

Evaluation, Prevention, and Management of Acne Scars: Issues, Strategies, and Enhanced Outcomes

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ABSTRACT

Acne is a common disease affecting a high percentage of the younger population. Without appropriate and effective primary prevention of scarring, post-acne scars occur in about 80-95% of all patients. Acne scarring is the result of an alteration of the healing process and it can have deep psychosocial implications for patients. Scars can involve textural change in the superficial and deep dermis and it can also be associated with erythema or pigmentation. While the most effective strategy to reduce acne scarring is to prevent its formation, over the past decades, numerous aesthetic and surgical techniques have been proposed to improve the appearance of acne scarring. However, scar treatment still remains suboptimal; indeed, acne scarring management is a difficult therapeutic challenge for dermatologists. Several treatment options have been described to treat various acne scar types and clinical responses may differ from various factors, such as skin types. Treatment approaches for acne scarring should be individualized and primarily determined by the morphological features of each patient's scars. Dermatologists need to better organize their assessment of acne scarring and develop a multistep treatment plans tailored to address patients' individual needs.

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INTRODUCTION

Evaluation of Acne Scars

Although several grading scales exist for acne scarring, there are many limitations in their application in daily clinical practice. Scars classifications is difficult even for acne experts, sometimes.

To simplify, there are two basic types of acne scars depending on whether there is a loss or gain of skin volume: 80-90% of patients having scars associated with a loss of collagen (atrophic scars) compared to a minority of subjects showing hypertrophic scars and keloids (with a ratio atrophic/hypertrophic scars 3:1).

Atrophic Scars

Atrophic scars can be sub-classified into ice-pick (60%-70% of total scars), boxcar (20%-30%), and rolling scars (15%-25%).¹ In Table 1 we summarize morphological features and corresponding clinical aspect of different type of atrophic scars. Among classifications and scales proposed by several authors, the qualitative scarring grading system proposed by Goodman and Baron² is simple and universally applicable (Table 2). The qualitative approach is useful in mild post acne scarring, but the main limitation of these scales is the subjectivity of the assessment. In the observation of severe cases, different patterns are simultaneously present and may be difficult to differentiate. For these cases, Goodman developed a quantitative global acne scarring assessment tool³ based on the type of scar and the number of scars. This system assigns fewer points to macular and mild atrophic scars, and highest score to moderate


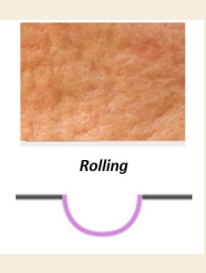
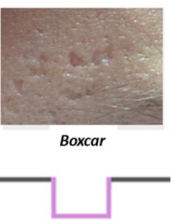
and severe atrophic scars (macular or mildly atrophic: 1 point; moderately atrophic: 2 points; punched out or linear-troughed severe scars: 3 points; hyperplastic papular scars: 4 points). The multiplication factor for these lesion types is based on the numerical range: for 1-10 scars, the multiplier is 1; for 11-20 scars, the multiplier is 2; for more than 20 scars, the multiplier is 3. Other systems have been proposed to improve the approach to the classification of acne scars. In 2017, the Global Alliance to Improve Outcomes in Acne presented a system based on the global grading scale.⁴ Tan et al proposed a six-category global severity scale (SCAR-S) for assessment of acne scarring at each of the face, chest, and back.⁵

The ECCA (Echelle d'Evaluation clinique des Cicatrices d'acné)⁶ for facial acne scarring is also a quantitative scale, designed for use in clinical practice with the aim of standardizing discussion on scar treatment and is based on the sum of individual types of scars and their numerical extent. The potential advantages of this system include independent accounting of specific scar types, thereby providing for separate atrophic and hypertrophic sub-scores in addition to total scores. Potential shortcomings include restriction to facial involvement, time intensity, and undetermined clinical relevance of score ranges.

