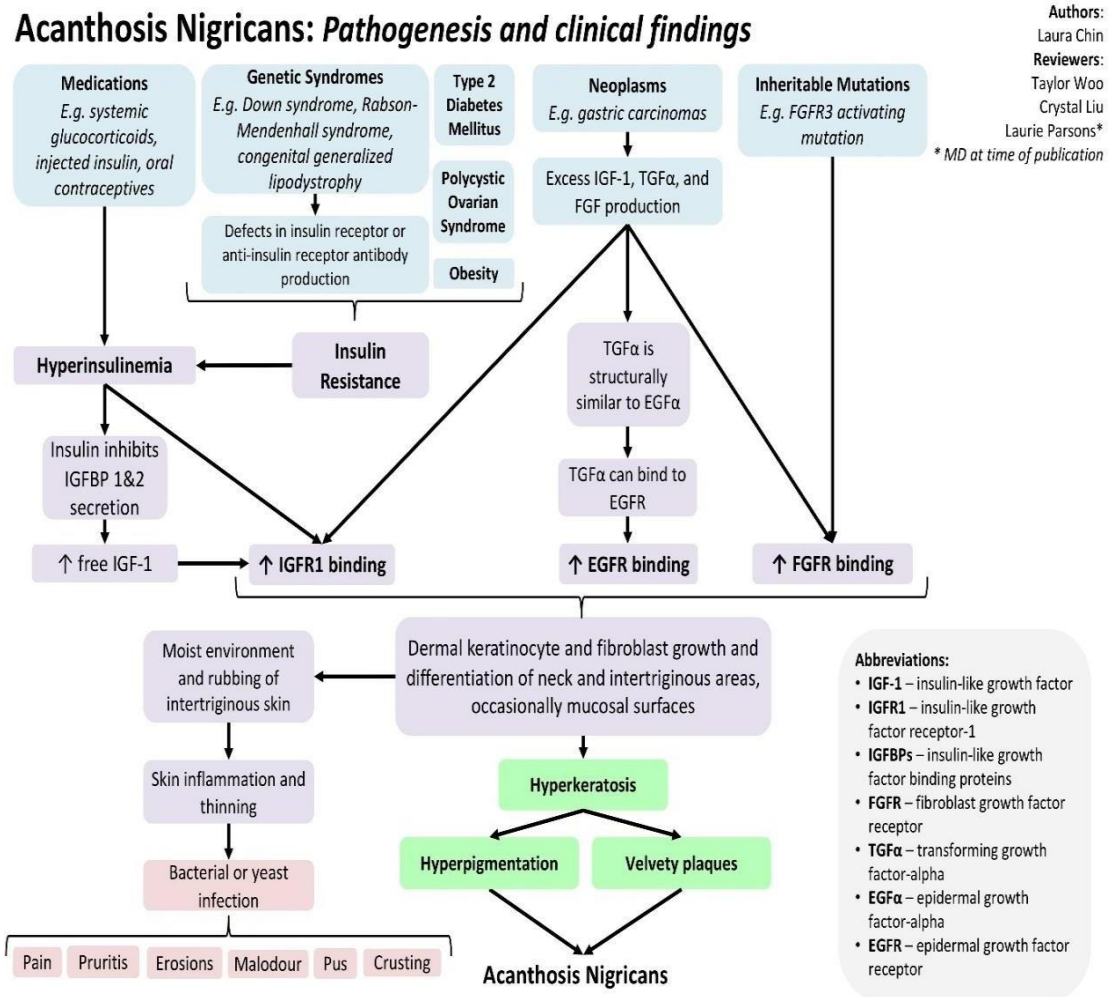


Figure 2: Pathophysiology and clinical findings of acanthosis nigricans[13]

Exogenous medications, like as insulin injections, have been recognized as possible etiological contributions, most likely via activating IGF receptors, especially at the injection site.[14,15] Certain therapeutic agents, such as palifermin— a synthetic version of keratinocyte

growth factor designed to alleviate mucositis in patients undergoing chemotherapy and stem cell transplantation— have been observed to trigger transient yet pronounced skin changes resembling acanthosis nigricans (AN). This effect is believed to stem from the activation of FGFR, which play a crucial part in cellular proliferation and tissue response mechanisms.[16]

Instances of ectopic anhidrosis have been documented in individuals with syndromic conditions requiring surgical intervention. A patient in one such instance had skin grafted from the groin to address syndactyly. Over time, the grafted areas exhibited a delayed onset of anhidrosis, suggesting a disruption in normal sweat gland function at the transplant sites.[17]

The aetiology of Acanthosis nigricans is influenced by a multitude of factors.[18]

Blood insulin levels that are elevated trigger "keratinocyte insulin-like growth factor (IGF) receptors," namely "IGF-1." Raised insulin levels may cause "IGF-1" to separate from its binding protein. High blood levels of "IGF" may lead to the proliferation of cutaneous fibroblasts and keratinocytes. Hereditary differences are linked to aberrations in fibroblast growth factors.

Acanthosis nigricans linked to malignancy appears to be caused by elevated transforming growth factor (TGF). Through the EGF receptor , TGF impacts on epidermal tissue.

Disorders and syndromes associated with AN

• Acromegaly and gigantism

• Bloom syndrome

• Beare–Stevenson syndrome

• Benign encephalopathy

• Chondrodystrophy with dwarfism

• Costello syndrome

• Crouzon syndrome [26,27]

• Diabetes

• Familial pineal body hypertrophy

• Gigantism

• HAIR-AN syndrome

• Hashimoto thyroiditis

• Laurence–Moon–Bardet syndrome

• Lawrence-Seip syndrome

• Lipoatrophic diabetes

• Phenylketonuria

• Polycystic ovary syndrome

• Prader–Willi syndrome

• Rud syndrome

• Systemic sclerosis

• Thanatophoric dwarfism

• Werner syndrome

Internal Cancers associated with AN

• Adenocarcinoma of GIT

• Transitional cell carcinoma

•Clear cell renal cell carcinoma

• Hepatocellular carcinoma and cholangiocarcinoma

Osteogenic sarcoma and Wilms tumour (in children

TYPES OF ACANTHOSIS NIGRICANS

Familial AN: An autosomal dominant trait may cause familial acanthosis nigricans, which may appear at birth or during infancy. Mutations in the "fibroblast growth factor receptor 3 (FGFR3)" are the cause of this.[19,20]

Obesity-associated AN: An established condition associated with AN is obesityIt was previously referred to as "pseudoacanthosis nigricans." It may be associated with IR. Dietary changes, weight loss, or pharmaceutical treatments for overweight can all help treat AN.[21,22]

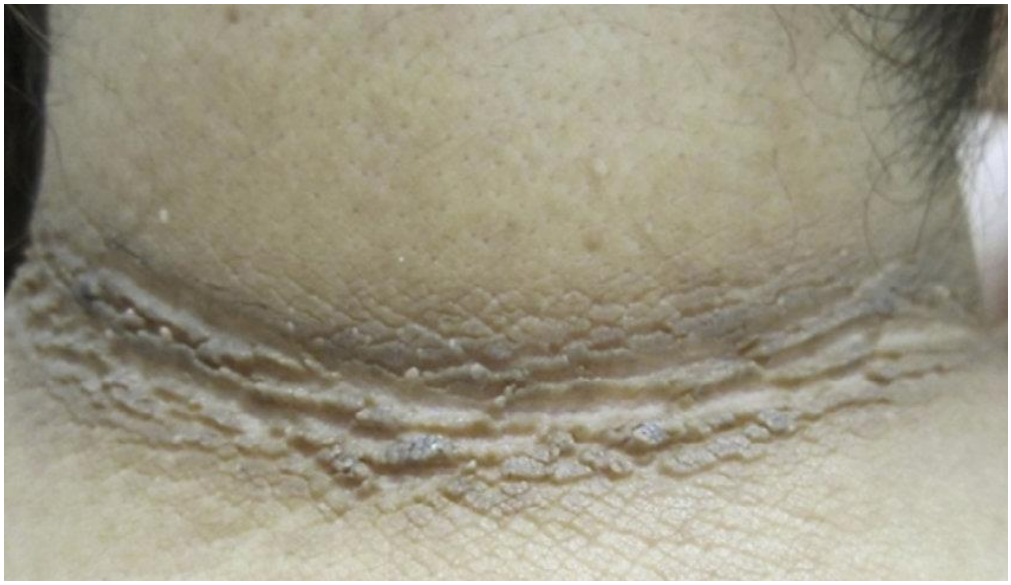


Figure 3: Obesity associated Acanthosis nigricans[23]

Medications related with AN: AN has been associated with a variety of pharmacological drugs. These consist of injectable insulin, niacin, growth hormone treatment, estrogen, diethylstilbestrol, systemic glucocorticoids, nicotinic acid, and protease inhibitors. Drug-induced acanthosis nigricans is reversible, as evidenced by the fact that the disease usually gets better or goes away after the offending medicine is stopped.[24-25]

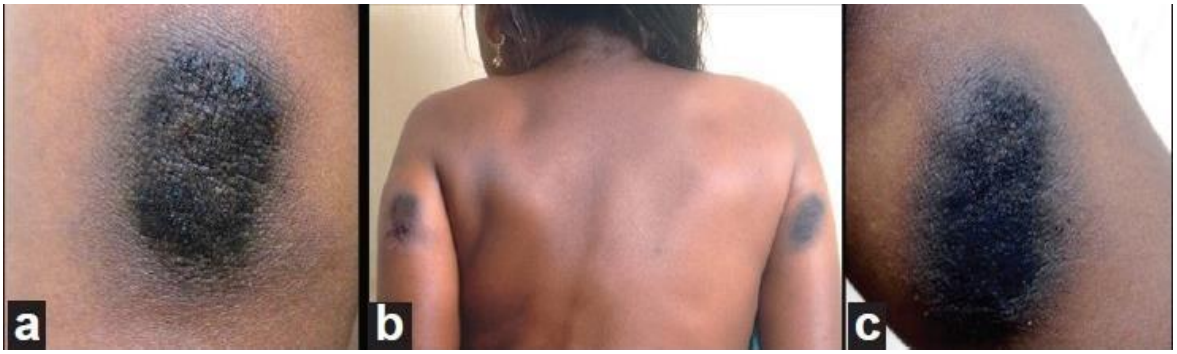


Figure 4: Medication associated acanthosis nigricans[27]

Endocrine-related acanthosis nigricans: People with obesity are often found to have endocrine-related acanthosis nigricans, which tends to develop gradually and stay relatively

localized. There are two forms of insulin resistance syndromes: Type A (HAIR-AN) and Type B.

The symptoms of type A syndrome include acanthosis nigricans, insulin resistance, and elevated testosterone levels. On the other hand, Type B syndrome mostly affects women and is frequently characterized by ovarian hyperandrogenism, uncontrolled high blood sugar, or related autoimmune diseases including scleroderma, Sjögren's syndrome, or systemic lupus erythematosus. Additionally, polycystic ovarian syndrome (PCOS) has been strongly linked to acanthosis nigricans, as affected individuals commonly exhibit both insulin resistance and elevated androgen levels.[28]

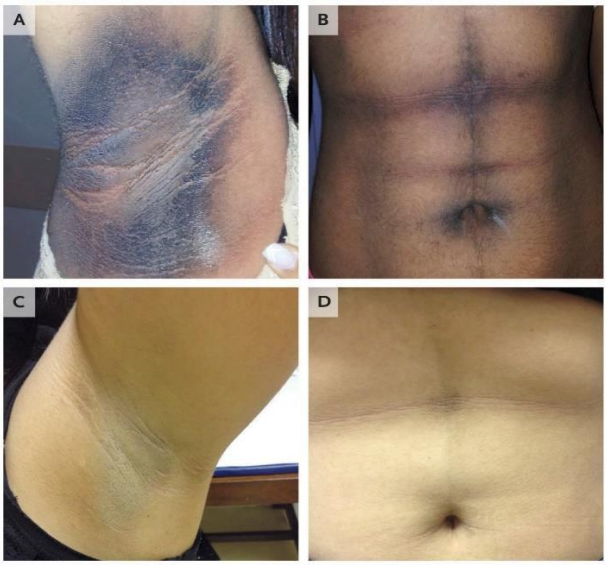


Figure 5: Acanthosis nigricans associated with endocrine dysfunction:[29]

Acral acanthotic anomaly: This localized variety of acanthosis nigricans mainly affects particular body parts, such as the the elbows, knees, knuckles, and the top of the foot. More often, those with darker skin tones exhibit it.[30,31]

Malignant AN is closely associated with various forms of internal malignancies, particularly gastrointestinal adenocarcinomas and cancers affecting the genitourinary system, such as

prostate, breast, and ovarian malignancies. While less common, lung cancer and lymphoma have also been sporadically linked to the condition. The onset of malignant acanthosis nigricans can vary—it may develop before, alongside, or after the diagnosis of an underlying malignancy. This form of acanthosis nigricans is characterized by its rapid progression and is frequently accompanied by additional dermatological manifestations, including skin tags, numerous seborrheic keratoses (which may signal the Leser-Trélat sign), and the distinct thickened ridges of tripe palms.[32,33]

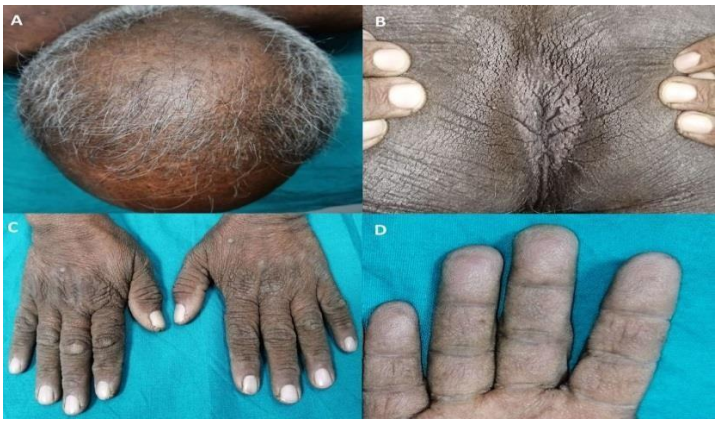


Figure 6: Malignant acanthosis nigricans syndrome[34]

Auto-immune AN: is linked to autoimmune illnesses that include systemic lupus erythematosus, Sjögren's syndrome, scleroderma, and Hashimoto's thyroiditis.[35]

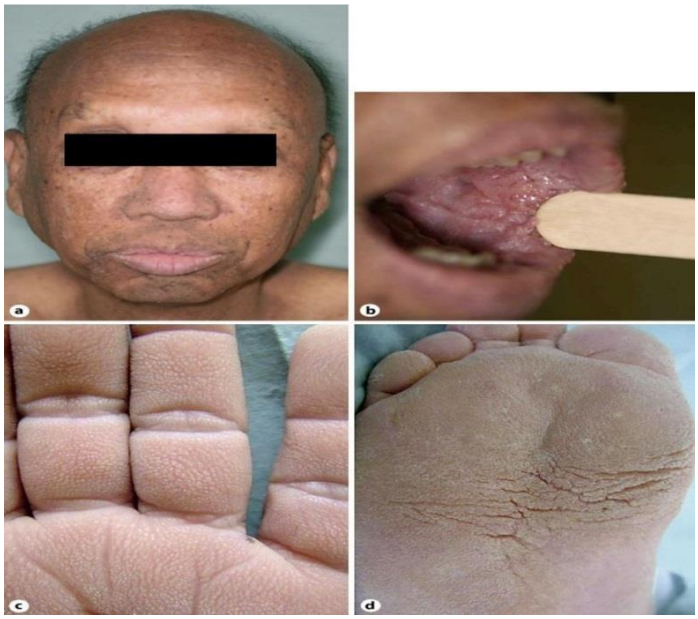


Figure 7: Auto-immune acanthosis nigricans[36]

Unilateral acanthosis nigricans: Another name for unilateral acanthosis nigricans is nevoid acanthosis nigricans. The transmission pattern is autosomal dominant, and it is extremely rare. One side of the body is affected. Throughout childhood, adolescence, or old life, lesions develop.[37,38]

HISTOPATHOLOGY OF ACANTHOSIS NIGRICANS

Histological analysis will reveal minor "hyperpigmentation," hyperkeratosis, and "papillomatosis." Epidermal thinning and an upward protrusion are common features of the dermal papillae. Usually, there is no inflammatory infiltration of the skin.

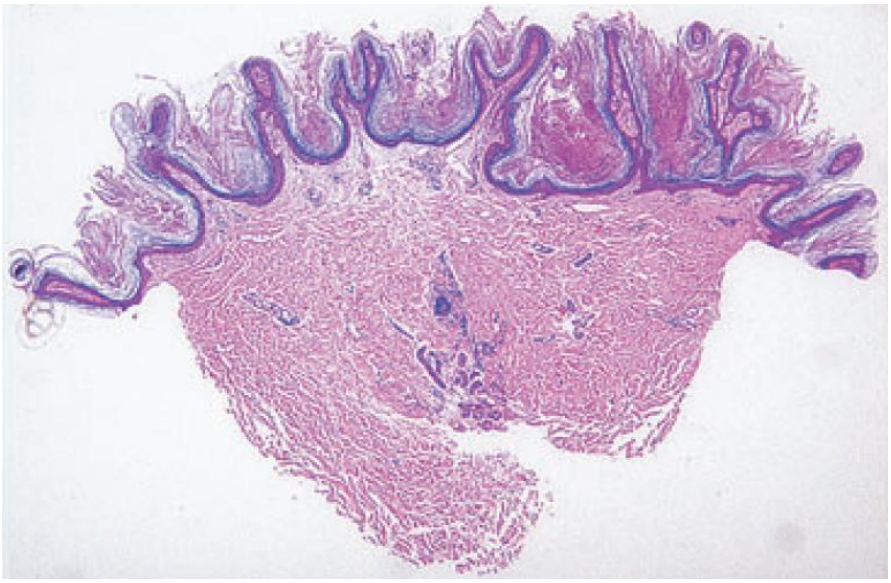


Figure 8: AN histology showing hyperkeratosis and papillomatosis.[39]

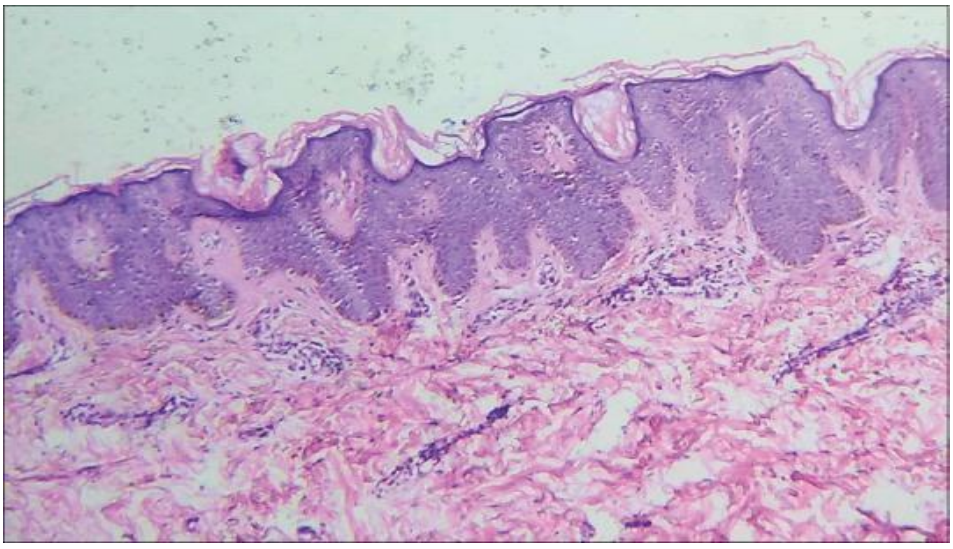


Figure 9: Facial AN histopathology reveals papillomatosis, acanthosis, moderate hyperkeratosis, and a rise in basal melanin.[39]

Dermascopy of Acanthosis Nigricans

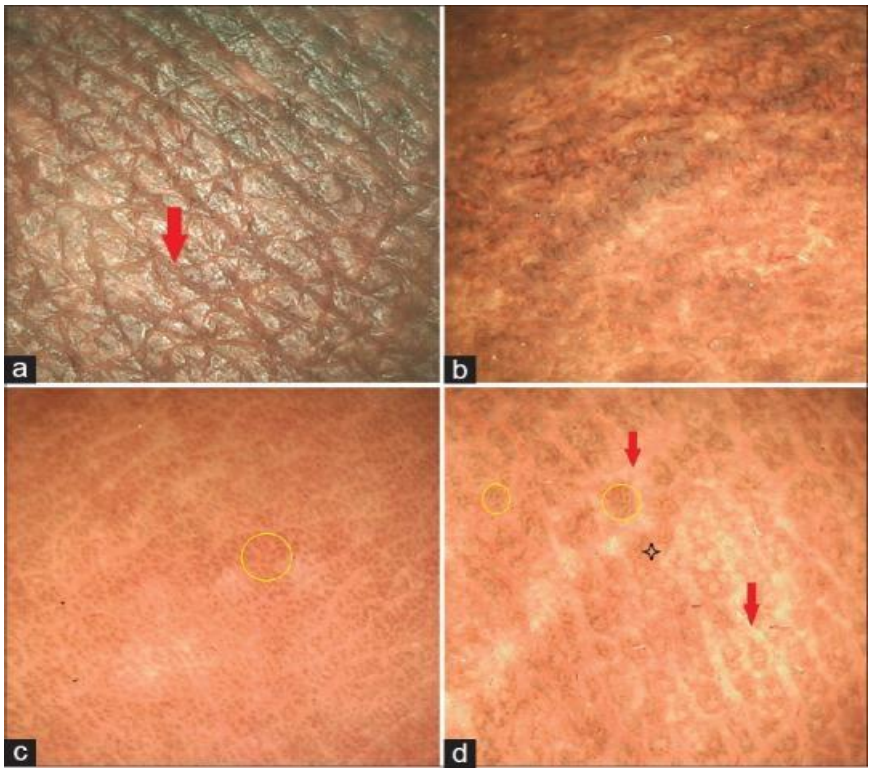


Figure 10 (a-d): A facial AN dermoscopy reveals hyperpigmented spots in the crista cutis (yellow circle), sulcus cutis (red arrow) & linear crista cutis (black star)[40]

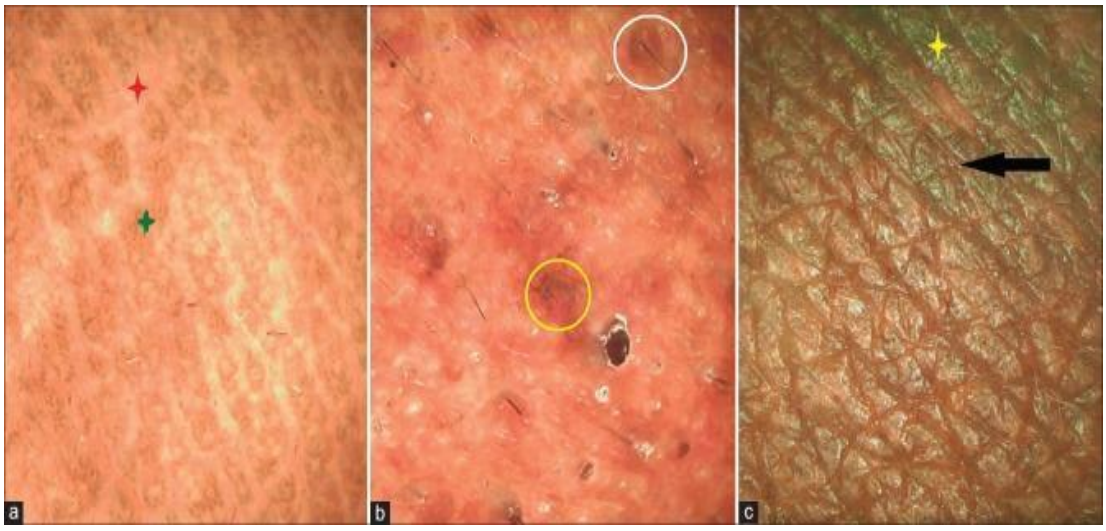


Figure 11 (a-c): Dermoscopy of Facial AN – (a) **Mild:** Characterized by uneven brown globules, perifollicular pigmentation, follicular plugging, and a weak sulci pattern.

