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VARIOUS MEDICAMENT USED IN WOUND HEALING: A REVIEW

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ABSTRACT

Wound healing involves a complex series of interactions between different cell types, cytokine mediators, and the extracellular matrix. The phases of normal wound healing include hemostasis, inflammation, proliferation, and remodeling. Since would healing is a vital body response, in ideally suited environment, the process may be hastened due to optimum biological response of the body. In order to create similar situations applications of different medicaments are suggested. The patho-physiology and treatment strategies vary depending on the nature of wound.

The present review compiled the data on various medicament used for wound healing in animals.

KEYWORDS: Wound healing, medicament, chronic wound, acute wound, treatment strategies.

INTRODUCTION

Wound healing involves a complex series of interactions between different cell types, cytokine mediators, and the extracellular matrix. The phases of normal wound healing include hemostasis, inflammation, proliferation, and remodeling. Each phase of wound healing is distinct, although the wound healing process is continuous, with each phase overlapping the next (MacKay and Miller 2003).

Successful wound healing requires adequate blood and nutrients to be supplied to the site of damage, the overall health and nutritional status of the patient influences the outcome of the damaged tissue (MacKay and Miller 2003).

Two broad categories exist for the classification of wounds: chronic and acute. Acute wounds undergo a complex interactive process involving a variety of cell types that leads to a healed wound. Conversely, chronic wounds have proceeded through portions of the repair process without establishing a functional anatomic result (Cohen *et al*., 1999).

VARIOUS TYPE OF MEDICAMENT

- **Activated Protein C (APC)**

Activated protein C (APC) promotes the migration and proliferation of endothelial cells and keratinocytes cells *in vitro*. In *in vivo* rat model, APC also enhanced wound healing compared to saline control, by up regulating matrix metalloproteinase (MMP-2) activity, increasing angiogenesis, promoting re-epithelialization and decreasing inflammation. These unique properties of APC make it an attractive therapeutic agent to promote the healing of chronic wounds (Jackson et al,2006).

- **Inducible Nitric Oxide synthase (iNOS)**

Nitric oxide plays an important role in normal wound repair. It observed that wound closure was delayed by 31% in iNOS knockout mice compared with wild type animals. Delayed wound healing in iNOS-deficient mice was completely reversed by a single application of an adenoviral vector containing human iNOS cDNA (AdiNOS) at the time of wounding (Kokushi et al,2010).

- **Calcium channel blockers**

The wound healing effect of two calcium channel blockers, nifedipine and amlodipine studied in rats using incision and excision wound models. In excision wound model, wound contraction was increased on day 4 and 16 but epitheliazation was not significantly altered. Drugs enhanced the skin tensile strength in incision wound model. It found that, calcium channel blockers can be used to enhance wound healing, especially if wound healing was suppressed by steroids (Bhaskar et al, 2004).

- **Platelet-Derived Growth Factor (PDGF)**

Role of platelet-derived growth factor (PDGF) on wound healing studied in full thickness linear incision wound model in rat. A single application of hPDGF or rPDGF-B (2-20 µg/wound) in a slow release vehicle at the time of wounding resulted in a dose-dependent, statistically significant increase in breaking strength of treated wounds. Wound healing in animals treated with rPDGF-B was 170% stronger and accelerated by 2 days during the first

week over control wounds and by 4-6 days over the next 2 wk. Histological evaluation of growth factor-treated wounds correlated with the *in vitro* chemotactic activity. The accelerated healing of wounds with a striking inflammatory cell infiltrate early after wounding, markedly increased formation of granulation tissue by 4 days, and increased fibrosis by 14 days in comparison to control wounds. Thus it concluded that rPDGF-B is fully active in *in-vitro* tests of mitogenesis and chemotaxis. PDGF also significantly advances wound healing in incisional wounds of experimental animals (Glenn et al, 1998).