Hypertrophic and Keloidal Scars

Keloids and hypertrophic scars are caused by cutaneous injury and inflammation. Notably, superficial injuries that do not reach the reticular dermis never cause keloidal and hypertrophic

TABLE 1.**Acne Scars Morphological Description and Clinical Aspect**

Acne Scars Subtype	Morphological Features	Clinical Aspect
<i>Icepick</i>	Ice-pick scars are narrow (<2 mm), deep, sharply margined epithelial tracts that extend vertically to the deep dermis or subcutaneous tissue.	
<i>Rolling</i>	Rolling scars occur from dermal tethering of otherwise relatively normal-appearing skin and are usually wider than 4 to 5 mm. Abnormal fibrous anchoring of the dermis to the subcutis leads to superficial shadowing and a rolling or undulating appearance to the overlying skin.	
<i>Boxcar</i>	Boxcar scars are round to oval depressions with sharply demarcated vertical edges, similar to varicella scars. They are clinically wider at the surface than ice-pick scars and do not taper to a point at the base. They may be shallow (0.1–0.5mm) or deep (≥0.5mm) and are most often 1.5 to 4.0 mm in diameter.	

scarring. This suggests that these pathological scars are due to injury of this skin layer and the subsequent aberrant wound healing therein by persistent inflammation. The reticular layer of keloids and hypertrophic scars contains inflammatory cells, increased numbers of fibroblasts, and newly formed blood vessels. Hypertrophic scars are typically pink, raised, and firm, with thick hyalinised collagen bundles that remain within the borders of the original site of injury and collagen deposits (Figure 1). Hypertrophic and keloidal scars are more common in darker-skinned individuals and occur predominantly on the trunk.

Prevention of Acne Scars

Prevention of acne scar development can be lead by controlling skin inflammation during acne treatment. Inflammation plays a crucial role in acne scars formation. By examining biopsy specimens of acne lesions from the back of patients with severe scars and without scars, Holland et al found that the inflammatory reaction at the pilosebaceous gland was stronger and had a longer duration in patients with scars versus those without;

FIGURE 1. Hypertrophic acne scars in a 24-year-old female.

in addition, the inflammatory reaction was slower in those with scars versus patients who did not develop scars. They showed a strong relationship between severity and duration of inflammation and the development of scarring, suggesting that treating early inflammation in acne lesions may be the best approach to prevent acne scarring.⁷ Among therapeutic options to control the inflammatory process in acne are topical retinoids that have shown high efficacy. Several clinical trials have demonstrated the efficacy of topical retinoids to prevent acne scars.⁸⁻⁹ Direct and indirect anti-inflammatory properties of topical retinoids are the molecular principle by which their activity is based on.

Different authors focused on the molecular events involved in the scar formation, explaining the activity of topical retinoids in acne scarring prevention.¹⁰ They described the inflammatory pathways active in vivo in acne lesions, showing the hyperactivation of two important transcriptional factors: NFK-B e AP-1. In particular, NFK-B activation increases the expression of various cytokines (especially TNF alpha and IL-1) that are able to break out the inflammatory cascade with different mechanisms, especially through the recruitment of circulating inflammatory cells. These cells, when "attracted" by these mediators, migrate from the circulation through the vessel wall reaching the inflammatory site. All these events contribute significantly to the histological damage occurring in the pilo-sebaceous unit, contributing to the appearance of disfiguring scars in patients suffering from acne (Figure 2).

AP-1 is a transcriptional factor able to modulate different genes and activate the expression of different Metalloproteinases (MMPs) such as MMP-1, MMP-3, MMP-9. These types of MMPs seem to be particular represented in the dermis and they are involved in extracellular matrix degradation, a crucial event in acne scars formation. The activities of NFK-B and AP-1 on molecular pathways involved in scarring events explain why the anti-inflammatory effect of retinoids is so important for their efficacy in acne scars prevention.¹¹ It has also been demonstrated that retinoids are able to reduce free fatty acids amounts in microcomedones, promoting the correct barrier function of infundibular wall by an indirect antinflammatory activity. Retinoic

