Heparin effect on wound healing and scar formation; recommendation of heparinized surgical suture threads to reduce scar: A practical hypothesis

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Cite as : Hamzeh Mohammadi Sardo, Faezeh Mirzaee, Seyede Mahsa Abbasnia, Mitra Seyedi, Mohammad Pourfridoni. Heparin effect on wound healing and scar formation; recommendation of heparinized surgical suture threads to reduce scar: A practical hypothesis. Canon Journal of Medicine. 2023 December; 4(4), 97-99.

The skin is the body's primary defense against external harm and is essential for overall homeostasis (1). A surgical wound is a cut or incision in the skin that occurs during surgery and is often created with a scalpel. Sutures are typically used to close them, but they are occasionally left open during healing. Researchers have always sought to find different solutions to heal wounds faster and reduce scar tissue after surgery. Heparin has been found to influence skin fibroblast mitogenesis and collagen production. By binding to growth factors, heparin stabilizes them and delays their release. The use of heparin-coated sutures has been shown to increase cell proliferation and accelerate wound healing. Additionally, studies have demonstrated that incorporating nanofibers with heparin can enhance tissue healing speed (2). The present study proposes a new method for utilizing heparin in wound healing, which has the potential to reduce tissue scars and accelerate the healing of surgical wounds.

The wound healing process is a complex series of events involving various growth factors, proteases, and cells. When a wound occurs, the first step is the entrance of thrombocytes and coagulation, leading to the formation of a clot using fibrin and platelets. This clot acts as a temporary matrix. Subsequently, growth factors and inflammatory cytokines are secreted, leading to angiogenesis and the progression of the healing process. Macrophages play a vital role in controlling the growth phase of the healing process by inducing the production of replacement extracellular matrix (ECM) and triggering neutrophil apoptosis (3). The two main growth factors involved in the healing of wounds are basic fibroblast growth factor (bFGF) and transforming growth factor beta (TGF-β1). bFGF promotes collagen degradation and angiogenesis, while TGF-β1 is crucial for controlling cellular growth, differentiation, and the production of ECM proteins like collagen. The absence of adequate perfusion in the new arteries results in hypoxic circumstances that cause the release of growth factors, leading to scarring. The extracellular matrix (ECM) is a critical structural component in the wound healing process, and its reorganization during the healing phases is essential for normal wound healing and the prevention of abnormal scarring (4,5).

Surgical wounds go through three stages of healing: the inflammatory phase, the proliferative phase, and the remodeling phase. The third stage of healing, scar formation, involves gradual modification of the granulation tissue (1). Fibroblasts are activated and changed into myofibroblasts during the modification of granulation tissue. The extracellular matrix components that replace the temporary matrix are made and deposited by these myofibroblasts. Atypical scars can result from an inappropriate fibrotic response, excessive collagen formation, messed up stop signals, and improper modulation of enzymatic degraders. They may be atrophic, hypertrophic, or keloid in nature (3). The primary structural protein in the dermis in a non-wound state, collagen I, is replaced by collagen III in this tissue, and then elastin develops. Certain growth factors directly influence the process of granulation tissue development. The entrance of fibroblasts is aided in this stage by the production of TGF-β1 and PDGF from inflammatory cells (Figure 1) (4,6).

Heparin, an anticoagulant, has been studied for its effects on wound healing. It inactivates various proteases, impacting endothelial cell repair, capillary circulation, and healing time. Heparin affects dermal fibroblast proliferation, collagen production, and the levels of growth factors like TGF-β1 and bFGF. It also influences the coagulation cascade, local blood circulation, and the interaction of proteins with cell receptors. Heparin's use has shown positive effects on TGF-β1, TNF-α, and the prevention of excessive inflammatory responses. Additionally, it can stop pain neuropeptides from stimulating immune cells and control the activation of complements (7). Heparin's sulfation patterns may interact with integrin adhesion molecules, disrupting nuclear factor kappa B

Receive Date: 15 December 2023
Revise Date: 12 January 2024
Accept Date: 26 January 2024
Published Date: 30 January 2024
Editor: MA. Pourhoseingholi (Conflict of Interests: None)
Reviewers: M. Allahverdi Khani (Conflict of interest: None), M. AkbariRad (Conflict of Interests: None).

