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Scar Formation, Healing Stages, and Advanced Treatment Strategies - Review

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Abstract

Introduction and Aim of the Study: Scarring is a major concern in clinical dermatology, affecting individuals' quality of life due to both physical and psychological impacts. This review aims to explore the pathophysiology of various scar types—hypertrophic, keloid, and atrophic—and evaluate the effectiveness of current and emerging treatments to inform better clinical practices and therapeutic strategies. **Description of the State of Knowledge**: Scar formation involves complex biological processes: inflammation, proliferation, and remodeling. The nature of the scar varies with the underlying cause and biological response, influenced by genetic factors, skin tension, and environmental elements such as UV exposure. Recent advances in treatments range from surgical techniques to laser therapy and biological agents like cytokines. **Conclusion**: The studies reviewed underscore the complexity of scar management, influenced by diverse genetic, biological, and environmental factors. No single treatment is universally effective, but a combination of preventative and therapeutic strategies shows the best promise.

Keywords: Scar, surgery, postoperative care, laser therapy, dermatology

Introduction

Each of us is exposed to injuries and damage to the continuity of the skin in our everyday lives. Damage at the level of the dermis may cause scarring while the damaged tissue is filled with connective tissue. During surgery, the basic step is to incise the skin, so it is important to develop techniques that reduce the risk of scar formation. Burns are associated with scars that

can cover a large area of the body. Acne scars are very common, located mainly on the face, they leave permanent marks and affect self-esteem. To sum up, any skin damage (including piercings, tattoos, laser tattoo removal) involving the dermis may result in the formation of a scar. Non-surgical procedures such as peelings, lasers, injections are becoming more and more popular. However, they disrupt the continuity of the skin and require recovery time, during which appropriate care is also important to avoid unwanted blemishes. Scars' unsightly appearance may cause discomfort to the patient, especially if they are disproportionately raised, depressed, wide or erythematous. Additionally, they may cause itching, tension, and pain in the patient.

Methodology

To explore effective strategies for healing scars after surgeries, we conducted an exhaustive literature review using PubMed as our primary resource. Our search utilized specific key terms including "Scars healing", "Postoperative", „Surgery", "Wound Care" and "Silicone Gel", "Steroid Injections", "Laser Therapy", "Polynucleotides" and "Preventive Measures", "Minimizing Tension" "Wound Healing". This initial search identified papers. After a detailed evaluation, 45 of these papers were selected for the study for their scientific relevance and rigor.

Types of Scars - Hypertrophic Scars, Keloid Scars, Atrophic Scars

There are three types of scars: Hypertrophic Scars, Keloid Scars and Atrophic Scars. The most common cause of hypertrophic scars is a protracted healing phase following a skin burn. Convex, firm, red scar tissue that protrudes above the skin's surface are characteristic features. A fibroproliferative condition called keloid development causes excessive extracellular matrix and collagen synthesis. Histological buildup of collagens and fibroblasts, refractory clinical symptoms including itching and topical invasiveness, and frequent postsurgical recurrence are characteristics of keloids. Once the wound has healed, they take shape. Atrophic scars are the most prevalent kind of skin scars, which are distinguished by a decreased collagen concentration. Recognized clinically as a skin imperfection resulting from the inflammatory process. Stretch marks, acne scars, and chicken pox scars have a specific place among atrophic scars. Concave scars, which have a base beneath the skin's surface, are characterized by their distinctive borders and boundaries.

Healing Stages

Three primary mechanisms comprise the generic wound healing model: inflammation, proliferation and remodeling. The inflammation phase as a local non-specific reaction to injuries is characterized by active hyperemia in the surrounding damaged tissues, increased capillary permeability resulting in exudate and edema, extravasation of granulocytes, lymphocytes, monocytes, plasma antibodies, and the production of cytokine and chemokines. Cleansing the wound and reducing inflammation, during which macrophages dominate, lasts four to seven days. Proliferation usually starts on day four or five, when the fibroblasts migrate into the wound matrix marks. After two to four weeks, the fibroblasts have fully proliferated and have replaced the fibrin with a stronger collagen fiber matrix. Day ten to twelve is when wound contraction starts, though this can vary depending on the patient's overall health and the severity of the wound. The remodeling phase often starts three weeks after tissue damage. At this stage, microscopic observations include stiffening of collagen fibers, obstruction of blood arteries and reductions in the number of fibroblasts. For around six months following injury, the mature wound matrix is remodeled because of ongoing collagen synthesis and breakdown. Currently, there is no discernible change. The scar characteristics are primarily the result of the remodeling process[1].