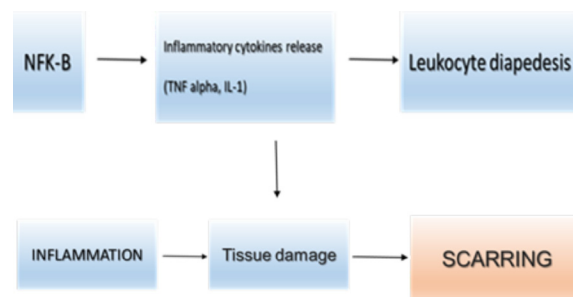
TABLE 2.**Qualitative Scarring Grading System** (adapted from Goodman and Baron, 2006)

Grades of Post Acne Scarring	Level of Disease	Clinical Features
1	Macular	These scars can be erythematous, hyper-, or hypopigmented flat marks. They do not represent a problem of contour like other scar grades but of color.
2	Mild	Mild atrophy or hypertrophy scars that may not be obvious at social distances of 50 cm or greater and may be covered adequately by makeup or the normal shadow of shaved beard hair in men or normal body hair if extrafacial.
3	Moderate	Moderate atrophic or hypertrophic scarring that is obvious at social distances of 50 cm or greater and is not covered easily by makeup or the normal shadow of shaved beard hair in men or body hair if extrafacial, but is still able to be flattened by manual stretching of the skin (if atrophic).
4	Severe	Severe atrophic or hypertrophic scarring that is evident at social distances greater than 50 cm and is not covered easily by makeup or the normal able to be flattened by manual stretching of the skin.

acid is able to increase fibroblast proliferation and extracellular matrix components synthesis in vitro.¹²⁻¹⁴ All these biological properties make retinoids a very useful tool for dermatologists in the prevention and treatment of acne scarring.

Management of Acne Scars

Anecdotal experience and medical investigations have shown that most cases of acne scarring cannot be solved by a single “best” treatment. Acne scars can vary for type and depths and each of the currently available treatments is ideally suited to ad-

FIGURE 2. NFK-B dependent inflammatory pathway involved in acne scars formation.

dress a subset of this spectrum. Below, we summarize the most used therapeutic techniques available for acne scars management, their indications/contraindications, evidence for efficacy, and potential adverse effects.

Chemical Exfoliation

Chemical exfoliation is obtained by applying chemicals to the skin to destroy the outer damaged layers and accelerate the repair process. Active inflammation, dermatitis or infection of the area to be treated, isotretinoin therapy within 6 months before peeling procedure, pregnancy, and delayed or abnormal wound healing are general contraindications for all types of chemical exfoliations. Different agents have different depths of penetration and therefore, chemical peels can be divided into four different groups based on the histologic level of necrosis that they cause (Table 3).

Glycolic acid (GA): GA is the most commonly used alpha hydroxyl acid as a peeling agent. GA acts by thinning the stratum corneum, promoting epidermolysis, and dispersing basal layer melanin. It increases dermal hyaluronic acid and collagen

TABLE 3.**Classification of Peeling Agents**

Depth of Penetration	Histologic Level	Peeling Agents
Very superficial	Destruction of the stratum corneum without creating a wound below the stratum granulosum	<ul style="list-style-type: none"> Glycolic acid, 30% to 50%, applied briefly (1 to 2 minutes) Jessner solution, applied in 1 to 3 coats TCA 10%, applied in 1 coat
Superficial	Destruction of part or all of the epidermis, anywhere from the stratum granulosum to the basal cell layer	<ul style="list-style-type: none"> Glycolic acid, 50% to 70%, applied for a variable time (2 to 20 minutes) Jessner solution, applied in 4 to 10 coats TCA, 10% to 30%
Medium Depth	Destruction of the epidermis and part or all of the papillary dermis	<ul style="list-style-type: none"> Glycolic acid 70%, applied for a variable time (3 to 30 minutes) TCA, 35% to 50% Augmented TCA (CO₂ plus TCA 35%; Jessner solution plus TCA 35%; glycolic acid 70% plus TCA 35%)
Deep	Destruction of the epidermis and papillary dermis, extending into the reticular dermis	<ul style="list-style-type: none"> Phenol 88% Baker-Gordon phenol formula

gene expression by increasing secretion of IL-6. The best results achieved for acne scars include five sequential sessions of 70% glycolic acid every two weeks. The disadvantages of GA are penetration often not uniform, mandatory neutralization, and high risk of overpeel if the time of application is too long or if the skin is inflamed. Persistent hyperpigmentation and irritation are the most common side effect of this chemical agent.

