International Journal of Dermatology, Venereology and Leprosy Sciences

E-ISSN: 2664-942X
P-ISSN: 2664-9411
www.dermatologypaper.com
Derma 2024; 7(2): 39-44
Received: 21-06-2024
Accepted: 26-07-2024

Lamiaa Abdelwahab Elzahaby
Department of Dermatology and Venerology, Faculty of Medicine, Tanta University, Tanta, Egypt

Yasmina Ahmed EL Attar
Department of Dermatology and Venerology, Faculty of Medicine, Tanta University, Tanta, Egypt

Doaa Waseem Nada
Department of Dermatology and Venerology, Faculty of Medicine, Tanta University, Tanta, Egypt

Tarek El-Sayd Aminand
Department of Dermatology and Venerology, Faculty of Medicine, Tanta University, Tanta, Egypt

Corresponding Author:
Lamiaa Abdelwahab Elzahaby
Department of Dermatology and Venerology, Faculty of Medicine, Tanta University, Tanta, Egypt

Hyaluronic acid for treatment of atrophic acne scars: A review

Lamiaa Abdelwahab Elzahaby, Yasmina Ahmed EL Attar, Doaa Waseem Nada and Tarek El-Sayd Aminand

DOI: https://doi.org/10.33545/26649411.2024.v7.i2a.191

Abstract
Background: Scarring resulting from acne represents a common and unpleasant outcome of acne that could have adverse effects on patient's mental health as well as overall quality of life. Different approaches have been established to address acne scars, showing varied levels of efficacy and safety.

Keywords: Acne scars, low intensity pulsed ultrasound, hyaluronic acid, sonophoresis

Introduction

Approximately 95% of individuals with acne develop scarring, representing a prevalent and permanent consequence of the condition. It often appears on the face [1].

While acne scarring is ultimately a harmless skin condition, the widely recognized psychological consequences of such a condition could be very stressful for some people. Therefore, it is crucial to identify a successful therapy for this problem. The precise mechanism of acne scarring remains uncertain. Nevertheless, there seems to be a correlation between the condition's duration [1] and the inflammation severity linked to acne [3].

Diverse approaches have been established to address acne scars [4], indicating different levels of safety as well as efficiency [5].

Hyaluronic acid (HA) is well-recognized in the field of medicine as dermal fillers and for operations aimed at revitalization. When utilized in higher concentrations within the human dermis, it allows for hydration while preserving the appropriate tissue volume, therefore protecting skin cells from mechanical breakdown. Alone or in conjunction with other compounds, HA allows for accelerated wound healing [6] as well as tissue regeneration in cases developing burns or ulcerations [7]. Moreover, it exhibits anti-inflammatory and bio-stimulating properties, Additionally, it is believed to stimulate subsequent signaling cascades when interacting with several cell membrane receptors [8].

Acne Scars

Approximately 80% of teenagers get acne vulgaris, representing a widespread condition [9]. It could result in permanent scarring, inducing considerable psychological stressfor these individuals. The three acne scar types involve hypertrophic, keloid, as well as atrophic scars. Among scar types, atrophic scars exhibit greater prevalence in comparison to keloid and hypertrophic conditions. Atrophic scarring resulting from acne could manifest in three main forms: rolling, boxcar, as well as icepick scars (Figure 1) [12].

