

Beta-Endorphins - A Novel Holistic Therapeutic Approach to Oro-Facial Disorders

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Abstract

Endorphins are an endogenous morphine neuropeptides produced from pituitary gland in response to stress and pain. There are three types of endorphins beta-endorphins, enkephalins, and dynorphins binds to mu (μ), kappa (κ), and delta (δ) receptors situated on nervous system and immune cells. Beta endorphin is an abundant endorphin synthesized and stored in the anterior pituitary gland. It has got various activities such as immune stimulatory, anti-inflammatory, analgesic, anti-aging, stress buster activity involved in holistic preventive, promotive, therapeutic, and palliative treatment of ulcerative, autoimmune disease, TMj disorders, Oral cancer, oro-facial pain without adverse effects and inexpensive. This article highlights about the new basic research findings of beta endorphins in management of oro-facial disorders.

Keywords: *Cortisol; Noradrenaline; ACTH; IL-1 β ; IL-6; TNF- α ; COX-2; NF-KB; STAT-3*

Abbreviations

PNS: Peripheral Nervous System; CNS: Central Nervous System; ACTH: Adrenocorticotrophic 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

Introduction

Oral cancer ranked 6th most common cancer in the world with 300,000 new cases of oral cancer, and annual death rate of 1,45,328. Most of all oral cancers are developed from oral potentially malignant lesions and conditions [1,2]. Majority of oral cancer cases are due to external environmental factors such as tobacco, alcohol, viruses such as HPV, and chronic psychological stress [1,2]. Advanced oral cancer treatment modalities such as surgery, chemotherapy, and radiotherapy fails to improve the prognosis of oral cancer with increasing morbidity, adverse drug reactions, mortality, and decreased survival rate. We can't kill cancer cells with any treatment without killing normal cells, cancer cells and normal cells work alike said by Albert zen gyorgi.

The current concept of 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 including cancer with reductionist chemical drugs yield better results without adverse effects. Adverse drug reactions are a major killer in the present world.

Most of all diseases are from human environment is human mind that is consciousness. Endorphins are endogenous morphine, neuro-peptides 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 [3-6,25,28-30].

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

Mechanism of action of beta-endorphins

Beta-endorphins is an abundant endorphin, potent than morphine, synthesized and stored in the anterior pituitary gland, it is a precursor of POMC (Proopiomelanocortin).

Most of all immune cells produce endorphins. In inflammatory state recruitment of immune cells to the site of inflammation by chemokines produce endorphins reduce inflammation by binding of endorphins to the receptors on peripheral nerves results in inhibition of substance p a neurotransmitter of pain and inflammation. Endorphins produced during yoga, intense physical exercise creates a psychological relaxed state known as “Runner’s high”, mindful meditation, pranayama, acupuncture, TENS therapy, Pranic healing, music therapy [3,4,5,7-17,25,28-30].

Chronic psychological stress induced release of CRH from hypothalamus activates HPA-axis through ANS release neuropeptides such as cortisol, noradrenaline and ACTH activates IL-1β, TNF-α, IL-6 and COX-2, inflammatory mediators, which activates NF-KB, STAT-3 transcription factors involved in chronic inflammation, autoimmunity and cancer [14,18,20,21,25-32] (Figure 1).