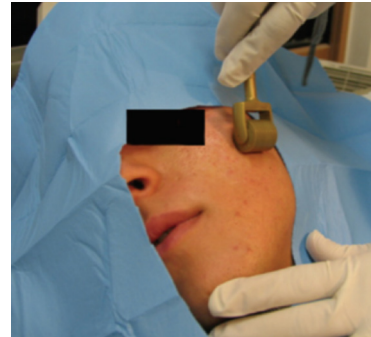
Jessner's solution (JS): JS is a combination of salicylic acid, resorcinol, and lactic acid in 95% ethanol, able to induce corneocyte detachment and subsequent desquamation of the stratum corneum, enhancing penetration of other agents. The depth of the peel depends on the number of coats of solution applied. Different patients may require different number of coats to achieve the same level of peel. This is because the penetration of the solution depends on a number of factors, including the preparation of the skin, the thickness of the corneum, and the sensitivity of the skin. The advantages of JS are that the peel is very superficial and safe, and rarely goes deeper than one would expect. Scaling, irritation, burning sensation, and persistent hyperpigmentation are the most frequent side effects of this chemical agent.

Pyruvic acid (PA): PA presents keratolytic, antimicrobial, and sebostatic properties, as well as the ability to stimulate new collagen production and the formation of elastic fibers. The use of 40 to 70% pyruvic acid has been proposed for the treatment of moderate acne scars. The advantages of pyruvic acid are the homogeneous penetration with uniform erythema, mild desquamation, short postoperative period, and the possibility of use for all skin types. Disadvantages include intense stinging and burning sensation, mandatory neutralization, and irritating vapors for the upper respiratory mucosa.

Salicylic acid (SA): SA is one of the best peeling agents for the treatment of acne scars. It is a beta hydroxy acid. SA removes intercellular lipids that are covalently linked to the envelope surrounding cornified epithelioid cells. The most efficacious concentration for acne scars is 30% in multiple sessions, 3 through 5 times, every 3 through 4 weeks.¹⁵ The side effects of salicylic acid peeling are mild and transient. The advantages of salicylic acid are an established safety profile in all skin types, post-inflammatory hyperpigmentation or scarring are very rare, and for this reason it is used to treat dark skin. The disadvantage of salicylic acid is the intense stinging and burning sensation.

Trichloroacetic acid (TCA): TCA causes protein denaturation, the so-called keratocoagulation, resulting in a readily observed white frost. The degree of the frosting correlates with the depth of solution penetration on the basis of different concentrations. TCA in a percentage of 10%–20% results in a very light superficial peel with no penetration below the stratum granulosum;

FIGURE 3. Skin needling procedure.



a concentration of 25%–35% produces a light superficial peel with diffusion encompassing the full thickness of the epidermis; 40%–50% can produce injury to the papillary dermis, and finally, greater than 50% results in injury extending to the reticular dermis. The use of TCA in concentrations greater than 35% should be avoided. It can be preferred in some cases of isolated lesions or for treatment of isolated ice-pick scars (TCA CROSS).¹⁶ The advantages of TCA are low cost, uniformity of application, and the ability to evaluate the penetration by the color of frost. The disadvantages include stinging and burning sensation during the application. High concentrations are not recommended in skin types V to VI due to the potential for hypo/hyperpigmentation.

Phenol: Phenol is a deep peel that can improve atrophic acne scars. However, it requires sedation and cardiovascular monitoring and it is not recommended in skin types IV to VI. Deep peels as phenol are more rarely used because of the downtime required for healing and the potential for complications and adverse events.

Skin Microneedling or Percutaneous Collagen Induction

Skin needling is a dermatologic treatment procedure performed to achieve percutaneous collagen induction (PCI), which is effective in improving depressed acne scarring. At first, facial skin must be cleansed, then a topical anaesthetic is applied and left for 60 minutes. The skin needling procedure is achieved by rolling a preformed tool comprising multiple thin microneedles on the cutaneous areas affected by acne scars: the skin is punctured in multiple directions, applying constant pressure (Figure 3).

