STUDY PROTOCOL

Comparative study between therapeutic effects of microneedling versus CO₂ laser in acne scars [version 1; peer review: awaiting peer review]

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Abstract

Objectives: To study the clinical aspect of acne scars while grading them on the basis of severity as well as to study and compare the therapeutic effects of CO₂ laser and microneedling in their management.

Methods: This study used prospective comparison as its method of study. Over the course of two years, from June 2021 to June 2023, 100 patients above 18 years of age having post-acne atrophic scars will be enrolled. Patients will be split into two groups and each group will be selected for fractional CO₂ laser (non-ablative) and microneedling respectively. Four treatments will be administered to each group of patients with a four-week gap between each session. All clinical findings will be recorded for data analysis and comparison. “Goodman and Baron's Qualitative and Quantitative grading system for scars” will be used after each session in order to compare the therapeutic effects for each group.

Results: At the end of each session, acne scar grading will be done in each group and data will be compiled to assess and compare the therapeutic effects between CO₂ laser and microneedling.

Conclusions: The findings of the protocol research will be used to form the conclusions.

Trial Registration: Submitted for registration to Clinical Trial Registry of India (CTRI).

Keywords
CO₂ laser, microneedling, fractional, acne scars, atrophic scars, inflammation
Introduction
Acne, a common inflammatory condition of the pilosebaceous unit, is characterized by comedones, papulo-pustules, and occasionally nodules. It mostly affects the face, followed by the chest and back. Remaining scarring is a usual adverse effect of acne treatment. Acne scarring can negatively affect quality of life, leading to low self-esteem and unpleasant feelings.1

Severity of the residual scarring depends on the duration and intensity of the inflammatory response during the active disease. There is weakening of the collagen synthesis caused by an increased ratio of tissue inhibitors of MMPs to matrix metalloproteinases (MMPs) during the extracellular matrix remodeling process.2

A classification system has been described to segregate atrophic scars post acne into three types: icepick, rolling, and boxcar scars. With the help of this classification, treatment options can be better tailored to each individual patient. Ice pick scars being less than 2 mm in diameter that extend vertically through the whole length of dermis. Boxcar scars are spherical skin depressions with flat bases and sharp edges that could be shallow (0.1-0.5 mm) or deep (>0.5 mm). Lastly, rolling scars are depressions which range in size from 4 to 6 mm and are shallower than boxcar type but have the largest circumference. The aberrant fibrous bands causing these scars pull the dermis down to attach to the subcutaneous layer.2

Microneedling is a commonly used minimally invasive technique used to treat acne scars. It involves creating skin punctures using sterile micro needles attached to a handheld rolling device which helps in disrupting dermal collagen fibers that connect the scar tissue. Growth factors are regenerated as a result, encouraging the dermal blood vessels to produce collagen and elastin.3 Microneedling works best for healing shallow boxcar and rolling scars since it only reaches the upper dermis.1 Fractional ablative CO2 lasers, which have only recently as of 2003 hit the market, are an efficient method of managing acne scars with least adverse effects. They work on the principle of fractional thermolysis. This refers to the creation of pixilated columnar zones of thermal injury to the dermis also known as micro thermal zones in order to promote collagen formation.4

The fractional component of the laser makes sure that the tissue injury is spatially well distributed in a precise pattern across the treated area, while retaining the healing function of the epidermis whereas the ablative component ensures fewer side effects, such as erythema, edema, hemorrhage, crusting, infection, and scarring since they target the dermis while leaving the epidermis intact.5

In carbon lasers, water acts as a chromophore which produces light at a wavelength of 10,600 nm. Due to the significant tissue water absorption of the carbon dioxide beam, depth penetration is limited. However, depths of over 2 mm can be reached by increasing irradiation over a very small region in a fractionated method and employing greater pulse energies. In addition to modifying dermal collagen, development of myofibroblasts and matrix proteins like hyaluronic acid is also aided by carbon dioxide lasers. Matrix metalloproteinases are present at exceptionally high concentrations promoting wound healing (MMPs).6

Therefore, by comparing the outcome between these two commonly used treatment modalities, we can have knowledge as to which intervention would be most effective in acne scar management.

Protocol
Rationale/need for the study
Scarring in post acne lesions is a very common, difficult, and upsetting issue for medical professionals and patients. It may negatively affect the quality of life of the patient. It is necessary to examine the pathophysiology and morphology of each scar in order to address this issue and treatment must be decided accordingly. An early and aggressive approach helps not only in improving cosmesis but also in limiting the further progression of severity.1

Acne scars can be primarily of three types: hypertrophic, atrophic and keloidal, with atrophic scars being associated with collagen loss and affecting 80–90% of patients. Keloids and hypertrophic scars only occur occasionally. It is crucial to further divide atrophic scars into ice pick, rolling, and boxcar categories so that treatment options can be more precisely catered to the needs of each patient.3,5,1 Rolling and boxcar types of acne scars respond well to fractional CO2 laser therapy and microneedling.5,1 Scar severity is another important aspect to be considered in the management of scars. It helps not only in identifying the treatment most suited to the patient but also in evaluating outcomes. One such grading scale is the “Goodman and Baron Qualitative scar grading system”, which will be used in this study.7

Nowadays, a multitude of modalities are available in managing post acne scars. Microneedling and fractional ablative CO2 lasers are very commonly used techniques which are effective and cause fewer side effects when compared to other
modalities. In this study, we compare the therapeutic effects between them in different cases of acne scars of varying severity which will help us decide which one is more effective in their management.

