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Perspective

Beta-Endorphins: A Novel Anti-Inflammatory Activity

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Abstract

Endorphins are endogenous morphine, produced in pituitary gland response to stress. There are three types of endorphins beta endorphins, enkephalins, and dynorphins binds to mu, kappa, and delta receptors situated on nervous system and immune cells. Beta-endorphins are an abundant endorphins, has an anti-inflammatory activity by inhibiting chronic psychological stress induced release of neuropeptides activates inflammatory mediators, which activates NF-KB key transcription factor involved in chronic inflammation and other mechanism of anti-inflammatory activity by production of anti-inflammatory cytokines. This article highlights about the basic research findings of beta-endorphins and its anti-inflammatory activity.

Keywords: *NF-KB; STAT3; IL-1; IL-6; TNF-α; Cortisol; ACTH; Noradrenaline; Chronic Psychological Stress*

Introduction

Endorphins are endogenous morphine, neuropeptides, produce in the pituitary gland in response to stress and pain. There are three types of endorphins beta-endorphins, enkephalins, and dynorphins binds to mu, kappa, and delta receptors respectively situated on nervous system and immune cells. Beta-endorphins are abundant endorphins, more potent than morphine, synthesized and stored in the anterior pituitary gland; it is a precursor of POMC (proopiomelanocortin). Chronic inflammation is the basis for most of all diseases including auto-immune diseases, heart diseases, cancer, Alzheimer's disease, infectious diseases, diabetes mellitus, and aging. Endorphin receptors are increased during stress such as inflammation abruptly binds with endorphins. Endorphins are produced during pranayama, mindful meditation, intense physical exercise creates a relaxed psychological state known as "Runner's high", music therapy, pranic healing, acupuncture, Love, Tender, Care, sympathy and empathy in caring the patient [1-3,22-24].

Beta endorphins: Anti-inflammatory activity

Endorphins are produced by most immune cells. In inflammatory state, recruitment of immune cells to the site of inflammation by chemokine's produces endorphins. Binding of beta-endorphins to the mu receptors situated on peripheral nerves results in inhibition of substance p, a neurotransmitter of pain and inflammation, produce IL-10, TGF-β, IFN-γ anti-inflammatory cytokines to reduce inflammation [22-24,27].

Beta-endorphins inhibits chronic psychological stress induced activation of NF-KB a key transcription factor by inhibiting HPA-axis (Hypothalamic pituitary adrenal axis) mediated release of neuropeptides such as cortisol, ACTH, noradrenaline through inhibition of autonomic nervous system (ANS) activate inflammatory mediators such as IL-1β, IL-6, TNF-α and COX-2, which activates NF-KB a key

transcription factor induced expression of chronic inflammatory mediators such as chemokine's, cytokines, growth factors, proteolytic enzymes involved in chronic inflammatory diseases such as (heart disease and Alzheimer's disease), autoimmune disease, cancer. NF-KB a key transcription factor involved in by conversion of Th1 lymphocytic type to TH2 lymphocytic type mediated by IL-4, STAT-6 transcription factor release IL-4, IL-5, IL-13 pro-inflammatory cytokines involved in chronic inflammation, tissue damage, immune modulation. Growth factors (EGF, FGF, VEGF) involved in cell proliferation and angiogenesis. Altered induced regulatory T cells (Tregs) formed from TH1 cells mediated by TGF-β, release IL-2, IL-4, IL-5, IL-10, IL-13, IL-17 pro-inflammatory cytokines involved in immune modulation. Reactive oxygen species (ROS) and reactive nitrogen species (RNS) released from neutrophils, macrophages, and dendritic cells during oxidative stress via NADPH oxidase pathway involved in cell aging, chronic inflammation, tissue damage, cell death, DNA damage and gene mutation. Proteolytic enzymes such as upa (urokinase plasminogen activator), MMp's (Matrix metallo proteinases)-2,9 involved in tissue damage by extracellular matrix degradation, NF-KB a key transcription factor activated by IL-1β, TNF-α, and COX-2, STAT-3 transcription factor activated by IL-6, EGF, FGF,PDGF involved in cell proliferation by activation of cyclin D,E cell cycle regulatory proteins and cell survival by activation of BCL-2, BCL-XL anti-apoptotic proteins involved in autoimmune disease, cancer [4-23].

Binding of beta-endorphins to the mu receptors present on innate and adaptive immune cells such as neutrophils, macrophages, dendritic cells, natural killer cells, mast cells, T cells, B cells, results in inhibition of IL-1β, TNF-α, IL-6 pro-inflammatory cytokines and produce TGF-β, IL-10, IFN-Ɣ anti-inflammatory cytokines.

Beta endorphins inhibits NF-KB a key transcription factor activated by chronic inflammatory mediators induced tumor progression by antagonizing P53 tumor suppressor gene, a guardian of the genome mutated in more than 50% of all cancer by NO(Nitric oxide),ROS,RNS free radicals, AID (Activation induced cytidine deaminase) enzyme expressed by NF-KB transcription factor [22,24-31].

Conclusion and Future Perspective

Beta-endorphins are an abundant endorphins synthesized and stored in the anterior pituitary gland. It has got anti-inflammatory activity by inhibiting various inflammatory mediators such as IL-1β, TNF-α, IL-6 and inhibits chronic psychological stress induced activation of NF-KB a key transcription factor mediated chronic inflammation induced immune modulation. Beta endorphins can be used in holistic preventive and therapeutic applications in treatment of various diseases, where chronic inflammation is considered as a basis for most diseases such as cancer, infectious diseases, and autoimmune diseases without adverse effects and inexpensive. Thorough understanding of beta-endorphins, mechanism of action and its anti-inflammatory activity, dose dependent duration of action, prognosis related to disease need to be studied. Basic human clinical trials in patients with chronic inflammatory diseases such as heart disease, Alzheimer's disease, auto-immune diseases, infectious diseases treated with laboratory exogenous beta-endorphins needed for future therapeutic applications of beta-endorphins.

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