The needles penetrate from 1.5 to 2 mm into the dermis. As expected, the skin bleeds for a short time. The skin develops multiple microbruises in the dermis. This damage induces the release of growth factors that stimulate the production of new collagen and elastin in the upper dermis. Several studies report that 6 months after collagen-induction therapy, histology shows a dramatic increase of new collagen and elastin fibers.¹⁷⁻¹⁸ Aust et al showed a considerable increase in collagen and elastin

TABLE 4.**Absolute Contraindications to a Skin Needling Procedure**

Presence of open wounds, cuts, or abrasions to the skin

Radiation treatment within the last year

A current outbreak of herpes simplex or any other infection or chronic skin condition in the area to be treated

Areas of the skin that are numb or lack sensation

Pregnancy or breast feeding

A history of keloid or hypertrophic scars or poor wound healing

TABLE 5.**Post-operative Precautions after Skin Needling Procedure**

Prevent hyperpigmentation by avoiding direct sunlight after treatment for 1 week

Apply SPF50+ sunscreen

Avoid topical product containing irritating ingredients such as glycolic/salicylic/TCA

Avoid invasive treatment (laser/chemical peel/microdermabrasion) until the skin is recovered.

deposition at 6 months' post-operation. The epidermis demonstrated a 40% thickening of stratum spinosum and normal rate ridges at 1-year post-operation.¹⁹

Results generally start to be seen after about 6 weeks, but complete improvement can take at least 3 months to occur, and, as the deposition of new collagen takes place slowly, the skin texture will continue to improve over a 12-month period.¹⁸ Most individuals will require around three treatments approximately 4 weeks apart. Some clinical conditions can be considered as absolute contraindications for a skin-needling procedure (Table 4). Several early reports suggested that performance of dermatosurgical procedures in patients on oral isotretinoin is associated with abnormal skin healing, keloid, or hypertrophic scar formation. However, a task force of experts from the American Society for Dermatologic Surgery concluded that there is insufficient evidence to justify delaying treatment with superficial and focal dermoabrasion and nonablative lasers for patients recently exposed to isotretinoin.²⁰

Complications are very rare, and when they occur, are represented by post-inflammatory hyperpigmentation, erythema, acne, and herpes flares superinfection. Allergic contact dermatitis from materials used in the needles has also been observed. Complications risk can be reduced following some simple post-operative precautions (Table 5). The management of these complications are different for different patients. In case hyperpigmentation occurs, it should be treated with a solution of glycolic acid (50%) or hydroquinone creams combined with sunscreen or laser therapy. In the case of infection, an antibiotic therapy has to be prescribed: either topical therapy with mupirocin 2% ointment, three-times daily for 10 days, alternatively, fusidic acid, and, in severe cases, systemic therapy with amoxicillin and clavulanic acid, twice daily for 6 days. If aggravation of acne occurs, it is possible to consider local or systemic antibiotic therapy, depending on the gravity of the condition. The observation of all the pre- and post-operative precautions and respect of contraindications may reduce the risk of adverse effects, which are minimal with this type of treatment and typically include minor flaking or dryness of the skin, milia, and hyperpigmentation, which can occur only very rarely and usu-

ally resolves after a month. Edema and erythema are the most frequent sequelae. Recovery may take 24 hours or up to a few days. Most patients are able to return to work the following day.

Skin needling provides good outcomes with negligible risks and can be safely performed on all skin colors and types. There is a lower risk of postinflammatory hyperpigmentation than other procedures such as dermabrasion, chemical peels, and laser resurfacing. A peculiar type of microneedling is fractional radiofrequency microneedling (FMR) in which insulated needles release radiofrequency waves to act deeper in the dermis, thus preventing epidermal damages. After damage to the reticular dermis, long-term dermal remodelling, neoelastogenesis, and neocollagenogenesis results in dermal thickening. The treatment is generally well tolerated with transient side effects such as mild erythema, post-inflammatory hyperpigmentation, and track marks of the device.²¹