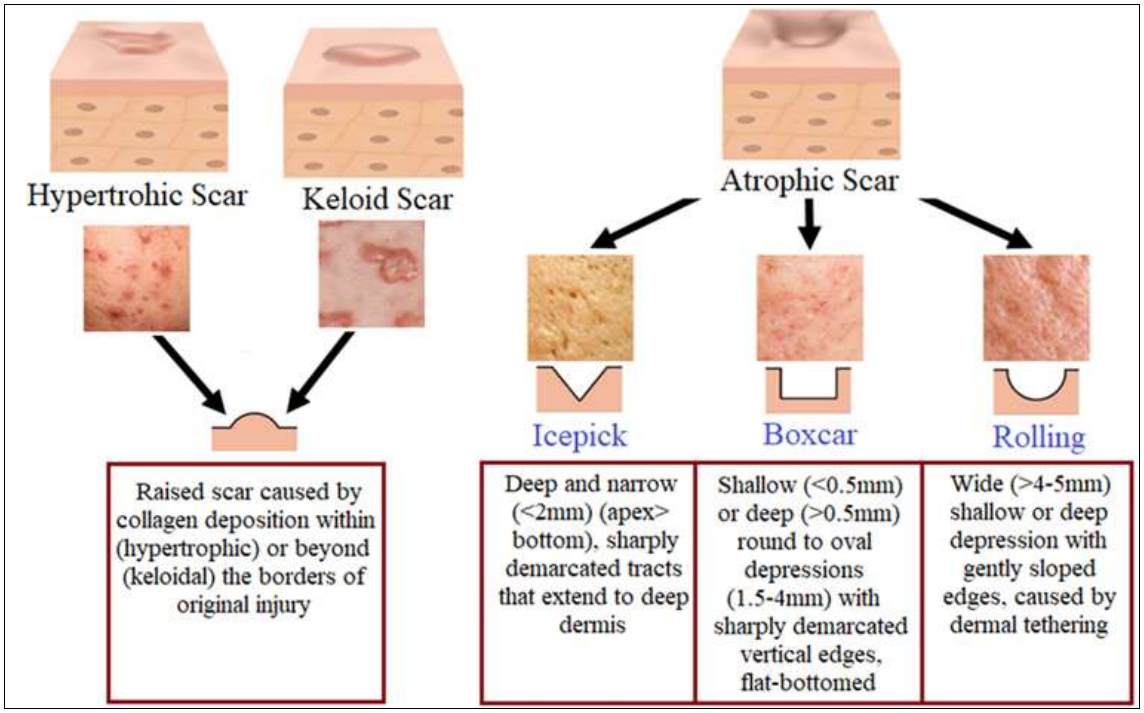

Fig 1: Acne scar types [12].

Icepick scars: Accounts for sixty to seventy percent of atrophic scars. The v-shaped epithelial tracts exhibit a width of less than 2 mm. They also have a sharp border, extending in a vertical direction to the deep dermis or subcutaneous tissue. Since they could be deep, icepick scars often shows resistance to traditional skin resurfacing techniques [13].

Boxcar scars: Account for twenty to thirty percent of atrophic scars. They often exhibit greater width, falling between 1.5 and 4.0mm. They are characterized by round-to-oval depressions, showing well-defined sharp vertical borders. Skin resurfacing technologies are effective for shallow or superficial boxcar scars measuring 0.1 to 0.5mm, while deep boxcar scars measuring ≥0.5mm resist such treatments [13].

Rolling scars: Account for fifteen to fifty-five percent of atrophic scars. They exhibit the greatest width, reaching a diameter of 5 mm. The dermis' fibrous anchoring to the subcutis leads to superficial shadowing with the scars being undulated in the appearance. Primary treatment should prioritize the subdermal component correction [13].

