

Review Article

A REVIEW OF SCAR TREATMENT RELATED TO ACNE AND BURN

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Abstract

Introduction: Annually in the developed world about 100 million patients get scars, several of them are a source of significant problems, as a result of elective operations or operations following trauma. It is assessed 11 million keloid scars and 4 million burn scars occur each year that 70% of these scars arise in children. People that have unusual skin with scarring may confront aesthetic, physical, social, and psychological consequences. One of the main reasons for skin scarring is acne and burn.

Objective: The aim of this study is a review of therapeutic method for scar treatment related to burn and acne.

Material and method: Broad research was conducted on some medical, pharmacological and surgical database of life sciences such as PubMed, EMBASE, MEDLINE, LILACS database, global independent network of Cochrane. By referencing these databases, a comprehensive literature review was carried out through combining numerous recent studies in terms of skin scarring, burn, acne treatment and management in accordance with many related articles published from 2000 to 2020 which could cover this area of recommendations.

Conclusion: Significant advancements have been seen in scare related burn and acne treatment in the recent decade, including advances in novel skin substitutes, pharmacological interventions, advanced surgical approaches such as laser therapy, fat grafting, skin grafting and coverage options for burn scar. For acne scarring treatment the laser therapy, cosmetic filler and pharmacological method have been introduced. As a result, by these new methods, treatment of scars improves significantly, however improvement of scar related to burn looks is more difficultly and numerous challenges still is essential to improve current scare.

Key words: skin scarring, burn, acne, pharmacological therapy, laser therapy, cosmetic filler.

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INTRODUCTION

Annually in the developed world about 100 million patients get scars, various of it is source of significant problems, as a result of elective operations or operations following trauma. It is assessed 11 million keloid scars and 4 million burn scars each year that 70% of these scars arise in children. People that have unusual skin with scarring may confront aesthetic, physical, social, and psychological consequences [1]. One of the main reasons of skin scarring is acne and burn.

Lesions caused by the closure of the sebaceous glands in the face, neck, back, shoulders, and chest are called acne. The scar result of acne can remain in all life and cause aesthetically problematic [2-5]. Although these scars can be repaired, they do not become like normal skin.

Burn-related injuries are the most traumas that can affect every organ in the body and cause morbidity. According to the World Health Organization (WHO), nearly 180000 death related-burns accrue annually [6]. All burn types initiate wound healing process including inflammation, cell recruitment, matrix deposition, epithelialization, and tissue regeneration. Additionally in severe large burns the persistent pathophysiological stress response can accrue [7].

The aim of this study is review of therapeutic method for scar treatment related burn and acne.

MATERIAL AND METHOD

Broad research was conducted on some medical, pharmacological and surgical database of life sciences such as PubMed, EMBASE, MEDLINE, LILACS database, global

independent network of Cochrane. By referencing these databases, a comprehensive literature review was carried out through combining numerous recent studies in terms of skin scarring, burn, acne treatment and management in accordance with many related articles published from 2000 to 2020 which could cover this area of recommendations.

SKIN SCARS

The scar is the final step of tissue repair in the mammal. The ideal purpose in the endpoint of each injury is formation of new original tissue instead of scar[8, 9]. But in many injuries, the rapid inflammatory response occurs to prevent infection and other injuries for the body. Therefore, these rapid responses cause scar forming.

Clinical problem of skin scarring

Scars occur after every dermal injury and usually considered trivial. But they can be aesthetically unpleasant and lead to a personal problem such as tenderness, severe itching, pain, sleep disturbance, depression, and anxiety[10].

The spectrum of skin scar types

Skin scars classify to a "normal" fine line or abnormal ones such as widespread scars, hypertrophic scars, atrophic scars, scar contractures, and keloid scars.



Figure 1. A fine line scar in forearm of a white man after a knife wound[11]

Widespread (stretched) scars are the result of surgery and become widened and stretched [12]. these scars are usually pale, flat, soft and symptomless.



Figure 2. Widespread scar (A) in the midline after surgical incision and a hypertrophic scar (B) after transverse surgical incision in an Asian woman [11].

Atrophic scars are small and deep and commonly occur after chickenpox or acne.



Figure 3. Atrophic scars after acne in upper back and shoulder area of a white man [11]

Scar contractures commonly occur after burn wound. These scars often are dysfunctional and disabling.