Lasers

The efficacy of lasers and radiofrequency in atrophic acne scarring is confirmed by many comparative and observational studies. Different types of laser, including the nonablative and ablative lasers, are very useful in treating acne scars. Ablative lasers achieve removal of the damaged scar tissue through melting, evaporation, or vaporization. Carbon dioxide laser and Erbium YAG laser are the most commonly used ablative lasers for the treatment of acne scars. Nonablative lasers do not remove the tissue but stimulate new collagen formation and cause tightening of the skin resulting in the scar being raised to the surface. Among the nonablative lasers, the most commonly used are the Nd:YAG and diode lasers.²² In Table 6, we summarize some characteristics of the most used ablative and nonablative lasers. Ideal candidates for laser treatment must present a skin disease with acne of at least 1 year; they should have stopped taking oral isotretinoin for at least 1 year; they should not have presented skin infections by herpes virus during the six months prior to treatment; they must not have a history of keloids or hypertrophic scarring. All ablative lasers showed high risk of complications and side effects. Nonablative skin remodeling systems have become increasingly popular for the treatment of acne scars because they decrease

TABLE 6.**Wavelength and Effects in Tissues of the Most Used Ablative and Nonablative Lasers**

Type of laser	Wavelength	Effects on Tissues
<i>Carbon dioxide (CO₂) laser</i>	10.600nm	Rapid heating and vaporization of tissue, which causes collagen remodelling and heat-mediated tissue contraction
<i>Erbium:yttrium-aluminum-garnet (Er:YAG)</i>	2940nm	Has a more superficial ablation profile and a smaller zone of thermal damage beneath the ablated layer leading to shorter healing time
<i>Neodymium:yttrium-aluminum-garnet (Nd:YAG) laser</i>	1 064 nm	Stimulates inflammatory mediator release, fibroblast activation, neocollagenesis, and dermal remodelling
<i>Diode laser</i>	<i>Diode laser</i>	Targets the water in the upper dermis, remodels the skin's underlying collagen, and promotes formation of new collagen.

the risk of side effects and the need for postoperative care. Although improvement was noted with these nonablative lasers, the results obtained were not as impressive as the results from those using laser resurfacing. For this reason, a new concept in skin laser therapy called fractional photothermolysis (FP) has been designed to create microscopic thermal wounds to achieve homogeneous thermal damage at a particular depth within the skin, a method that differs from chemical peeling and laser resurfacing. The benefits of this system are less downtime and side effects compared to the conventional ablative laser, and an increased efficacy of tissue regeneration compared to the nonablative methods. Skin resurfacing is a new technology that delivers heat energy directly to the skin. After treatment, fibroblasts depositing new collagen and elastin fibers can be seen. Side effects are rare and can include temporary hyperpigmentation, erythema, edema, epidermal de-epithelialization, and infection.

Subcision

Subcision is a stand-alone treatment for depressed scars and wrinkles designed to address the underlying pathophysiology of rolling acne scars.²³ Despite their superficial appearance, rolling scars result from deep fibrous attachments gathering the epidermis to the subcutis. Subcision is designed to cut these fibrous bands while causing minimal damage to the overlying skin. Typically, this technique results in elevation of the depressed scar to the level of the surrounding skin. In the weeks following subcision, additional augmentation of the depressed defect is typically observed. This subsequent elevation is thought to result from trauma caused during the procedure,

which initiates a wound-healing response culminating in the deposition of new connective tissue beneath the scar surface. The main advantage of subcision is that it has the potential to produce long-term improvement in the appearance of rolling acne scars while causing minimal injury to overlying skin. The procedure is easy to perform and it is generally safe and well tolerated. One disadvantage of subcision is that a single treatment is not guaranteed to produce substantial improvement. The final result of the procedure depends on the individual wound-healing response, and it is often difficult to predict the outcome of an initial treatment. Subcision may be readily combined with other treatments such as filler injection, laser resurfacing, needling, or trichloroacetic acid peeling.