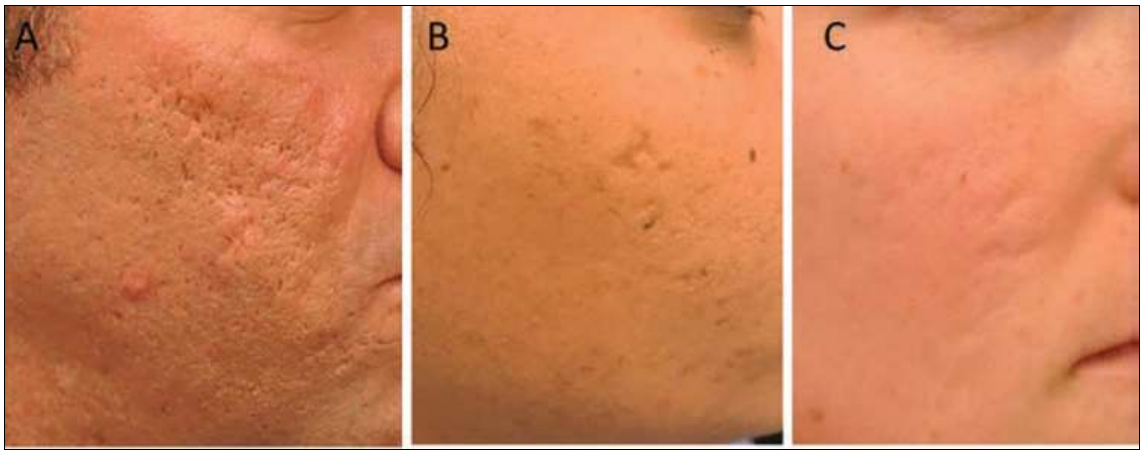

Fig 2: The three atrophic acne scar types: a) icepick, b) boxcar, c) rolling [13].

The Atrophic Acne Scars Treatment Approaches

Topical

A research investigation has shown that Adapalene 0.3% is very beneficial in reducing the atrophic acne scars appeatance by fifty to eighty percent [14]. Additionally, tazarotene has been effective in reducing acne scars [15].

In order to enhance effectiveness while reducing retinoid dermatitis, retinoids have been synergistically coupled with other active bioactive compounds. Examples of such a combination involve adapalene at dosages of 0.1% and 0.3%, along with benzoyl peroxide at 2.5% [16].

Office procedures

- **Skin Needling (Percutaneous Collagen Induction Therapy)**

  Needling represents a therapeutic technique that operates on the basis of percutaneous collagen induction (PCI). Creating microclefts along with dermal

traima, utilizing this method, promotes wound healing process, triggering a series of growth factors, which lead to collagen synthesis [17].

- **Chemical Peeling**
  Chemical peeling represents the application of chemicals to the skin in order to eliminate the outer damaged layers while accelerating the process of repair. In relation to acne scars, the most favorable outcomes could be obtained in macular scarring [18]. Four distinct categories of chemical peels may be established according to the histologic necrosis degree they induce. As illustrated on Table 6, the peeling agent's classification is provided [19].

Table 1: The peeling agent's classification [19]

Depth of penetration	Histologic level	Peeling agent
Very superficial	Destroying stratum corneum without any wounds underneath the stratum granulosum	▪ A 30-50% Glycolic acid application is briefly conducted over one to two minutes. ▪ Jessner solution, given one to three coats. ▪ TCA 10%, given in one coat.
Superficial	Partial or total epidermis destruction, at any area from the stratum granulosum to the basal cell layer	▪ A 50-70% Glycolic acid, given over a period falling between two and twenty minutes ▪ Jessner solution, given in four to ten coats. ▪ TCA, 10-30%.
Medium depth	Destroying epidermis along with partial or total destruction of the papillary dermis	▪ Glycolic acid 70%, given over a period between three and thirty minutes). ▪ TCA, 35% to 50%. ▪ Augmented TCA (CO_2 plus TCA 35%; Jessner solution plus TCA 35%; glycolic acid 70% plus TCA 35%).
Deep	Destroying the epidermis as well as papillary dermis, that could extend into the reticular dermis	▪ Phenol 88%. ▪ Baker-Gordon phenol formula.