Figure 4. Scar contracture of forearm and wrist after a burn injury to a white woman [11].

Hypertrophic scars as a raised scars stay in the original lesion boundaries and spontaneously regress following the initial

injury. These scars are commonly inflamed, itchy, red, and painful. They usually arise later burn injury [13].

Keloid scars also known as raised scars that develop on the original wound margins and the surrounding normal skin is invaded in a specific way.

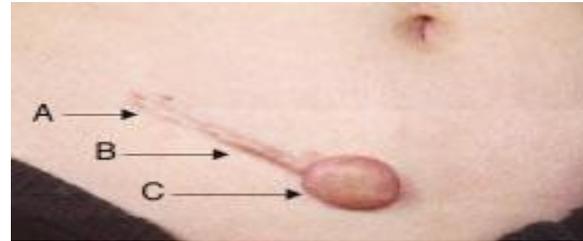


Figure 5. Presence of multiple scar types in same anatomical site of a white woman after surgery—widespread scar (A), hypertrophic scar(B), and keloid scar (C) [11]

TREATMENT OF ACNE

Acne is an inflammatory process localized on the face, upper arms, chest, and back[14, 15]. Due to the age of the disease and its apparent effect on beauty, complications and scarring, the need to treat it is more necessary[16].

Pharmacological method

Many oral and topical drugs are used for acne treatment. The purpose of acne treatment is to improve and prevent lesions. In this regard, it is very important to prevent long-term acne scarring because it's adverse psychological effects on patients in social communication and its related problems.

One of majority treat for acne is antibiotics; systemic antibiotic therapy is common in this procedure[17]. But extensive use of these compounds causes many problems such as bacteria resistance. So using of non-antibiotic drugs became common. Consumption of certain derivatives of vitamin A, in particular isotretinoin and tretinoin, has a significant effect on glands and is caused by a decrease in sebaceous gland size[18]. These drugs use as a solution, gel and cream. Also such drugs have a comedolytic effect and is excreted in comedones and converted to closed comedones. Continuation of treatment can prevent the formation of new comedones[19].

One of the major reason for development acne is increasing of sebum volume that cause to Linoleic acid decreasing. Some of anti-acne drugs such as cyproterone compound improve acne lesion by decreasing of sebum release[20].

One reason for acne appearance is insulin resistance and increasing insulin-like growth factor (IGF)-1 especially in women with polycystic ovary syndrome (PCOS) disease. So metformin has effect in treatment of acne in women with PCOS. In our provirus study, we investigated metformin and isotretinoin effect on 70 females with late-onset acne or acne resistant for 6 months. We funded effective of metformin in late-onset or resistant acne treatment and metabolic status improvement, devoid of severe side effects[21].

ACNE SCAR TREATMENT

Several methods are used for acne scar treatment (table 1). A summary of these method is provided below.

Table 1. Methods for acne scar treatment

Cosmetic filler	a) Hyaluronic Acid b) Calcium Hydroxyapatite c) Poly-L-Lactic Acid
Photodynamic Therapy	
Laser therapy	a) carbon dioxide b) erbium laser c) PDLs d) Fractional Laser
Microneedling	
Chemical peels	a) Superficial peeling agents (resorcinol, tretinoin, glycolic acid, lactic acid, salicylic acid, and trichloroacetic acid) b) Medium-depth peeling agents (phenol, TCA 35% to 50%, and Jessner solution (resorcinol, lactic acid, and salicylic acid in ethanol)) c) Deep peeling agents (Baker-Gordon or Litton phenol formulas)
Microdermabrasion	
Platelet-rich plasma	
Subcision	a) Cannula b) needle
Fractional radiofrequency	

Cosmetic Fillers

Recently, the injectable fillers have been developed in cosmetic field, these filler include temporary fillers such as hyaluronic acid (HA), semi-permanent and permanent fillers [22]. Numerous cosmetic fillers have been utilized for acne scars treatment by increasing of tissue volume in these wounds and collagen production stimulating [23]. Many of acne scars respond successfully to cosmetic fillers, occasionally these fillers combined with other component to enhance their function [24]. We summarized these fillers following.