(b) **Moderate:** Features more pronounced sulci with larger brown globules, as well as noticeable perifollicular hyperpigmentation.

(c) **Severe:** Marked by deeply recessed sulci and distinctly elevated cristae, indicating advanced progression of the condition.[40]

TREATMENT MODALITIES

Acanthosis nigricans is not amenable to treatment. By treating the underlying reason, insulin resistance, it could eventually go away. Blood glucose control with diet and exercise often reduces symptoms. Less severe cases of skin pigmentation can be reduced using topical fade creams. Malignant AN may resolve if the underlying tumor is successfully removed.[41,42]

Treating the underlying illness is the goal of treatment. The majority of individuals have the procedure done purely for aesthetic reasons. Losing weight and improving insulin resistance can lessen the severity of hyperkeratotic lesions in certain people. Pharmacological treatments for acanthosis nigricans associated with IR include rosiglitazone & metformin, which act as insulin sensitizers.[43]

All triggering agents and drugs must be terminated. The goal should be to reduce the lipid profile. Evidence indicates that the consumption of fish with niacin may be beneficial.

Topical retinoids, such as "topical tretinoin 0.1% or a combination of tretinoin 0.05% and 12% ammonium lactate," and "podophyllin," are examples of keratolytics that dermatologists occasionally prescribe.[44,45] Topical vitamin D analogs, such as ―calcipotriol (calcipotriene)‖ 0.005%, function by reducing ―keratinocyte proliferation‖ & enhancing the condition of AN lesions.[46] These treatments have varying degrees of effectiveness. Etetinate and metformin are other medications that have been explored. According to one study, octreotide considerably helped an insulin-resistant diabetic.[47]

By improving inflammatory conditions and "insulin sensitivity," melatonin could alleviate cutaneous symptoms in overweight individuals with AN.[48]

A variety of cosmetic procedures have been tried: "chemical peels, dermabrasion, and Alexandrite laser". [49] Surgical excision is an essential treatment for malignant lesions.[50]

Treatment ladder

1st line - Topical retinoids have the potential for minimizing hyperkeratosis.

2nd line: By lessening hyperkeratosis, topical α-hydroxyacids and keratolytics like salicylic acid might improve appearance.

3rd line: Oral isotretinoin - tried in numerous situations with varying degrees of efficacy.

Topical retinoids

Topical retinoids are widely recognized as 1st line treatment option for managing acne necrotica.[47] A study conducted on a cohort of 30 individuals revealed notable clinical improvement in cases of anorexia nervosa that had previously been resistant to treatment. This positive response was observed following a two-week regimen of 0.05% tretinoin application, suggesting its therapeutic potential in addressing dermatological complications associated with the condition[51]. Out of the 30 patients studied, 24 (80%) achieved full resolution of their condition within 16 weeks. However, maintaining these improvements required intermittent use of tretinoin, as symptoms reappeared within four weeks after discontinuing treatment. Histopathological analysis demonstrated that key features, such as hyperkeratosis and keratotic accumulations between the papillae, showed significant reduction upon biopsy after eight weeks of tretinoin therapy, highlighting its effectiveness in modifying tissue abnormalities.

The use of a 0.1% tretinoin topical formulation has been shown to produce favorable outcomes for acanthosis nigricans, as illustrated by two separate case reports. In one case, after approximately 10 days of treatment, the lesions on the neck of an female patient with alopecia areata completely disappeared. Additionally, within a two-week period, there was a notable improvement in the pigmentation and reduction of hyperkeratotic changes in her axillary regions.[52] In another case, a patient achieved complete resolution of acanthosis nigricans in the left axilla after applying a 0.1% tretinoin gel two times a day for two weeks, the untreated rt axilla, which was used as a control, showed no improvement.[44]

Two studies utilizing adapalene gel for pediatric acne vulgaris exhibited inconsistent outcomes.[53,54] The darkening of skin on one side of the neck of 16 Thai children with acanthosis nigricans was reduced after using 0.1% adapalene, according to a randomized controlled trial. There was little to no skin irritation, and the change in epidermal keratinization was thought to be the cause of the therapeutic effect.[53] A comparative study conducted in India discovered that 16 pediatric patients with acne vulgaris who received 0.1% adapalene gel noted a reduction in their mean skin color ratio, which is 60.7%±28.5%. At weeks two and four, the treatment side showed a considerably lower mean skin color ratio than the not treated side, indicating considerable improvement.[54]

Additionally, AN may be effectively treated with an array of therapies. According to one case study, acanthosis nigricans associated with obesity was remitted when 0.05% tretinoin cream and 12% ammonium lactate cream were used together.[45]

A triple-combination cream depigmenting regimen was shown to be beneficial in a reported case of idiopathic acanthosis nigricans. This formulation, which was administered overnight in addition to daily sunscreen protection, contained 0.05% tretinoin, 0.01% fluocinolone acetonide and 4% hydroquinone. Remarkable improvements were observed within a month,

demonstrating the potential of this treatment strategy in addressing pigmentation and textural irregularities associated with the condition.[55]

Topical vitamin D derivatives

Calcipotriene, a synthetic vitamin D analog, serves as an alternative topical therapy for acanthosis nigricans. By raising intracellular calcium and cyclic GMP concentrations within keratinocytes, it is believed to prevent excessive keratinocyte proliferation while fostering cellular differentiation, enhancing the texture and look of skin.[47] Lowering keratinocyte levels could help lessen the skin-related impact of insulin.[43] An obese man's flexural areas with mixed-type acanthosis nigricans improved following three months of twice-daily administration of 0.005% calcipotriol cream, according to a published case report.[47,56] Another case study found that an obese female with alopecia areata experienced an obvious reduction in her skin lesions after taking calcipotriol ointment two times per day for three months.[57] Gregoriou et al. highlighted calcipotriol as a reliable therapeutic option for acanthosis nigricans, demonstrating its safety, efficacy, and high tolerability. This treatment is particularly valuable when specific etiological medications are either inaccessible or unavailable, providing an alternative approach for managing the condition.[46,47]

Chemical peels

Although superficial chemical peels qualify as cosmetic, they are a somewhat secure and efficient alternative therapy for AN. A chemical exfoliant termed trichloroacetic acid (TCA) damages the epidermis and then causes it to repair and rejuvenate.[47] TCA causes skin proteins to coagulate and precipitate since it is a caustic agent, which leads to epidermal necrosis. After this damage, re-epithelialization and improved skin texture result from inflammation and the start of wound healing.[47] In an initial research, Zayed et al. reported that six female

individuals who received trichloroacetic acid peels had a reduction in acanthosis nigricans. Hyperpigmentation, thickness, and general appearance were all shown to be improved. [58]TCA offers numerous advantages: it is secure, readily accessible, cost-effective, and simple to prepare. Moreover, TCA is a stable substance characterized by established precipitation, absorption, and peel depth, facilitating straightforward assessment of its endpoint exfoliation.[47]

ORAL THERAPY

Oral retinoids

Oral retinoids, including isotretinoin and acitretin, may serve as viable therapeutic alternatives for AN. Nonetheless, enhancement necessitates substantial dosages and prolonged treatments, with recurrences documented in the literature.[9,18,47] The normalization of epithelial proliferation and differentiation is one of the speculated mechanisms of action for these medications.[47,59] Isotretinoin (3 mg/kg/day) has been effective in treating extensive AN associated with obesity; nevertheless, relapse happened when the treatment was withdrawn.[60] After using 80 mg of isotretinoin daily for two months, another patient reported a 90% improvement in palmar acanthosis nigricans and a 50% improvement in axillary AN. Following a year of progressively reducing the dosage until the cumulative intake exceeded 30 grams, the patient's skin lesions reappeared; however, a significant improvement was noted after starting a 1000 mg bi-daily metformin regimen.[61] After starting oral isotretinoin therapy for nodulocystic acne, a girl with Costello syndrome exhibited a significant reduction in acne nodules on the back of her hands and neck. [62]

The literature contains limited findings on the treatment of acanthosis nigricans (AN) with acitretin; yet, the available studies indicate successful outcomes in instances with syndromic and benign AN.[47] An 18-year-old man with generalized idiopathic anorexia nervosa improved

significantly after taking acitretin for 45 days at a dose of 0.8 mg/kg (50 mg) given two times a day. After beginning maintenance treatment with 25 mg of acitretin once a day for two months, the lesions returned. After that, 0.1% retinoic acid was used topically to dissolve the lesions.[63] The prolonged ultimate elimination half-life and decreased lipophilicity of acitretin may limit its use and increase the risk of an early recurrence.[63] Due to acitretin's extended final elimination half-life and reduced lipophilicity, its use may be constrained, resulting in a risk of early recurrence.[47,64] A published case report described the effective management of acanthosis nigricans in a patient with extensive lipodystrophy using oral etretinate, a 2nd generation systemic retinoid, leading to a successful therapeutic outcome.

Metformin with rosiglitazone

The traditional insulin-sensitizing drugs, such as metformin, can be utilized for the treatment of AN linked to IR. Metformin enhances peripheral insulin sensitivity, leading to decreased glucose production, hyperinsulinemia, body weight, and fat mass, while simultaneously improving insulin sensitivity in individuals with insulin resistance and anorexia nervosa.[18,47,65,66] A recent clinical trial in India administered 500 mg of metformin thrice daily for 3 months to 40 patients with anorexia nervosa and IR, as determined by the HOMA-IR. Metformin-treated individuals showed statistically and clinically significant reduction in AN of the neck and axilla, but not in acanthosis nigricans of the knuckles, fingers, or elbows, when compared to 20 control patients who received a placebo. In a case series, three obese individulas began receiving metformin while implementing adjustments to their diets. All of the patients had previously tried topical calcipotriol or corticosteroid treatments for AN without success. After a year, there were no relapses observed in any of the three patients, who all showed subjective improvement.[18,43,67]

For 12 weeks, a prospective, randomized, open-label trial assessed the effects of rosiglitazone and metformin in 27 insulin-resistant patients. Both drugs showed only slight reduction in AN thickness and texture, although rosiglitazone led to a more notable reduction in fasting insulin levels.[68] The duration of medication may influence the observation of clinical alterations in the skin, as metformin enhances both androgen levels and IR when administered for six months or longer.[65] Since metformin increases insulin resistance and testosterone levels when taken for six months or more, the length of treatment may affect the appearance of clinical changes in the skin.[65]

Alternative oral medications

The use of metformin and thiazolidinediones together , which enhance insulin sensitivity in muscles present in the periphery, has demonstrated favorable outcomes in individuals with AN.[69,70] Individuals diagnosed with HAIR-AN syndrome, characterized by hyperandrogenemia and insulin resistance, can be effectively managed through a combined therapeutic approach utilizing metformin and oral contraceptives. This treatment strategy helps regulate hormonal imbalances while addressing insulin sensitivity, contributing to overall symptom improvement.[4] It has also been demonstrated that TZD pioglitazone plus sitagliptin, a DPP4 inhibitor that boosts insulin production, can spontaneously improve acanthosis nigricans in a patient who lacks insulin.[71] Prolonged ocreotide use, a synthetic somatostatin analog, led to decrease in body weight and a sustained improvement in anorexia nervosa in a male patient who was extremely obese and had insulin resistance; these effects continued for six months after the drug was discontinued.[72]

Alternative treatments

Additionally, case studies have shown that oil from fish, and a combination regimen consisting of urea, salicylic acid, and a triple-combination depigmenting cream are effective

therapeutic agents for controlling acanthosis nigricans. In one case, even after six months of treatment, despite continuing niacin use, fish oil, which is high in omega-3 fatty acids, significantly reduced the dark pigmentation and smoothens the skin texture of a person with acanthosis nigricans and Diabetes in a lipodystrophic type.[9,73] Application of 20% podophyllin in alcohol has been reported to provide temporary relief from acanthosis nigricans lesions on the hands. However, before improvement was observed, the treatment initially triggered a localized reaction at the application site.[9,74] Other methods of therapy, including the use of topical urea and salicylic acid, have shown variable effectiveness in managing acanthosis nigricans, with outcomes differing across cases.[47]

The alexandrite laser is a good cosmetic therapy option for enhancing AN lesions. After seven sessions of long-pulsed (5 msec) alexandrite laser treatment spaced four to eight weeks apart, there was over 95% clearance in the left axilla.[49] It was assumed that by targeting the melanin in hair, this laser would improve the skin's pigmentation in the affected areas. . The use of an alexandrite laser to treat AN offers promise for the future, despite the fact that it is not as economical as alternative topical and oral therapies.

Counselling and lifestyle modification

The physicians' report indicates that the identification of AN prompted conversations on diabetes prevention, implying that this disorder may alter the dynamics of initial care interactions. Appearance of AN can affect clinicians' decisions to engage in discussions regarding type 2 diabetes risk reduction (e.g., by altering patient receptivity to lifestyle modification recommendations).

A relatively new research found characteristics that influence doctors' verdicts to incorporate overweight avoidance counselling during brief inital visits, potentially elucidating their

responses to conventional diabetes mellitus risk factors. Clinicians' verdicts about time provision and engagement in preemptive counselling were influenced by many steady and factors related to the situation, including patients' absence of motivation. The visible characteristics of acanthosis nigricans may affect patient motivation amidst competing demands during the brief interaction.

FRACTIONAL CO_2 LASERS

Laser resurfacing is a technique that employs targeted energy of particular wavelength to decrease thickness of the uppermost layers of the skin. It can be performed as a full ablation, where the entire treatment area is affected, or as a fractional procedure, which selectively ablates smaller sections while leaving adjacent regions untouched, typically forming a pattern of alternating treated and untreated zones.

CO2 Lasers generate energy at a highest wavelength of 10,600 nm, effectively targeting intracellular water for selective absorption. This interaction facilitates precise tissue ablation, making CO_2 lasers a widely used tool in dermatological and surgical procedures requiring controlled removal of skin layers or other biological tissues.[75] The epidermis absorbs this wavelength, effectively eliminating its outermost layers and initiating a regeneration process.[76] The heat damage beneath the ablation area triggers the contraction of collagen fibers, leading to structural remodeling within the dermis and contributing to tissue regeneration.[77] The collagen fibrils contract to provide the skin its tightening effect. In contrast to other laser types, including the ed Yag , CO_2 lasers produce increased thermal energy and improve the coagulation of small dermal blood vessels, which greatly reduces bleeding when huge skin regions are removed. Additionally, the heat produced by photocoagulation activates deeper dermal layers, speeding up re-epithelialization while ensuring a nearly sterile ablated surface.

In carbon dioxide lasers, the lasing medium is responsible for producing a highly focused, coherent, and monochromatic beam of light. In medical applications, this medium consists of a gas mixture containing CO_2, nitrogen, hydrogen, and helium, which generates infrared radiation at a peak wavelength of 10,600 nm. Water is a primary chromophore that absorbs electrons at this wavelength, allowing and enabling precise interaction with biological tissues.

Both the laser operator and the patient must wear appropriate protective eyewear to ensure safety during laser procedures. Moist gauze and opaque, photoprotective eye covers can be used to protect the patient's eyes. Meanwhile, the operator and all personnel involved are required to use laser-protective goggles specifically designed for 10,600 nm wavelengths. CO_2 laser goggles are typically transparent.

CO_2 laser resurfacing requires a qualified medical team, including a primary operator who may be a board-certified dermatologist, otolaryngologist, plastic surgeon, or oral surgeon. Alternatively, a clinician with specialized laser training may perform the procedure under physician supervision. Physician assistants and nurses proficient in laser-based cutaneous ablation can offer critical procedural support. Every healthcare provider involved must undergo rigorous laser safety training.

Beyond execution, the team is responsible for conducting pre-procedure evaluations, providing patient counseling, and ensuring comprehensive follow-up following a procedure. A detailed patient history and physical examination are essential components of the assessment process. Determining the patient's Fitzpatrick skin type is fundamental to evaluating risks, predicting laser treatment efficacy, and selecting the optimal technique for energy delivery.

During pre-procedure consultations, clinicians must offer patients a realistic understanding of expected results and necessary pre- and post-treatment care. Patients should also be fully informed about any potential complications following the procedure, ensuring thorough preparation and informed decision-making.

To minimize the risk of severe post-procedural herpetic outbreaks that could result in significant scarring, prophylactic antiviral therapy should be initiated before perioral skin resurfacing. Treatment can begin either the day prior or on the morning of the procedure. A recommended regimen includes valacyclovir 500 mg taken orally twice daily for a duration of 14 days.[78]

A suitable approach to pain management must be determined. For full facial CO_2 laser resurfacing, general or dissociative anesthesia is typically utilized. In cases of partial or localized resurfacing, sequential applications of topical anesthetics, followed by either local anesthetic infiltration or a nerve block, can effectively maintain patient comfort. Depending on the treatment area, protective eyewear options such as occlusive inserts, glasses, or laser goggles should be used, with careful attention given to the potential for light reflection onto the cornea.[79,80]

Currently, antiviral therapy is started for all individuals considering many people might have been exposed to the HSV. By taking this precaution, the chance of infection-related problems is greatly decreased. Following the procedure, commonly prescribed antibiotics include cefadroxil, dicloxacillin, doxycycline, or ciprofloxacin to further support recovery and infection control.[81] Patients undergoing antifungal treatment, including fluconazole, tend to have shorter healing times. As a preventive measure, antifungal medication is commonly administered on the same day as laser therapy to support recovery.

A pulse length of less than 1 millisecond and a fluence of 5 J/cm2 are used to achieve efficient skin ablation with the least amount of heat damage.[82] Enough thermal relaxation of the skin can be assured by a brief pulse duration. In accordance with the guidelines provided by the individual laser device manufacturers, the precise penetration depth and pulse length should be customized to the patient's particular problems and skin type.

The skin typically undergoes re-epithelialization within 6 to 7 days following treatment. During the recovery phase, the exposed skin may develop crusting and release a serous discharge in the affected area.[83] Swelling, tenderness, and redness can persist for one to two weeks after treatment, with the inflammatory response typically diminishing over the following six weeks. However, in some cases, this inflammation may continue for up to six months after the procedure.

Beginning with erythema, desquamation, and skin irritation, the typical post-procedural progression might last up to three months after the procedure. The development of milia and acneiform lesions in the afflicted area are examples of short-term therapy side effects. Patients with a history of documented herpes simplex virus infection may need to receive preventive valacyclovir treatment due to the possibility of HSV reactivation. Pigmentation changes, including hyperpigmentation and hypopigmentation, are common. Fortunately, hyperpigmentation is the more common result and is more likely to resolve on its own than hypopigmentation.[78]

Pigmentation changes, including hyperpigmentation and hypopigmentation, are common.