- **Chemical Reconstruction of Skin Scars (CROSS):** The atrophic scars focal treatment utilizing very high TCA concentrations (50-100%), has shown superior effectiveness while reducing complications [17].
- **Dermabrasion/Microdermabrasion:** Dermabrasion as well as microdermabrasion represent facial resurfacing procedures, employing mechanical ablation to remove damaged skin at various levels, thus stimulating the regeneration of epithelial tissue. Both methods demonstrate efficacy in treating scars [20].
- **Subcision:** Subcision represents a surgical technique involving the needle insertion under the skin and its passage in many directions. Iris most suitably used for treating rolling acne scarring. This process leads to the release of fibrous tissue, which in turn induces scar elevation [17].
- **Punch Techniques:** Punch procedures, involving punch excision, elevation, grafting, or float methods, represent the established criteria for treating punched-out scars, with a width of three to four mm, as well as deep boxcar and large icepick scarring [21].
- **Platelet-Rich Plasma:** Platelet-rich plasma (PRP) injection represents a therapeutic application, utilizing the patient's own plasma to address and correct acne scarring. It involves many therapeutic growth factors such as platelet-derived growth factor (PDGF), transforming growth factor (TGF), vascular endothelial growth factor (VEGF), as well as insulin-like growth factor (IGF). These growth factors stimulate the collagen and elastin regeneration. Although beneficial for boxcar as well as rolling scars, its effectiveness is restricted when applied to icepick scarring [22].
- **Mesotherapy:** Mesotherapy represents a rejuvenation method, involving the injection of hormones, vitamins, as well as plant extracts into the skin, thus promoting skin regeneration as well as tightening [23].
- **Botulinum toxin:** When highly atrophic (grade 3) acne scars are exacerbated by regular muscle movement, some researchers suggest that botulinum toxin may be advantageous, particularly for acne scars on the forehead, glabella, as well as chin [17].
- **Thread lifting:** Thread lifting represents a non-surgical procedure that involves inserting a long barbed suture into the face's subcutaneous layer. Furthermore, it provides mechanical support to the skin while activating fibroblasts and producing collagen [24].
- **Fillers:** Fillers are utilized to enhance the soft tissue augmentation and are particularly efficient in treating soft rolling or boxcar scarring. They may be utilized either alone or in conjunction with previous surgical procedures, thus improving the visual aesthetics of atrophic acne scars. Hyaluronic acid, calcium hydroxyapatite, as we; as poly-L-lactic acid (PLLA) fillers are often used for treating atrophic acne scars [25].

Other lines

- **Fat Transplant:** This procedure has two stages: acquiring the graft and positioning it. Surgical liposuction is performed, and the excised fat is then injected into the atrophic scar. An investigation revealed that fat transplantation enhances collagen organization, decreases fibrosis, and stimulates the development of new blood vessels by using the growth factors already present within the lipoaspirate [17].
- **Stem cell therapy:** A class of adult stem cells derived from mesoderm, mesenchymal stem cells (MSCs) has the ability to self-renew, self-replicate, and differentiate. They have been utilized in tissue regeneration due to their exceptional capacity to differentiate into several cell types such as adipocytes, fibroblasts, and others [26].
- **Epidermal growth factor:** Epidermal growth factor (EGF) represents a growth factor, produced as part of the tissue response to inflammation. Experimental evidence has shown that the interaction between EGF and its receptor could stimulate the keratinocyte stem

cells growth in living organisms while accelerating skin regeneration. When topically administered, it has the ability to induce neo-collagenesis as well as skin thickening [27].

Laser and light therapy

- **Intense Pulsed Light (IPL):** Recently, intense pulsed light (IPL) has been identified as a very effective therapy for scars. Detecting the IPL mechanism is incomplete. However, it potentially affects the vascular proliferation that is crucial for collagen overgrowth while influencing the pigmentation that occurs during the scar formation [23].
- **Laser Therapy**
- **Ablative lasers**

Fractional Carbon dioxide (CO_2) laser.

A fractional CO2 laser generates a fractionated light beam that effectively induces tissue vaporization within a depth range of 20 to 100µm. This process also creates zones of thermal necrosis that extend up to 50µm. Direct skin heating below the ablation zone triggers a wound-healing reaction that leads to collagen remodeling as well as tissue contraction mediated by heat [28].

Erbium: yttrium-aluminum-garnet (Er:YAG)

Er:YAG with a field strength of 5J/cm induces tissue vaporization to a depth of 20 to 25 micrometers, along with a 5 to 10 micrometers zone of thermal necrosis. Consequently, it exhibits a shallower ablation profile and a narrower area of thermal damage below the ablated layer, resulting in reduced healing duration as well as a decreased incidence of complications. Re-epithelialization with Er:YAG requires a time frame of four to seven days [29].

- **Nonablative lasers**

In recent years, nonablative skin remodeling techniques have gained popularity in managing acne scars due to their ability to reduce complications along with streamlining postoperative care. Nonablative lasers are specifically engineered to avoid damaging the epidermis while stimulating new collagen synthesis [30].