How Scars Form

The reticular layer of the dermis contains inflammatory cells, an increased number of fibroblasts, newly formed blood vessels, collagen deposits, and increased expression of pro-inflammatory factors such as interleukin (IL)-1α, IL-1β, IL-6 and tumor necrosis factor-α . This means increased sensitivity to trauma, which promotes chronic inflammation that can cause the invasive growth of keloid scars. A hypertrophic scar occurs when there is no negative feedback during the remodeling phase and the synthesis and degradation of collagen fibers is not stopped, leading to continuous production of collagen fibers in the wound[1].

The pathogenesis of atrophic acne scarring is most likely related to inflammatory mediators and enzymatic degradation of collagen fibers and subcutaneous fat[2].

Factors Affecting Scar Healing

The incision may heal slowly and painfully, leaving more noticeable scars, if it is situated in an area that is continually stretched (such as the knee, the bend of the elbows, etc.), in an area with insufficient blood supply, or in an area with thin skin. It has been noted that mucous membranes, the soles of the feet, or the palms of the hands are not typically the sites of hypertrophic scarring, especially on the shoulders, sternum and auricles. Scars on the hands or face that are exposed to the sun, which emits UV radiation, typically have a darker, more unsightly appearance. Chemical and thermal burns, as well as lacerations, usually heal much difficultly than incised wounds, the risk of which can be reduced if they were created during surgery using developed surgical techniques. Some diseases may promote the formation of scars. Diabetes is a metabolic disease, in which the white blood cell system responsible for fighting infections, in this case wounds, is impaired. Moreover, diabetes impairs blood circulation, which causes the wound to be poorly nourished and oxygen-deprived, and therefore regenerates slowly. High concentration of glucose in the blood, resulting in the formation of glycation end products causing changes in the nerves, such as demyelination or changes in the nerve fibers themselves, cause diabetic neuropathy manifested by sensory loss, especially in the distal parts of the body - hands and feet. This means that the patient does not feel and therefore often does not notice the place of injury, which may deepen the injury, increasing the risk of improper healing and scar formation. Contamination and infection of the wound are another cause of difficult healing and therefore a greater risk of scar formation[3]. Infection is a major problem in burn wounds, with multidrug-resistant (MDR) organisms and fungi being the main challenges. Estrogen has been shown to regulate cytokine levels, which may speed up skin wound healing in addition to its effects on aging skin. In fact, it has been discovered that topical estrogen helps elderly men and women heal their wounds quickly and effectively[4].

Biological Factors - Genetics, Age, Skin Type

The patients must be aware of personal and clinical circumstances that cannot be modified, such as age, ethnicity, skin type and genetics.

In older people, skin tension and the activity of sebaceous glands decrease, which is why hypertrophic scars are less frequently observed in elderly people when compared to younger people[1].

The pathophysiology of keloids is significantly influenced by both genetics and epigenetics. Different chromosomal locations, susceptibility genes, and single nucleotide polymorphism (SNP) are among the genetic factors that may have an impact on the pathophysiology of keloids. Moreover, keloids may develop as a result of epigenetic changes such DNA methylation and non-coding RNA. It appears from all these findings that keloid patients are genetically susceptible. While many studies have suggested that keloid is caused by gene mutations, the precise gene responsible for the condition has not yet been identified. Thus, it is very crucial to identify the precise gene mutation location that causes keloid scars. It was also discovered that individuals with darker skin tones have a much higher risk of keloid formation[5].

The skin type classification system is a technique used to determine the likelihood of inflammatory skin illnesses' aftereffects and to forecast how the skin will react to damage. It may help to prevent hyperpigmentation and scarring. It comprises the photoaging and skin phototype[6]. The gold standard is still the Fitzpatrick Skin Phototype Classification. Six skin types (phototypes) are classified based on how the skin responds to UV light, which sets it apart. When applied appropriately, ablative lasers, non-ablative lasers, and radiofrequency microneedling can all be effective therapies for acne scarring in ethnic skin (skin phototypes IV–VI)[7].

