CHRONIC POSTSURGICAL PAIN

Essay

Submitted in Partial Fulfillment of the Master Degree
In Anesthesia

Presented by

Eyman Fawzy Hassan Radwan
M.B., B.Ch.

Under supervision of

Prof. Dr./ Nabil Mohamed Abd Elmoety
Professor of Anesthesia,
Intensive Care and Pain Management
Faculty of medicine - Ain Shams University

Prof. Dr./ Sameh Michel Hakim
Professor of Anaesthesia
Intensive Care and Pain Management
Faculty medicine - Ain Shams University

Dr./ Mohamed Yousef Mohamed Abo Elmagd
Lecturer in Anaesthesia,
Intensive Care and Pain Management
Faculty of medicine - Ain Shams University

Faculty of medicine
Ain Shams University
٢٠١٣

٢٠١٣

List of contents

Page

All praise is to **Allah** *and all thanks. He has guided and enabled me by His mercy to fulfill this thesis, which I hope to be beneficial for people.*

Words can never express my deepest gratitude and appreciation to ***Prof. Dr./ Nabil Mohamed Abd Elmoety,*** *Professor of Anesthesia, Intensive Care and Pain Management, Faculty of medicine, Ain Shams University, for his close supervision, continuous guidance, valuable instructions, indispensable advice and patience. He has generously devoted much of his valuable time and effort to present this work in an ideal form. It was a great honor to me to work under his supervision.*

I would like to express my sincere thanks and deepest gratitude to ***Prof. Dr./ Sameh Michel Hakim,*** *Professor of Anaesthesia, Intensive Care and Pain Management, Faculty medicine, Ain Shams University, for his gracious supervision, valuable guidance, valuable scientific suggestions, generous help, support and continuous encouragement through the whole research. I am deeply affected by his characters, perfection, care and consideration.*

I would like to express my utmost and sincere gratitude and cordial appreciation to ***Dr./ Mohamed Yousef Mohamed Abo Elmagd,*** *Lecturer in Anaesthesia, Intensive Care and Pain Management, Faculty of medicine, Ain Shams University, for his continuous encouragement, generous assistance and valuable guidance during the whole period of this work.*

List of abbreviations

δ	: Delta
μ	: Mu
σ	: Sigma
AA	: Arachidonic acid
ACTH	: Adrenocorticotrophic Hormon
APS	: Acute pain services
ASA	: Acetylsalicylic acid
ATP	: Adenosine triphosphate
BP	: Blood pressure
cAMP	: Cyclic adenosine monophosphate
CCK	: Cholecystokinin
CGRP	: Calcitonin gene-related peptide
COX-٢	: Cyclooxygenase ٢
CRF	: Corticotrophin-releasing factor
CRP	: Cervical radiculopathy
CRPS	: Complex regional pain syndrome
DAG	: Diacylglycerol
DBS	: Deep brain stimulation
GABA	: γ -aminobutyric acid
GDNF	: Glial cell line-derived neurotrophic factor
HR	: Heart rate
ICP	: Intracranial pressure
IM	: Intramuscular
IP٣	: Inositol triphosphate
IV	: Intravenous
K	: Kappa
MSIR	: Morphine sulfate instant release
NMDA	: N-methyl-D-aspartate
NRM	: nucleus raphe magnus
NSAIDs	: Nonsteroidal anti-inflammatory drugs
OTFC	: Oral Transmucosal Fentanyl Citrate
PAG	: Peri-aqueductal grey area
PC	: Phosphatidylcholine
PCA	: Patient controlled analgesia
PGE٢	: Prostaglandin E٢
PKC	: Protein kinase C
PLA٢	: Phospholipase A٢

List of abbreviations (Cont.)

PLC	: Phospholipase C
PRF	: Pulsed radiofrequeny
PVG	: Periventricular gray matter
RCTs	: Randomisedcontrolled trials
RF	: Radiofrequency
SAN	: Sino-atrialnode
SC	: Subcutaneous
SCS	: Spinal cord stimulation
SG	: Substantia gelatinosa
SP	: Substance P
TDS	: Transdermal system
TENS	: Transcutaneous electrical nerve stimulation
TTS	: Transdermal therapeutic system
VIP	: Vasoactive intestinal peptide

List of Tables

Page

List of Figures

Page

بسم الله الرحمن الرحيم

صدق الله العظيم

سورة النساء آية
(١١٣)

INTRODUCTION

The International Association for the Study of Pain defined pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" ***(Godfrey, ٢٠٠٥)***. Chronic or 'persistent' post-surgical pain (CPSP) is defined as pain of at least ٣-٦ months duration which has developed after a surgical procedure, where other causes such as disease recurrence or a preexisting pain syndrome have been excluded ***(Macrae, ٢٠٠١)***.

