

Wound Healing: Assessment by Various Markers

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Abstract

Wound healing is the progression by which skin or other body tissue repairs itself after trauma. The phases of normal wound healing comprises of homeostasis, inflammation, proliferation, and remodeling. In stage first, there is an initiation of tissue injury which clears the wound. In stage second, there is a visibility of erythema, swelling and warmth which is associated with pain which increases the vascular permeability. While in third phase, there is formation of granulation of tissue and which results in epithelialization. So, by the use of various biomarkers we can easily detect the main cause of the disease and their stage of occurrence.

Keywords: Wound healing; Proliferation; Inflammation phase; Matrix; Cytokine; Trauma

Introduction

Wound healing is a difficult process which involves interaction between several tissues like connective tissue and cell types, cytokine mediators, extracellular matrix and various biological pathways in a multi-step and highly coordinated series of events. The phases of normal wound healing comprises of homeostasis, inflammation, proliferation, and remodeling. In first phase, tissue injury initiates a response that clear the wound of devitalized tissue and foreign material which surrounds the stage for tissue healing and regeneration. The primary vascular response engrosses a brief and transient period of vasoconstriction and homeostasis. In second phase of wound healing i.e. the inflammatory phase, shows erythema, swelling and warmth which is often associated with pain. This phase increases the vascular permeability, which results in migration of neutrophils responsible for engulfing debris and microorganisms and acts as a defense against infection and monocytes in the surrounding tissues. In the third phase i.e. the proliferative phase, formation of granulation of tissue and epithelialization occurs. Chemo tactic and growth factors released from platelets and macrophages activates wound fibroblasts' which releases substances for wound repair like glycosaminoglycans mainly hyaluronic acid, chondroitin-4-sulfate, dermatan sulfate and heparin sulfate and collagen. In the late phase i.e. the wound remodeling phase, comprises of reorganization of new collagen fibers, which results in increment of tensile strength. The process of remodeling continues to be about a two years which is achieving 40% to 70% of the strength of undamaged tissue at four weeks [1-3].

Types of Wounds

Abrasions

Abrasions are made when the skin is rubbed off. Rope burns, floor burns and skinned knees are common example [4]. This kind of wounds can become easily infected by dirt and germs which are embedded in the tissues. It is caused by superficial damage to the skin, no deeper than epidermis. It is less severe than lacerations and bleeding. Mild abrasions are also known as scrapes, do not scare or bleed but deep abrasions may lead to the formation of scars [4-7].

Punctures

Punctures are caused by objects that penetrate into the tissue while leaving a small surface opening. This type of wound can be done by nails, wire and bullets are usually punctures. Small punctures will

leak freely while in case of large punctures may cause severe internal bleeding [8-11].

Lacerations

This type of wound is cut by the torn rather than cut. They have ragged and irregular edges and mass of torn tissue underneath. A wound made by a dull knife is considered to be a laceration as compared incision [12-14].

Avulsions

It is defined as the tearing away of the tissue from the body part. Bleeding is usually heavy. In certain case torn tissue may be surgically attached. It is made by the shearing stress of force and friction which results in significant shearing and destruction of tissue [15-17].

Amputations

A traumatic amputation is the nonsurgical removal of limb from the body. In this case bleeding is heavy [18].

Incisions

Incisions commonly called as cuts or wounds which are made by knives, razors and broken glasses. There is a little damage to surrounding tissue. They are least infected when compared to others types of wounds [19].

Assessment of Wound Healing by Biomarkers

Wound healing can be assessed by various biomarkers. Biomarkers can be defined as a characteristics which is objectively measured and evaluated as an indicator of normal biological or biochemical features that can be used to assess the progress of a disease or the effects of treatment. There are various biomarkers which is associated with assessment of wound healing [20-22].

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Nitric oxide (NO)

Nitric oxide seems to be a diagnostics tool for assessment of wound healing. Nitric oxide is formed from the amino acid L-arginine and oxygen by three distinct isoforms of nitric oxide synthase (NOS). The inducible isoform (i NOS) synthesized in the inflammatory phase of wound healing by inflammatory cells is mainly due to macrophages [23-26]. NO is an essential biological factor for wound repair and is a significant supervisor of wound inflammation, epidermal cell migration, wound angiogenesis, collagen deposition, and wound tensile strength. The stable end-oxidation products of NO which is measured in tissues and fluids was determined NO bioactivity in wounds [27].

Matrix metalloproteinase (MMPs)

Another biomarker which is used for assessment of wound healing is matrix metalloproteinase (MMPs). They belong to family of zinc endopeptidase which helps in degradation of extracellular matrix and play a key role in every phase of healing process [28-30]. The main function is to damaged protein, destroy the provisional extracellular matrix, facilitate the migration, to the center of wound, remodel the granulation tissue and modulate angiogenesis (formation of new blood vessels through the activation of HIF- α). The level of MMPs declines and the closure progresses in normal condition of wound healing. While in case of chronic non-healing wounds such as venous ulcers, pressure ulcers, and diabetic foot ulcers the level of MMPs declines [5].

Platelet derived growth factor (PDGF)

PDGF is a cationic, heat stable protein stored in the α -granules of circulating platelets which is released from the platelets into the serum during blood clotting and is a potent mitogen for cells of mesenchymal origin such as fibroblasts and arterial smooth muscles cells. PDGF stimulates the release of Insulin Growth Factor (IGF) in cultured human fibroblasts which play an important role in the initiation of the repair process of wounds [6,31-33].

Tissue inhibitors of the metalloproteinase (TIMPS)

TIMPS are specific inhibitors which bind with MMP in a ratio 1:1 stoichiometry. There are four TIMP isoforms (TIMP-1, TIMP-2, TIMP-3, TIMP-4) found in vertebrates which is regulated during development and tissue remodeling. Under pathological conditions, which is associated with unbalanced MMP activities, which leads to direct decline in the level of TIMP and considered to be the important as these directly affect the level of MMP activity [7,34-36].

Conclusion

From the current study one can conclude that wound is a difficult process which involves interaction with several tissues, cell types and various cytokine receptors like IL-6. Interleukin 6 is a pleiotropic cytokine with roles in generating acute phase responses, inflammation, and lymphocyte differentiation. Numerous cell types produce IL-6, especially at sites of inflammation. IL-6 functions are mediated by binding to its specific receptor, IL-6Ra (gp80 and CD126). IL-6Ra is the only known receptor for IL-6, and its expression is predominantly restricted to hepatocytes and immune cells. So, it plays a major role in wound healing which is a tightly regulated process in which platelets and fibrin immediately fill the wound bed with an insoluble clot, and significant neutrophil immigration occurs shortly thereafter. Re-epithelialization proceeds by adjacent keratinocyte proliferation and migration over the wound area. Neutrophils in wounds are important for microbe neutralization, but their absence from sterile wounds does

not delay healing. Monocyte/macrophages are subsequently recruited and play roles in the clearance of debris and the provision of growth and angiogenic factors. Macrophages in wounds typically express markers indicating alternate activation pathways with functions in tissue remodeling and angiogenesis, rather than classically activated macrophages that function to kill pathogens. Therefore, biomarkers are used for the assessment of wound healing by various markers like nitric oxide (NO), matrix metalloproteinase (MMPs), platelet derived growth factor (PDGF), tissue inhibitors of the metalloproteinase (TIMPS) are used.

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