Bleaching agents and chemical peels can be employed to diminish the visibility of dark discolouration, either preventively or as a treatment. Because of the degree of heat damage and subsequent inflammation, hypopigmentation happens more often with CO2 lasers than

with other laser modalities; this effect can be difficult to control. Strong pulsed light, blue laser treatments, fractionated CO2 laser therapy, and UV light exposure are common methods for treating hypopigmentation. [84]

Chemical peels application

Careful patient assessment and the efficient implementation of a thorough treatment plan can yield dependable, secure, & fulfilling results during a chemical peel process.

Many pigmentary skin conditions support chemical peeling as a skin resurfacing technique.[85–89] Chemical face peels are frequently divided into three categories based on their effects and depth of penetration: superficial, medium and deep.

Retinoic acid peel

Clinical enhancement correlates with the extent of penetration. Superficial peels need successive treatment to get the desired outcome. In comparison to previous peels, the healing process is expedited and deemed safer. Medium and deep peels are conducted in one session, resulting in an extended epithelization phase, which increases the risk of infection. A 2001 case study involving 15 patients examined clinical and histological changes in the skin. The procedures were conducted bi-monthly at doses ranging from 1% to 5%. The research demonstrated favourable clinical and histological outcomes when the peel was applied for 6 to 8 hours on individuals types I to IV, resulting in a rapid decrease in pigmentation.[90]

Another study by Khunger et al., indicated that a 1% tretinoin peel was likely as efficient as

the usual 70% GA peel in diminishing pigmentation associated with melasma in persons with dark skin.[91]

Retinoic acid applied once a day to the skin causes melanin dispersion and changes to the epidermis. For those with melasma, a superficial peel called a retinoin peel may produce comparable results and provide the advantages of quicker and less invasive treatment. Furthermore, the daily application of 0.1% tretinoin cream took 24 weeks to get comparable results, whereas the 1% tretinoin peel produced advantages in a relatively shorter amount of time—12 weeks.

Few studies evaluate the drug concentration maintained in the various skin layers in vivo, despite the results on the efficacy and safety of high-concentration tretinoin peels. Now, an experimental study uses cream and a solution made of equal parts ethanol and propylene glycol to assess the in vitro penetration of tretinoin at dosages of 0.25%, 1%, and 5%. When given in a 5% solution, there was improved drug retention with regard to the viable epidermis.[92,93]

But there is still disagreement over the effectiveness of retinoin peels at a high concentration

in comparison to the continued usage of low dosages. According to a 2015 study, the stratum corneum retained the majority of the tretinoin peel.[94] Retinoic acid peel will be retained in the st corneum. The fact that tretinoin peel is retained superficially indicates that its primary effect is to exfoliate the stratum corneum; it has no effect on the retinoic acid receptors of living keratinocytes in the deep layers of the skin. Therefore, the daily application of tretinoin cream for melasma and photoaging may have different outcomes than sequential peels.

Peeling works better for people with diffuse photodamage and broad actinic keratosis than the existing methods for treating isolated lesions.

Glycolic acid peels

Alpha-hydroxy peels are a well-established and commonly utilized dermatological treatment that has been used for many years. They typically involve superficial or medium-depth peels and have minimal recovery time. They give both therapeutic and cosmetic advantages when applied to the skin. The main AHA peel ingredient is glycolic acid (GA), which is obtained from cane.[95]

Peels containing glycolic acid (GA) have keratolytic, antioxidant, and anti-inflammatory effects. GA affects the corneocytes by promoting its degradation and decreasing cohesion, resulting in peeling. The potency of the peel is dictated by the acid concentration, the medium used for its application, the quantity of acid utilized, and the procedure implemented.[96]

―Fabbrocini et al. classify 70% concentrations of glycolic acid as superficial when applied for 2 to 5 minutes or as medium depth when applied for 3 to 15 minutes‖. Icthymia et al. utilized this concentration to cure AN.[97,98]

Ferulic acid peels

Ferulic acid represents a novel enhancement to the treatment options available with chemical peels. It is a potent phenolic antioxidant that is found abundantly and in significant concentrations in plants. Research has been conducted on its application as a skin-lightening agent, based on its capacity to inhibit the activity of the enzyme tyrosinase, which is a limiting factor in the melanogenic.[99]

Consequently, favorable outcomes are anticipated in pigmentary illnesses such as melasma and constitutional forms of post-inflammatory hyperpigmentation, where sun exposure enhances the melanogenic capacity of keratinocytes.[99]

Ferulac peel is a superficial chemical exfoliant composed of ferulic acid, phloretin, fruit acids, and retinoids. Ferulic acid was extracted from Ferula foetida. It is frequently present in commelinid plants, grasses, cereals, vegetables, flowers, fruits, leaves, beans, coffee seeds, peanuts, and nuts.[100,101]

Similar to various other phenolic compounds, FA exhibits significant antioxidant activity against free radicals. It demonstrates significant anti-inflammatory properties. FA is an effective absorber of ultraviolet (UV) photons, exhibiting consistent absorption rates at both acidic and neutral pH levels. It provides significant protection to the skin against UVB-induced erythema in a time-dependent way. Consequently, it enhances protection against UV rays.[102,103]

Ferulic acid's structure resembles that of tyrosine, and as a non-competitive inhibitor of tyrosinase, it exhibits depigmenting characteristics. Phloretin is a potent antioxidant that interacts with the lipids of the stratum corneum, facilitating enhanced penetration of peels and other active components. Moreover, phloretin inhibits matrix metalloproteinase-1, thereby reducing the breakdown of collagen and elastin.[104]

All components in the Ferulac peel are encased in nanosomes, little vesicles measuring 50 to 200 nm that are fully assimilable by the body. The nanosomes possess resurfacing, anti-inflammatory, antibacterial, clarifying, and sebum-regulating characteristics, and due to their size, they may selectively deliver active substances to the right skin layers.

Indications

The primary prescription for this peel is photoaging, with supplementary advantages for melasma, acne, and rosacea. It effectively diminishes indicators of photoaging, including fine wrinkles, promotes uniform skin tone by mitigating hyperpigmentation, and restores skin

to its natural luminosity by boosting cellular turnover. The overall texture of the skin is said to enhance, and the therapy elevates hydration by augmenting ceramide levels in the skin to mitigate water loss. Treatment for people with rosacea and acne can decrease sebum production, enhance scar appearance, and minimize pore size.

Contraindications[105]

Active infection

Open wound

Dermatitis

Sunburn or recent suntan

Impaired healing

Excessively dry skin

Unrealistic patient expectations

Pregnancy/lactation

Body dysmorphic disorder

Complications

Very rare following Ferulac peel. There may be mild discomfort or dryness after the peel.

SCORING IN ACATHOSIS NIGRICANS:

ACANTHOSIS NIGRICANS AREA AND SEVERITY INDEX (ANASI) SCORE.[106]

It is a clinical scoring system used to objectively assess the severity and extent of Acanthosis Nigricans

Components of ANASI Scoring:

1. **Area(A):**

- The percentage of skin involved in regions typically affected by AN, especially the neck.

- Scored from 0 to 5, depending on the extent of involvement.

2. **Thickness(T):**

- Clinical impression of how thick or velvety the skin is.
- Score: 0 (normal) to 4 (severe).

3. **Pigmentation(P):**

- Intensity of hyperpigmentation in the lesion.
- Score: 0 (normal) to 4 (severe).

4. **Texture(Te):**

- Assessment of the skin's roughness or rugosity.
- Score : 0 (normal) to 4 (severe).

The figure depicts the procedure for quantifying the size of both total and affected regions of the neck. The total area of the neck side was determined by multiplying the measurement from A to B by the measurement from B to C.

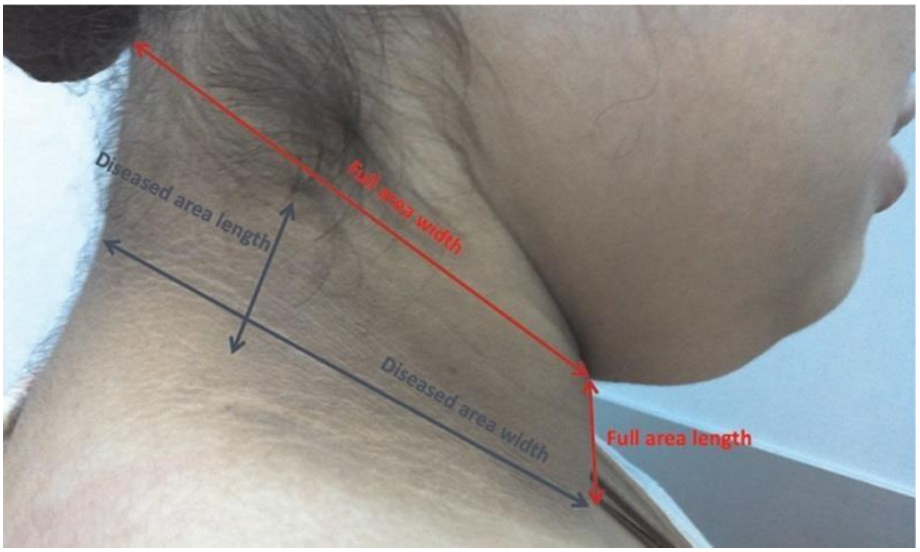


Figure 12: Calculating area involvement in ANASI score

By multiplying its greatest length by its greatest width, the affected area is determined.

Figure 2 was utilized to ascertain the numerical values for area, pigmentation, and thickness indices, hence facilitating the calculation of the overall score.

Figure 13: ANASI score for assessment of right and left sides of the neck.

BURKE'S ACANTHOSIS NIGRICANS SCORING SYSTEM (BURKE SCALE)[107]

Most commonly used in epidemiological and clinical studies, especially in children and adolescents.

MATERIALS AND METHODS

MATERIALS AND METHODS

Source of study: This study was conducted in outpatient clinic of Dermatology, Venereology and Leprosy in R L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar from May 2023 to November 2024.

Study design: Randomized controlled trial (RCT)

Sample size calculation:

Sample size was estimated by using the difference in textural improvement % of 68.7% that if group A with fractional Co2 laser of pseudo acanthosis nigricans from recent article Comparative study between fractional carbon dioxide laser versus retinoic acid chemical peel in the treatment of acanthosis nigricans study by Ahmed Fathy State et. al. and fair improvement % of 33.3% in group B with ferulic acid 12% peel in peri orbital hyperpigmentation a study done by Surabhi Dayal.

So with 95% Confidence interval, Alpha error 5% and Power value of 80% - the estimated total sample size for the study was 60 and the sample size per group is 30.

Hypothetical proportion of group A with exposure = 68.7%

Hypothetical proportion of group B with exposure = 33.3%

Required Sample size for each group = 30.

Total sample size for study = 60.

$$N_1 = \left\{ z_{1-\alpha/2} * \sqrt{\bar{p} * \bar{q} * (1 + \frac{1}{k})} + z_{1-\beta} * \sqrt{p_1 * q_1 + (\frac{p_2 * q_2}{k})} \right\}^2 / \Delta^2$$

$$q_1 = 1 - p_1$$

$$q_2 = 1 - p_2$$

$$\bar{p} = \frac{p_1 + kp_2}{1 + K}$$

$$\bar{q} = 1 - \bar{p}$$

$$N_1 = \left\{ 1.96 * \sqrt{0.51 * 0.49 * (1 + \frac{1}{1})} + 0.84 * \sqrt{0.687 * 0.313 + (\frac{0.333 * 0.667}{1})} \right\}^2 / 0.354^2$$

$$N_1 = 30$$

$$N_2 = K * N_1 = 30$$

p_1, p_2 = proportion (incidence) of groups #1 and #2
$\Delta = |p_2 - p_1|$ = absolute difference between two proportions
n_1 = sample size for group #1
n_2 = sample size for group #2
α = probability of type I error (usually 0.05)
β = probability of type II error (usually 0.2)
z = critical Z value for a given α or β
K = ratio of sample size for group #2 to group #1

Sample size: Total sample size for the study is 60.

Sample size per group is 30.

30 participants will be treated with fractional co2 laser and other 30 participants will be treated with ferulic acid 12.0% followed by 8.0% peel.

Inclusion criteria:

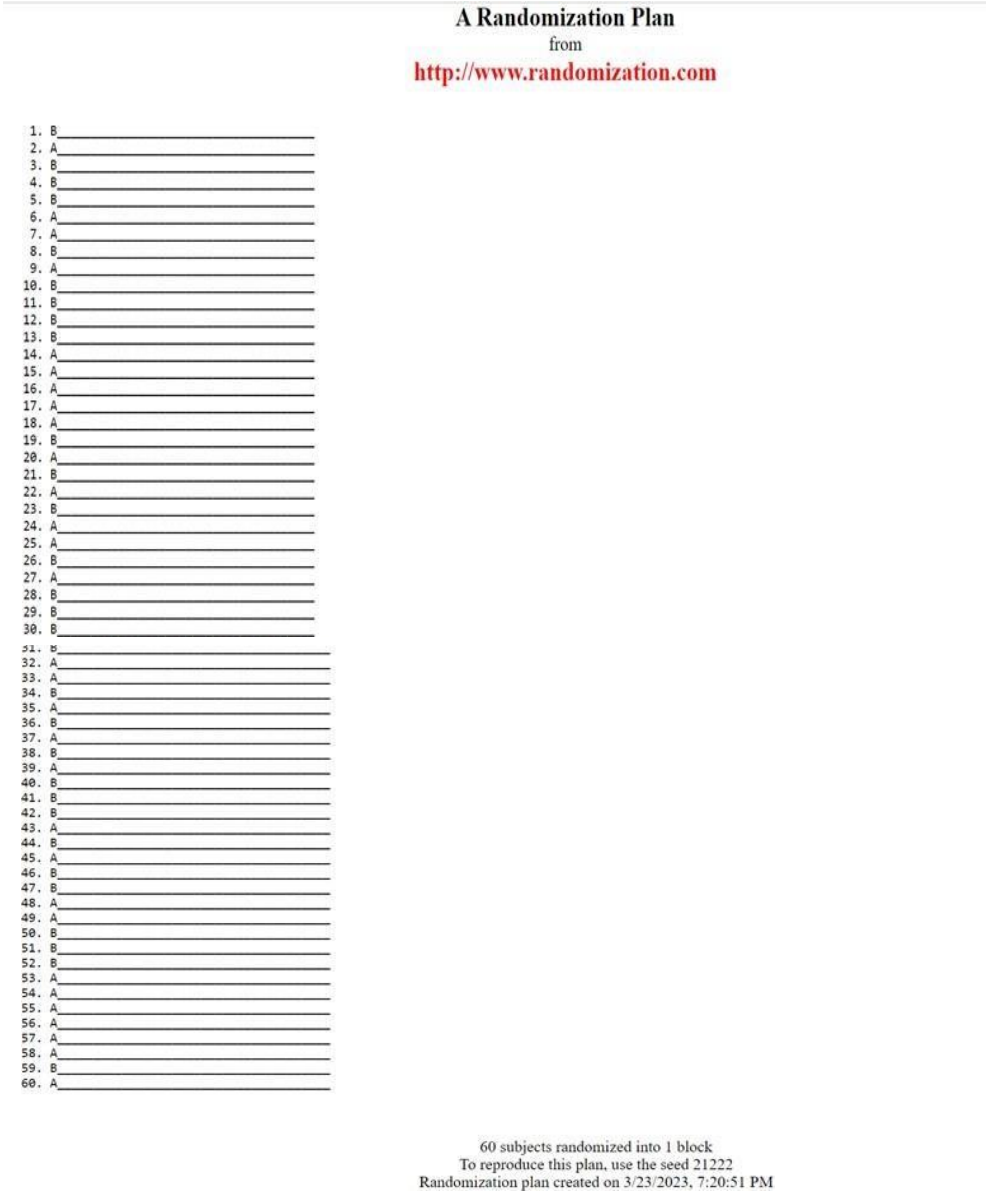
- All the patients of both sexes with age >18 years with neck acanthosis nigricans will be included in the study.

Exclusion criteria:

- Patients with recent history of any topical treatment and any procedures for neck acanthosis nigricans at least 1month before enrolment into the study.
- Patients who received systemic retinoids six months prior to the start of study.
- Patients with keloidal tendency.

- Pregnant or lactating women.

Randomization: Computer generated block randomization.



A Randomization Plan
from
http://www.randomization.com

1. B
2. A
3. B
4. B
5. B
6. A
7. A
8. B
9. A
10. B
11. B
12. B
13. B
14. A
15. A
16. A
17. A
18. A
19. B
20. A
21. B
22. A
23. B
24. A
25. A
26. B
27. A
28. B
29. B
30. B
31. B
32. A
33. A
34. B
35. A
36. B
37. A
38. B
39. A
40. B
41. B
42. B
43. A
44. B
45. A
46. B
47. B
48. A
49. A
50. B
51. B
52. B
53. A
54. A
55. A
56. A
57. A
58. A
59. B
60. A

60 subjects randomized into 1 block
To reproduce this plan, use the seed 21222
Randomization plan created on 3/23/2023, 7:20:51 PM

METHODS OF DATA COLLECTION:

All patients who satisfied the inclusion criteria were divided into two groups as follows:

Group A: Participants were treated with Fractional CO_2 Laser over the AN site. This was repeated at intervals of 2 weeks until complete disappearance, reduced pigmentation and texture or for a maximum of four sessions.

Group B: Participants were treated with ferulic acid 12% peel followed by ferulic acid 8% peel over the neck AN site. This was repeated at intervals of 2 weeks until complete disappearance, reduced pigmentation and texture or for a maximum of four sessions.

Group A Participants: A topical anaesthetic containing a mixture of lidocaine 2.5% w/w and prilocaine 2.5% w/w in a cream base was applied for 1 hour under occlusion on the area to be treated. After satisfactory anaesthesia was achieved, eyes were covered with eye shields. Fractional CO_2 LASER was then delivered to the neck at a fluence of low power (10 W), duration (1 ms), short distance (1 mm), with two passes on the affected area. Post-procedurally, ice packs for cooling were immediately applied after laser sessions. This procedure was repeated at intervals of 2 weeks until complete disappearance or reduced pigmentation, textural improvement for a maximum of four sessions.

Group B Participants: Pre-procedurally, neck skin was cleaned with a cotton pad. Patients were subjected to 2–3 coats of Ferulac Peel Classic solution (Ferulic acid 12% + 5% Phloretin) over the area to be treated. After the solution dried and appeared as a light white mask, 2 coats of Ferulac Peel Plus (Ferulic acid 8%, Phloretin 5%, Malic acid 5%, Citric acid 5%, Lactic acid 5%, Retinol 0.2%) were applied and allowed to dry. After approximately 12 hours, the patients washed the area with mild cleansing gel. Sunscreen was advised for one week after peeling. Each patient underwent four sessions at 2-week intervals.

The severity and area involved in Acanthosis nigricans were assessed using the ANASI score system.[8]

AREA (A) INDEX

0	1	2	3	4	5
NO INVOLVEMENT	<10%	10-29%	30-49%	50-69%	70-100%

SEVERITY INDEX

Pigmentation (P)

0	1	2	3	4
absent	mild	Moderate	marked	severe

Thickness (T)

0	1	2	3	4
none	mild	moderate	marked	severe

Right neck side	Left neck side
P + T = × A = Right ANASI	P + T = × A = Left ANASI

Participants were required to undergo serial photography at baseline and at subsequent sittings.

- All series images were taken with the same lighting and positioning.
- A third, blind observer evaluated the serial photos independently.
- Using the Global Photograph Assessment (GPA) scale, the third observer graded the therapy modality's effectiveness.
- At the conclusion of each session, participants' perceptions of their level of satisfaction with the treatment modality were recorded using the Visual Analogue Scale, which has a score range of 0 to 10.
- The Visual Discomfort Scale (scoring from 0 to 10) was used to record the subjective discomfort of the participants, such as pain, burning sensation, and any other peculiar discomforts following the procedure at each sitting.

STATISTICAL ANALYSIS

The data was collected using Microsoft 365 Excel and analyzed using SPSS v27.0. The normality test (Shapiro-Wilk Test) was performed to analyze the data, and the results were expressed as frequency with percentage and mean with standard deviation or median with interquartile range. Association between categorical variables was assessed using Chi-square test or Fisher's exact test. Association between quantitative variables was assessed using independent t test. All the statistical analyses were carried out at a 5% level of significance, and results with the P value < 0.05 were considered statistically significant.