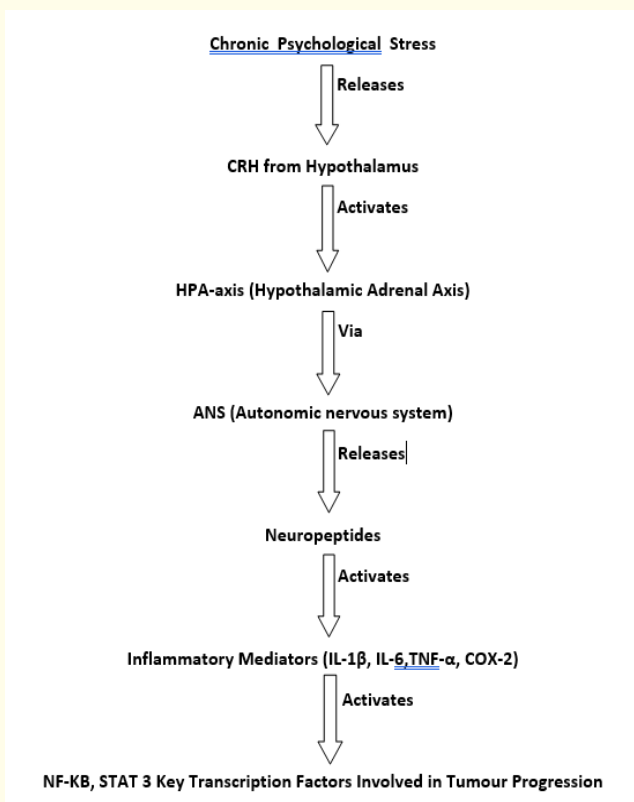


Figure 1: Shows the correlation between chronic psychological stress and cancer

In the peripheral nervous system (PNS) binding of beta-endorphins to the mu receptors on peripheral nerves results in inhibition of substance P a neurotransmitter of pain and inflammation, produce IL-10, IL-18 and IFN- γ anti-inflammatory cytokines to reduce inflammation [7,13,17,20,28-32] (Figure 2).

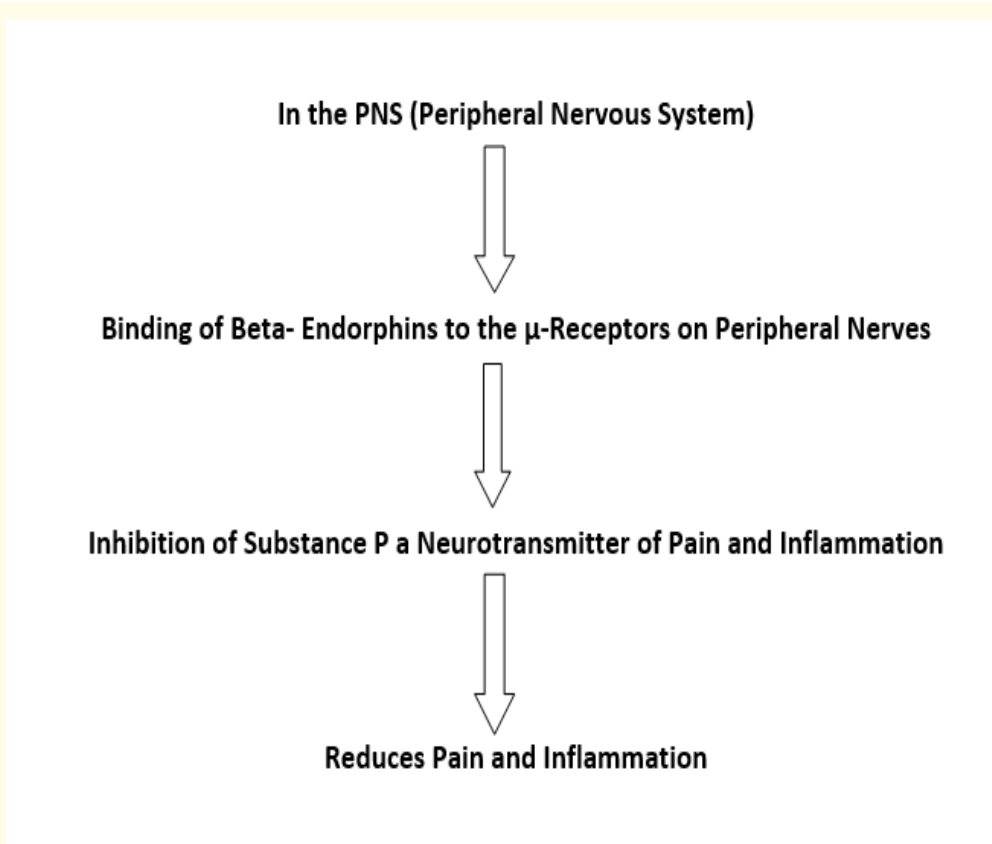


Figure 2: Mechanism of action of beta endorphins on PNS in reduction of pain and inflammation.

In the central nervous system (CNS) binding of beta endorphins to the mu receptors on central nervous system instead of inhibiting substance p, it inhibits GABA (Gama amino butyric acid) inhibitory neurotransmitter, activates dopamine neurotransmitter involved in analgesic activity, euphoria, tranquility of mind, self-reward, cognitive development and stress buster activity [7,17,18,28-30] (Figure 3).