Neodymium: yttrium-aluminum-garnet (Nd:YAG) laser

The Nd:YAG laser is reserved for individuals developing hyperpigmented or very sensitive skin. It selectively affects the underlying water as well as collagen without causing any damage to the skin's outer layer. Thermal damage triggers the inflammatory mediators, fibroblast activation, new collagen synthesis, as well as remodeling of dermis [13].

Diode laser

The 1450 nm diode laser in the infrared spectrum specifically focusses on the water within the upper dermis, causing collagen remodeling under the skin while stimulating the production of new collagen proteins. Collagen production and deposition showed a persistent rise up to six months following such a laser treatment [31].

Drug delivery and ultrasound for scar therapy

Transdermal drug delivery (TDD) offers an alternate method to needle injection, which causes pain and leads to unequal drug distribution. The stratum corneum serves as both a barrier and a constraint in achieving effective medication delivery. A significant number of protein-based therapies are unable to penetrate the subcutaneous layer because of their large molecular weight as well as hydrophilic properties [32].

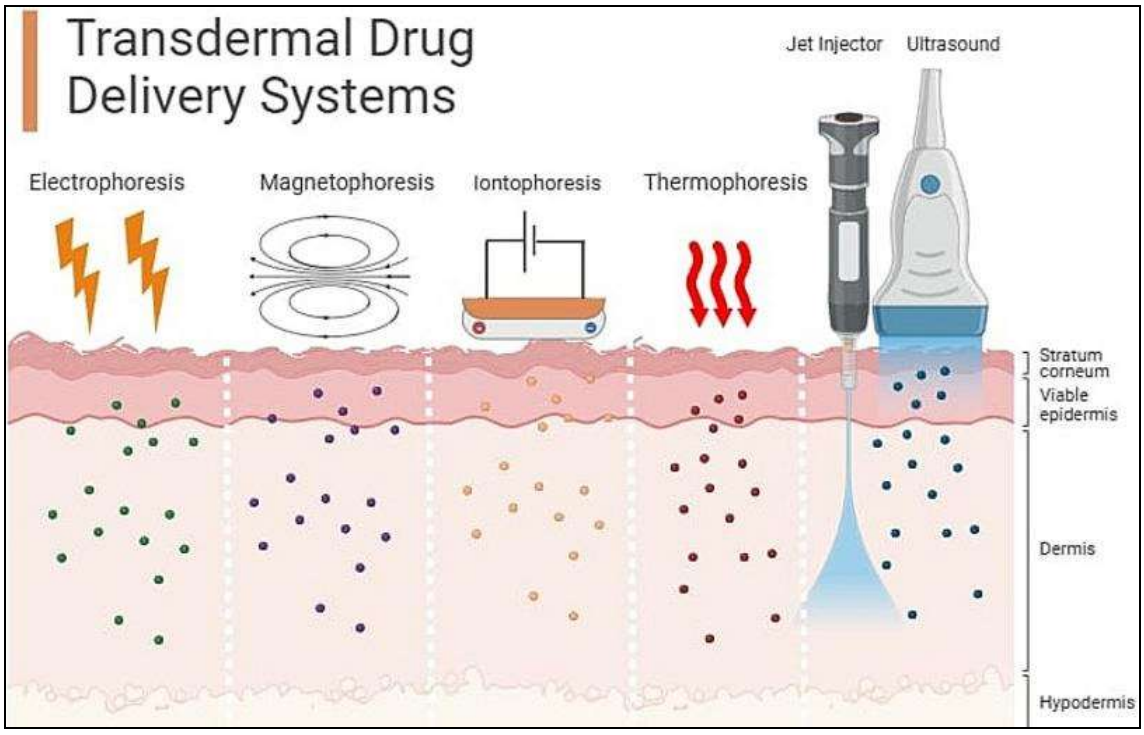

Fig 3: Transdermal drug delivery systems [33]

Many new technologies have been created to transiently enhance skin permeability in order to enhance the TDD effectiveness. The techniques involved in this category are radio frequency (RF) cell ablation, iontophoresis,

electroporation, micro-needles, ablative fractional laser, as well as sonophoresis [34, 35]. The efficacy of iontophoresis as a TDD technique has been extensively researched over the last three decades. Its primary drawback is the need to ionize medicines before administration. Electroporation employs short, high voltage pulses to enhance the skin permeability. Nevertheless, the scope of its use is restricted due to the pain-inducing nature of the electrical pulses [36].