RESULTS

RESULTS

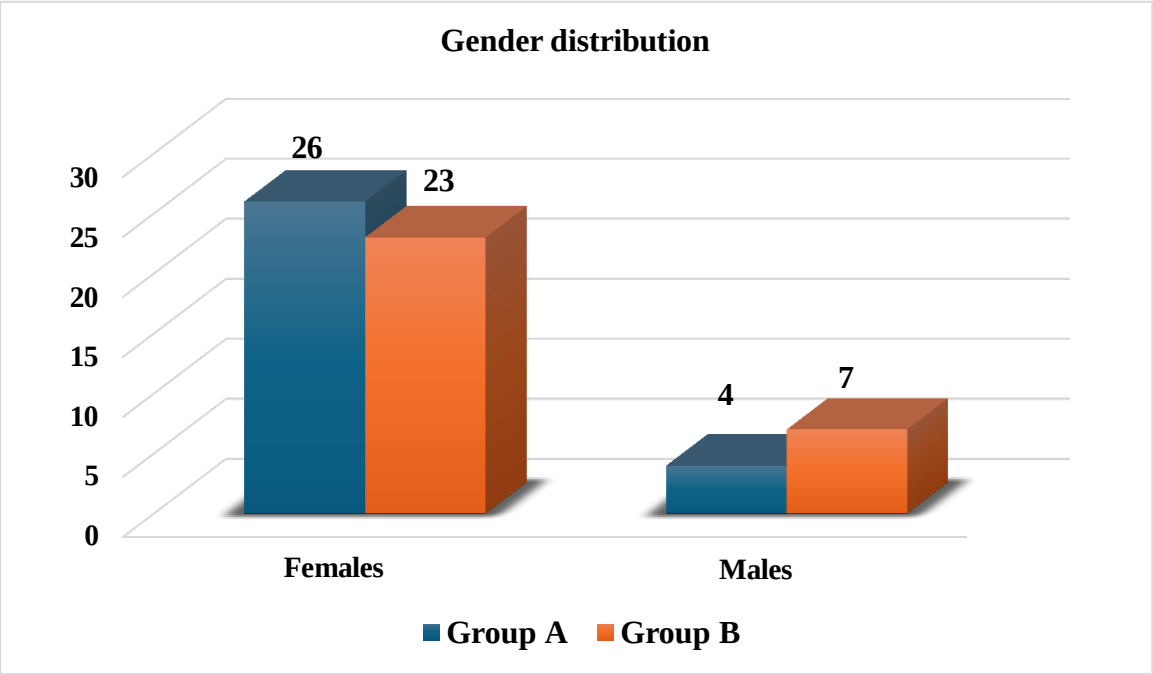
Table 1: Baseline characteristics (Age and gender) & clinical severity of lesions.

		Group A	Group B	t/ Chi-square value	P value
Age	Mean ± SD	36.13 ± 7.56	32.50 ± 8.64	1.731	0.089
	Range	21 – 45 years	21 – 45 years		
Gender	Females	26 (86.7)	23 (76.7)	1.002	0.317
	Males	4 (13.3)	7 (23.3)		
Baseline severity of lesions	Mild	8 (26.7)	5 (16.7)	3.307	0.191
	Moderate	10 (33.3)	17 (56.7)		
	Severe	12 (40.0)	8 (26.7)		

In this study the mean age of the study participants in group A was 36.13 ± 7.56 years and that of group B was 32.50 ± 8.64 years. There is no significant difference in the distribution of age between the two groups (p = 0.089). In this study both males and females were almost equally distributed (p = 0.317) between the two groups with 26 (86.7%) females in group A and 23 females in group B (76.7%). There were 4 males (13.3%) in group A and 7 males (23.3%) in group B in this study.

Considering the baseline severity of the lesions, in group A 12 (40.0%) subjects had severe lesions, 10 (33.3%) had moderate lesions and 8 (26.7%) had mild lesions in this study. In group B, 17 (56.7%) subjects had moderate lesions, 8 (26.7%) had severe lesions and 5 (16.7%) had mild lesions. This difference in severity of lesions at the baseline was not statistically significant.

Graph 1: Graph representing gender distribution of study participants



Graph 2: Graph showing Baseline severity of lesions

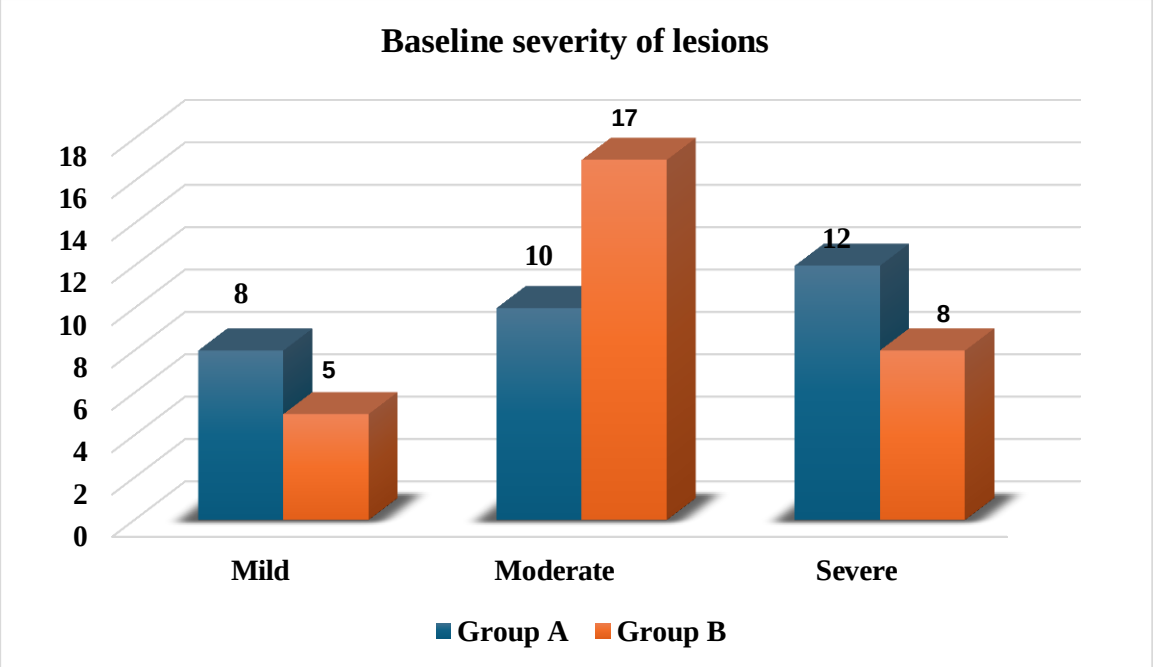


Table 2: Severity of lesions at various intervals

Severity of lesions		Group A	Group B	t/ Chi-square value	P value
2 weeks	Mild	8 (26.7)	5 (16.7)	3.307	0.191
	Moderate	10 (33.3)	17 (56.7)		
	Severe	12 (40.0)	8 (26.7)		
4 weeks	Mild	9 (30.0)	7 (23.3)	0.642	0.725
	Moderate	12 (40.0)	15 (50.0)		
	Severe	9 (30.0)	8 (26.7)		
6 weeks	Mild	11 (36.7)	9 (30.0)	0.627	0.731
	Moderate	11 (36.7)	14 (46.7)		
	Severe	8 (26.7)	7 (23.3)		
8 weeks	Mild	12 (40.0)	15 (50.0)	2.133	0.407
	Moderate	14 (46.7)	14 (46.7)		
	Severe	4 (13.3)	1 (3.3)		

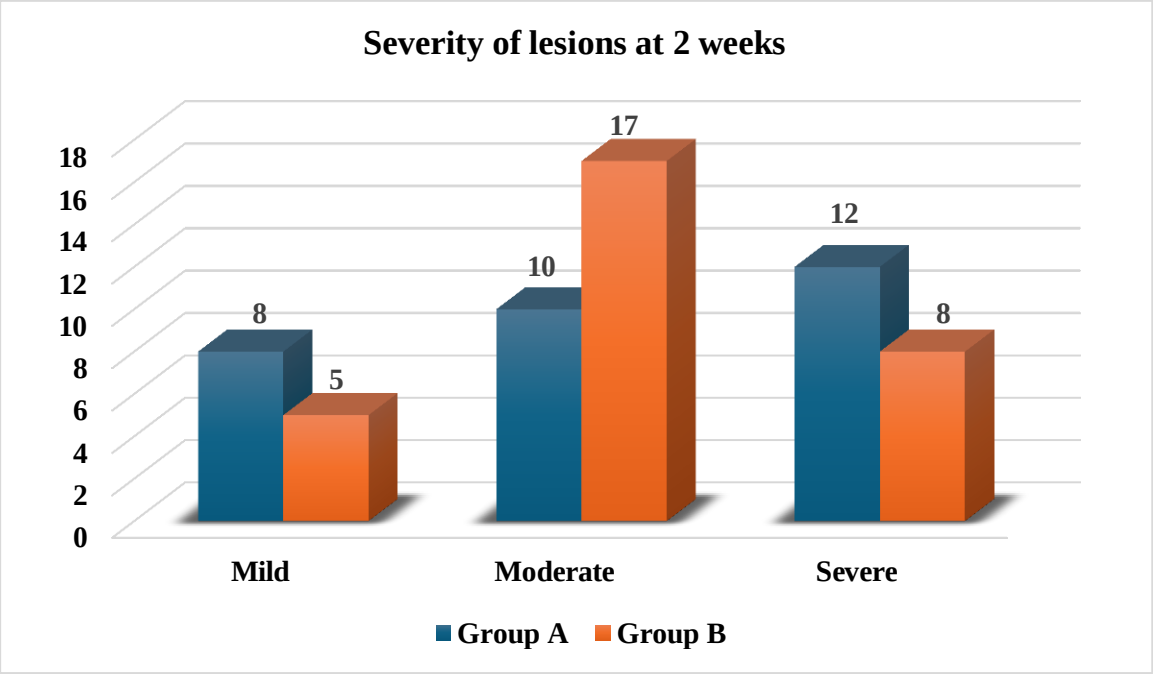
During 2 weeks of therapy, there was no change in the severity of lesions compared to the baseline lesions. At 2 weeks in group A ,12 (40.0%) subjects had severe lesions, 10 (33.3%) had moderate lesions and 8 (26.7%) had mild lesions. In group B, 17 (56.7%) subjects had moderate lesions, 8 (26.7%) had severe lesions and 5 (16.7%) had mild lesions.

At 4 weeks the severity of lesions has reduced in both the groups, with moderate lesions more prominent in the group A (40.0%) compared to severe and mild lesions (30.0% each). In group B also moderate lesions were showing higher predominance with 50.0% and severe and mild lesions showing 26.7% and 23.3% respectively.

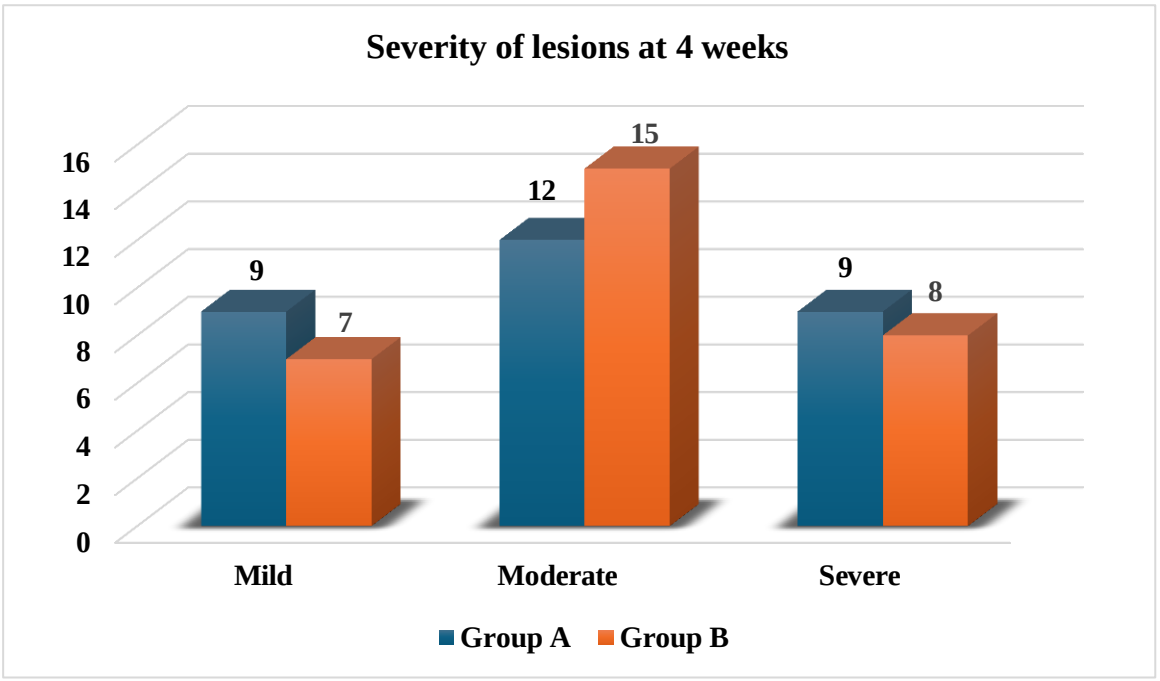
At 6 weeks, the severity of lesions has again decreased and thereby in the group A there were equal numbers of mild and moderate cases (36.7%) and a lesser number of severe cases (26.7%). In group B there were more moderate cases (46.7%) compared to mild (30.0%) and severe cases (23.3%).

At 8 weeks the severity of lesions decreased considerably with only 4 (13.3%) and 1 (3.3%) cases showing severe lesions in group A and B respectively. Moderate cases were almost equal in both groups at 8 weeks (46.7% each) and mild cases were the predominant ones at the end of 8 weeks.

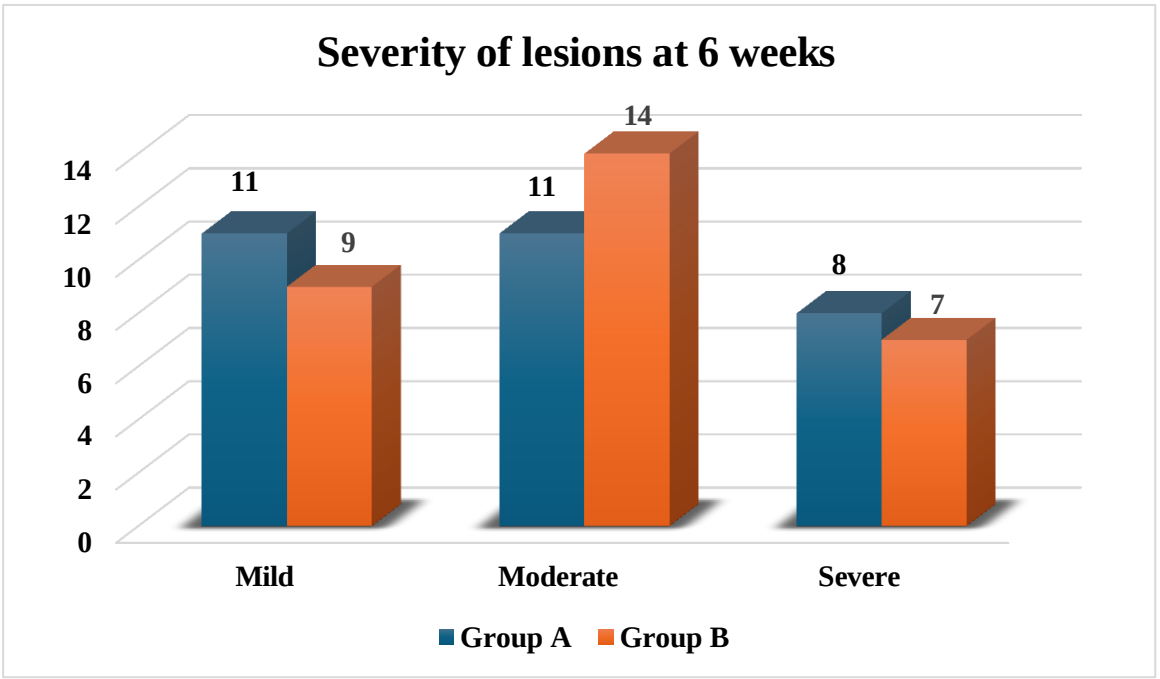
Graph 3: Graph depicting Severity of lesions at 2 weeks



Graph 4: Graph depicting Severity of lesions at 4 weeks



Graph 5: Graph depicting Severity of lesions at 6 weeks



Graph 6: Graph depicting Severity of lesions at 8 weeks

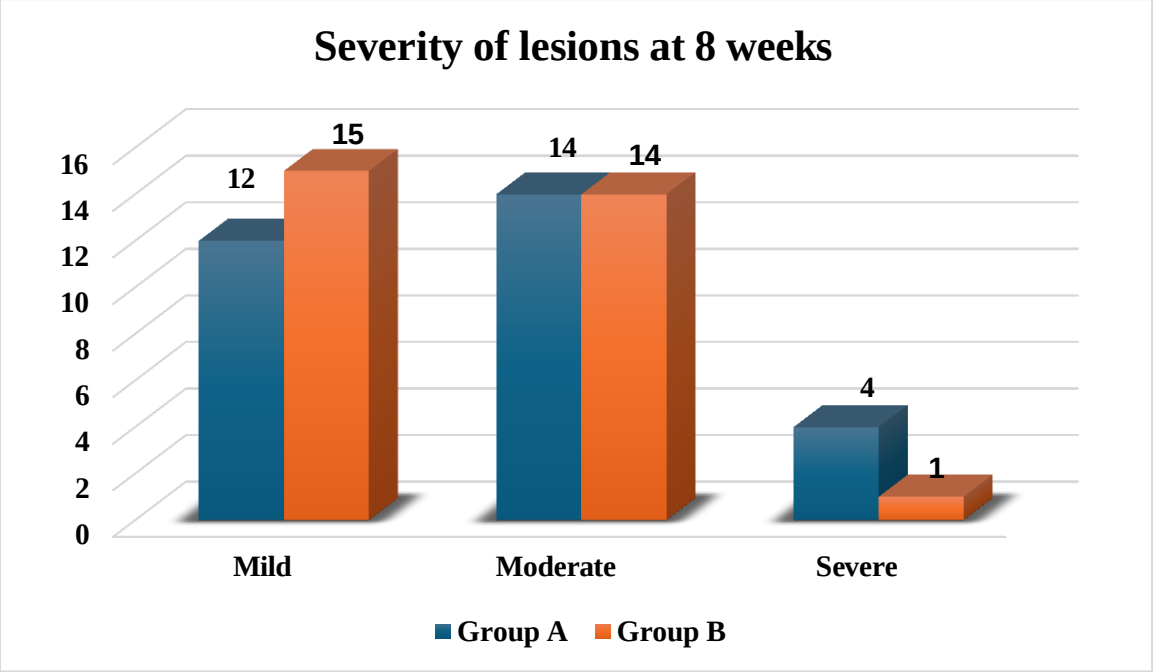


Table 3 : Mean ANASI scores at various intervals

ANASI scores	Group A	Group B	P value
Baseline	17.87 ± 9.08	17.00 ± 7.21	0.684
2 weeks	17.53 ± 8.84	16.67 ± 6.95	0.675
4 weeks	15.73 ± 8.54	14.73 ± 6.95	0.621
6 weeks	14.33 ± 8.27	12.93 ± 7.02	0.483
8 weeks	12.33 ± 7.46	10.20 ± 6.37	0.239

The mean ANASI scores were almost equally distributed in both the groups during the study period even though the score was slightly lower in the B group compared to the A group. But this difference was not statistically significant. Also, the ANASI score gradually decreased from baseline to 8 weeks in both the groups.