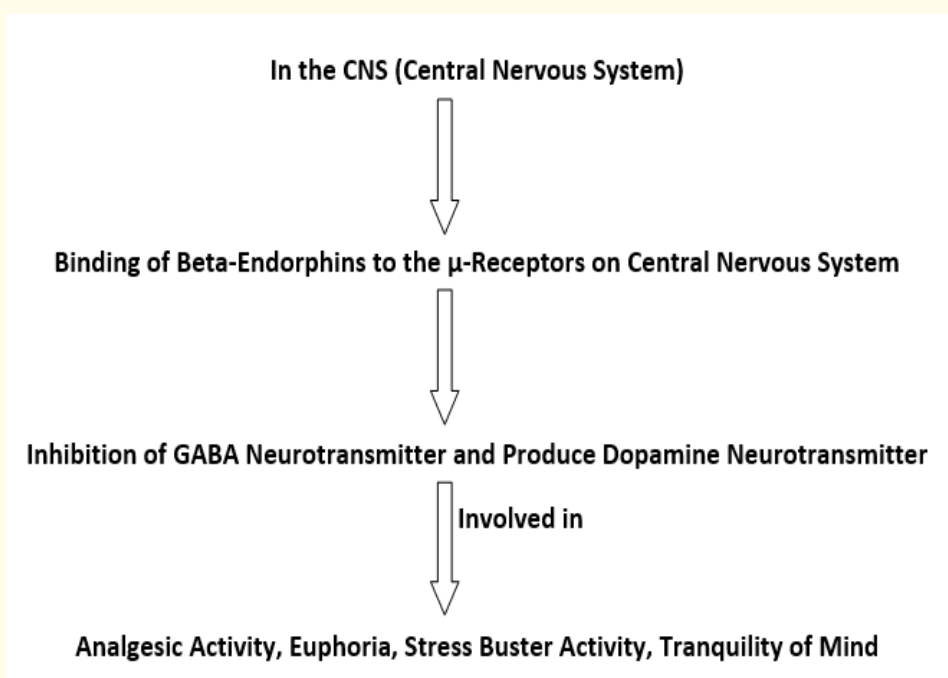


Figure 3: Mechanism of action of beta- endorphin on CNS on reduction of pain and stress.

Endorphin receptors are situated on immune cells. Binding of beta endorphins to the mu receptors on immune cells such as NK cells, DC's, neutrophils, macrophages, T cells and B cells results in activation and release of opsonin, granzyme-B, IFN- γ , and antibodies involved in antiviral, antibacterial, antitumor and anti-inflammatory activity [8-10,12-14,20,25,28-30] (Figure 4).