- **Extracorporeal Shock-Wave Therapy (ESWT)**

Extracorporeal shock-wave therapy (ESWT) has a significant positive effect in accelerating chronic wound healing in a streptozotocin-induced diabetic Wistar rats receiving different session of ESWT (one session on day 3, 2 session on day 3and 7 and 3session on day 3, 7and 10) .The results revealed that the wound size was significantly reduced in the ESWT treated rats, especially in the ESW-2 and ESW-3 groups as compared with the control. They found that an optimal session of ESWT significantly enhanced diabetic wound healing associated with increased neo-angiogenesis and tissue regeneration, and topical anti-inflammatory response (Kuo et al, 2009).

- **Human Urine**

The effect of human urine studied inburn wound models and the effects compared with an antiseptic agent, povidine iodine solution. The human urine applied topically in the, burn wounds. The data showed a significant decrease in period of epithelialization and wound contraction-50% in all the treatment groups when compared to control. It was found that human urine applied topically or administered orally (10 ml/kg, p.o) possesses wound healing activity (Ramesh et al, 2010).

- **Chemokines Receptor (CX3CR1)**

Chemokines receptor CX3CR1 regulates skin wound healing in a mouse. Selected male CX3CR1 knockout (KO) mice and wild-type (WT) mice infused with anti-CX3CR1-neutralizing Ab using excision wound model. In WT mice, wound areas were reduced with linear kinetics whereas wound closure was significantly delayed in CX3CR1 KO mice. Multiple reparative processes were affected by the receptor, including inflammation, fibrosis, neovascularization, and regeneration of parenchymal cells (Ishida et al, 2008).

- **Linoleic and oleic acids**

The effect of linoleic and oleic acids on the inflammatory phase of excisional wound healing studied in rats. Fatty acids were topically administered and they assessed the total area and mass of the wound tissue, total protein and DNA contents of the tissue samples, vascular permeability and neutrophil migration to the injured area. It found that both oleic and linoleic acids increased the wound healing tissue mass, total protein and DNA contents of the wounds but did not affect vascular permeability. The number of neutrophils in the wounded area and air pouches was increased and the thickness of the necrotic cell layer edge around the wound was decreased. There was a dose-dependent increase in vascular endothelial growth factor-alpha (VEGF-α) and interleukin-1beta (IL-1ß) by neutrophils incubated in the presence of oleic and linoleic acid and oleic acid also stimulated the production of cytokine-induced neutrophil chemoattractant in inflammation (CINC-2α/β) (Pereira et al, 2007).

Table 1: Medicament used in wound healing

Medicament	Therapeutic Use	Mechanism of Action
Activated protein C(APC)	In cutaneous wound healing	By upregulatingexpression and activation of matrix metalloproteinase-2 (MMP-2)
Inducible nitric oxide synthase (iNOS)	Improve wound healing in iNOS-deficient states such as diabetes,	Increased NO production resulting from upregulation of iNOS expression could promote wound healing Angiogenesis is a key component of normal wound healing, and NO has been shown to be necessary for expression of macrophage angiogenic activity
Calcium channel blockers, (Nifedipine and Amlodipine)	Enhance wound healing, when wound healing was suppressed by steroids	By acting on voltage gated Ca2+ channels alter the intracellular calcium and also have antioxidant activity
Platelet-derived growth factor (PDGF)	In incisional wound healing	By having chemotactic and stimulatoryactivities for inflammatory cells and fibroblasts.
Extracorporeal shock-wave therapy (ESWT)	Diabetic wound healing	Increased neo-angiogenesis and tissue regeneration, and topical anti-inflammatory response
Human urine	Burn wound	Wound healing activity of human urine due to combination of its antibacterial, antioxidant and growth promoting effects.
Chemokine receptor (CX3CR1)	Surgery, chronic ulcers, and other pathologic conditions	CX3CR1 mediates direct recruitment of bone marrow-derived monocytes/macrophages which release profibrotic and angiogenic mediators
Linoleic and oleic acids	Cutaneous wound healing	These fatty acids stimulate neutrophils to release and shows a pro-inflammatory effect

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