Graph 7: Graph depicting ANASI scores at various intervals

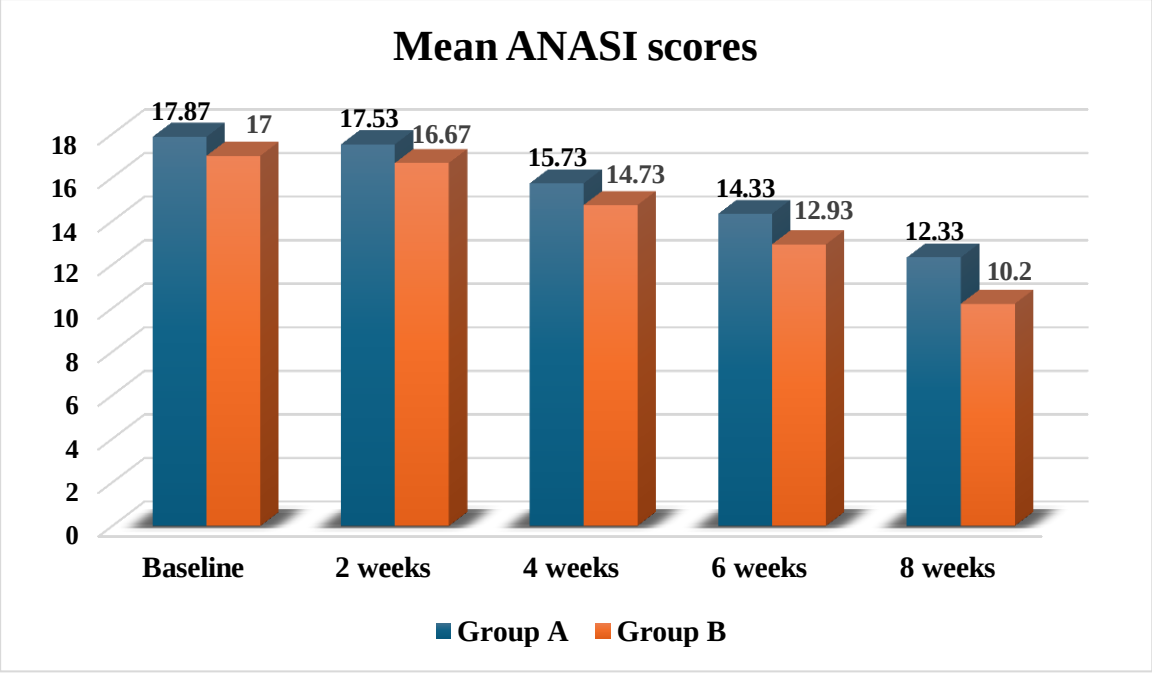


Table 4 : Therapeutic response at various intervals

Therapeutic response	Response percentage	Group A	Group B	t/ Chi-square value	P value
2 weeks	<25 %	8 (50.0)	8 (50.0)	0.000	1.000
	25 – 50%	22 (50.0)	22 (50.0)		
	51 – 75%	0	0		
	>75%	0	0		
4 weeks	<25 %	0	0	5.455	0.020*
	25 – 50%	18 (66.7)	9 (33.3)		
	51 – 75%	12 (36.4)	21 (63.6)		
	>75%	0	0		
6 weeks	<25 %	0	0	3.268	0.071
	25 – 50%	0	0		
	51 – 75%	28 (54.9)	23 (45.1)		
	>75%	2 (22.2)	7 (77.8)		
8 weeks	<25 %	0	0	16.596	<0.001*
	25 – 50%	0	0		
	51 – 75%	13 (100.0)	0		
	>75%	17 (36.2)	30 (63.8)		

*p value <0.05; Hence statistically significant

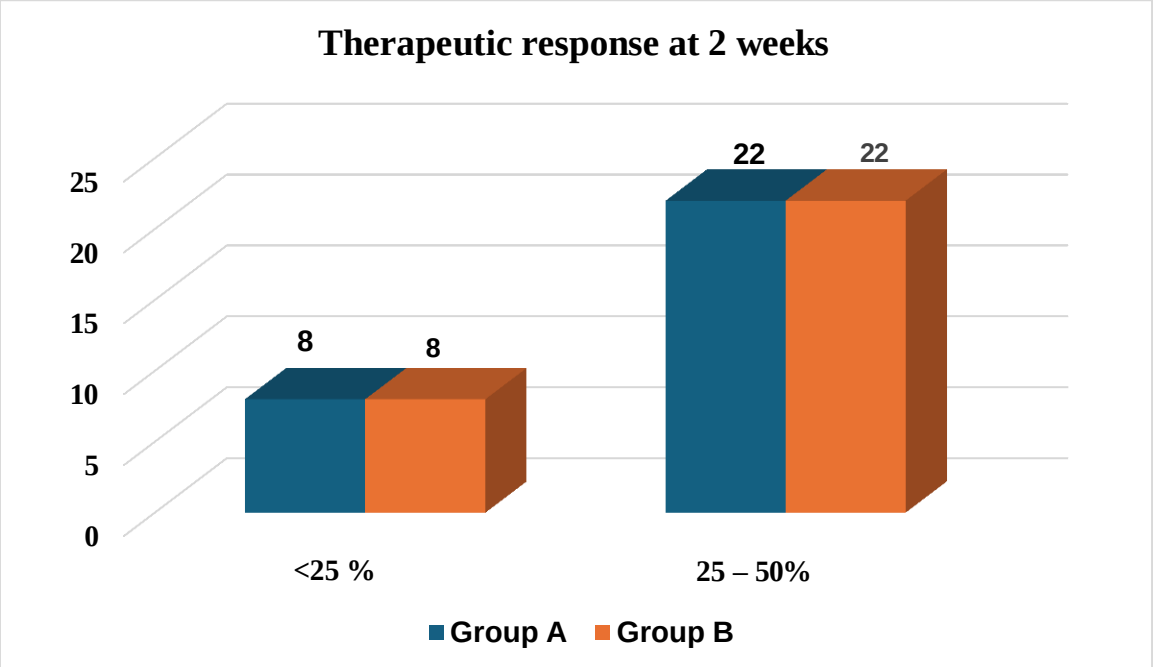
Looking at therapeutic response of both the drugs under study it was found that, there was no significant response after 2 weeks of therapy and both the treatment modalities showed equal response. Less than 25% response was shown by 8 subjects in both the groups and 25 to 50% response (moderate response) was shown by 22 subjects in each group. At 4 weeks moderate

response (25 – 50%) was shown by 18 subjects in group A and 9 subjects in group B, while marked response (51 – 75%) was shown by 12 subjects in group A and 21 subjects in group B. This difference in response to the drugs were statistically significant (p = 0.020).

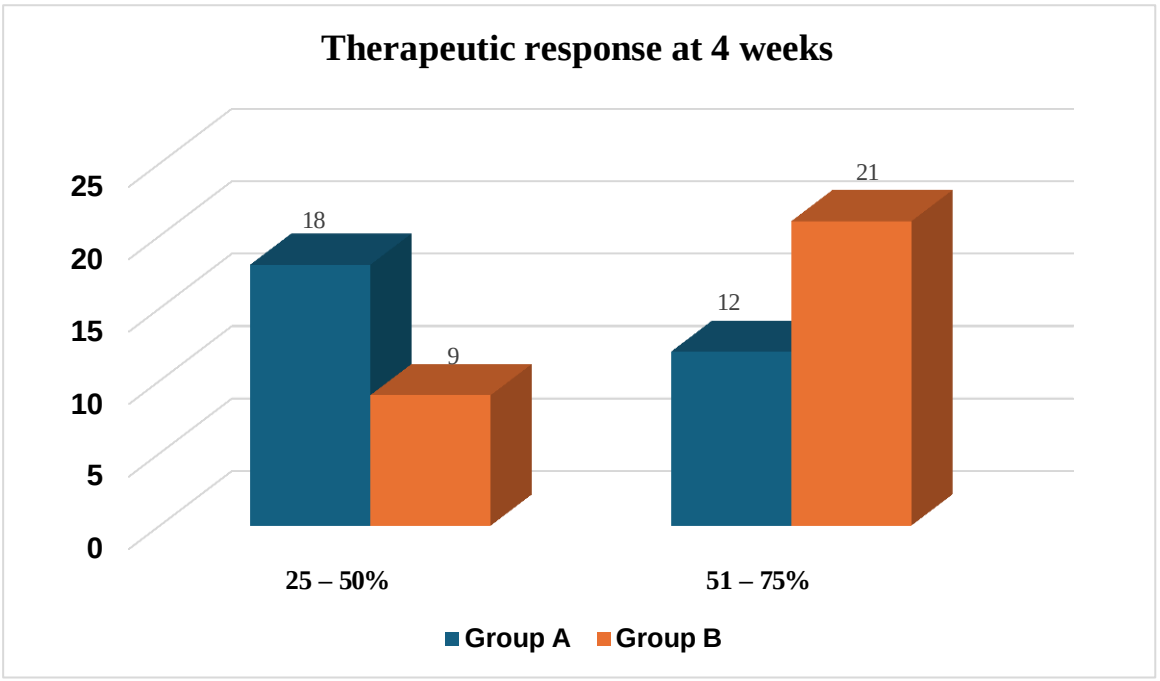
At 6 weeks of therapy, the response was marked (51 – 75%) in 28 subjects in group A and 23 subjects in group B. During the same time period excellent response (>75%) was observed among 2 subjects in group A and 7 subjects in group B.

At 8 weeks of therapy the response was excellent (>75%) in all the subjects in group B and 17 subjects in group A. Rest of the 13 subjects in group A had a marked response (51 – 75%) at 8 weeks of therapy. This difference was found to be statistically significant as well (p <0.001).

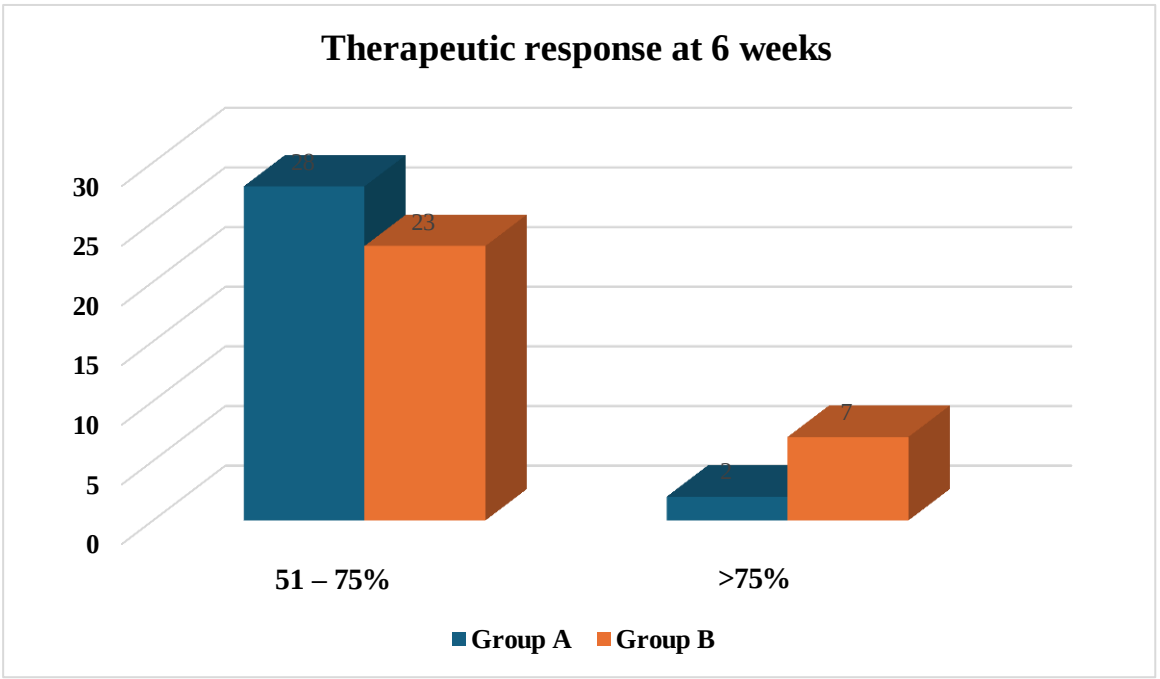
Graph 8: Graph depicting Therapeutic response at 2 weeks



Graph 9: Graph depicting Therapeutic response at 4 weeks



Graph 10: Graph depicting Therapeutic response at 6 weeks



Graph 11: Graph depicting Therapeutic response at 8 weeks

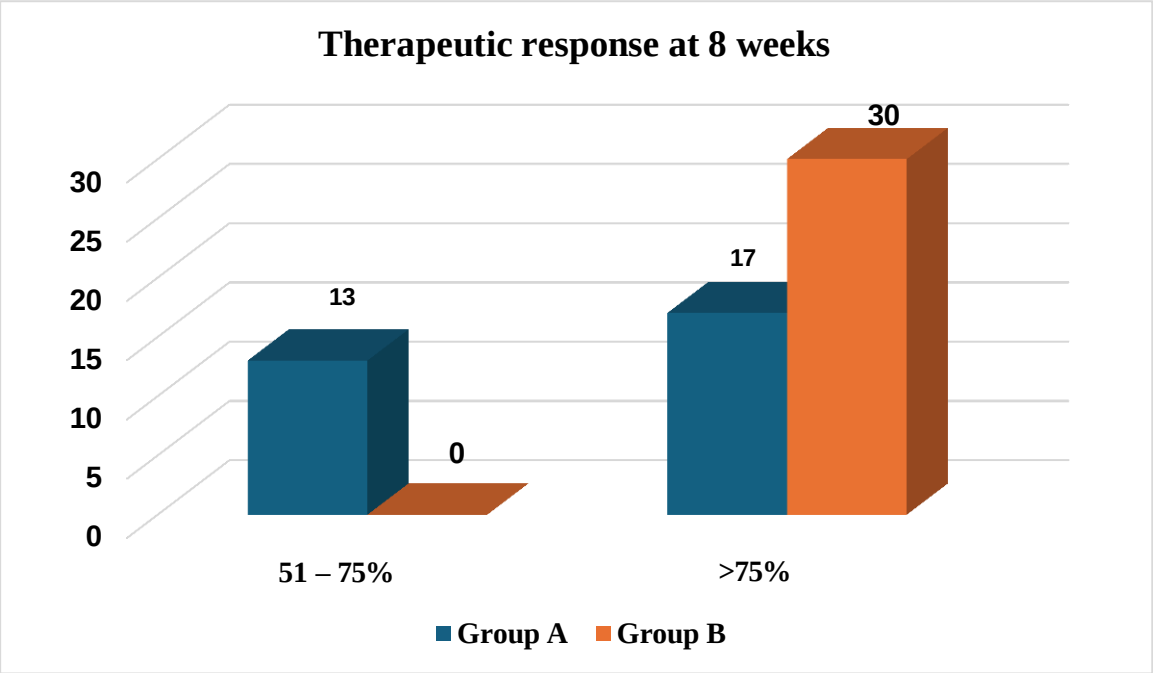


Table 5: Adverse effects observed in both the groups

Adverse effects		Group A	Group B	Total	t/ Chi-square value	P value
Erythema	Present	19 (70.4)	8 (29.6)	27 (100.0)	8.148	0.004*
	Absent	11 (33.3)	22 (66.7)	33		
Post procedure hyperpigmentation	Present	9 (75.0)	3 (25.0)	12	3.750	0.053
	Absent	21 (43.8)	27 (56.3)	48		
Burning sensation	Present	5 (62.5)	3 (37.5)	8	0.577	0.706
	Absent	25 (48.1)	27 (51.9)	52		
Peeling of skin	Present	1 (33.3)	2 (66.7)	3	0.351	1.000
	Absent	29 (50.9)	28 (49.1)	57		

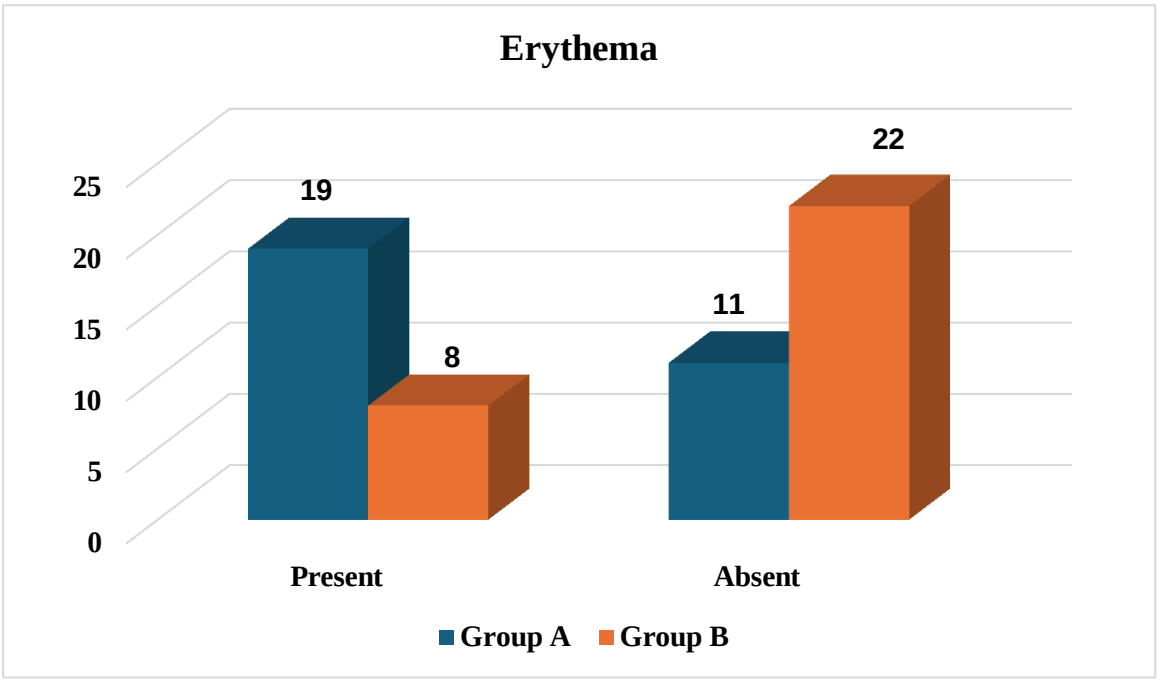
*p value <0.05; Hence statistically significant

Looking at the side effects it was found that erythema was found more among patients in group A who received fractional CO_2 laser compared to patients in group B who received Ferulac Peel Classic solution. This difference was found to be statistically significant (p = 0.004).

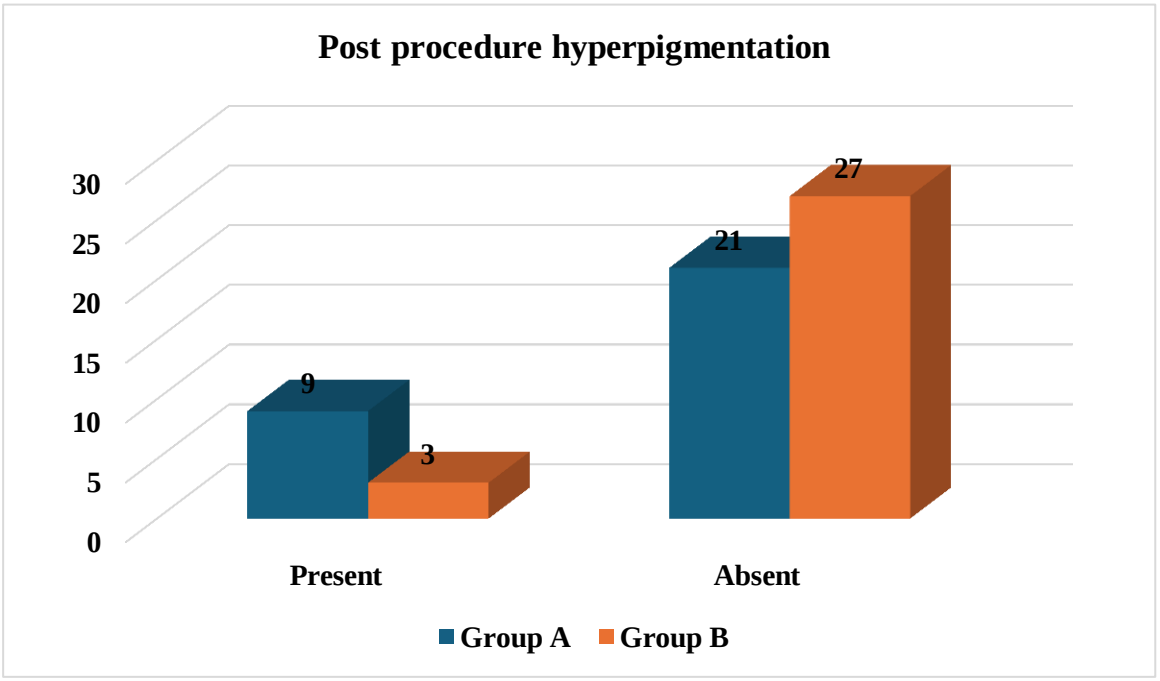
Post procedure hyperpigmentation was also found to be higher in group A compared to group B, but this difference was not found to be statistically significant.

Burning sensation and peeling of skin was almost equally distributed among the study participants in both the groups and no significant difference was found between group A and group B with respect to the both the adverse effects.

