شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأفلام قد أعدت دون أية تغيرات

يجب أن

تحفظ هذه الأفلام بعيدا عن الغبار

في درجة حرارة من ١٥-٢٥ مئوية ورطوبة نسبية من ٢٠-٤٠%

To be Kept away from Dust in Dry Cool place of 15-25- c and relative humidity 20-40%

بعض الوثائـــــــق الاصليـــــة تالفـــة

بالرسالة صفحات لم ترد بالاصل

GENE THERAPY AS A NEW INNOVATION IN CHRONIC PAIN MANAGEMENT IN CANCER PATIENTS

An essay submitted in partial fulfillment of requirements of the Master degree of Anaesthesia

By

Mostafa Mohamed El Adany
MB.BCH.
Suez Canal University

Supervisors

Dr. Alaa El Dean Mohammed El Kassaby
Professor and head of Anaesthesia and Intensive care department
Faculty of Medicine
Suez Canal University

Dr. Mohammed Hamid El Sharkasy
Professor of Anaesthesia and Intensive care
Faculty of Medicine
Suez Canal University

Dr. Magdy Abd-El Hamid Mahmoud Abo El Nasr
Lecturer of Anaesthesia and Intensive care
Faculty of Medicine
Suez Canal University

Faculty of Medicine
Suez Canal University
2005

Contents

ACKNOWLEDGEMENT

Praise to Allah, The master of the universe and most merciful.

I wish to thank Prof. Alaa El Dean Mohammed El Kassaby Professor and head of Anaesthesia and Intensive care department, for his help ,support and patience.

I also like to express my appreciation to Prof. Mohammed Hamid El Sharkasy Professor of Anaesthesia and Intensive care for his encouragement and guidance to me .

My sincerest gratitude to Dr. Magdy Abd-El Hamid Mahmoud Abo El Nasr Lecturer of Anaesthesia and Intensive care for his cooperation during this study.

List of figures

Introduction

Pain was defined by The International Association for the Study of Pain as "an unpleasant sensory and emotional experience in association with actual or potential tissue damage, or described in terms of such damage." There are many other ways to define pain. A useful definition is from pain expert Margo McCaffrey: "Pain is whatever the experiencing person says it is, and exists whenever he says it does."[1]

Pain is transmitted through the body by the nervous system when our nerve endings detect damage to a part of the body. The nerves transmit the warning through defined nerve pathways to the brain, where the signals are interpreted as pain. Sometimes pain results when the nerve pathways themselves are injured. Pain happen when brain receives the signal from nerves that damage is occurring. All types of pain are transmitted this way, including cancer pain.[2]

Pain can be acute or chronic: Acute pain usually starts suddenly, may be sharp, and often triggers visible bodily reactions such as sweating, an elevated blood pressure, and more. Acute pain is generally a signal of rapid-onset injury to the body, and it resolves when pain relief is given and/or the injury is treated.

Chronic pain lasts, and pain is considered chronic when it lasts beyond the normal time expected for an injury to heal or an illness to resolve. Chronic pain, sometimes called persistent pain, can be very stressful for both the body and the soul, and requires careful, ongoing attention to be appropriately treated.

Non pharmacological management of chronic pain includes Physical therapy, Relaxation and Massage, Chiropractic manipulations, Spiritual healing, Biofeedback and Hypnosis, Magnetic and Low power Laser therapy, Transcutaneaus electrical nerve stimulation, Homeopathy, Acupuncture and Prayer. [5]

However, many patients with chronic pain, in particularly those of neuropathic origin, are most often not satisfactorily managed with currently available agents and some patient even suffer from the side effects of these agents.

Hence there is an increasing need for more effective modalities for chronic pain management with fewer side effects.

Gene-bases approaches may contribute to the search for a better management of chronic pain.

A report from the Recombinant DNA Advisory Committee lists 393 approved human gene therapy protocols of these, 33 are for infectious diseases, 49 for monogenic diseases (mostly cystic fibrosis), 237 for cancer, 35 for other disorders, and the remainders for non-therapeutic trials. [6]

Gene therapy offers the tantalizing possibility of specific and selective targeting of a single point in the synthesis of proteins. [7]

Gene therapy based on introducing therapeutic proteins into some targeted structures, where it would be continuously synthesized and exert its biological effect in the near vicinity of, or inside the cells, might avoid some drawbacks of classical drugs. [8]

In March 15,1999 _ Using a gene vector developed by the University of. PITTSBURGH a university of South Carolina-led research team was

CHRONIC PAIN

Definition of pain:

According to the International Association of the Study of Pain. pain is defined as "an unpleasant, sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage." (11)

Types of pain :

A. Acute Pain: caused by noxious stimulation due to injury, a disease process, or abnormal function of muscle or viscera. This type of pain is typically associated with a neuroendocrine stress that is proportional lo intensity. It is frequently referred lo as nociceptive pain. (nociception, describe the neural response to traumatic or noxious stimuli.)