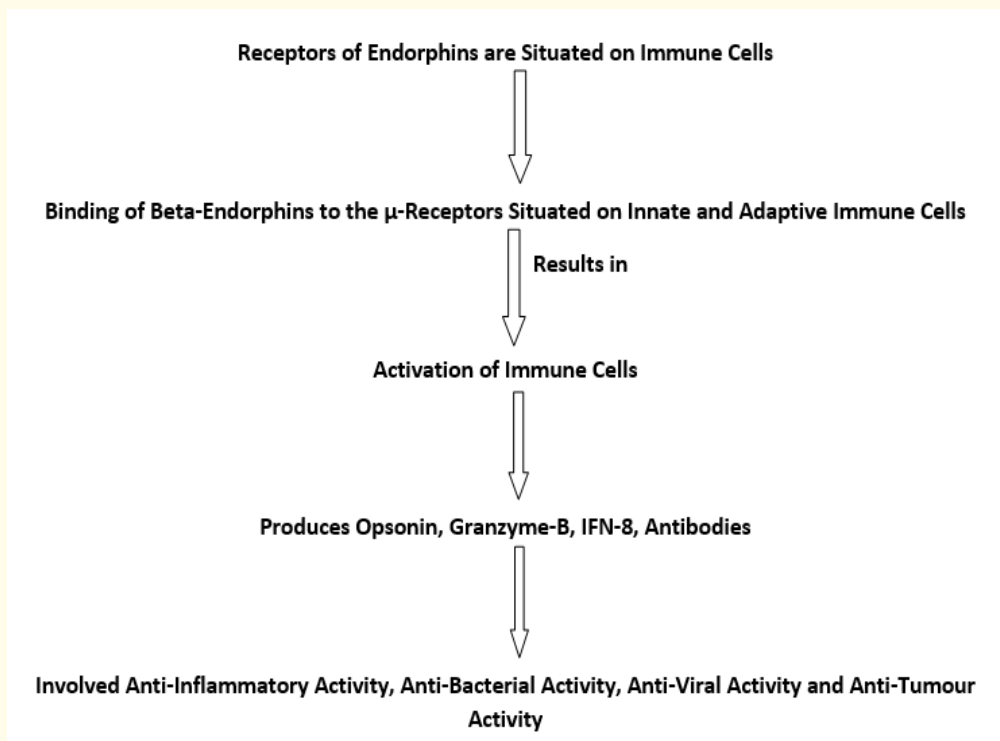


Figure 4: Mechanism of action of beta-endorphins on immune cells.

Endorphins inhibits chronic psychological stress induced sympathetic nervous system activity and activates parasympathetic nervous system activity mediated inhibition of release of neuropeptides such as cortisol, ACTH, noradrenaline, through HPA-axis results in inhibition of inflammatory mediators such as IL-1 β , TNF- α , IL-6 and COX-2, which activates NF-KB, STAT-3 transcription factors involved in chronic inflammation, autoimmunity, and cancer [24-32].

Beta endorphins inhibits NF-KB transcription factor through inhibiting HPA-axis mediated release of neuropeptides activates inflammatory mediators, which activated NF-KB transcription factor NF-KB a key transcription factor induced expression of inflammatory mediators involved in cell survival by BCL-2, BCL-XL, surviving. Chronic inflammation and immune modulation by MHC-1, MHC-11, Cytokines. Invasion and metastasis by MMP-2, 9, E-selectin, ICAM-1, VCAM-1, ELAM-1, Fibronectin. Angiogenesis by IL-8, VEGF and COX-2. Cell proliferation by cyclin D [4,5,8,13,14,22-25,28-32].

NF-KB a key transcription factor involved in progression of oral cancer antagonize the P53 tumor suppressor gene, a guardian of the genome mutated in more than 50% of all cancers, including oral cancer patients by inflammatory mediators such as NO (nitric oxide), ROS, RNS, AID (Activating cytidine deaminase) enzyme [22,28-30].

Beta endorphins express epithelial E-Cadherin involved in epithelial attachment, loss of E-cadherin involved in EMT (epithelial mesenchymal transition) induced tumor invasion [22,23,28-30].

Endorphins delay aging by lengthening telomeres, which otherwise shorten with aging and other mechanism is by inhibiting free radicals (ROS, RNS) release during oxidative stress via NADPH oxidase pathway produced by inflammatory cells such as neutrophils, macrophages, and dendritic cells involved in cell aging, genetic mutation and cell death [28-30].

Endorphins inhibit chronic psychological stress induced activation of NF- κ B a key transcription factor which induce inflammatory mediators involved in conversion of TH1 lymphocytic type to TH2 lymphocytic type release IL-4, IL-5, IL-13 pro-inflammatory cytokines, along with TH17 cells involved in chronic inflammation, tissue damage, and immune modulation. Altered induced Tregs (Regulatory T cells) formed from TH1 cells mediated by TGF- β inflammatory mediator release IL-2, IL-4, IL-5, IL-10, IL-13, IL-17 pro-inflammatory cytokines involved in immune modulation otherwise normally regulatory T cells participate in self-tolerance and immune homeostasis, growth factors such as (EGF, FGF, VEGF) involved in cell proliferation and angiogenesis, MMP's 2,9 (matrix metalloproteases 2,9) involved in tissue damage, all these changes lead to autoimmune disease [13,14,16,18,26-32].

Application of beta-endorphins in orofacial disorders

Oral ulcers, Oral cancer, autoimmune disorders, TMJ disorders, Oro-facial pain, headache, Oral potentially malignant lesions and conditions.

Conclusion and Future Perspective

Beta-endorphins synthesized and stored in the anterior pituitary gland, it is an abundant endorphin, has immune stimulatory, anti-inflammatory, stress buster activity, analgesic activity, anti-aging activity, anti-inflammatory activity. Endorphins are endogenous morphine acts as a holistic preventive, therapeutic, health promotive, and palliative treatment of oro-facial disorders without adverse effects and inexpensive. In future, thorough understanding of endorphins, types, mechanism of action, dose dependent duration of action, prognosis related to oro-facial disorders useful for future therapeutic purpose.

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