Hyaluronic Acid

Hyaluronic acid contains of a water-retaining glycosaminoglycan polysaccharide that is a naturally component in the connective tissue. Hyaluronic acids as a temporary fillers utilize for 3 to 12 months. Hasson and Romero examined the HA effect on 12 patient with acne scar, and 74% of them had good to excellent results after 1 month [25].

Calcium Hydroxyapatite

Calcium hydroxyapatite as a semi-permanent and biocompatible filler is synthesized of CaHA microspheres (25- to 45-µm) in an aqueous gel including glycerin, water, and carboxymethylcellulose [26]. Calcium hydroxyapatite invoke a local response of fibroblasts and histiocytes and cause collagen fabrication [27]. In a clinical study of acne scars of 10 people were treated with CaHA, after 12 months 30% of patients exhibited about 75% improvement and 60% of them indicated 50% to 75% improvement in acne scars [28].

Poly-L-Lactic Acid

Poly-L-lactic acid is a biodegradable and non-immunogenic artificial polymer by collagen production ability through increasing the number of fibroblasts [29]. The improvement ability of PLLA has been shown on 20 patients with acne and varicella scarring [30].

Laser therapy

Lasers used to treat acne scars are divided into three categories;

1) These include carbon dioxide and erbium laser. These lasers are often used to treat depleted scars. These lasers stimulate collagen production and treat scar by cutting very fine-grained skin layers with micron precision [31-33].

2) The non-destructive lasers (PDLs) that used in the treatment of acne scars. These lasers modify the lower layers by preserving the upper layers of the skin. They are usually used to treat hypertrophic and red acne [34-37].

3) These groups known as Fractional Laser [38]. They destroy a small part of the skin but leave most of it healthy. This causes the healthy part of skin quickly repair its damaged part. With this technology, the effects of destructive lasers are reduced and the patient returns to work faster, but more sessions are needed to achieve therapeutic effects [38, 39].

Fractional CO₂ laser is a highly advanced technology in the treatment of acne scars, pimples, burns, pores, rejuvenation and tightening of the skin and cracks. Fractional CO₂ Laser is a modified CO₂ laser that eliminates the complications of a conventional CO₂ laser [40-42]. The Erbium Laser is the newest laser technology in the treatment of wrinkles, open pores of the face, facial clearance and welding. This laser is less invasive than the CO₂ laser and has low penetration under the skin. Also, it has fewer post-laser burns and complications, and the skin is healed earlier [38, 43].

Microdermabrasion

Microdermabrasion is one of the most widely used cosmetic technologies in the field of cosmetic medicine in the world. It was first developed in 1985 by Marini and LoBrutto in Italy, and its final application was later suggested by Montelleone to treat scars [44]. In this procedure the plastic surgeon removes the posterior skin layers with special abrasive tools (using a rotary or abrasive device) in a rotational and rapid manner. This method is applied in such a way that new, soft, and thick layers of skin replace instead previous layers [45]. There are various ways to perform microderms that change with the advent of new technologies over time. Crystalline Hydrogen Microderm and Diamond Hydrogen Microderm are the most common ones [46].

Microneedling

Microneedling as an induction of percutaneous collagen has been used during 2 decades ago[47]. Microneedling popularity has increased in the treatment of acne and scarring related acne[48, 49]. Alam et al assessed effect of microneedling on acne scarring treatment. Mean scar scores were significantly decreased over 6 months. The pain and limited erythema and edema were observed in patients[50]. Numerous clinical trials have confirmed positive clinical effect of microneedling[51-53].

Chemical Peels

Chemical peels are broadly used in acne scarring treatment. Scar improve with peels through damaging of skin layers and cause rejuvenation, exfoliation and remodeling of tissue. Superficial peeling agents for dermoepidermal junction including glycolic acid, tretinoin, salicylic acid, lactic acid, and trichloroacetic acid (TCA) 10% to 35%. Medium-depth peeling agents cover the upper reticular dermis including Jessner solution (lactic acid, resorcinol, and salicylic acid in ethanol) followed by TCA, 35%phenoland, and TCA 35% to 50%. And the deep peeling agents effects reach the mid reticular dermis and contain the Litton phenol formulas or Baker-Gordon[54].

fractional radiofrequency (fRF)

Fractional radiofrequency (fRF) as a new technology developed for acne scar treatment. fRF uses electrodes with regularly spaced arrays for inducing thermal necrosis in skin and providing improved thermal penetration capability and less side effects compared to fractional laser therapy. fRF can penetrated deep into layer of reticular dermis, therefore encouraging dermal remodeling by new collagen and elastin forming[55].