Its most common forms include posttraumatic, postoperative, and obstetrical pain. as well as that associated with acute medical illnesses such as myocardial infarction, and renal calculi. Three types of acute pain superficial., deep somatic, and visceral are differentiated based on origin and features.

1. **Superficial:** nociceptive input arising from skin. subcutaneous tissues, and mucous membranes. It is characteristically well-localized and described as a sharp, pricking, throbbing, or burning sensation,
2. **Deep somatic**: Deep somatic pain arises from muscles, tendons, joints, or bones. It usually has a dull, I aching quality and is less well-localized- An additional feature is that both the intensity and duration of the stimulus affect the degree of localization.
3. **Visceral** : due to a disease process or abnormal function of an internal organ or its covering (e.g., parietal pleura, pericardium, or peritoneum). Four subtypes are described: (1) true localized visceral pain, (2) localized parietal pain, (3) referred visceral pain, and (4) referred parietal pain. True visceral pain is dull, diffuse, and usually midline- It is frequently associated with either abnormal sympathetic or parasympathetic activity causing nausea, vomiting, sweating, and changes in blood pressure and heart rate. Parietal pain is typically sharp and often described as a stabbing sensation that is either localized lo the area around the organ or referred to a distant site . The phenomenon of visceral or parietal pain referred to cutaneous areas results from patterns of embryologic development and migration of tissues, and the convergence of visceral and somatic afferent input into the central nervous system . (12)

B. Chronic Pain: defined as pain persists beyond the usual course of an acute disease or after a reasonable time for healing to occur; this period varies between 1 to 6 month. Chronic pain may result from peripheral nociception, or peripheral or central nervous system dysfunction.

Usually associated with mood and psychological disturbances and attenuated neuroendocrine stress response . The most common forms of chronic pain include those associated with musculoskeletal disorders, chronic visceral disorders, lesions of peripheral nerves, nerve roots, or dorsal root ganglia (including phantom limb pain, and post herpetic

Most of first-order neurons send the proximal end of their axons into the spinal cord via the dorsal (sensory) spinal root

Some unmyelinated afferent (C) fibers send proximal branches via the ventral nerve (motor) root, so some patients continue lo feel pain even after transection of the dorsal nerve root (rhizotomy) and report pain following ventral root stimulation.

In the dorsal horn, first-order neurons synapse with second-order neurons, the axons of may synapse with interneurons, sympathetic neurons, and ventral horn motor neurons.

Pain fibers originating from the head are carried by the trigeminal (V), facial (VI) gloss pharyngeal (IX), and vagal (X) nerves. (14)

Second-Order Neurons

First –order neurons synapse with second –order neurons in the gray matter (direct or through interneurons)

Gray matter was divided by Rexed into 10 areas ;6 areas receive all afferent impulses

Second –order neurons are two types :nociceptive-specific neurons and wide dynamic range neurons (WDR)

As nociceptive-specific neurons receive only pain (noxious stimulations) and arranged in lamina I ,respond only to high threshold noxious stimulations

And wide dynamic range neurons (WDR) receive non noxious afferent input from Aβ,Aδ, and C fibers. They are the most prevalent neurons ,and are more in lamina V ,after repeated stimulation they increase their firing rate (Wind up)

The Spinothalamic Tract; The axons of most second-order neurons cross the midline close to their level of origin (at the anterior commissure) to the contralateral side of the spinal cord before they form the spinothalamic tract and send their fibers to the thalamus, the reticular formation, the nucleus raphe magnus, and the periaqueductal gray. The spinothalamic tract. considered the major pain pathway, lies antrolaterally in the white matter of the spinal cord.

Alternate Pain Pathways: other ascending pain pathway, spinoreticular tract thought to mediate arousal and autonomic responses to pain. The spinomesencephalic Tract may be important in activating anti-nociceptive, descending pathways. The spinohypothalamic and spinotelencephalic tracts activate the hypothalamus and evoke emotional behavior The spinocervical tract ascends uncrossed to the lateral cervical nucleus, which relays the Fibers to the contralateral thalamus: this tract is likely a major alterative pain pathway

Integration With the Sympathetic and Motor Systems: Somatic and visceral afferents are fully integrated with the skeletal motor and sympathetic systems in the spinal cord. brainstem. and higher centers. Afferent dorsal horn neurons synapse both directly and indirectly with anterior horn motor neurons, These synapses are responsible for reflex muscle activity—whether normal or abnormal—that is associated with pain. In a similar fashion, synapses between afferent nociceptive neurons and sympathetic neurons in the intermediolateral column result in reflex sympathetically mediated vasoconstriction, smooth muscle spasm, and the release of catecholamines, both locally and from the adrenal medulla. (15)

Third-Order Neurons

located in the thalamus and send fibers to somatosensory areas I and V in the post- central gyrus of the parietal cortex and the superior wall of the sylvian fissure, respectively.