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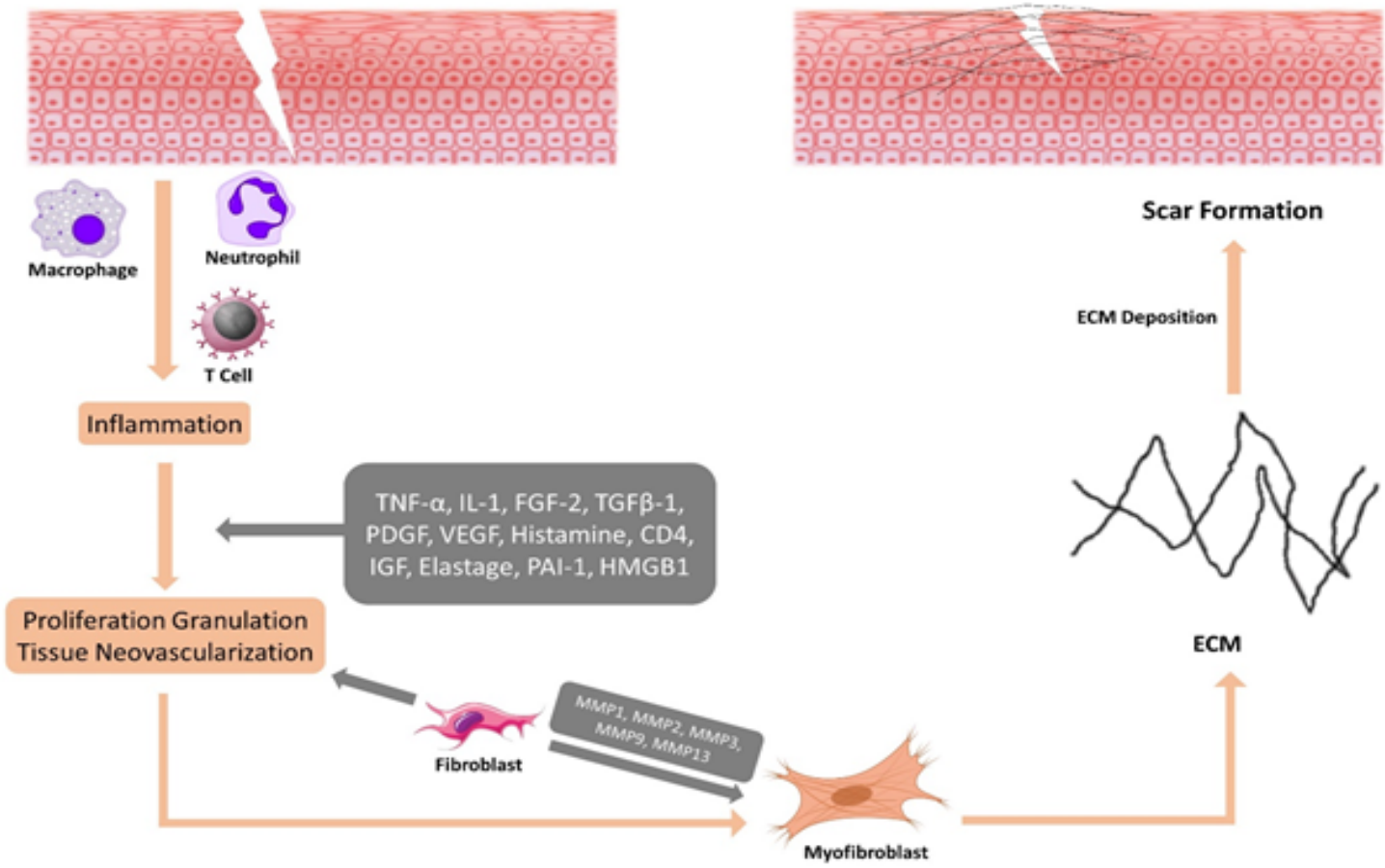

Figure 1. General mechanisms of scar formation

signaling. While heparin has a short half-life, nanotechnology has been developed to increase its half-life and reduce negative effects. Heparin can be safely used as an adjunct to standard wound care in selected patients with diabetic foot ulcers and critical limb conditions (8).

Heparin has been shown to affect skin fibroblast mitogenesis and collagen production by changing the level of these growth factors (7). Heparin also increases capillary blood circulation and tissue perfusion, which accelerates wound healing and reduces scarring. Recent studies have shown that heparinization of suture threads by molecular methods causes increased cell proliferation and helps to heal wounds faster. Heparinized surgical sutures offer several benefits, including reducing inflammation and infection, sustaining delivery of growth factors, improving wound strength, reducing friction and tissue response, and reducing scarring and potential for bioactive sutures (9,10). However, the use of molecular or nanotechnology methods to produce heparin sutures is time-consuming and costly and may not be available everywhere. The suggested technique for suturing a skin wound involves several steps. First, the used suture thread is removed from the sterile cover and placed in a heparin solution. Then, the area to be intervened is prepped and draped. After completing these prerequisites, the suture thread is removed from the heparin solution, and the wound is sutured in the shortest possible time. This method allows a small amount of heparin to enter the layers of the skin, which can leave the effects of tissue improvement and faster wound healing. The risk of unforeseen complications is very low due to the small amount of heparin injected into the skin in this technique.

Heparin, a compound known for its anticoagulant properties, has been found to play a significant role in wound healing and scar reduction. Studies have demonstrated the benefits of heparin in wound healing, such as increased cell proliferation and faster wound healing when heparin is applied to suture threads. A proposed technique involves heparinization of surgical suture threads before use, aiming to reduce scar tissue and heal surgical wounds faster with minimal side effects. However, further studies are needed to prove its effectiveness.

ETHICAL CONSIDERATION

The study adhered to Helsinki guideline.

CONFLICT OF INTERESTS

The authors declare that they have no competing interests.

AVAILABILITY OF DATA AND MATERIALS

Data sharing is not applicable to this article as no new data were

created or analyzed in this study.

ABBREVIATIONS

TGF; Transforming growth factor, PDGF; Platelet-derived growth factor, FGF; Fibroblast growth factor, EGF; Epidermal growth factor, IGF; insulin-like growth factor, HB-EGF; Heparin-binding EGF, VEGF; Vascular endothelial growth factor, CTGF; Connective tissue growth factor, HSPG; Heparan Sulfate Proteoglycans.

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