Both ablative fractional laser as well as microneedling may generate arrays of micro-channels on the scar, enabling safe and effective delivery of therapeutic drugs into the deeper scar tissues [37].

Ultrasound has been shown to induce increased cellular and organ absorption of medicines. Employing US waves ranging from high-frequency (0.7-3 MHz) to low-frequency (20-100 kHz), the technique known as sonophoresis has been studied for transdermal medication delivery purposes. The fundamental concept behind sonophoresis is to generate cavitation microbubbles that move towards the surface, resulting in the formation of a microjet by the bubble asymmetrical collapse. Although not fully addressed, cavitation is regarded as the main factor responsible for higher skin permeability as well as drug penetration [34].

Hyaluronic acid (HA) is a significantly abundant component of the extracellular matrix found within the skin and has a crucial function in the dermis metabolic processes. Due to its capacity to keep a humid environment suitable to healing as well as the growth factors activation, cellular components, and the migration of diverse cells required for healing, it plays a crucial role in wound healing along with tissue repair processes [38].

Hyaluronic acid represents a vital component of connective tissues, responsible for moisturizing, lubricating, and restoring skin elasticity, therefore preserving tissue shape while improving its tone strength [38].

Due to its viscoelastic characteristics as well as exceptional biocompatibility, HA has been widely utilized in the field of cosmetology. Topical cosmetics containing HA replenish the skin's hydration as well as elasticity, therefore producing an anti-wrinkling action [38].

A range of HA fillers has been authorized for the purpose of treating excessive nasolabial folds, tear troughs, as well as cheek augmentation [38].

Topical treatments that including HA along with human growth factors could be especially suitable for cosmetic skin rejuvenation [39]. Mesotherapy using an intradermal hyaluronic acid formulation has also been employed for skin renewal [40].

The most appropriate therapy for facial lines caused by the volume loss linked to aging is injectable fillers, which effectively diminish and reinforce the static lines. Being linked to favorable results, HA fillers are easily administered by injection and have been associated with only a limited number of complications, involving some pain, redness, as well as bruising [41].

Conclusion

We concluded that Sonophoresis using hyaluronic acid in treating atrophic acne scars could show safety and effectiveness.