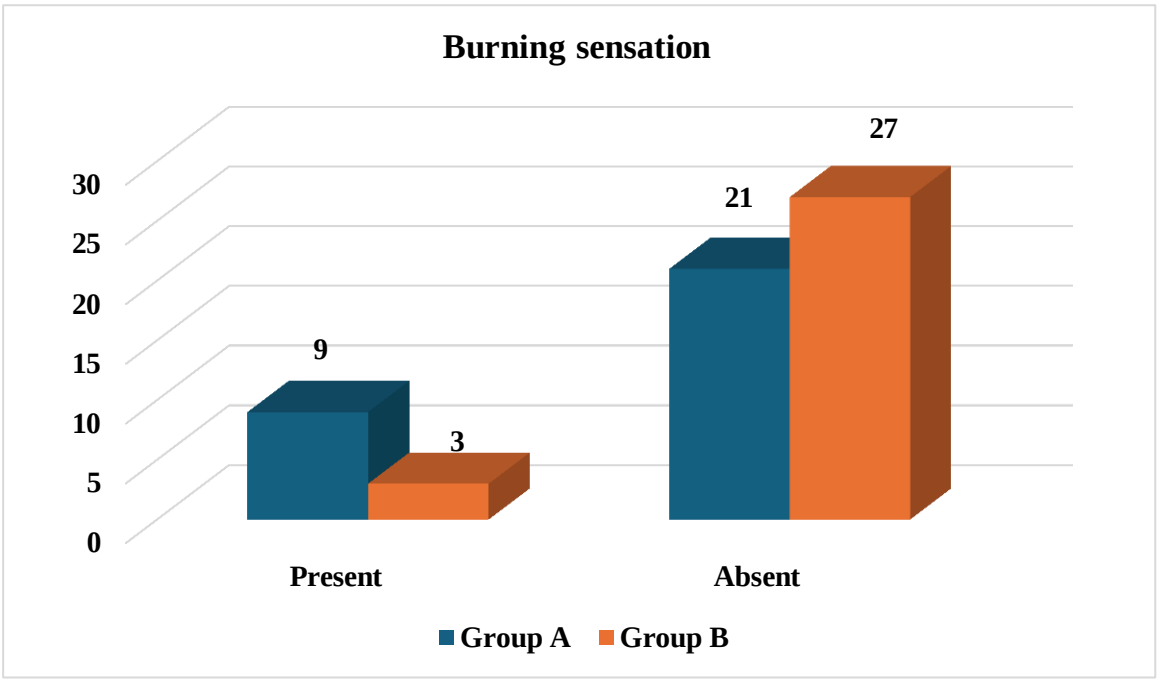
Graph 12: Graph depicting Erythema following procedures in both the groups



Graph 13:Graph depicting Post procedure hyperpigmentation following procedures in both the groups



Graph 14:Graph depicting burning sensation following procedures in both the groups



Graph 15:Graph depicting Peeling of skin following procedures in both the groups

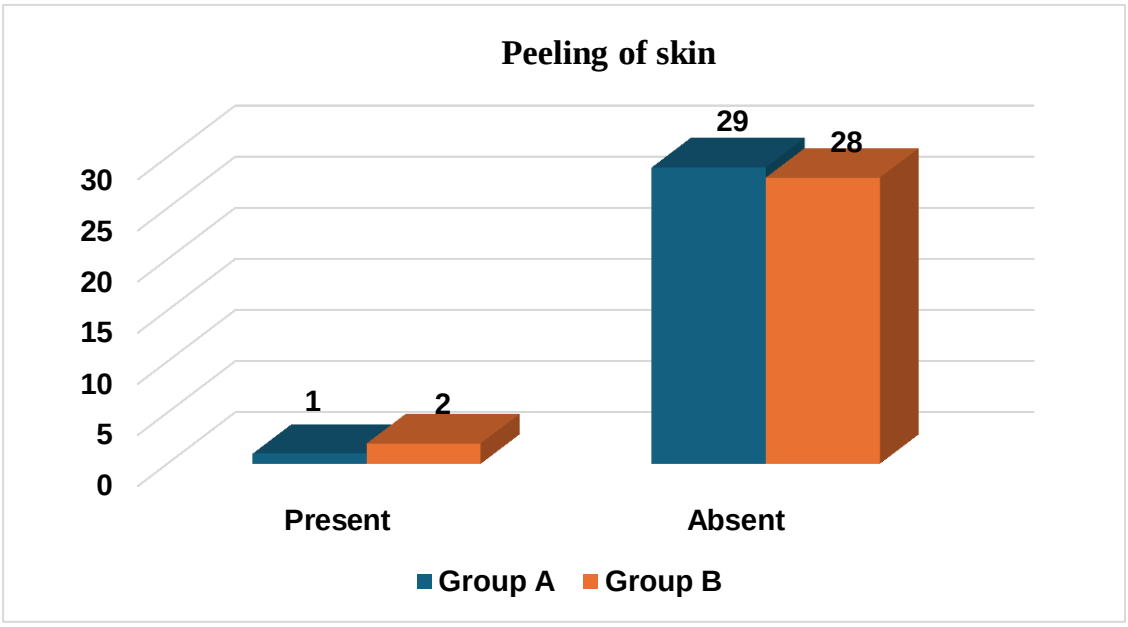


Table 6: Visual discomfort scale for side effects

	Mean value			t value	P value
	Group A	Group B	Mean difference		
Visual discomfort scale for side effects	4.90 ± 1.29	3.83 ± 1.34	1.067	3.133	0.003*

*p value <0.05; Hence statistically significant

The mean visual discomfort scale was found to be higher in group A (4.90 ± 1.29) compared to the group B (3.83 ± 1.34). Patients in group A were found to be at a higher level of discomfort compared to the patients in group B and this difference was found to be statistically significant (p = 0.003).

Graph 16 : Graph depicting Visual discomfort scale

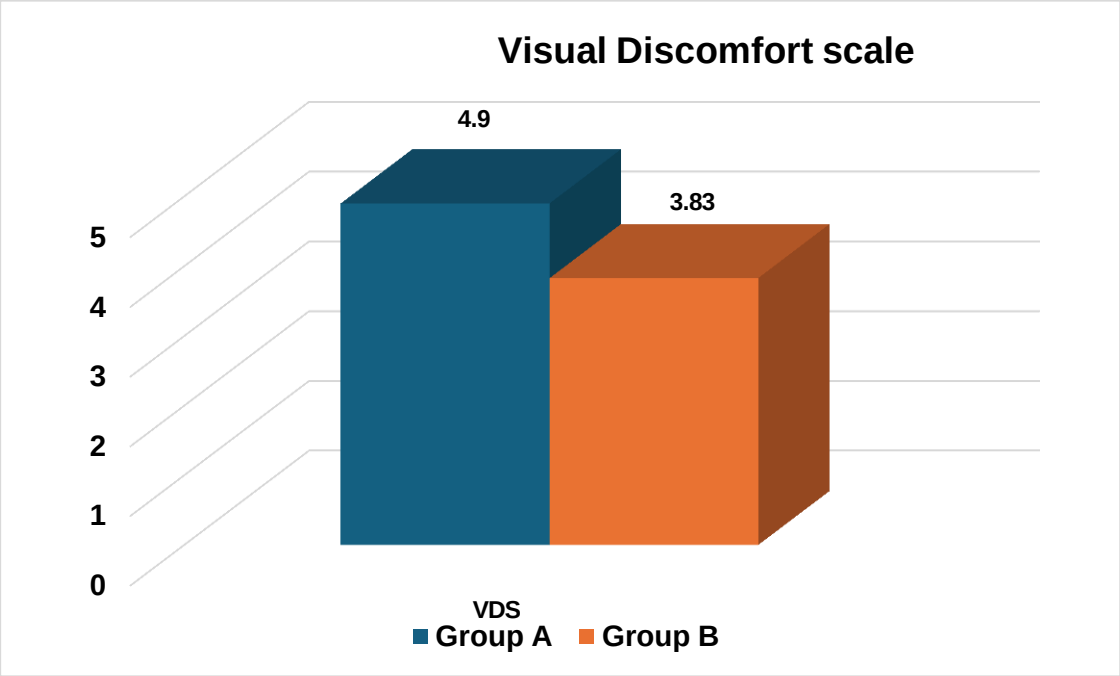
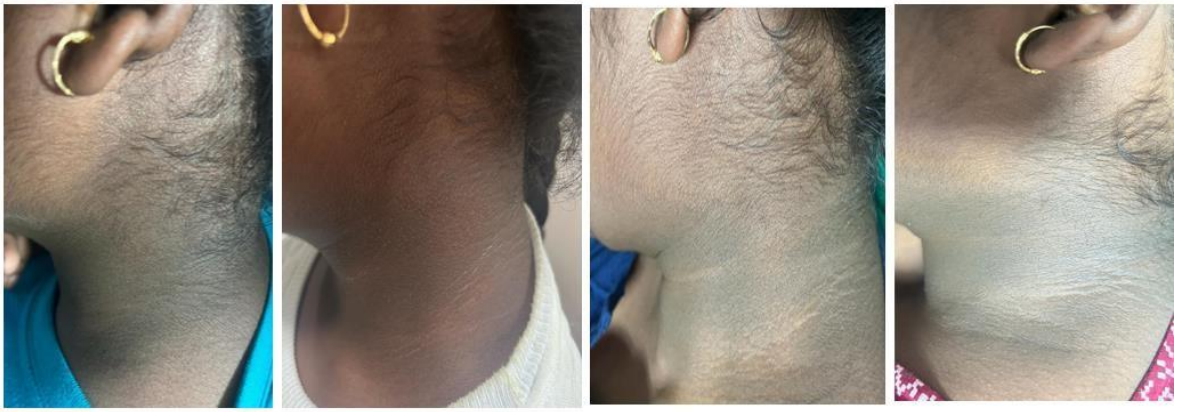
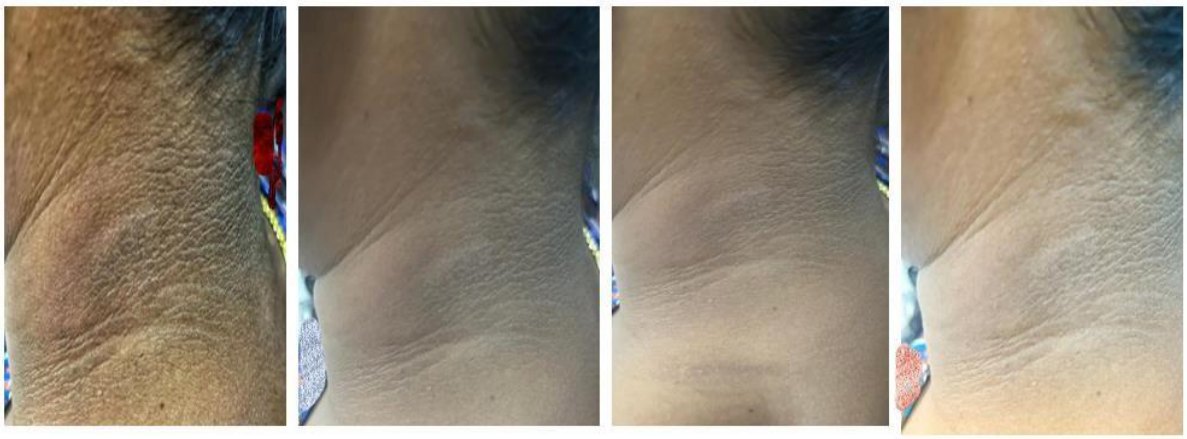


FIGURE-14: GROUP A- FRACTIONAL CO2 LASER



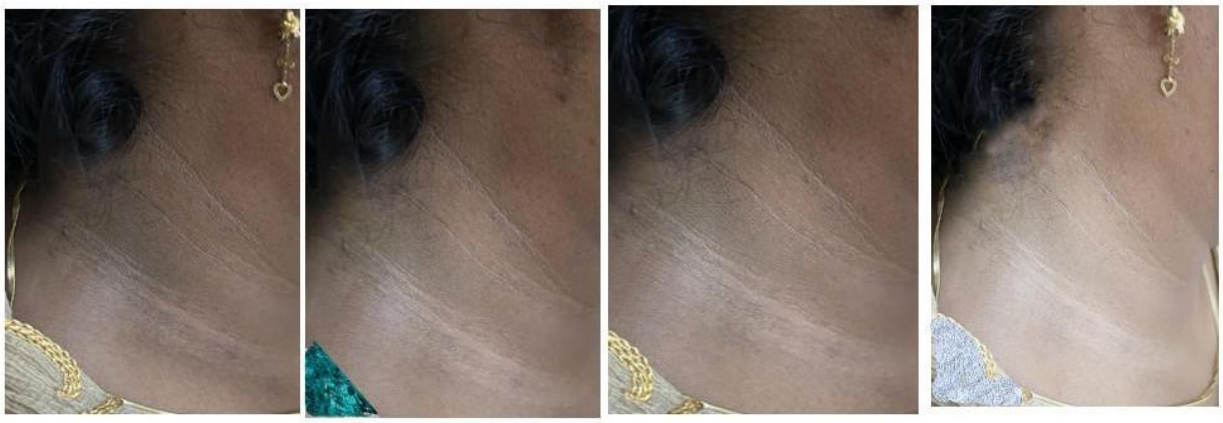
BASELINE	4 WEEKS	6WEEKS	8 WEEKS
ANASI – 18	ANASI – 18	ANASI –14	ANASI -12

FIGURE 15 : FERULIC ACID SEQUENTIAL (12% & 8%) PEEL



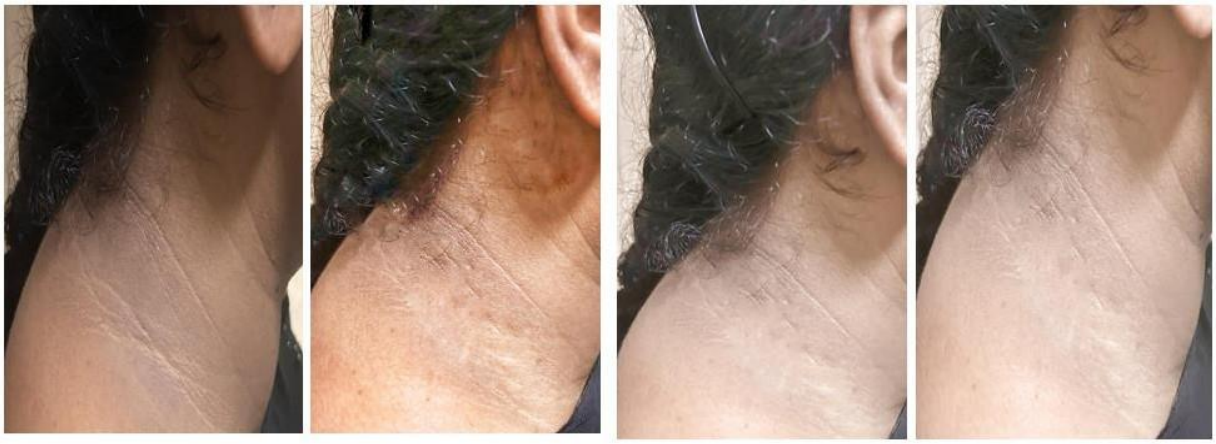
BASELINE	4 WEEKS	6 WEEKS	8 WEEKS
ANASI – 20	ANASI – 18	ANASI – 12	ANASI – 10

FIGURE 16 : GROUP A- FRACTIONAL CO2 LASER



BASELINE	4WEEKS	6WEEKS	8WEEKS
ANASI – 18	ANASI – 16	ANASI – 14	ANASI – 10

FIGURE 17 : GROUP B- FERULIC ACID SEQUENTIAL (12% &



BASELINE	4WEEKS	6WEEKS	8WEEKS
ANASI – 16	ANASI – 12	ANASI – 10	ANASI – 6

DISCUSSION

DISCUSSION

This study was conducted among 60 subjects who received either fractional CO2 laser (group A) or ferulic acid sequential peel (Group B) for the treatment of acanthosis nigricans. The main objectives of the study were to evaluate the efficacy of fractional co2 laser and ferulic acid sequential peel (12% and 8%) in the treatment of neck acanthosis nigricans and to document the post procedural side effects of fractional co2 laser and ferulic acid sequential peel (12% and 8%) in the treatment of neck acanthosis nigricans.

In this study the mean age of the study population was 36.13 ± 7.56 years in those who received fractional CO2 laser 32.50 ± 8.64 years in those who received the ferulic acid sequential peel. In the Eldeeb et al., study the mean age in the laser group was 30.6 ± 7.8 years, while in the TCA group it was 28.9 ± 6.0 years.[108] In the Oun et al., study the mean age was 27.15 ± 8.93 years.[2] In the study conducted by Zaki et al., the mean age of the study population was 27.5 ± 8.10 years.[109] It is interesting to note that people with higher ages sought treatment in our study compared to other studies.

In our study both males and females were almost equally distributed (p = 0.317) between the two groups with 26 (86.7%) females in laser group and 23 females in ferulic acid group (76.7%). In the Eldeeb et al., study females constituted the majority with 75.0% and 90.0% in TCA and laser group respectively.[108] In the Zaki et al., study there was only one male and 19 females in the study.[109] Females are more concerned about their beauty and thereby approached dermatologist for the treatment of acanthosis nigricans.

Considering the baseline severity of the lesions, in the fractional CO2 laser group, 12 (40.0%) subjects had severe lesions, 10 (33.3%) had moderate lesions and 8 (26.7%) had mild lesions in this study. In the group that received ferulic acid peel treatment, 17 (56.7%) subjects had

moderate lesions, 8 (26.7%) had severe lesions and 5 (16.7%) had mild lesions. This difference in severity of lesions at the baseline was not statistically significant. Eldeeb et al., study also showed similar distribution of lesions with moderate cases showing higher frequency followed by severe and mild cases.[108]

The mean ANASI scores in the study were almost similar in both the groups of the study. But the score gradually decreased during the treatment course. ANASI scores decreased at a better rate in the group that received the ferulic acid peel treatment compared to the laser treatment. In the study conducted by Oun et al., the laser treatment group had better ANASI scores compared to the peeling treated group.[2]

In the study conducted by Zaki et al., the mean ANASI scores were 23.55 ± 8.68 and 23.50 ± 8.85 in the glycolic acid group and laser group respectively before the treatment. After the GA treatment sessions on the left side of the neck, it was 13.50 (± 8.33). The improvement was statistically significant and after the laser treatment sessions, it became 19.10 ± 7.62, (P value = 0.1) which shows no statistical improvement.[109]

Looking at therapeutic response of both the drugs under study it was found that, there was no significant response after 2 weeks of therapy and both the treatment modalities showed equal response. At 4 weeks moderate response was shown by 18 subjects in laser group and 9 subjects in ferulic acid peel group, while marked response was shown by 12 subjects in laser group and 21 subjects in ferulic acid peel group. Hence ferulic acid peel was found to be significantly better than laser in the treatment of AN at 4 weeks.

During 6 weeks of therapy, marked response was more in laser group while excellent response was more in ferulic acid peel group. Therefore, ferulic acid peel is a better choice for 6 weeks of therapy for AN. At 8 weeks of therapy the response was excellent in all the

subjects in ferulic acid peel group and 17 subjects in the laser group. Hence without doubt we can say that ferulic acid peel is superior to fractional Co2 laser for the treatment of AN.

The laser treatment done in that study was devoid of any complications, scarring or recurrence.[110] The same findings were reported by Wijnberg et al., as well.[111]

In the study conducted by Oun et al., retinoic acid peel was used, and significant improvement was noticed with just 4 peeling sessions.[2]

Considering the side effects, it was found that erythema was found more among patients who received fractional CO_2 laser compared to patients who received Ferulic Peel Classic solution. Post procedure hyperpigmentation was also found to be higher in laser group. Burning sensation and peeling of skin was almost equally distributed among the study participants in both the groups. In the Eldeeb et al., study the side effects were increased in the TCA group when compared to the laser group and the common side effect was burning sensation. The TCA group in the study had higher levels of post-inflammatory hyperpigmentation. Because the normal skin around the microthermal zones serves as a reservoir for tissue regeneration, the laser-ablated skin regenerates quickly, which may explain the decreased incidence of post-inflammatory hyperpigmentation (PIH) linked to fractional CO2 laser treatment.[108]

In the study by Zaki et al., the most frequent side effect observed after laser application was PIH. No side effects were observed with the use of GA peeling in this study.[109]

For the treatment of infantile AN, Treesirichod et al. applied topical 0.1% adapalene gel and 0.025% tretinoin cream. In every case, the treatments reduced minor cutaneous irritation and AN, which improved during the course of the research.[112]

Ferulac peel is composed of ferulic acid, phloretin, fruit acids, and retinoids. Ferulic acid in the ferulic peel is a strong UV absorber and also has depigmenting properties. Phloretin is a potent antioxidant which interacts with lipids in stratum corneum and thereby helps in better penetration of the peels. The fruit acids including malic, citric and lactic acids can enhance penetration of the peels and retinol gives an antiaging effect. All these components have a synergistic effect on the treatment for acanthosis nigricans. And thereby Ferulac peel performs better than fractional CO2 lasers.

CONCLUSION

CONCLUSION

After 8 weeks of ferulic acid peel treatment improvement was seen in texture, thickness and pigmentation of acanthosis nigricans.

Overall, the response with ferulic acid peel was better compared to the fractional CO2 laser treatment. The side effect profile of both the treatment showed significant difference with ferulic acid peel having lesser side effects compared to the CO2 laser treatment.

Compared to other peels the ferulic acid peel has better safety and better therapeutic effect. The ferulic acid peel is cheaper compared to the costlier procedure of fractional CO2 laser and thereby the general population will be able to afford it. Along with its cost effectives, increased therapeutic effect and better safety profile, ferulic acid peel is the best option for treatment of acanthosis nigricans.

SUMMARY

SUMMARY

This study was conducted among 60 subjects who received either fractional CO2 laser (group A) or ferulic acid sequential peel (Group B) for the treatment of acanthosis nigricans. The main objectives of the study were to evaluate the efficacy of fractional co2 laser and ferulic acid sequential peel (12% and 8%) in the treatment of neck acanthosis nigricans and to document the post procedural side effects of fractional co2 laser and ferulic acid sequential peel (12% and 8%) in the treatment of neck acanthosis nigricans.

- In this study the mean age of the study participants in group A was 36.13 ± 7.56 years and that of group B was 32.50 ± 8.64 years.
- Considering the baseline severity of the lesions, in group A 12 (40.0%) subjects had severe lesions, 10 (33.3%) had moderate lesions and 8 (26.7%) had mild lesions in this study. In group B, 17 (56.7%) subjects had moderate lesions, 8 (26.7%) had severe lesions and 5 (16.7%) had mild lesions.
- At 8 weeks the severity of lesions decreased considerably with only 4 (13.3%) and 1 (3.3%) cases showing severe lesions in group A and B respectively. Moderate cases were almost equal in both groups at 8 weeks (46.7% each) and mild cases were the predominant ones at the end of 8 weeks.
- The mean ANASI scores were almost equally distributed in both the groups during the study period even though the score was slightly low in the B group compared to the A group.
- At 8 weeks of therapy the response was excellent (>75%) in all the subjects in group B and 17 subjects in group A. Rest of the 13 subjects in group A had a marked response (51 – 75%) at 8 weeks of therapy.

- Looking at the side effects it was found that erythema and post procedure hyperpigmentation was found more among patients in group A who received fractional CO_2 laser compared to patients in group B who received Ferulac Peel Classic solution.
- Burning sensation and peeling of skin was almost equally distributed among the study participants.
- The mean visual discomfort scale was found to be higher in group A (4.90 ± 1.29) compared to the group B (3.83 ± 1.34).

LIMITATIONS

- A smaller sample size is the limitation of the study
- Follow up for longer time to see clinical improvement is needed

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Fathy A, Elsayed G, Elsayed M, Elmongy S, Mohammed E. Fractional Carbon Dioxide Laser versus Glycolic Acid Peel in Treatment of Pseudo-Acanthosis Nigricans 85, The Egyptian Journal of Hospital Medicine. 2021.

