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BETA-ENDORPHINS - THERAPEUTIC BOON

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INTRODUCTION

Endorphins are endogenous morphine, neuropeptides produced in pituitary gland, response to stress and pain. 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 abundant endorphins, more potent than morphine, synthesized and stored in the anterior pituitary gland, it is a precursor of POMC (pro opiomelanocortin). Endorphin receptors are increased during stress such as inflammation, binds abruptly with endorphins.

Holistic healing is a whole person healing. Human body works as a whole. If we consider human body as a whole rather than as parts in treating any disease with reductionist chemical drugs yield better results without adverse effects.

Adverse drug reactions are a major killer in the world. Cancer is a major threat to mankind, Majority of cancers more than 90% of all cancers are due to external environmental factors such as tobacco, alcohol, and infectious agents (such as HBV, EBV). Human environment is a most important factor in any disease including cancer. Very important part of human environment is human mind; human mind is a human consciousness. Chronic psychological stress is one of the important factors for human cancer. "Cancer cells works exactly like normal cells, I do not know any treatment how to kill the cancer cells without killing normal cells" said by Nobel laureate Albert Zen gyorgi. Advanced cancer treatment modalities such as surgery, radiotherapy, and chemotherapy failed to improve the prognosis of the cancer with increasing morbidity, adverse drug reactions, and decreased survival rate. Endorphins are produced during yoga, mindful meditation, pranayama, pranic healing, intense physical exercise creates a psychological relaxed state known as" runner's high", Love, tender, care, sex, music therapy, acupuncture, sympathy and empathy in caring the patient.[1-5]

Mechanism of actions of beta-endorphins

In inflammatory state, recruitment of immune cells to the site of inflammation by chemokines produces endorphins. Binding of endorphins to the receptors on peripheral nerves results in inhibition of substance P, a neuro transmitter of pain and inflammation, produce IL-10, IFNY, TGF-β anti inflammatory cytokines to reduce inflammation. In the PNS, binding of beta endorphins to the μ receptors situated on peripheral nerves results in inhibition of substance P, a neurotransmitter of pain and inflammation. In the CNS, binding of beta endorphins to the mu receptors situated on central nervous system results in inhibition of GABA inhibitory neurotransmitter, produce dopamine neurotransmitter involved in analgesic activity, stress buster activity, euphoria, and tranquillity of mind, cognitive development, self reward, and addiction. Endorphin receptors are situated on most innate and adaptive immune cells. Binding of beta endorphins to the mu receptors situated on innate and adaptive immune cells such as neutrophils, macrophages, mast cells, dendritic cells, natural killer cells, T cells, B cells, results in activation of immune cells(immune stimulatory activity) release opsonin, granzyme-B, interferon Y and antibodies involved in antibacterial activity, antiviral activity, antitumor activity and anti inflammatory activity. Beta endorphins inhibits chronic psychological stress induced sympathetic nervous system activity and activation of parasympathetic nervous system activity(results in release of IL-2,IFN-γ immune stimulatory cytokines) of ANS through inhibition of HPA- axis mediated release of neuropeptides such as cortisol, ACTH, and nor adrenaline activate inflammatory mediators such as IL-1β, IL-6, TNF-α, and COX2, which activates NFKB and STAT-3 key transcription factors involved in chronic inflammatory diseases such as heart disease, Alzheimer's disease, cancer, auto- immune disease, infectious diseases,

diabetes mellitus, and aging. Beta endorphins inhibits chronic psychological stress induced activation of NF-KB a key transcription factor induced inflammatory mediators involved in 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 along with TH17 cells involved in chronic inflammation, tissue damage, and immune modulation. Growth factors such as EGF, FGF, VEGF, involved in cell proliferation, cell survival, and angiogenesis. Altered induced regulatory T cells formed from TH1 cells mediated by TGF-β inflammatory mediator, release IL-3,IL-4, IL-5, IL-10, IL-17 pro inflammatory cytokines involved in immune modulation, otherwise normally regulatory T cells involved in self-tolerance and immune homeostasis. Proteolytic enzymes such as upA, matrix metalloproteases 2, 9 involved in tissue damage, tumor invasion and metastasis. IL-1 β, TNFα, COX2 pro inflammatory cytokines activate NF-KB a key transcription factor and IL-6, EGF, FGF, PDGF, pro-inflammatory mediators activates STAT-3 transcription factor, both transcription factors work together involved in cell proliferation by activation of cell cycle regulatory proteins such as cyclin D, E and apoptosis (cell survival) by activation of anti apoptotic proteins such as BCL-XL, BCL-2, all these changes lead to autoimmune disease and tumour progression. Beta endorphins inhibits chronic psychological stress induced activation of NF-KB a key transcription factor involved in tumour progression, which antagonise P53 tumour suppressor gene, a guardian of the genome mutated in more than 50% of all cancers by inflammatory mediators such as NO (nitric oxide), ROS, RNS, free radicals, AID (activation induced cytidine deaminase) enzyme expressed by NF-KB a key transcription factor. Beta endorphins express epithelial E- cadherin helps in cell adhesion, loss of epithelial E-cadherin mediated epithelial to mesenchymal transition induced tumour invasion. Beta endorphins delay aging by lengthening telomeres which otherwise shortened with aging. Other mechanism of delay aging by inhibiting ROS, RNS free radicals from inflammatory cells such as neutrophils, macrophages, dendritic cells during oxidative stress via NADPH oxidase pathway involved in cell aging, tissue damage, DNA damage, gene mutation and cell death. Beta endorphins are abundant endorphins useful in natural holistic preventive, therapeutic, health promotive, and palliative treatment of various diseases such as heart disease, Alzheimer's disease, cancer, infectious diseases, aging, auto immune disease and diabetes mellitus without adverse effects and inexpensive by its immune stimulatory activity, stress buster activity, analgesic activity and anti- inflammatory activity.[1,2,3,4,6-11]

ABBREVIATIONS

PNS- Peripheral nervous system
CNS- Central nervous system
ACTH- Adrenocorticotropic hormone
HPA- axis- Hypothalamic pituitary adrenal axis.
STAT 3- Signal transducer and activator of transcription protein 3
NF-kB – Nuclear factor kappa- light- chain –enhancer of activated B cells
CRH- Corticotropin releasing hormone
COX-2- Cyclooxygenase 2
TNF- α –Tumor necrosis factor – Alfa
IFN- γ- Interferon Gamma.

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