Conflict of Interest

Not available

Financial Support

Not available

References

1. Layton A, Henderson C, Cunliffe W. A clinical evaluation of acne scarring and its incidence. Clinical and Experimental Dermatology. 1994;19:303-308.
2. Dréno B, Tan J, Kang S, Rueda M, Torres Lozada V, Bettoli V, *et al*. How people with facial acne scars are perceived in society: an online survey. Dermatology and Therapy (Heidelberg). 2016;6:207-218.
3. Holland D, Jeremy A, Roberts S, Seukeran D, Layton A, Cunliffe W. Inflammation in acne scarring: A comparison of the responses in lesions from patients prone and not prone to scar. British Journal of Dermatology. 2004;150:72-81.
4. Hession M, Graber E. Atrophic acne scarring: a review of treatment options. Journal of Clinical and Aesthetic Dermatology. 2015;8:50-8.
5. Zaleski-Larsen L, Fabi S, McGraw T, Taylor M. Acne Scar Treatment. Dermatologic Surgery. 2016 May;42-49.
6. D'Agostino A, Stellavato A, Busico T, Papa A, Tirino V, Papaccio G, *et al*. *In vitro* analysis of the effects on wound healing of high- and low-molecular weight chains of hyaluronan and their hybrid H-HA/L-HA complexes. BMC Cell Biology. 2015;11(16):19.
7. Dicker K, Gurski L, Pradhan-Bhatt S, Witt R, Farach-Carson M, Jia X. Hyaluronan: a simple polysaccharide with diverse biological functions. Acta Biomaterialia. 2014;10(4):1558-1570.
8. Vigetti D, Karousou E, Viola M, Deleonibus S, De Luca G, Passi A. Hyaluronan: biosynthesis and signaling. Biochimica et Biophysica Acta. 2014;1840(8):2452-2459.
9. Kranning K, Odland G. Prevalence, morbidity and cost of dermatological diseases. Journal of Investigative Dermatology. 1979;73(5):395-401.
10. Johnson M, Roberts J. Skin conditions and related need for medical care among persons 1-74 years. United States, 1971-1974. Vital and Health Statistics. 1978;11(212):61-72.
11. Koo J. The psychosocial impact of acne: patient's perceptions. Journal of the American Academy of Dermatology. 1995;32(5):26-30.
12. Junayed M, Islam M, Jeny A, Sadeghzadeh A, Biswas T, Shah A. ScarNet: development and validation of a novel deep CNN model for acne scar classification with a new dataset. IEEE Access. 2021;10:1245-1258.
13. Connolly D, Vu H, Mariwalla K, Saedi N. Acne Scarring-Pathogenesis, Evaluation, and Treatment Options. Journal of Clinical and Aesthetic Dermatology. 2017 Sep;10(9):12-23.
14. Loss M, Leung S, Chien A, Kerrouche N, Fischer A, Kang S. Adapalene 0.3% gel shows efficacy for the treatment of atrophic acne scars. Dermatology and Therapy. 2018 Jun;8:245-257.
15. Afra T, Razmi T, Narang T, Dogra S, Kumar A. Topical Tazarotene Gel, 0.1%, as a Novel Treatment Approach for Atrophic Postacne Scars: A Randomized Active-Controlled Clinical Trial. JAMA Facial Plastic Surgery. 2019;21(2):125-132.
16. Jennings T, McLarney M, Renzi M, Duffy R, Heymann W, Decker A, *et al*. Acne scarring-pathophysiology, diagnosis, prevention and education - Part 1. Journal of