Surgical Factors - Surgical Technique: Precise techniques reduce scarring., Wound Care: Proper care prevents complications and improves healing

Prevention of scar formation begins with planning the surgical incision site, selecting surgical tools, making appropriate sutures, and ending with caring for the wound and scar after surgery.

The cutting site should be made in Langer's lines, i.e. lines running perpendicular to the long axis of the muscles underlying the skin, where the tension is the most reduced, which allows the scar to remain flexible and at least partially hidden in the natural folds of the skin[1]. To prevent scarring surgical techniques, compose an important aspect. The five "A" of intraoperative methods are asepsis, absence of tension, accurate approximation, avoidance of raw surface, and atraumatic tissue handling

The next important stage is placing the stitches, to offer "approximation without tension" is the function of sutures. The fibroblasts and collagen fibers, not the sutures, are responsible for keeping the wound closed[8].

Treating burns and avoiding infection, often of large wound surfaces, is another important element in preventing scar formation. Over the last decade, many new treatments have been developed, such as: novel skin substitutes, application of new antimicrobial wound dressings and enhanced systemic drug delivery for wound infection, testing new pharmacological interventions and finding new targets for wound pain control[3].

In addition to the skin incision technique, it is also important to choose a tool that will be sharp to precisely make the cut with as little tissue damage as possible. A good example of this skin incision technique is the picosecond infrared laser (PIRL). Incisions on rats' skin exhibited less formation of scar tissue than those produced with a knife or electrosurgical equipment[9].

Improving Scar Healing

It's critical to optimize skin preparation and post-procedure supportive skin care management to safeguard the skin, promote wound healing and regeneration, avoid problems, and reduce scarring[10].When avoiding scarring, skin benefits may be increased with post-procedure skin care with healing, anti-inflammatory substances and supplementary skin care with antioxidant, anti-aging, and lightening characteristics.

Medical Interventions

Silicone gel, hypochlorous acid

Nowadays, a lot of silicone-based products are utilized to prevent and treat surgical scars[11].

As surgical scar preventives, silicone gel sheets and topical silicone gels were tested for both effectiveness and ease of application, it has been shown that topical silicone gels are more convenient to apply than other products, although there is no discernible difference in efficacy between the two.

It has been demonstrated that hypochlorous acid (HOCL) is a safe, effective therapy for treating and preventing hypertrophic and keloid scars following surgical procedures. Scar gel, dermal spray, and solution formulations are available. HOCL solution has been linked to a decreased in wound infection when compared to povidone-iodine because of its strong broad spectrum antibacterial activity and antibiofilm properties. By increasing oxygenation at the wound’s location, it may speed up the healing process. It has been shown that the safety of HOCL solution is equivalent to that of common local antiseptics. The efficiency of HOCL's

scar gel formulation has been shown in reducing pain and pruritus and enhancing the appearance of hypertrophic and keloid scars. It seems that HOCL scar gel is well-tolerated and safe. To further validate the utility of HOCL in post procedure treatment and scar control, larger head-to-head trials against other currently used products and bacterial eradication studies are required[12].

The study comparing the effects of topical silicone gel and corticosteroid cream for preventing hypertrophic scar and keloid formation following Pfannenstiel incisions were finished by thirty-nine patients (eighteen in the control group and twenty-one in the treatment group). All groups (control, silicone, and methylprednisolone groups) showed a significant decrease in all parameters (height, pigmentation, vascularity, pliability, and total the modified Vancouver Scar Scale (MVSS) score) at the 6th month evaluation compared to the 3rd month evaluation, according to intragroup comparisons of the MVSS scores from the third and sixth months. When comparing the methylprednisolone group to the silicone group at the sixth month, there were significant improvements in all MVSS indices, as well as in the metrics related to height, vascularity, and pigmentation, when compared to the control group. Patients in the methylprednisolone group reported higher levels of satisfaction and neither group suffered any negative effects, which suggests a promising use of the methylprednisolone cream[13].