Aim
To study and compare the therapeutic effects between CO₂ laser and microneedling in acne scars.

Objectives
1. To evaluate the characteristics and clinical features of acne scars
2. To grade acne scars on the basis of their severity
3. To evaluate CO₂ lasers’ therapeutic effect in post atrophic acne scars
4. To evaluate the therapeutic effects of microneedling in acne scars
5. Comparison between the therapeutic effects of CO₂ laser and microneedling in atrophic post acne scars

Methods
Study participants
In the current study, 100 cases including both males and females with post-acne atrophic scars and age of above 18 years are included presenting in the department of dermatology, venereology and leprosy at AVBRH, Sawangi.

Study design
The method used in this study is prospective comparative.

Study period
The study will be conducted over the course of two years (June 2021 to June 2023).

Eligibility criteria
Inclusion criteria
a) Patients of both genders above 18 years of age.

b) Patients willing to participate in the study with their informed consent.

c) Patients with clinical diagnosis of post acne atrophic scars will be included.

Exclusion criteria
a) Patients having any major systemic disease and uncontrolled medical or surgical illness.

b) Patients having any active infection (Viral e.g. Herpes or bacterial/fungal infections).

c) Female patients who are pregnant or lactating.

d) Patients having keloid/hypertrophic scar.

e) Patients on anti-coagulant medications.

f) Patients with immunocompromised conditions e.g. HIV infection.

Sample size
\[ n = \left[ Z_{0.025} \right]^2 \times \frac{P(1-P)}{d^2} \]
\[ n = (1.96)^2 \times 0.15 \times (1 - 0.15)/(0.07)^2 \]
n = 99

n = 99 patients needed for the study

Where,

n = sample size

$Z_{0.025}$ is the level of significance at 5%, that is, 95% confidence interval = 1.96

P = Prevalence of atrophic acne scars = 15% = 0.15

d = Desired error of margin = 7% = 0.07

**Sample size for the present study will be 100 cases**

Cases will be defined as any patient above 18 years of age, irrespective of gender, coming to the Department of Dermatology, Venereology and Leprosy and having acne scars.

**Methods**

Prospective comparison is used as the method in this study in which 100 patients having acne scars coming to the Department of Dermatology at AVBRH, Wardha, will be enrolled after considering the various exclusion and inclusion criteria’s from June 2021 to June 2023. Institutional Ethical Committee (IEC) clearance will be obtained. Written and signed informed consent in their vernacular language will be taken from all the participants for voluntary participation. A detailed history including name, age, sex, past history and family history will be taken. A detailed clinical examination will be performed for all patients presenting with post acne atrophic scars.

Based upon the severity of acne scars, patients will be classified into four grades according to the “Goodman and Baron Qualitative scar grading system” (Table 1). The patients will be split into two groups with 50 patients each, Group A and Group B. Participants will be randomly assigned to either groups with a 1:1 allocation as per a computer generated randomisation schedule stratified by site and using permuted blocks of random sizes. The block sizes will not be disclosed, to ensure concealment. The group A will be selected for fractional ablative CO2 laser using Futura CO2 Fractional Laser System®. The group B will be selected for microneedling using the Dermapen 4™. Four treatments will be given to patients in both groups, with a four-week interval between each session. There will be a clinical evaluation of the progress made based on “Goodman and Baron Qualitative scar grading system” at the end of each session by a side by side comparison of pre-operative and post-operative photographs. All patients from both the groups will be prescribed a topical sunscreen and moisturizer post procedure. Additionally, one month following the fourth session, patients will be questioned regarding how scars have improved in order to determine patient satisfaction using the Visual Analogue Score (VAS). In order to improve adherence of patients to the study, patients will be counselled in detail about the procedures and the improvement they can expect with successive therapies. A thorough follow up shall be done using patients contact information collected during the enrollment process along with adjusting dates of treatment according to the patient’s comfort. During the period of the study, patients will not be receiving any concomitant therapy for their acne scars in order to prevent bias in the therapeutic effects of the modalities being compared in the study. Both treatment interventions shall be discontinued in case of any adverse reaction or worsening of existing lesions. The time schedule of enrolment, interventions, assessments, and visits for participants has been explained in the participant timeline figure (Table 2). The progress of the study will be monitored by the departmental committee headed by the Head of the Department of Dermatology.