the American Academy of Dermatology. 2022 Jul 2 (22)00677-6.
17. Bhargava S, Cunha P, Lee J, Kroumpouzos G. Acne scarring management: systematic review and evaluation of the evidence. American Journal of Clinical Dermatology. 2018;19:459-477.
18. Alster T, Graham P. Microneedling: A Review and Practical Guide. Dermatologic Surgery. 2018 Mar;44(3):397-404.
19. Gozali M, Zhou B. Effective treatments of atrophic acne scars. Journal of Clinical and Aesthetic Dermatology. 2015;8(5):33-40.
20. Roh M, Chung K. Acne Scars: How They Form and How to Undo Them. Springer eBooks. 2019 Nov 30:97-103.
21. Goodman G. Treating scars: addressing surface, volume, and movement to expedite optimal results. Part 2: more-severe grades of scarring. Dermatologic Surgery. 2012;38:1310-1321.
22. Schoenberg E, Hattier G, Wang J, Saedi N. Platelet-rich plasma for facial rejuvenation: an early examination. Clinical Dermatology. 2020 Mar 1;38(2):251-253.
23. Goodarzi A, Behrangi E, Ghassemi M, Nobari N, Sadeghzadeh-Bazargan A, Roohaninasab M. Acne scar; a review of classification and treatment. Journal of Critical Reviews. 2020;7(5):815-823.
24. Donnarumma M, Vastarella M, Ferrillo M, Cantelli M, D'andrea M, Fabbrocini G. An innovative treatment for acne scars with thread-lift technique: our experience. Italian Journal of Dermatology and Venereology. 2019 Jan;156:(1-6):40-41.
25. Tam C, Khong J, Tam K, Vasilev R, Wu W, Hazany S. A comprehensive review of non-energy-based treatments for atrophic acne scarring. Clinical, Cosmetic and Investigational Dermatology. 2022;15:455-469.
26. Li F, Cai Y, Deng C. Research advances on mesenchymal stem cells and their derivatives in the treatment of acne scars. Chinese Journal of Burns. 2022;38(6):595-600.
27. Ibrahim Z, Eltatawy R, Ghaly N, Abd El-Naby N, Abou El Fetouh H, Abd Elateef A, *et al*. Autologous bone marrow stem cells in atrophic acne scars: A pilot study. Journal of Dermatological Treatment. 2015;26(3):260-265.
28. Omi T, Numano K. The Role of the CO2 Laser and Fractional CO2 Laser in Dermatology. Laser Therapy. 2014 Mar 27;23(1):49-60.
29. Chen K, Tam K, Chen I, Huang S, Tzeng P, Wang H, *et al*. A systematic review of comparative studies of CO2 and erbium: YAG lasers in resurfacing facial rhytides (wrinkles). Aesthetic Surgery Journal. 2017;19(4):199-204.
30. Mirza H, Mirza F, Khatri K. Outcomes and adverse effects of ablative vs nonablative lasers for skin resurfacing: A systematic review of 1093 patients. Dermatology and Therapy, 2021, 34(1).
31. Rathod D, Foroughi A, Mekokishvili L, Wollina U, Lotti T, Rajan A, *et al*. A cross-sectional, multi-center study on treatment of facial acne scars with low-energy double-pass 1450-nm diode laser. Dermatology and Therapy, 2020, 33(3).
32. Haedersdal M, Erlendsson A, Paasch U, Anderson R. Translational medicine in the field of ablative fractional laser (AFXL)-assisted drug delivery: A critical review from basics to current clinical status. Journal of the American Academy of Dermatology. 2016;74(5):981-1004.
33. Wang R, Bian Q, Xu Y, Xu D, Gao J. Recent advances in mechanical force-assisted transdermal delivery of macromolecular drugs. International Journal of Pharmaceutics. 2021;602:120598.
34. Singh P, Muhammad I, Nelson N, Tran K, Vinikoor T, Chorsi M, *et al*. Transdermal delivery for gene therapy. Drug Delivery and Translational Research. 2022;12(11):2613-2633.
35. Azagury A, Khoury L, Enden G, Kost J. Ultrasound mediated transdermal drug delivery. Advanced Drug Delivery Reviews. 2014 Jun;72:127-143.
36. Wang H, Fan P, Guo X, Tu J, Ma Y, Zhang D. Ultrasound-mediated transdermal drug delivery of fluorescent nanoparticles and hyaluronic acid into porcine skin *in vitro*. Chinese Physics B. 2016;25(12):124314.
37. Nieboer M, Meesters A, Almasian M, Georgiou G, de Rie M, Verdaasdonk R, *et al*. Enhanced topical cutaneous delivery of indocyanine green after various pretreatment regimens: comparison of fractional CO2 laser, fractional Er
38. Laser, microneedling, and radiofrequency. Lasers in Medical Science. 2020;35(6):1357-1365.
39. Keen M. Hyaluronic Acid in Dermatology. Skinmed. 2017;15(6):441-448.
40. Vasvani S, Kulkarni P, Rawtani D. Hyaluronic acid: A review on its biology, aspects of drug delivery, route of administrations and a special emphasis on its approved marketed products and recent clinical studies. International Journal of Biological Macromolecules. 2020;151:1012-1029.
41. Tedeschi A, Lacarrubba F, Micali G. Mesotherapy with an intradermal hyaluronic acid formulation for skin rejuvenation: An intrapatient, placebo-controlled, long-term trial using high-frequency ultrasound. Aesthetic Plastic Surgery. 2015;39:129-133.
42. Gutowski K. Hyaluronic acid fillers: Science and clinical uses. Clinics in Plastic Surgery. 2016;43(3):489-496.

How to Cite This Article
Elzahaby LA, EL Attar YA, Nada DW, El-Sayd Aminand T. Hyaluronic acid for treatment of atrophic acne scars: A review. International Journal of Dermatology, Venereology and Leprosy Sciences. 2024; 7(2): 39-44.