Platelet concentrate (APC) and autologous dermo-epidermal skin grafts (DESG)

Deep burns are being treated using autologous dermo-epidermal skin grafts (DESG), which have become the gold standard. Furthermore, in the context of wounds, human autologous thrombin-activated autologous platelet concentrate (APC) has acquired popularity. It has been studied that the addition of platelets (a source of growth factors and inhibitors necessary for tissue repair) to DESG (a source of progenitor cells and tissue proteases necessary for the spatial and temporal control of growth regulators released from platelets) creates an optimal environment for cell interaction in healing deep injuries, which reduces the risk of pathological scar formation.

Platelet-rich plasma.

After split-thickness skin grafting, the application of platelet-rich plasma gel can accelerate wound healing, reduce the formation of scars, and ease discomfort at the donor site[14].

Pressure garment therapy.

Scar contraction was reported to be effectively reduced by pressure garment therapy at 10 mmHg. The application of pressure garment therapy also produced modest changes in the biomechanics and the structure of scar tissue[15].

Modern techniques for preventing and treating scars also include laser therapy.

A straightforward, risk-free, and painless method to greatly enhance the appearance of the scar is to perform a single presurgical laser treatment at the site of the intended incision[15].Better results can be obtained with the fractional erbium-doped yttrium aluminum garnet (Er:YAG) laser plus intense pulsed light (IPL) than with fractional Er:YAG laser alone or without therapy. During the initial stages of wound healing, this innovative fractional Er:YAG laser and IPL combo treatment may prove to be a safe and efficient means of preventing scarring[16]. When applied immediately after surgery**,** the 2,940-nm erbium:YAG laser treatment can make a surgical scar look better. Findings from the study, which enrolled patients undergoing intricate closures of at least 1.5 cm in length, were presented. Shortly after skin closure, a 2,940 erbium:YAG laser was used to treat half of the wound. Follow-up took place one week and twelve weeks after surgery. At the last appointment, the patient completed a self-evaluation. Three dermatologic surgeons who were blinded to the images assessed them[17]. For healing linear surgical scars, a continuous ablative CO2 laser with a fine beam size works just as well as a fractional CO2 laser. We propose the use of a 595-nm Nd:YAG laser as an alternative to a PDL since it produces effects that are comparable to those of a Q-switched PDL. Furthermore, compared to a fractional CO2 laser, the combination of a continuous ablative CO2 laser with a 595-nm Nd:YAG laser has superior effects on pigmentation[18]. To minimize the need for acute surgical reconstruction after facial burns, the combination of CO2-AFL and non-surgical scar contracture therapy was examined[19].

In the early stages of acute care, panfacial scarring and contractures that can cause significant functional deficits can be effectively managed with this combination of treatments. They may also remove the need for additional conventional surgical reconstructive procedures, which are frequently necessary to be carried out as soon as possible to preserve functional capacity.

After surgery, a single session with the 1210-nm Laser-Assisted Skin Healing (LASH) Technology can significantly improve both objectively and subjectively the look of scars. When patients are getting ready for surgery, this information can be helpful[20].

In full thickness wounds, a single low-to medium-fluence NAFL therapy given one day beforehand or during the initial stages of wound healing may be able to minimize scar formation[21].

Within a month after autografting, fractional carbon dioxide or pulsed dye laser therapy appears safe and lowers scar contraction in comparison to control; however, there was no statistically significant difference between the two laser modalities or the use of both modalities. Though these differences were not statistically significant, overall, erythema, scar texture, and scar mechanics appear to improve somewhat more with FX CO2 therapy. Even if the evidence supports the benefits of laser therapy, more research is needed to fully comprehend the connection between the parameters of laser administration and result[22].

The study about effectiveness of a 595 nm pulsed-dye-laser (PDL) in the treatment of surgical scars following a knee arthroplasty showed that the use of the cryogen cooled 595 nm PDL is an effective, well-tolerated and safe treatment option[23].

The effectiveness of moist exposed burn therapy (MEBT) and moist exposed burn ointment (MEBO) in post-treatment PDL was investigated in conjunction with UltraPulse fractional CO2 for juvenile, red hypertrophic scars. The outcomes demonstrated that MEBT/MEBO therapy might lessen post-treatment discomfort, speed up the healing process for wounds, improve the quality of scar tissue repair, and lessen pigmentation[24].