2. Abu Oun AA, Ahmed NA, Hafiz HSA. Comparative study between fractional carbon dioxide laser versus retinoic acid chemical peel in the treatment of acanthosis nigricans. J Cosmet Dermatol. 2022 Mar 31;21(3):1023–30.

3. Khunger N, Chanana C. A perspective on what's new in chemical peels. Cosmoderma. 2022 Feb 15;2:14.

4. Sinha S, Schwartz RA. Juvenile acanthosis nigricans. J Am Acad Dermatol. 2007 Sep;57(3):502–8.

5. Smid CJ, Modaff P, Alade A, Legare JM, Pauli RM. Acanthosis nigricans in achondroplasia. Am J Med Genet A. 2018 Dec 31;176(12):2630–6.

6. Gupta M. Cutaneous manifestations of obesity in children: A prospective study. Indian Journal of Paediatric Dermatology. 2017;18(1):28.

7. Lause M, Kamboj A, Fernandez Faith E. Dermatologic manifestations of endocrine disorders. Transl Pediatr. 2017 Oct;6(4):300–12.

8. Torley D, Bellus GA, Munro CS. Genes, growth factors and acanthosis nigricans. British Journal of Dermatology. 2002 Dec;147(6):1096–101.

9. Higgins SP, Freemark M, Prose NS. Acanthosis nigricans: a practical approach to evaluation and management. Dermatol Online J. 2008 Sep 15;14(9):2.

10. Berk DR, Spector EB, Bayliss SJ. Familial Acanthosis Nigricans Due to K650T FGFR3 Mutation. Arch Dermatol. 2007 Sep 1;143(9).

11. Sharda S, Panigrahi I, Gupta K, Singhi S, Kumar R. A Newborn with Acanthosis Nigricans: Can It Be Crouzon Syndrome with Acanthosis Nigricans? Pediatr Dermatol. 2010 Jan;27(1):43–7.

12. Krawczyk M, Mykała-Cieśla J, Kołodziej-Jaskuła A. Acanthosis nigricans as a paraneoplastic syndrome. Case reports and review of literature. Pol Arch Med Wewn. 2009 Mar;119(3):180–3.

13. Puri N. A study of pathogenesis of Acanthosis nigricans and its clinical implications. Indian J Dermatol. 2011;56(6):678.

14. Mailler-Savage EA, Adams BB. Exogenous insulin-derived Acanthosis nigricans. Arch Dermatol. 2008 Jan;144(1):126–7.

15. Kudo-Watanuki S, Kurihara E, Yamamoto K, Mukai K, Chen KR. Coexistence of insulin-derived amyloidosis and an overlying acanthosis nigricans-like lesion at the site of insulin injection. Clin Exp Dermatol. 2013 Jan;38(1):25–9.

16. Lane SW, Manoharan S, Mollee PN. Palifermin-induced acanthosis nigricans. Intern Med J. 2007 Jun 24;37(6):417–8.

17. Wu JC, Cunningham BB. Ectopic acanthosis nigricans occurring in a child after syndactyly repair. Cutis. 2008 Jan;81(1):22–4.

18. Hermanns-Le T, Scheen A, Pierard GE. Acanthosis Nigricans Associated with Insulin Resistance. Am J Clin Dermatol. 2004;5(3):199–203.

19. Fukuchi K, Tatsuno K, Matsushita K, Kubo A, Ito T, Tokura Y. Familial acanthosis nigricans with p.K650T <*scp*>*FGFR*</*scp*> *3* mutation. J Dermatol. 2018 Feb 25;45(2):207–10.

20. Rakeshkumar G, Pavan P, Srinivas M. Conceptual Study on Prameha Pidakas w.s.r. to Skin Lesions In Diabetes. Journal of Ayurveda and Integrated Medical Sciences (JAIMS). 2017 Aug 22;2(4).

21. Ng HY. Acanthosis nigricans in obese adolescents: prevalence, impact, and management challenges. Adolesc Health Med Ther. 2016 Dec;Volume 8:1–10.

22. Kuroki R, Sadamoto Y, Imamura M, Abe Y, Higuchi K, Kato K, et al. Acanthosis nigricans with Severe Obesity, Insulin Resistance and Hypothyroidism: Improvement by Diet Control. Dermatology. 1999;198(2):164–6.

23. Plascencia Gómez A, Vega Memije ME, Torres Tamayo M, Rodríguez Carreón AA. Skin Disorders in Overweight and Obese Patients and Their Relationship With Insulin. Actas Dermo-Sifiliográficas (English Edition). 2014 Mar;105(2):178–85.

24. Stals H, Vercammen C, Peeters C, Morren MA. Acanthosis nigricans Caused by Nicotinic Acid: Case Report and Review of the Literature. Dermatology. 1994;189(2):203–6.

25. Mellor-Pita S, Yebra-Bango M, Alfaro-Martinez J, Suarez E. Acanthosis Nigricans: A New Manifestation of Insulin Resistance in Patients Receiving Treatment with Protease Inhibitors. Clinical Infectious Diseases. 2002 Mar 1;34(5):716–7.

26. Fleming MG, Simon SI. Cutaneous insulin reaction resembling acanthosis nigricans. Arch Dermatol. 1986 Sep;122(9):1054–6.

27. Kanwar A, Sawatkar G, Dogra S, Bhadada S. Acanthosis nigricans--An uncommon cutaneous adverse effect of a common medication: Report of two cases. Indian J Dermatol Venereol Leprol. 2013;79(4):553.

28. Schmidt TH, Khanijow K, Cedars MI, Huddleston H, Pasch L, Wang ET, et al. Cutaneous Findings and Systemic Associations in Women With Polycystic Ovary Syndrome. JAMA Dermatol. 2016 Apr 1;152(4):391.

29. Lauria MW, Saad MJ. Acanthosis Nigricans and Insulin Resistance. New England Journal of Medicine. 2016 Jun 16;374(24):e31.

30. Anand V, Das A, Kumar P, Kumar R, Hassan S. Acral acanthosis nigricans (acral acanthotic anomaly). Indian Dermatol Online J. 2014;5(6):140.

31. Xiao Q, Zhou R, Li Y, Zhao L, Xiong L, Tang J, et al. Symmetrical Acrokeratoderma: A Case Report and Literature Review. Clin Cosmet Investig Dermatol. 2022 Feb;Volume 15:247–52.

32. Liu XK, Li J. Hyperpigmentation in the skin folds. BMJ. 2018 Jan 18;j5729.

33. Yu Q, Li XL, Ji G, Wang Y, Gong Y, Xu H, et al. Malignant acanthosis nigricans: an early diagnostic clue for gastric adenocarcinoma. World J Surg Oncol. 2017 Dec 25;15(1):208.

34. Devi KN, Devi GC, Sethy P, Hazarika N. Malignant acanthosis nigricans: a cutaneous marker of hepatocellular carcinoma. BMJ Case Rep. 2022 Oct 25;15(10):e252287.

35. Kondo Y, Umegaki N, Terao M, Murota H, Kimura T, Katayama I. A Case of Generalized Acanthosis Nigricans with Positive Lupus Erythematosus-Related

Autoantibodies and Antimicrosomal Antibody: Autoimmune Acanthosis Nigricans. Case Rep Dermatol. 2012 Mar 30;4(1):85–91.

36. Kondo Y, Umegaki N, Terao M, Murota H, Kimura T, Katayama I. A Case of Generalized Acanthosis Nigricans with Positive Lupus Erythematosus-Related Autoantibodies and Antimicrosomal Antibody: Autoimmune Acanthosis Nigricans. Case Rep Dermatol. 2012 Mar 30;4(1):85–91.

37. Das A, Bhattacharya S, Kumar P, Gayen T, Roy K, Das N, et al. Unilateral nevoid acanthosis nigricans: Uncommon variant of a common disease. Indian Dermatol Online J. 2014;5(5):40.

38. Bansal M, Yadav J, Bansal A. Unilateral nevoid acanthosis nigricans. BMJ Case Rep. 2015 Jun 29;2015:bcr2015210614.

39. Higgins SP, Freemark M, Prose NS. Acanthosis Nigricans: A practical approach to evaluation and management. Dermatol Online J. 2008 Sep 1;14(9).

40. Ankad B, Drago N, Koti V, Nikam B. Dermoscopic approach to hyperpigmented lesions in skin of color. Clinical Dermatology Review. 2020;4(2):84.

41. Charnvises K, Weerakiet S, Tingthanatikul Y, Wansumrith S, Chanprasertyothin S, Rojanasakul A. Acanthosis nigricans: Clinical predictor of abnormal glucose tolerance in Asian women with polycystic ovary syndrome. Gynecological Endocrinology. 2005 Jan 7;21(3):161–4.

42. Patel NU, Roach C, Alinia H, Huang W, Feldman S. Current treatment options for acanthosis nigricans. Clin Cosmet Investig Dermatol. 2018 Aug;Volume 11:407–13.

43. Romo A, Benavides S. Treatment Options in Insulin Resistance Obesity–Related Acanthosis Nigricans. Annals of Pharmacotherapy. 2008 Jul 27;42(7–8):1090–4.

44. Darmstadt GL, Yokel BK, Horn TD. Treatment of acanthosis nigricans with tretinoin. Arch Dermatol. 1991 Aug;127(8):1139–40.

45. Blobstein SH. Topical therapy with tretinoin and ammonium lactate for acanthosis nigricans associated with obesity. Cutis. 2003 Jan;71(1):33–4.

46. Gregoriou S, Anyfandakis V, Kontoleon P, Christofidou E, Rigopoulos D, Kontochristopoulos G. Acanthosis nigricans associated with primary hypogonadism: Successful treatment with topical calcipotriol. Journal of Dermatological Treatment. 2008 Jan 1;19(6):373–5.

47. Phiske M. An approach to acanthosis nigricans. Indian Dermatol Online J. 2014;5(3):239.

48. Sun H, Wang X, Chen J, Gusdon AM, Song K, Li L, et al. Melatonin Treatment Improves Insulin Resistance and Pigmentation in Obese Patients with Acanthosis Nigricans. Int J Endocrinol. 2018;2018:1–7.

49. Rosenbach A, Ram R. Treatment of Acanthosis Nigricans of the Axillae Using a Long-Pulsed (5-msec) Alexandrite Laser. Dermatologic Surgery. 2004 Aug;30(8):1158–60.

50. Ghosh S, Roychowdhury B, Mukhopadhyay S, Chowdhury S. Clearance of acanthosis nigricans associated with insulinoma following surgical resection. QJM. 2008 Jul 29;101(11):899–900.

51. Lahiri K, Malakar S. Topical tretinoin in acanthosis nigricans. Indian J Dermatol Venereol Leprol. 1996;62(3):159–61.

52. Berger BJ, Gross PR. Another use for tretinoin--pseudoacanthosis nigricans. Arch Dermatol. 1973 Jul;108(1):133–4.

53. Schwartz RA. Efficacy of topical 0.1% adapalene gel for use in the treatment of childhood acanthosis nigricans: a pilot study. Dermatol Ther. 2015 Jul;28(4):266–266.

54. Treesirichod A, Chaithirayanon S, Wongjitrat N, Wattanapan P. The efficacy of topical 0.1% adapalene gel for use in the treatment of childhood acanthosis nigricans: A pilot study. Indian J Dermatol. 2015;60(1):103.

55. Adigun C, Pandya A. Improvement of idiopathic acanthosis nigricans with a triple combination depigmenting cream. Journal of the European Academy of Dermatology and Venereology. 2009 Apr 17;23(4):486–7.

56. BÖhm, Luger, Metze. Treatment of mixed-type acanthosis nigricans with topical calcipotriol. British Journal of Dermatology. 1998 Nov 4;139(5):932–4.

57. Lee HW, Chang SE, Lee MW, Choi JH, Moon KC, Koh JK. Hyperkeratosis of the nipple associated with acanthosis nigricans: Treatment with topical calcipotriol. J Am Acad Dermatol. 2005 Mar;52(3):529–30.

58. Zayed A, Sobhi RM, Abdel Halim DM. Using trichloroacetic acid in the treatment of acanthosis nigricans: a pilot study. Journal of Dermatological Treatment. 2014 Jun 1;25(3):223–5.

59. Jeong KH, Oh SJ, Chon S, Lee MH. Generalized acanthosis nigricans related to type B insulin resistance syndrome: a case report. Cutis. 2010 Dec;86(6):299–302.

60. Katz RA. Treatment of acanthosis nigricans with oral isotretinoin. Arch Dermatol. 1980 Jan;116(1):110–1.

61. Walling HW, Messingham M, Myers LM, Mason CL, Strauss JS. Improvement of acanthosis nigricans on isotretinoin and metformin. J Drugs Dermatol. 2003 Dec;2(6):677–81.

62. Sriboonnark L, Arora H, Falto-Aizpurua L, Choudhary S, Connelly EA. Costello Syndrome with Severe Nodulocystic Acne: Unexpected Significant Improvement of Acanthosis Nigricans after Oral Isotretinoin Treatment. Case Rep Pediatr. 2015;2015:1–4.

63. Özdemi˙r M, Toy H, Mevli˙toğlu İ, Demi˙rkesen C. Generalized idiopathic acanthosis nigricans treated with acitretin. Journal of Dermatological Treatment. 2006 Jan 1;17(1):54–6.

64. Pilkington T, Brogden RN. Acitretin. Drugs. 1992 Apr;43(4):597–627.

65. Tankova T, Koev D, Dakovska L, Kirilov G. Therapeutic approach in insulin resistance with acanthosis nigricans. Int J Clin Pract. 2002 Oct;56(8):578–81.

66. Atabek ME, Pirgon O. Use of Metformin in Obese Adolescents with Hyperinsulinemia: A 6-month, Randomized, Double-blind, Placebo-controlled Clinical Trial. Journal of Pediatric Endocrinology and Metabolism. 2008 Jan;21(4).

67. Lee PJ, Cranston I, Amiel SA, O’Rahilly S, Green AA. Effect of Metformin on Glucose Disposal and Hyperinsulinaemia in a 14-Year-Old Boy with Acanthosis Nigricans. Horm Res. 1997;48(2):88–92.

68. Bellot-Rojas P, Posadas-Sanchez R, Caracas-Portilla N, Zamora-Gonzalez J, Cardoso-Saldaña G, Jurado-Santacruz F, et al. Comparison of metformin versus rosiglitazone in

patients with Acanthosis nigricans: a pilot study. J Drugs Dermatol. 2006 Oct;5(9):884–9.

69. Barbato MT, Criado PR, Silva AK da, Averbeck E, Guerine MB, Sá NB de. Association of acanthosis nigricans and skin tags with insulin resistance. An Bras Dermatol. 2012 Feb;87(1):97–104.

70. Roemmich J, Clark P, Lusk M, Friel A, Weltman A, Epstein L, et al. Pubertal alterations in growth and body composition. VI. Pubertal insulin resistance: relation to adiposity, body fat distribution and hormone release. Int J Obes. 2002 May 17;26(5):701–9.

71. Adderley-Rolle E, Peter S. Regression of Acanthosis Nigricans with the Addition of Sitagliptin and Pioglitazone. West Indian Medical Journal. 2014 Oct 17;

72. Lunetta M, Di Mauro M, Le Moli R, Burrafato S. Long-term octreotide treatment reduced hyperinsulinemia, excess body weight and skin lesions in severe obesity with acanthosis nigricans. J Endocrinol Invest. 1996 Nov 4;19(10):699–703.

73. Sherertz EF. Improved acanthosis nigricans with lipodystrophic diabetes during dietary fish oil supplementation. Arch Dermatol. 1988 Jul;124(7):1094–6.

74. Epstein E. Podophyllin Therapy in Acanthosis Nigricans. Journal of Investigative Dermatology. 1951 Jul;17(1):7.

75. Reilly MJ, Cohen M, Hokugo A, Keller GS. Molecular Effects of Fractional Carbon Dioxide Laser Resurfacing on Photodamaged Human Skin. Arch Facial Plast Surg. 2010 Sep 1;12(5).

76. Orringer JS, Kang S, Johnson TM, Karimipour DJ, Hamilton T, Hammerberg C, et al. Connective Tissue Remodeling Induced by Carbon Dioxide Laser Resurfacing of Photodamaged Human Skin. Arch Dermatol. 2004 Nov 1;140(11).

77. Fitzpatrick RE, Rostan EF, Marchell N. Collagen tightening induced by carbon dioxide laser versus erbium: YAG laser. Lasers Surg Med. 2000;27(5):395–403.

78. Gilbert S, McBurney E. Use of Valacyclovir for Herpes Simplex Virus-1 (HSV-1) Prophylaxis After Facial Resurfacing: A Randomized Clinical Trial of Dosing Regimens. Dermatologic Surgery. 2000 Jan;26(1):50–4.

79. Kilmer SL, Chotzen VA, Silva SK, McClaren ML. Safe and effective carbon dioxide laser skin resurfacing of the neck. Lasers Surg Med. 2006 Aug 22;38(7):653–7.

80. Woodward JA, Fabi SG, Alster T, Colón-Acevedo B. Safety and Efficacy of Combining Microfocused Ultrasound With Fractional CO2 Laser Resurfacing for Lifting and Tightening the Face and Neck. Dermatologic Surgery. 2014 Dec;40(Supplement 12):S190–3.

81. Victor Ross CE, Amesbury EC, Barile A, Proctor-Shipman L, Feldman BD. Incidence of postoperative infection or positive culture after facial laser resurfacing: A pilot study, a case report, and a proposal for a rational approach to antibiotic prophylaxis. J Am Acad Dermatol. 1998 Dec;39(6):975–81.

82. Ramsdell W. Fractional Carbon Dioxide Laser Resurfacing. Semin Plast Surg. 2012 Nov 1;26(03):125–30.

83. Goldman MP, Roberts TL, Skover G, Lettieri JT, Fitzpatrick RE. Optimizing wound healing in the face after laser abrasion. J Am Acad Dermatol. 2002 Mar;46(3):399–407.

84. Mysore V, Anitha B, Hosthota A. Successful treatment of laser induced hypopigmentation with narrowband ultraviolet B targeted phototherapy. J Cutan Aesthet Surg. 2013;6(2):117.

85. Sun HF, Lu HS, Sun LQ, Ping WD, Mao DS, Li D. Chemical Peeling with a Modified Phenol Formula for the Treatment of Facial Freckles on Asian Skin. Aesthetic Plast Surg. 2018 Apr 26;42(2):546–52.

86. Reserva J, Champlain A, Soon SL, Tung R. Chemical Peels: Indications and Special Considerations for the Male Patient. Dermatologic Surgery. 2017 Nov;43(2):S163–73.

87. Chen X, Wang S, Yang M, Li L. Chemical peels for acne vulgaris: a systematic review of randomised controlled trials. BMJ Open. 2018 Apr;8(4):e019607.

88. Castillo DE, Keri J. Chemical peels in the treatment of acne: patient selection and perspectives. Clin Cosmet Investig Dermatol. 2018 Jul;Volume 11:365–72.

89. Kaminaka C, Yamamoto Y, Yonei N, Kishioka A, Kondo T, Furukawa F. Phenol peels as a novel therapeutic approach for actinic keratosis and Bowen disease: Prospective pilot trial with assessment of clinical, histologic, and immunohistochemical correlations. J Am Acad Dermatol. 2009 Apr;60(4):615–25.

90. Kligman DE. Regarding Tretinoin Peeling. Dermatologic Surgery. 2001 Jun;27(6):608–608.

91. Khunger N, Sarkar R, Jain RK. Tretinoin Peels versus Glycolic Acid Peels in the Treatment of Melasma in Dark-Skinned Patients. Dermatologic Surgery. 2004 May;30(5):756–60.

92. Ghersetich I, Troiano M, Brazzini B, Arunachalam M, Lotti T. Melasma: Treatment with 10% tretinoin peeling mask. J Cosmet Dermatol. 2010 Jun;9(2):117–21.

93. Bagatin E, Bontempo E, Aguiar Jr N, Campos PM, Wagemaker T. Skin penetration of tretinoin in three concentrations as an agent for superficial chemical peeling. In: JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY. MOSBY-ELSEVIER 360 PARK AVENUE SOUTH, NEW YORK, NY 10010-1710 USA; 2011. p. AB73–AB73.

94. Bagatin E, Wagemaker TAL, Aguiar Júnior N dos R, Gianeti MD, Gonçalves EMB, Campos PMBGM. Tretinoin-based formulations-influence of concentration and vehicles on skin penetration. Brazilian Journal of Pharmaceutical Sciences. 2015;51:85–90.

95. Tung RC, Bergfeld WF, Vidimos AT, Remzi BK. Alpha-Hydroxy Acid-Based Cosmetic Procedures. Guidelines for patient management. Am J Clin Dermatol. 2000 Mar;1(2):81–8.

96. Sharad J. Glycolic acid peel therapy - a current review. Clin Cosmet Investig Dermatol. 2013 Nov;281.

97. Fabbrocini G, De Padova M, Tosti A. Chemical Peels: What's New and What Isn't New but Still Works Well. Facial Plastic Surgery. 2009 Dec 18;25(05):329–36.

98. Ichiyama S, Funasaka Y, Otsuka Y, Takayama R, Kawana S, Saeki H, et al. Effective treatment by glycolic acid peeling for cutaneous manifestation of familial generalized acanthosis nigricans caused by FGFR3 mutation. Journal of the European Academy of Dermatology and Venereology. 2016 Mar 27;30(3):442–5.