Subcision

The Subcision was first introduced in 1995 by a German physician named Dr. Orentreich. The purpose of the term " Subcision " was to describe minor surgery to treat scars by making a hole in the surface of the skin using a three-sided needle for subcutaneous injection[47]. The primary mechanism of this surgery is based on breaking the fibrotic fibers in the subcutaneous tissue. The release of fibrotic fibers and the production of new collagen results in improved scar appearance[56].

CLINICAL PRACTICE IN THE TREATMENT OF BURN INJURY

Skin grafting

When burn injuries eradicate all three skin layers, common therapeutic methods such as suturing cannot treat injury and cause to large scar and additionally surgical method are needed[57]. The gold-standard for such deep injuries is autografts. In this procedure the necrotic tissue removed and autologous skin have grafted. These autologous skin grafts can be consisting of epidermis and dermis or the epidermis and upper part of the dermis. But this method limited because of graft limitation and additional surgery[58, 59].

Skin substitutes

In large burn lesion due to limited in autografts skin, the skin substitutes can be utilized. These substitutes enhance wound healing, decrease subsequent scarring and inflammatory responses [60-63]. Nearly 30 new skin substitutes were examined or used in the treatment of burn wounds (table 2). Skin substitutes can be classified into synthetic substitutes(Integra, composed of lyophilized collagen, supplemented and cross-linked), biological substitutes(natural scaffolds such as Alloderm, an intact, de-cellurised anddermal human matrix), or a mixture of both [64].

Table 2. Treatment method for burn wounds

Skin substitute	Composition
KaroSkin[65]	Human cadaver skin with dermal and epidermal cells
GraftJacket@[65, 66]	Human acellular pre-meshed dermis
StrataGraft™[67]	Human dermal fibroblasts and stratified epidermis derived from Near-diploid Immortalised Keratinocyte S (NIKS)
GlyaDerm@[68, 69]	Glycerol preserved acellular dermal collagen-elastin matrix
OASIS® Wound Matrix[70]	Porcine acellular lyophilized small intestinal collagen matrix
XenoDerm[71, 72]	Lyophilised acellular porcine dermis
Permacol™[73]	Porcine acellular diisocyanite cross-linked dermis
PermaDerm™[74, 75]	Autologous keratinocytes and fibroblasts cultured with bovine collagen
OrCel@[76]	Bilayered type I collagen matrix
RenoSkin@[77]	Bilayer dermal matrix – silicone film and porous crosslinked bovine collagen
TransCyte@[78, 79]	Porcine collagen-coated nylon mesh
Integra@[80-82]	Cross-linked bovine tendon collagen and glycosaminoglycan, and polysiloxane (silicone)
Pelnac@[83, 84]	Porcine tendon derived atelocolla

Wound dressings

Wound dressings are utilized for wound coverage, re-epithelialization aiding, and infection and skin desiccation preventing.one type of wound dressing is biological-based that include allograft, xenograft and human amnion skin. Although

this wound dressing improves burn injuries they can have an immunological response[85]. The conventional dressings such as Vaseline gauze or silicone sheets are used for temporarily covering of wounds. However these dressings may adhere to wound surface and need to dressing frequent changes[86, 87].

Also, biosynthetic dressings have a biomimetic function by mimicking epidermis or dermis, or both.

SCARRING AND MANAGEMENT

After reducing mortality related to severe burn wounds, second purpose is to aimed scar management[88]. The keloid and hypertrophic scarring cause morbidity because of the outcomes of cosmetic and poor functional. Burn scars may cause several debilitating effects such as pruritus, pain, heat intolerance and dyspigmentation.

Stem cells

Recently for scar treatment stem cell-based wound dressing is developed. Stem cells are involved in all wound healing phases [89-91]. In the initial phase of inflammatory, the migrations of endogenous stem cells to the injury site happen. This migration facilitates wound closure rat, re-epithelialization and angiogenesis[92]. Adipose-derived (ADSCs) and mesenchymal stem cells(MSCs)have been commonly investigated for scar treatment[93].

