Endorphins – A Novel Holistic Therapeutic Approach to Cancer

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Abstract: Endorphins are endogenous morphine, neuropeptides produced from pituitary gland in response to stress and pain. These are of three types- beta-endorphins, dynorphins, enkephalins, binds to mu, kappa, delta receptors found on immune cells and nervous system. Beta-endorphins is the most abundant endorphin synthesized and stored in the anterior pituitary gland. It has got various activities such as Immune stimulatory activity, anti-inflammatory activity, analgesic activity, stress buster, and anti-aging activity. Immune stimulatory activity by activation of NK cells, macrophages, T-lymphocytes, anti-inflammatory activity by production of cytokines, such as IL-18, 1L-10, analgesic activity by inhibiting substance-p, anti-ageing by suppressing ROS, RNS, free radicals and lengthening telomeres, stress buster activity by decreasing cortisol and nor-adrenaline, dopamine release involved in holistic, preventive, promotive, therapeutic and palliative treatment of cancer without any adverse affects and inexpensive. This article brief's about the current concept of novel actions of endorphins in holistic treatment of cancer .

Keywords: Cortisol, HPA –axis, Noradrenaline, NF-KB, STAT-3.

INTRODUCTION

Cancer is a major cause of death worldwide. Majority of cancers are mainly due to external environmental factors such as tobacco in the chewable and non-chewable form, chemical ingestion, alcohol consumption, dietary factors and viruses such as HPV(Human Papilloma virus). Chronic inflammation is considered as a seventh hallmark of cancer. Cancer cells work like normal cells, I do not know how to kill the cancer cells without killing normal cells said by a Nobel laureate hungarian biochemist Albert Szent-Gyorgyi [1,2,5].

Advanced treatment modalities such as surgery, radiotherapy, and chemotherapy fail to improve the cancer prognosis with an increasing morbidity and mortality rate. The present concept of holistic healing rather than healing a part of the body yields better results with less complications [2,5].

Endorphins are endogenous morphine, neuropeptides produced 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 situated on nervous system and immune cells.

Beta-endorphin is an abundant endorphin, it is a precursor of POMC(pro-opiomelanocortin), synthesized and stored in the anterior pituitary gland. Most of all immune cells produce endorphins. In inflammatory state, recruitment of immune cells by chemokines to the site of inflammation produce endorphins reduce inflammation by affecting endothelial adhesion of immune cells, epithelial expression of adhesion molecules, and interfere with recruitment of leucocytes. Increase in the receptors throughout the peripheral nerves during inflammatory condition results in production of IL-10, IL-18, IFN-Gamma anti-inflammatory cytokines after binding of beta-endorphins to the receptors on peripheral nerves [3-6].

FACTORS RESPONSIBLE FOR RELEASE OF ENDORPHINS

The endorphins produced during yoga, meditation, physical exercise, pranic healing, music therapy, acupuncture, pranayama, chacolate consumption, love, care, sympathy and empathy [3,5,7-10,14].

MECHANISM OF ACTIONS OF ENDORPHINS

In the Peripheral nervous system (PNS), binding of beta-endorphins to the receptors present on peripheral nerves inhibits substance p, a neurotransmitter of pain and a mediator of inflammation during inflammatory painful condition [5,24].

Beta-endorphins binds to its receptors present on most immune cells. It is involved in immune stimulatory activity by activating immune cells such as NK- cells, macrophages, T-cells, neutrophils, B-cells, results in production of IFN- gamma, opsonin, granzyme-b, and antibodies involved in antiviral activity, antitumor activity, and anti-inflammatory activity. Beta-endorphins involved in reduction of chronic psychological stress by reducing ACTH, cotisol, and noradrenaline, neuropeptides release by inhibiting

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sympathetic nervous system activity and activating parasympathetic nervous system activity of ANS (Autonomic nervous system) through inhibiting CRH release from hypothalamus. Which activates HPA-axis (Hypothalamic pituitary adrenal axis), and also inhibiting the release of ACTH, cortisol, and noradrenaline neuropeptides mediated release of IL-1β, TNF-α, IL-6, and COX-2 inflammatory mediators, which activate key transcription factors NF-KB and STAT-3 involved in tumor progression by cellular proliferation (cyclin D, C-myc, P21), cell survival (BCL-2, BCL-XL, CFLIP, survivin), angiogenesis (IL-8, VEGF, COX-2), genomic instability (ROS, RNS, NO), immune suppression (TGF-Beta, IL-10, iNOS), invasion and metastasis (MMP-2, 9, E-selectin, CXCR4, uPA, Fibronectin, ICAM-1, ELAM-1,VCAM-1) [6-8,21-24].

In the Central nervous system (CNS), binding of beta-endorphins to the receptors present on central nervous system instead of inhibiting substance p, it inhibits GABA inhibitory neuro-transmitter, results in release of dopamine neurotransmitter involved in analgesic activity, self reward, euphoric effect, tranquility of mind, cognitive development and stress buster activity [11-13,18,19].

Beta-endorphins inhibits ageing by lengthening telomeres, which otherwise shorten with ageing and other mechanism is by inhibiting free radicals release such as ROS (Reactive oxygen species), RNS (Reactive nitrogen species) from inflammatory cells such as neutrophils, dendritic cells, macrophages, during oxidative stress through NADPH oxidase pathway by cytokines such as IL-1, TNF-α, and IL-8 [15-17,19,24].

P53 a guardian of the genome is a tumor suppressor gene, mutated in more than 50% of all cancers by inflammatory mediators such as ROS, RNS and NO (NITRIC OXIDE). NF-KB a key transcription factor in inflammatory tumor micro-environment antagonize the p53 tumor suppressor gene. Suppression of inflammatory mediators such as ROS, RNS, free radicals, nitric-oxide (NO) and a key transcription factor NF-KB in tumor micro-environment by beta-endorphins, which inhibits suppression and mutation of p53 tumor suppressor gene [23,24]. Beta Endorphins promote epithelial E-cadherin expression, which involve in cell adhesion prevents/inhibits invasion of cancer [21].

Beta-endorphin is involved in holistic preventive, therapeutic, promotive, and palliative treatment of cancer without adverse effects and inexpensive.

CONCLUSION AND FUTURE PERSPECTIVE

Endorphins are neuropeptides produced from pituitary gland in response to pain and stress such as yoga, meditation, intense physical exercise, and pranayama. Chronic psychological stress induced release of CRH from hypothalamus activate HPA-Axis. Which release ACTH, cortisol and nor-adrenaline mediated activation of inflammatory mediators IL-1ß, TNF-α, IL-6, from inflammatory cells activate NF-KB, STAT-3, Key transcription factors involved in tumor progression. Beta-endorphins is a type of endorphin synthesized and stored in the anterior pituitary gland involved in anti-tumor activity by immune stimulation, anti-viral activity, stress buster activity and anti-inflammatory activity. In future, thorough understanding of beta-endorphins, their mechanism of action and dose dependent prognosis of cancer helps in preventive, therapeutic, promotive and palliative holistic treatment of cancer without adverse affects.

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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