The research examined the clinical formation of scars following three non-ablative fractional laser (NAFL) exposures. The study focused on the areas of inflammation, proliferation, and remodeling during the wound healing phases in both patients and untreated controls. The results indicated that scars treated with NAFL exhibited a minor improvement when compared to untreated control scars[25].

Low-level laser therapy and pulsed dye laser are both effective treatments for minimization of scar formation following the primary closure of surgical wounds with comparable treatment outcomes, which suggest the study in which the placebo-controlled trials, the use of energy-based devices and lasers for surgical scar reduction has been thoroughly assessed[26].

Remodeling

Formation closure of hypertrophic and keloid scar development is a complicated problem.

Combinations of laser therapy, biologics, and intralesional steroid therapy have all been studied as medical possibilities. The cornerstones of care continue to be excision and closure surgery for prevention[27]. Keloid scars are difficult to treat when they recur despite surgical excision and may deepen the unsightly appearance of the scar. To minimize the risk of recurrence, a method of keloid reconstruction with bilaminar dermal substitute and epidermal skin grafting was developed. Potential applications include the reconstruction of full-thickness skin defects without donor site complications[28]. 4- Dermabrasion, needling and subcision, punch excision and grafts, fillers, non-ablative fractional lasers, ablative and fractional ablative lasers, and platelet-rich plasma (PRP) are scar revision alternatives for atrophic scars.[27] For refractory cases, radiation therapy has also been employed, with varying degrees of success.

Polynucleotides

In addition to its well-known ability to accelerate wound healing, research on the role polydeoxyribonucleotide (PDRN) plays a role in preventing scarring from surgical wounds and has demonstrated that early postoperative PDRN injection is a safe and effective treatment for hypertrophic scars[29]. Another study showed that when combined with traditional fractional laser treatment, adjuvant polynucleotides administration improved wound healing and reduced the risk of post-operative scarring following a conventional open total thyroidectomy[30].

Adipose-derived stem cells (ASCs)

Adipose-derived stem cells (ASCs) have the ability to replace various tissue types and secrete growth factors that promote regeneration. High-dose ASCs may improve scar quality in excisional wounds healing by secondary intention, speed up wound contraction, and promote neovascularization[31].

Erythema, hyperpigmentation, and hypopigmentation treatment

For erythematous scars, non-ablative fractional lasers, silicone, onion extract, methyl aminolevulinate-photodynamic treatment (MAL-PDT), pulsed dye laser, intense pulsed light (IPL), and moist exposed burn ointment (MEBO) are scar revision possibilities. Non-ablative fractional lasers, IPL, and tyrosinase inhibitors can all be used to treat hyperpigmented scars. Medical tattoos, excimer lasers, prostaglandin analogs, retinoids, calcineurin inhibitors, needle dermabrasion, autologous cell transplantation, and non-ablative fractional lasers are some of the treatments available for hypopigmented scars[32].

Conclusion

To effectively prevent the formation of scars and treat those that have already occurred, it is necessary to understand the pathophysiology of their formation and the factors influencing the healing process, and thus increase the risk of creating an unsightly scar. Despite many risk factors that we have no control over, such as age, skin phototype and genetics, known risk factors such as UV radiation allow us to consciously avoid them and use appropriate photoprotection.

Treating underlying diseases, including diabetes, where healing is difficult, as well as developing an effective treatment for burns to avoid wound infections is crucial to avoid scarring.

The development of optimal surgical techniques, appropriate selection of tools and cutting sites made it possible to reduce the risk of developing hypertrophic and keloid postoperative scars.

The studies analyzed in this article that could demonstrate effectiveness in preventing the formation and treatment of existing scars included silicone gel, hypochlorous acid, corticosteroid cream, platelet-rich plasma, pressure garment therapy, polynucleotides, adipose-derived stem cells (ASCs) and platelet concentrate (APC) and autologous dermo-epidermal skin grafts (DESG) in the treatment of burns, remodeling of hypertrophic and keloid scars, as well as many types of lasers.

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