Review

Role of nitric oxide, nitroxidative and oxidative stress in wound healing

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Abstract:
Redox-regulated processes are relevant to wound healing. A balance between bioavailable nitric oxide (NO) concentration and a level of oxidative and nitroxidative stress in wounds may be crucial in wound repair. The highly beneficial effect of bioavailable NO is attributed to scavenging of superoxide, which is the main component of oxidative stress. Also, the high level of NO can influence angiogenesis and endothelial/skeletal muscle cell remodeling and proliferation. However, under conditions of excessive and prolonged production of O$_2^-$ in wounds, the supplementation of NO can be evolved in significant increase in nitroxidative stress due to production of peroxynitrite (ONOO$^-$) and peroxynitrous acid (ONOOH). ONOOH can trigger a cascade of events leading to the generation of highly reactive and damaging radicals and oxidative species. These species (mainly CO$_2^+$, NO$_2^-$, NO$_2$, N$_2$O$_5$, OH$^-$) can impose significant damage in biological milieu and impair the process of wound healing. Therefore, a general strategy for an acceleration of the wound healing process may include an intervention(s) leading to the decrease in oxidative stress (treatment with antioxidants and/or prevention of O$_2^-$ generation by uncoupled constitutive nitric oxide synthase, cNOS) and delivery of NO (treatment with NO donors, cNOS gene therapy). Here we briefly review the role of NO, and focus on O$_2^-$ and ONOOH (major components of oxidative and nitroxidative stress respectively) in the normal and impaired process of wound healing.

Key words: nitric oxide, wound healing, oxidative stress, nitroxidative stress, acute wounds, chronic wounds, antioxidants, oxidative damage


Introduction

Damage of a tissue triggers a cascade of repair events, which begin with the formation of a fibrin clot. The clot, formed as a result of leakage of blood, provides protection to the underlying tissues, serves as a provisional matrix through which cells can move and also acts as a reservoir for growth factors and cytokines [11]. The growth factors initiate the inflammation, epithelization, wound contraction and angiogenesis process [32]. Platelet derived growth factor (PDGF) and tissue growth factor (TGF) released from platelets can act as chemoattractants for neutrophils and monocytes/macrophages. The major role of neutrophils is to kill the invading microorganisms by their characteristic respiratory burst activity and also to activate keratinocytes and fibroblasts [25]. The monocytes in the inflamed tissues can mature into macrophages and are responsible for phagocytosis of dying neutrophils,