**Table 1. Goodman and Baron Qualitative system for grading acne scars.**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Level of disease</th>
<th>Clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Macular</td>
<td>Macular erythematous, hyperpigmented or hypopigmented flat marks</td>
</tr>
<tr>
<td>2</td>
<td>Mild</td>
<td>Mild atrophic or hypertrophic scarring that may not be obvious at social distances of 50 cm or greater and easily covered by makeup or beard hair in men</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
<td>Moderate atrophic or hypertrophic scarring that is obvious at social distances of 50 cm or greater and is not covered easily by makeup or beard hair in men but can still be flattened by manual stretching of skin</td>
</tr>
<tr>
<td>4</td>
<td>Severe</td>
<td>Severe atrophic or hypertrophic scarring not flattened by manual stretching of skin</td>
</tr>
</tbody>
</table>
Outcome measure
This study can help us better understand the response outcome of CO2 lasers and microneedling in acne scars which can further help us decide the most appropriate intervention amongst the two in treatment of acne scars.

Statistical method
All standard parametric and non-parametric data will be assessed by standard statistical methods.

A ‘p’ value of <0.05 will be considered significant.

Limitation of the study
Limitation is that this is a hospital based and not a population based study also other types of post acne scars like keloidal and hypertrophic scars are not included in this study.

Discussion
Bhalla M, Arora A, in the year 2022, studied the role of fractional CO2 lasers in acne scars and found that fractional carbon dioxide lasers showed effectiveness in skin renewal in atrophic acne scars. They explained the mechanism by which fractional lasers work and the proper treatment protocol to be followed for best results. They concluded that counselling, patient selection with pre and post procedure care guidelines are crucial factors upon which the treatment outcome depends. Jordan R, Cummins C et al., in the year 2000, carried out research to determine how laser resurfacing can reduce the appearance of face acne scars. They discovered that the patient efficacy ranged from 25 to 90% for both the carbon dioxide laser and the erbium: YAG laser. Although lasting a few weeks, pigmentation changes as a side effect were experienced by up to 44% of individuals. After receiving the carbon dioxide laser, patients experienced erythema for 1.5 to 4 months before re-epithelialization occurring after 7 to 14 days. Up to 84% of individuals can expect their acne or milia to return. It was discovered that the likelihood of serious consequences, such as hospitalization because of a systemic infection, was quite low. They arrived to the conclusion that high-quality randomized controlled studies with standardized scar ratings and validated patient outcome measures are needed to assess the effectiveness of laser resurfacing.

In the year 2012, Levy LL, Zeichner JA, et al. discussed and analyzed the various minimally invasive methods for treating acne scarring with a focus on pharmacologic agents, such as isotretinoin for acne scars that are atrophic and corticosteroids with chemotherapeutic drugs for scars that are hypertrophic. They discuss various in office and minimally invasive
techniques like chemical peels, dermabrasion, tissue augmentation, and punch excision. They conclude that no single strategy has emerged as first line as we must individualize the treatment in accordance with the type of acne scars present. Moreover, they emphasize on managing patient expectations and setting realistic goals. They also suggest a combination of approaches with lasers in order to achieve best results thereby improving patient’s quality of life.  

Zaleski-Larsen LA, Fabi SG et al., in the year 2016, conducted a research to examine the efficacy and safety of combining multiple modalities in the treatment of acne scars. Results of the hyaluronic acid filler were discovered to be evident immediately and to continue to stimulate neocollagenesis for a period of 12 to 24 months. With fat transplantation, optimal effects were typically seen 3 months after the procedure. Treatment options for 45 individuals with atrophic acne scars included skin needling combined with PRP, 100% TCA CROSS, and PRP. Improvement was found in 46.7%, 26.7% and 60% of the patients respectively. Non-ablative fractional lasers with 20% TCA improved atrophic acne scars by 78.27%. Autologous bone marrow stem cells were administered to 14 patients and implanted beneath the acne scars. At six months after the surgery, the acne scars had significantly improved. CONCLUSION: Combining acne scar treatment techniques is safe and leads to optimal patient outcome.  

To evaluate the efficacy of fractional CO2 laser and fractional radiofrequency microneedling in the treatment of facial acne scars, Reddy KY, Swaroop R et al. did a study in 2020. According to the findings, 20% of patients in the MnRF group had improved by three grades one month following their final session, compared to 13.3% of patients in the fractional CO2 group.  

Scope:
This study shall help us decide which intervention amongst CO2 laser and microneedling carries the most therapeutic effectiveness in treating acne scars. It will also reduce the psychological stress brought on by acne scars which shall further improve the patient’s quality of life. Knowledge about the best intervention will also help save time and effort for both the patient and the clinician.

Study status:
All patients having post acne atrophic scars in both CO2 laser (Group A) and microneedling (Group B) groups have been enrolled and necessary treatment sessions in four-week intervals have been conducted. Pre and post procedure photographs had been taken. Scar grade based upon the severity of acne scars at every four week interval to each patient has been allotted. Patient’s satisfaction one month following the last session using the Visual Analogue Score (VAS) has been recorded. Data compilation has been initiated to assess the comparative effects between the two modalities.

Ethical considerations:
Clearance from Institutional Ethics Committee (IEC) and Scientific Scrutiny Committee/Institutional Research Committee has been obtained.

Data availability:
No data are associated with this article.

References:


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