Excision, Punch Elevation, and Punch Grafting

Excision and punch techniques have been used for several decades in the treatment of deep, atrophic acne scars.²⁴ These techniques remain indispensable for the correction of acne scars whose depth precludes correction by resurfacing and whose irregular scar bases and sharply defined walls make them unsuitable candidates for filler correction. Elliptical or punch excision should be used when one's aesthetic goal is to replace a prominent scar with a less conspicuous linear, superficial scar. Punch excision is indicated for the treatment of ice-pick and deep boxcar scars that are <3.5 mm in diameter. Excision is also often the best option for the treatment of acne scars with cutaneous bridges or persistent cysts and tunnels. Excision and punch techniques have a distinct advantage over nonsurgical scar revision techniques in their capability to substantially improve the appearance of ice-pick and deep boxcar scarring. The primary disadvantage of all excision and punch techniques is that they necessitate an injury that can stimulate an abnormal healing process.

Additional Modalities and Future Developments

Although many of the surgical treatments for acne scarring have been used for decades, there has been a limited amount of evidence evaluating the long-term response to these treatments, comparing outcomes from different modalities. While some modalities, novel treatments, newer protocols, and more comparative studies continue to be reported. Recent work in stem-cell biology and regenerative medicine suggests that novel approaches to scar revision may be available in the future. Great strides have been made in elucidating the differences between the process of fibrotic wound healing that leads to scarring and the pathways of regeneration of injured tissues.²² A recently described therapeutic intervention study involves the use of stem cells for visual improvement of scars. Ibrahim et al found a significant qualitative and quantitative improvement in 14 patients where acne scars were directly injected with autologous bone marrow stem cells.²⁵ The use of stem cells may be considered as a single treatment or in conjunction with surgical management for potentially improved outcomes.

Autologous fat transplantation, or fat grafting, is another treatment option that has been more recently explored for its use in acne scarring. An additional potential adjunctive treatment that has undergone investigation is the use of low-level light therapy (LLLT). Although additional research is necessary, LLLT is thought to possibly decrease IL-6 and modulate TGF- β , which are associated with abnormal wound healing. The clinician should consider the combination of the traditional surgical modalities with non-surgical and resurfacing procedures together with some innovative treatments options, which potentially may act synergistically in order to achieve better result.

CONCLUSION

Various modalities have been used to treat scars, but limited efficacy and problematic side effects have restricted their application. In order to optimize the best treatment, we need to consider which option offers the most satisfactory result. There are also promising procedures for the future, such as stem cell therapy. A deep knowledge of the therapeutic options is mandatory for correct selection of the best therapeutic strategy for treatment of acne scars, whether it may be unique or combined, and for reducing or avoiding side effects and complications. Because severe acne scars are frequently the source of profound social and emotional distress for patients, the knowledge of all available techniques is essential for the cosmetic dermatologist.