99. FUNASAKA Y, KOMOTO M, ICHIHASHI M. Depigmenting Effect of α-Tocopheryl Ferulate on Normal Human Melanocytes. Pigment Cell Res. 2000 Jun 17;13(s8):170–4.

100. Guo T, Sun Y, Sui Y, Li F. Determination of ferulic acid and adenosine in Angelicae Radix by micellar electrokinetic chromatography. Anal Bioanal Chem. 2003 Mar 26;375(6):840–3.

101. Bourne LC, Rice-Evans C. Bioavailability of Ferulic Acid. Biochem Biophys Res Commun. 1998 Dec;253(2):222–7.

102. Graf E. Antioxidant potential of ferulic acid. Free Radic Biol Med. 1992 Oct;13(4):435–48.

103. Saija A. In vitro and in vivo evaluation of caffeic and ferulic acids as topical photoprotective agents. Int J Pharm. 2000 Apr 10;199(1):39–47.

104. Barreca D, Bellocco E, Laganà G, Ginestra G, Bisignano C. Biochemical and antimicrobial activity of phloretin and its glycosilated derivatives present in apple and kumquat. Food Chem. 2014 Oct;160:292–7.

105. Small R, O'Hanlon K. 22 - Chemical Peels. In: Usatine RP, Pfenninger JL, Stulberg DL, Small R, editors. Dermatologic and Cosmetic Procedures in Office Practice

[Internet]. Philadelphia: W.B. Saunders; 2012. p. 259–73. Available from: https://www.sciencedirect.com/science/article/pii/B9781437705805000224

106. Zaki NS, Hilal RF. Use of a novel quantitative tool for evaluation of pseudo-acanthosis nigricans. Journal of the Egyptian Women's Dermatologic Society. 2021 May;18(2):119–28.

107. Burke JP, Hale DE, Hazuda HP, Stern MP. A quantitative scale of acanthosis nigricans. Diabetes Care. 1999 Oct 1;22(10):1655–9.

108. Eldeeb F, Wahid RM, Alakad R. Fractional carbon dioxide laser versus trichloroacetic acid peel in the treatment of pseudo-acanthosis nigricans. J Cosmet Dermatol. 2022 Jan 28;21(1):247–53.

109. Zaki NS, Hilal RF, Essam RM. Comparative study using fractional carbon dioxide laser versus glycolic acid peel in treatment of pseudo-acanthosis nigricans. Lasers Med Sci. 2018 Sep 30;33(7):1485–91.

110. Bredlich, KRÄhn, Kunzi-Rapp, Wortmann, Peter. Continuous-wave carbon dioxide laser therapy in pseudoacanthosis nigricans. British Journal of Dermatology. 1998 Nov 4;139(5):937–8.

111. Wijnberg DS, Deutman HC, Steijlen PM, Spauwen PHM. CO 2 laser treatment of benign juvenile acanthosis nigricans. Eur J Plast Surg. 2000 May 22;23(4):238–40.

112. Treesirichod A, Chaithirayanon S, Wongjitrat N. Comparison of the efficacy and safety of 0.1% adapalene gel and 0.025% tretinoin cream in the treatment of childhood acanthosis nigricans. Pediatr Dermatol. 2019 May 18;36(3):330–4.

ANNEXURE

ANNEXURE - I

PROFORMA

- **Name:**
- **Age:**
- **Sex:**
- **Occupation:**
- **UHID number:**
- **Phone number:**
- **Address:**
- **Date :**

History of Presenting Illness:

1. Age of Onset:
2. Site of onset:
3. Duration:
4. Any Associated Symptoms: itching/ burning/ pain
5. Mode of spread: static/ growing/ receding
6. Use of any drugs before onset of illness

7. Aggravating factors: Occupational/ hobbies/ trauma/ drug/ work/ sunlight/ emotional factors/ menstruation/ pregnancy/ food/ cosmetics/ chemicals/ any other:

8. Recovery: Some/ good/ poor/ no response

Past history:

- Associated systemic diseases: DM/ HTN/ Thyroid disease.
- Associated cutaneous diseases:

Family history:

A. Similar complaints:

B. Other skin problems:

C. Personal history:

D. Diet: veg/ nonveg/ mixed

E. Bowel/ Bladder habits: regular/ altered.

F. Sleep- adequate/ disturbed

G. Appetite-

H. Habits: smoking/ tobacco chewing/ alcoholism

GENERAL PHYSICAL EXAMINATION:

- Built and nourishment
- Pallor/Icterus/Cyanosis/Clubbing/Generalised Lymphadenopathy/Edema

VITALS :

- Pulse :
- BP :
- Temperature :
- Respiratory Rate :

SYSTEMIC EXAMINATION:

1. CVS
2. RS
3. PER ABDOMEN
4. CNS

LOCAL EXAMINATION :

INSPECTION:

- SITE
- SIZE
- NUMBER
- SYMMETRY
- BORDER

PALPATION :

- LOCAL RISE OF TEMPERATURE
- TENDERNESS
- NUMBER
- SIZE
- SURFACE
- BORDER

Nail examination :

- **INVESTIGATIONS :**
- **FINAL DIAGNOSIS :**
- **TREATMENT :**
- **REMARKS OF THE GUIDE :**

ANNEXURE – II

INFORMED CONSENT FORM

I Mr./Mrs._____have been explained in my own understandable language, that I will be included in a study which is **—A COMPARATIVE STUDY OF FRACTIONAL CO2 LASER VS FERULIC ACID SEQUENTIAL PEEL(12% & 8%) IN THE TREATMENT OF NECK ACANTHOSIS NIGRICANS‖**.

Hence as per the computer generated randomization of the study – I am allotted to

Group -_____for whom_____will be given as a treatment modality for my illness.

I have been explained about the randomization of the treatment modality I receive and that my clinical findings, investigations, intra operative findings will be assessed and documented for study purpose.

I have been explained my participation in this study is entirely voluntary, and I can withdraw from the study any time and this will not affect my relation with my doctor or the treatment for my ailment.

I have been explained about the necessity of the intervention, possible benefits and adverse effects due to interventions, in my own understandable language.

I have understood that all my details found during the study are kept confidential and while publishing or sharing of the findings, my details will be masked.

The principal investigator will bear the cost of the study.

I have principal investigator mobile number for enquiries.

I in my sound mind give full consent to be added in the part of this study. No monetary benefits will be given to me during the study.

- Signature of the patient Signature of the witness
- Name: Name:
- Date: Relation to patient:
- Place:
- For any further clarification you can contact the study investigator:
- Dr. Akshata Yadav.S
- Mobile no: 9483145396.
- E-mail id: akshatayadav453@gmail.com

ಮಾಹಿತಿ ನೀಡಿದ ಒಪ್ಪಿಗೆ ನಮೂನೆ

[illegible]/[illegible]. ____________ [illegible] CO2 [illegible] VS [illegible] (12%&8%) [illegible].

[illegible] - [illegible]

[illegible] - _____ [illegible] ____ [illegible].

[illegible].

[illegible].

[illegible].

[illegible].

[illegible].

[illegible].

• [illegible]

• [illegible]:

• [illegible]:

• [illegible]:

[illegible]

• [illegible]

• Mobile no: 9483145396.

E-mail id: akshatayadav453@gmail.com

ANNEXURE – III

PATIENT INFORMATION SHEET

STUDY TITLE :

―A COMPARATIVE STUDY OF FRACTIONAL CO2 LASER VS FERULIC ACID SEQUENTIAL (12%&8%) PEEL IN THE TREATMENT OF NECK ACANTHOSIS NIGRICANS‖

PLACE OF STUDY: R.L Jalappa Hospital and Research Centre, Tamaka, Kolar.

OBJECTIVES :

- To evaluate the efficacy of fractional co2 laser and ferulic acid sequential peel (12% and 8%) in the treatment of neck acanthosis nigricans.
- To document the post procedural side effects of fractional co2 laser and ferulicacid sequential peel (12% and 8%) in the treatment of neck acanthosis nigricans.

Acanthosis nigricans (AN) is a dermatosis that manifests as asymptomatic and symmetrical darkening affecting the skin of intertriginous areas, in particular the axillae, groins, sub mammary folds and neck. Acanthosis nigricans has now become a concern of cosmetological importance to many. Acanthosis nigricans can be diagnosed by clinical examination.

In this study two treatment modalities for are documented.

In this study, Group A Participants: A topical anaesthetic, containing a mixture of lidocaine-2.5% w/w + prilocaine-2.5% w/w in a cream base will be applied for 1 hour under occlusion on the area to be treated. After satisfactory anaesthesia is achieved, eyes will be protected with eye shields. Fractional ablative CO2 LASER will be then delivered to the neck at the

fluence of low power (10 W), duration (1 ms), short distance (1mm), with two passes on the affected area. Post- procedurally, ice packs for cooling will be immediately applied after laser sessions This procedure will be repeatedwith interval gap of 2 weeks until complete clearance or for a maximum of four sessions.

Group B Participants – Pre- procedurally, neck skin will be cleaned with a cotton pad. Patients will be subjected to 2-3 coats of Ferulac Peel Classic solution (Ferulic acid 12 % + 5% Phloretin) over the area to be treated. Wait until the solution is dried, appearing as light white mask. This is followed by 2 coats of Ferulac Peel Plus (Ferulic acid 8%, Phloretin5%, Malic acid5%,Citric acid 5%,Latic acid 5%,Retinol 0.2%) and allowed to dry. After approximately 12 hrs, the patient should wash the area with a mild cleansing gel. Sunscreen will be advised for patient for 1 week after peeling. Each patient will have four sessions with 2 weeks apart.

Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in this study we will collect information (as per proforma) from you. Relevant blood investigations will be carried out if required. This information collected will be used for dissertation and publication only. NO MONETARY BENEFITS WILL BE MADE AVAILABLE FOR PARTICIPANTS OF THE STUDY. Even If you are not willing to participate in this study the care, treatment & relationship with doctor will not affect All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. The expenses required for the above study will be taken care by the principal investigator. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee.

There is no compulsion to agree to this study. The care you will get will not change if you

don’t wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

- Left Thumb Impression/Signature of the Patient
- Left Thumb Impression/Signature of the Witness
- For any further clarification you can contact the study investigator:
- Dr. Akshata Yadav. S
- Mobile no: 9483145396 , Email:akshatayadav453@gmail.com

ರ'ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳ'

- **ಶೋರ್ಷಿಕ'**: " CO2 VS (12%&8%) l.
- **ಸ್ಟ್ರಟ್ಗುರಿ:**
- CO2 (12% 8%) .
- 2 (12% 8%) .
- ( ) , , , , , . . .
- .
- , **ಗ್ರೂಪ್ ಎ** : -2.5% w/w + -2.5% w/w , 1 . , . CO2 (10 W), (1 ms), (0.5mm), . , 2 .
- **ಗ್ರೂಪ್ ಬಿ** - , . 12% . 2-3 (12 % +

5% □□□□□□□□□□□□)

[illegible] 2 [illegible] (8%, [illegible] 5%, [illegible] 5%, [illegible] 5%, [illegible] 5%, [illegible] 0.2%) [illegible] 12 [illegible] 1 [illegible] 2 [illegible]

- [illegible]
- [illegible]
- [illegible]
- Mobile no: 9483145396. Email:akshatayadav453@gmail.com

ANNEXURE -IV

KEY TO MASTER CHART

GROUP 1 = GROUP A

GROUP 2 = GROUP B

ANASI SCORE= Acanthosis Nigricans Area Severity Index Score

Mild Cases = <10

Moderate Cases = 10-20

Severe cases = >20(20-40)

GPA= Global Photographic Assessment

SCORE 0=< 25% RESPONSE, 1 = 25-50% ,2 = 51-75% , 3 = > 75% RESPONSE SEEN

ERY= ERYTHEMA

PPH = POST PROCEDURE HYPERPIGMENTATION

BS = BURNING SENSATION

POS = PEELING OF SKIN

SIDE EFFECTS = > 0= ABSENT, 1= PRESENT

MASTER CHART

MASTER CHART

SLNO	AGE	SEX	UHID	GROUP	BASELINE	@2WEEK	@4WEEK	@6WEEK	@8WEEK	GPA	@2WEEK	@4WEEK	@6WEEK	@8WEEK	FERY	PPH	BS	POS	VDS	Baseline	@2weeks	@4weeks	@6weeks	@8weeks_ANASI
1	41	2.00	128004	2	8	8	6	4	2	0	1	2	3	3	0	0	0	0	1	1.00	1.00	1.00	1.00	1.00
2	25	2.00	158570	1	26	24	20	20	16	0	1	2	2	3	1	0	1	0	6	3.00	3.00	2.00	2.00	2.00
3	45	2.00	164495	2	6	6	4	4	2	0	0	1	2	3	1	0	0	0	4	1.00	1.00	1.00	1.00	1.00
4	21	2.00	169475	2	14	14	12	10	6	0	0	1	2	3	0	0	0	0	3	2.00	2.00	2.00	2.00	1.00
5	24	2.00	172383	2	18	16	16	14	10	0	1	2	3	3	0	0	0	1	6	2.00	2.00	2.00	2.00	2.00
6	43	2.00	186046	1	28	26	24	22	18	0	1	2	3	3	1	0	1	0	5	3.00	3.00	3.00	3.00	2.00
7	21	2.00	173850	1	6	6	4	2	2	0	0	1	2	3	0	0	0	0	6	1.00	1.00	1.00	1.00	1.00
8	25	1.00	180107	2	10	10	8	6	6	0	0	1	2	3	0	0	0	0	4	2.00	2.00	1.00	1.00	1.00
9	38	2.00	133031	1	8	8	6	6	4	0	1	2	3	3	1	0	1	0	5	1.00	1.00	1.00	1.00	1.00
10	23	2.00	129697	2	26	26	24	24	20	0	0	1	2	3	1	0	1	0	4	3.00	3.00	3.00	3.00	2.00
11	34	1.00	186391	2	30	30	28	26	22	0	0	1	2	3	0	1	0	0	3	3.00	3.00	3.00	3.00	3.00
12	25	2.00	174698	2	18	18	16	14	10	0	0	1	2	3	1	0	0	1	6	2.00	2.00	2.00	2.00	2.00
13	39	2.00	186410	2	28	28	26	24	20	0	0	1	2	3	0	0	1	0	5	3.00	3.00	3.00	3.00	2.00
14	38	2.00	159921	1	12	12	10	8	8	0	0	1	2	2	1	1	0	0	6	2.00	2.00	2.00	1.00	1.00
15	30	2.00	186874	1	18	18	16	16	14	0	0	1	2	3	1	0	0	0	4	2.00	2.00	2.00	2.00	2.00
16	45	1.00	187285	1	30	28	26	26	22	0	1	1	2	3	0	0	0	0	3	3.00	3.00	3.00	3.00	3.00
17	34	2.00	122829	1	14	14	12	10	8	0	0	1	2	3	1	0	0	0	5	2.00	2.00	2.00	2.00	1.00
18	35	2.00	187271	1	34	32	30	28	24	0	1	2	2	2	0	1	0	0	6	3.00	3.00	3.00	3.00	3.00
19	34	1.00	177338	2	6	6	4	2	2	0	0	1	2	3	0	0	0	0	1	1.00	1.00	1.00	1.00	1.00
20	23	1.00	178370	1	16	16	14	12	10	0	0	1	2	3	1	1	0	0	6	2.00	2.00	2.00	2.00	2.00
21	39	1.00	188096	2	8	8	6	4	2	0	1	2	2	3	0	0	0	0	4	1.00	1.00	1.00	1.00	1.00
22	45	2.00	188199	1	18	18	16	12	12	0	0	1	2	2	1	0	0	0	2	2.00	2.00	2.00	2.00	2.00
23	41	2.00	167017	2	18	18	16	14	10	0	1	2	3	3	0	0	0	0	2	2.00	2.00	2.00	2.00	2.00
24	31	2.00	188394	1	12	12	10	8	8	0	0	1	2	2	1	0	0	0	2	2.00	2.00	2.00	1.00	1.00
25	39	2.00	184017	1	24	24	22	20	18	0	1	1	2	3	0	0	0	1	6	3.00	3.00	3.00	2.00	2.00
26	22	2.00	179053	2	12	12	10	8	6	0	1	2	3	3	1	0	0	0	6	2.00	2.00	2.00	1.00	1.00
27	43	2.00	181234	1	22	22	20	20	16	0	1	1	2	2	1	0	1	0	7	3.00	3.00	2.00	2.00	2.00
28	25	1.00	183403	2	12	12	10	8	6	0	1	2	2	3	0	0	0	0	3	2.00	2.00	2.00	1.00	1.00
29	36	2.00	190161	2	8	8	6	4	2	0	1	2	2	3	0	0	1	0	4	1.00	1.00	1.00	1.00	1.00
30	41	2.00	190270	2	26	26	24	22	20	0	1	2	2	3	0	0	0	1	5	3.00	3.00	3.00	3.00	2.00

31	40	2.00	190160	2	16	16	14	12	8	0	1	2	2	3	1	0	0	0	4	2.00	2.00	2.00	2.00	1.00
32	35	2.00	190253	1	26	26	24	22	20	0	1	1	2	2	0	1	0	0	6	3.00	3.00	3.00	3.00	2.00
33	39	2.00	198615	1	6	6	6	4	4	0	1	2	2	3	1	0	1	1	7	1.00	1.00	1.00	1.00	1.00
34	28	2.00	190763	2	10	10	8	6	4	0	1	2	3	3	0	0	0	0	4	2.00	2.00	1.00	1.00	1.00
35	40	2.00	191192	1	10	10	8	8	6	0	1	2	2	3	1	1	0	0	6	2.00	2.00	1.00	1.00	1.00
36	32	2.00	189136	2	18	16	14	10	8	0	1	2	2	3	0	0	0	0	3	2.00	2.00	2.00	2.00	1.00
37	36	2.00	134129	1	22	22	20	18	14	0	1	1	2	2	0	0	0	0	4	3.00	3.00	2.00	2.00	2.00
38	28	2.00	223301	2	14	14	12	10	8	0	1	2	2	3	0	0	0	0	3	2.00	2.00	2.00	2.00	1.00
39	44	1.00	247744	1	6	6	6	4	4	0	1	2	2	3	0	0	0	0	3	1.00	1.00	1.00	1.00	1.00
40	44	2.00	227739	2	16	16	14	12	10	0	1	2	2	3	1	0	0	0	5	2.00	2.00	2.00	2.00	2.00
41	21	2.00	247742	2	28	28	26	22	20	0	1	2	2	3	1	0	0	0	5	3.00	3.00	3.00	3.00	2.00
42	44	2.00	237842	2	18	18	16	14	10	0	1	2	2	3	0	0	0	0	4	2.00	2.00	2.00	2.00	2.00
43	34	2.00	227178	1	8	8	6	6	4	0	1	2	2	3	1	0	0	0	5	1.00	1.00	1.00	1.00	1.00
44	42	2.00	248156	2	14	14	12	12	10	0	1	2	3	3	0	0	0	0	4	2.00	2.00	2.00	2.00	2.00
45	41	2.00	233356	1	30	30	28	26	26	0	1	1	2	2	1	0	0	0	4	3.00	3.00	3.00	3.00	3.00
46	24	1.00	213286	2	26	24	22	22	18	0	1	2	2	3	0	0	0	0	2	3.00	3.00	3.00	3.00	2.00
47	21	1.00	243306	2	20	20	18	16	12	0	1	1	2	3	0	1	0	0	6	2.00	2.00	2.00	2.00	2.00
48	37	2.00	223342	1	18	18	16	16	12	0	1	2	2	3	1	0	0	0	5	2.00	2.00	2.00	2.00	2.00
49	36	2.00	213318	1	18	18	18	16	14	0	0	1	2	2	0	1	0	0	4	2.00	2.00	2.00	2.00	2.00
50	39	2.00	208988	2	24	24	22	20	18	0	1	2	2	3	0	0	0	0	3	3.00	3.00	3.00	2.00	2.00
51	45	2.00	229269	2	28	24	22	22	18	0	1	2	2	3	0	0	0	0	4	3.00	3.00	3.00	3.00	2.00
52	31	2.00	219398	2	16	16	14	12	8	0	1	2	3	3	0	0	0	0	4	2.00	2.00	2.00	2.00	1.00
53	41	1.00	221198	1	8	8	6	6	4	0	1	2	2	2	1	0	0	0	5	1.00	1.00	1.00	1.00	1.00
54	36	2.00	231491	1	6	4	4	2	2	0	1	1	2	3	1	0	0	0	6	1.00	1.00	1.00	1.00	1.00
55	21	2.00	242855	1	26	26	24	22	20	0	1	1	2	3	0	0	0	0	4	3.00	3.00	3.00	3.00	2.00
56	44	2.00	69781	1	14	14	12	12	10	0	1	2	2	3	0	0	1	0	4	2.00	2.00	2.00	2.00	2.00
57	45	2.00	174696	1	32	32	30	28	26	0	1	1	2	2	1	0	0	0	5	3.00	3.00	3.00	3.00	3.00
58	21	2.00	130624	1	8	8	6	6	4	0	1	2	2	2	0	0	0	0	5	1.00	1.00	1.00	1.00	1.00
59	21	2.00	233280	2	14	14	12	10	8	0	1	2	2	3	1	0	0	0	3	2.00	2.00	2.00	2.00	1.00
60	44	2.00	144820	1	30	30	28	24	20	0	1	1	2	2	1	1	0	0	5	3.00	3.00	3.00	3.00	2.00