Various studies have confirmed the positive effects of MSCs in hypertrophic scarring reduction by reduced myofibroblast marker expression and the collagen I down-regulation production [94-96]. Recently the ADSCs have been investigated in several studies and its potential in hypodermis, dermis and epidermis regeneration has been proved[97]. Also, many studies have been confirmed fat grafting technique efficacy in reconstructive and aesthetic cases[98-100].

Silicone in scar treatment

For years silicone has been used as a gold standard for burn-related hypertrophic scar management [101-103]. In recent studies, one of the effective non-surgical burn scar treatment methods is using of silicone surfaces. Various mechanisms have been proposed to account for the effect of silicon, including mechanisms of moisture, pressure, temperature, oxygen transfer and silicon absorption. But its mechanism of action is still unclear. Since 1982 in Australia, Perkins et al have been using silicone gel to treat burn scars. They showed significant improvement in the treatment of burn scars using silicone[104, 105]. Silicone gel alone (without the pressure on the scar) provides the most flexibility and softness for the scars, but we have no physiopathological explanation for this phenomenon. In the study of Ahn et al, silicone gel was effective in the prevention and treatment of hypertrophic scars[105].

Pharmacological method

Corticosteroids are also used to reduce scars height and volume.[103, 106-108] studies have proved TGF- β 1 and TGF- β 2 effect in scar formation but TGF- β 3 showed opposite behavior. Therefore, aiming in TGF- β 3 release can help in prevent of scar formation. The TGF- β 3 expression agents such as decorin can be utilized[109].

Laser therapy

Pulsed dye laser therapy

The PDL is the commonly laser that studied for hypertrophic scarring treatment[110]. Recently, the PDL has been displayed in many studies to give expressive and long-term progress in hypertrophic scars[111]. This laser targets the reticular dermis up to a depth of 1.2 mm. But its mechanism in scar improvements is unknown, however most theories considered vascular proliferation as a key role in scar management. Useful PDL effects on burn scar pruritus have been detected. Following PDL treatment the mast cell count or amounts of substance P and calcitonin gene-related peptide (the vascular response mediate in skin) may be decreased[112].

Ablative / non ablative fractional lasers

Fractional resurfacing cause organized damage of tissue columns, also recognized as microscopic treatment zones (MTZs), without considerably collateral damage. Similar to a z-plasty, the laser disturb collagen fibrils that formed the scar, causing repair of scare regions in a more controlled fashion. However, a main volume of epidermis and dermis remains healthy, which helps in wound healing.

Erbium -YAG laser

Studies shows that fractional erbium laser cause improvement of scar between 60 -90%[113] . Two studies investigated non ablative fractional erbium laser effect on mature burn scars and similar lack of improvement in thick scars was found[114, 115]. In a study improvement of hypertrophic burn scars in 24 patients on face, neck, or low neckline, and eight on the hands was seen with erbium:YAG lasers[114].

CO₂ laser

The CO₂ laser targets the water in abnormal collagen several millimeters below the skin surface. In fractional ablative CO₂ laser studies for scar treating , a collagen subtype (types I and III collagen) profile resembling that of non-wounded skin was seen[116]. Also problematic related pinpoint bleeding is much less in fractional ablative CO₂ laser compared to erbium: YAG laser. The fractional ablative CO₂ laser has been exhibited to be greatly effective in hypertrophic scars treatment [117, 118].

MICRONEEDLING FOR SCAR TREATMENT

For first time, Fernandes proposed microneedling for skin rejuvenation. Now days it is used for scar treatment. Microneedling potential in scar treatment have been related to releasing the growth factors, responsible in cell proliferation, improved deposition and synthesis of collagen - elastin complex, and transformation of collagen I to collagen III. In our study, we compared the therapeutic effect of microneedling with carbon dioxide laser in hypertrophic burn scars in clinical investigation and the more effectively of microneedling has been demonstrated [41].

CONCLUSION

Significant advancements have been seen in scare related burn and acne treatment in the recent decade, including advances in novel skin substitutes, pharmacological interventions, advanced surgical approaches such as laser therapy, fat grafting, skin grafting and coverage options for burn scar. For acne scaring treatment the laser therapy, cosmetic filler and pharmacological method have been introduced. As a result, by these new methods, treatment of scars improves significantly, however improvement of scar related to burn looks is more difficultly and numerous challenges still is essential to improve current scare.

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