REFERENCES

- Jacob CI, Dover J.S., Kaminer MS. Acne scarring: a classification system and review of treatment options. *J Am Acad Dermatol*. 2001;45(1):109-117.
- Goodman GJ, Baron JA. Postacne scarring: a qualitative global scarring grading system. *Dermatol Surg*. 2006;32(12):1458-1466.
- Goodman GJ, Baron JA. Postacne scarring—a quantitative global scarring grading system. *J Cosmet Dermatol* 2006;5(1):48-52.
- Thiboutot DM, Dréno B, Abanmi A, et al. Practical management of acne for clinicians: An international consensus from the Global Alliance to Improve Outcomes in Acne. *J Am Acad Dermatol*. 2018;78(2S1):S1-S23.e1. doi:10.1016/j.jaad.2017.09.078.
- Tan JK, Tang J, Fung K, et al. Development and validation of a scale for acne scar severity (SCAR-S) of the face and trunk. *J Cutan Med Surg*. 2010;14(4):156-60.
- Dréno B, Khammari A, Orain N, et al., ECCA grading scale: an original validated acne scar grading scale for clinical practice in dermatology. *Dermatol-ogy*. 2006; 214(1):46-51.
- Holland DB, Jeremy AH, Roberts SG, et al. Inflammation in acne scarring: a comparison of the responses in lesions from patients prone and not prone to scar. *Br J Dermatol*. 2004;150(1):72-81.
- Dréno B, Bissonnette R, Gagné-Henley A, et al. Prevention and reduction of atrophic acne scars with adapalene 0.3%/benzoyl peroxide 2.5% gel in subjects with moderate or severe facial acne: results of a 6-month randomized, vehicle-controlled trial using intra-individual comparison. *Am J Clin Dermatol*. 2018;19(2):275-286. doi: 10.1007/s40257-018-0352-y.
- Dreno B, Tan J, Rivier M, et al. Adapalene 0.1%/benzoyl peroxide 2.5% gel reduces the risk of atrophic scar formation in moderate inflammatory acne: a split-face randomized controlled trial. *J Eur Acad Dermatol Venereol*. 2017;31(4):737-742. doi: 10.1111/jdv.14026. Epub 2016 Dec 7.
- Heymann WR. Toll-like receptors in acne vulgaris. *J Am Acad Dermatol*. 2006;55(4):691-2.
- Jones DA. The potential immunomodulatory effects of topical retinoids. *Dermatology Online J*. 2005;11(1):3.
- Angeles AM, Kahari V-M, Chen YQ, et al. Enhanced collagen gene expression in fibroblast cultures treated with alltrans retinoic acid: evidence for up-regulation of the $\alpha 2(1)$ promoter activity. *J Invest Dermatol*. 1990;94:504.
- Schwartz E, Cruikshank FA, Mezick JA, Kligman H. Topical all-trans retinoic acid stimulates collagen synthesis in vivo. *J Invest Dermatol*. 1991;96:976-978.
- Varani J, Mitra RS, Gibbs D, et al. All-trans retinoic acid stimulates growth and extracellular matrix production in growth-inhibited cultured human skin fibroblasts. *J Invest Dermatol*. 1990;94:717-723.
- Fabbrocini G, Annunziata MC, D'Arco V, et al. Acne scars: pathogenesis, classification and treatment. *Dermatol Res Pract* 2010; 2010:893080. Epub 2010 Oct 14.
- G. Fabbrocini, S. Cacciapuoti, N. Fardella, F. Pastore, and G. Monfrecola, CROSS technique: chemical reconstruction of skin scars method, *Dermatologic Therapy*, 21:3:S29-S32, 2008.
- Fabbrocini G, Fardella N, Monfrecola A et al. Acne scarring treatment using skin needling. *Clin Exp Dermat*. 2009;34(8):874-9.
- Fabbrocini G, De Vita V, Monfrecola A, De Padova MP, Brazzini B, Teixeira F, Chu A. Percutaneous collagen induction: an effective and safe treatment for post-acne scarring in different skin phototypes. *J Dermatol Treat*. 2014;25(2):147-52.
- Aust MC, Fernandes D, Kolokythas P, Kaplan HM, Vogt PM. Percutaneous collagen induction therapy: an alternative treatment for scars, wrinkles, and skin laxity. *Plast Reconstr Surg*. 2008;121(4):1421doi:10.1097/01.prs.0000304612.72899.02
- Waldman A, Bolotin D, Arndt KA, Dover JS, et al. ASDS Guidelines Task Force: Consensus recommendations regarding the safety of lasers, dermabrasion, chemical peels, energy devices, and skin surgery during and after isotretinoin use. *Dermatol Surg*. 2017;43(10):1249-1262.
- Cho SI, Chung BY, Choi MG, et al. Evaluation of the clinical efficacy of fractional radiofrequency microneedle treatment in acne scars and large facial pores. *Dermatol Surg*. 2012;38:1017-24.
- S. Nelson. An introduction to laser and laser-tissue interactions in dermatology, in Principles and Practices in Cutaneous Laser Surgery, A. N. B. Kauvar, Ed., p. 70, Taylor and Francis Group, Boca Raton, Fla, USA, 2005.
- Alam M, Omura N, Kaminer MS. Subcision for acne scarring: technique and outcomes in 40 patients. *Dermatol Surg*. 2005;31:310-7.
- Gurtner GC, Werner S, Barrandon Y, Longaker MT. Wound repair and regeneration. *Nature*. 2008;453:314-21.
- Ibrahim ZA, Elatawy RA, Ghaly NR, et al. Autologous bone marrow stem cells in atrophic acne scars: A pilot study. *J Dermatolog Treat*. 2015;26(30):260-265.