Although pain is a psychological sensory experience, it is caused by various factors e.g., nociceptive, inflammatory, and neuropathic pain. Acute postoperative pain is followed by persistent pain in ١٠–٥٠٪ of individuals after common operations, such as groin hernia repair, breast and thoracic surgery, leg amputation, and coronary artery bypass surgery. Since chronic pain can be severe in about ٢–١٠٪ of these patients, persistent postsurgical pain represents a major, largely unrecognised clinical problem. Iatrogenic neuropathic pain is probably the most important cause of long-term postsurgical pain. Consequently, surgical techniques that avoid nerve damage should be applied whenever possible. Also, the effect of aggressive, early therapy for postoperative pain should be investigated, since the intensity of acute postoperative pain correlates with the risk of developing a persistent pain state.

Finally, the role of genetic factors should be studied, since only a proportion of patients with intraoperative nerve damage develop chronic pain. Based on information about the molecular mechanisms that affect changes to the peripheral and central nervous system in neuropathic pain, several opportunities exist for multimodal pharmacological intervention. Here, we outline strategies for identification of patients at risk and for prevention and possible treatment of this important entity of chronic pain ***(Kehlet et al., ٢٠٠٦)***.

AIM OF WORK

The aim of this work is to outline the problem of chronic or persistent pain developing after surgical procedures with particular emphasis on its epidemiology, pathophysiology, chronic postsurgical pain syndromes, clinical presentation, management and prevention.

NEUROANATOMY OF PAIN

Pain is conducted through three neuron pathways that transmit noxious stimuli from the periphery to the cerebral cortex. Most nociceptors are free nerve endings that sense heat and mechanical and chemical tissue damage and are characterized by a high threshold for activation and encode the intensity of stimulation by increasing their discharge rates in graded fashion. Noxious sensations can often be broken down into two components: a fast, sharp, and well-localized sensation ("first pain"), which is conducted with a short latency (٠,١ s) by Aδ-fibers (tested by pinprick); and a duller, slower onset, and often poorly localized sensation ("second pain"), which is conducted by C fibers. In contrast to epicritic touch sensation, which may be transduced by specialized end organs on the afferent neuron (eg, pacinian corpuscle for touch), protopathic pain sensation is transduced mainly by free nerve endings ***(Stantonhicks, ٢٠٠٩).***

Classification of Nociceptors According to the Site *(Stantonhicks, ٢٠٠٩):*

Nociceptors can be divided according to their location into:

- Cutaneous nociceptors.
- Deep somatic nociceptors.
- Visceral nociceptors

Cutaneous Nociceptors:

Nociceptors are present in both somatic and visceral tissues. Primary afferent neurons reach tissues by traveling along spinal somatic, sympathetic, or parasympathetic nerves. Somatic nociceptors include those in skin (cutaneous) and deep tissues (muscle, tendons, fascia, and bone), whereas visceral nociceptors include those in internal organs.

Deep Somatic Nociceptors:

Deep somatic nociceptors are less sensitive to noxious stimuli than cutaneous nociceptors, but are easily sensitized by inflammation. The pain arising from them is characteristically dull and poorly localized. Specific nociceptors may exist in muscles and joint capsules; they respond to mechanical, thermal, and chemical stimuli.

Visceral Nociceptors:

Visceral organs are generally insensitive tissues that mostly contain silent nociceptors. Some organs appear to have specific nociceptors, such as the heart, lung, testis, and bile ducts. Most other organs, such as the intestines, are innervated by polymodal nociceptors that respond to smooth muscle spasm, ischemia, and inflammation (algogens) ***(Stantonhicks, ٢٠٠٩).***

Pain Pathways:

Pain is conducted through three neuron pathways that transmit noxious stimuli from the periphery to the cerebral cortex ***(Brandsborg, ٢٠٠٩).***

First Order Neurons:

Located in the dorsal root ganglia, the majority of first order neuron sends the proximal end of their axons into the spinal cord via the dorsal (sensory) spinal root at each cervical, thoracic and sacral level. The first order neurons synapse with the second order neurons. Alternatively they may synapse with interneurons, sympathetic neurons or ventral horn motor neurons.

Second order neurons:

As afferent fibers enter the spinal cord they segregate according to size with small unmyelinated fibers becoming lateral and large myelinated fibers becoming medial (Fig.١)**.** Pain fibers may ascend or descend one to three spinal cord segments in lissauer's tract before synapsing with second order neurons in the gray matter of the ipsilateral dorsal horn. A cross section of the spinal cord shows ١٠ anatomical and physiologically distinct layers called Rexed Laminae. Lamina I responds primarily to noxious (nociceptive) stimuli from cutaneous and deep somatic tissues. Lamina II, also called the substantia gelatinosa, contains many interneurons and is believed to play a major role in processing and modulating nociceptive input from cutaneous nociceptors***(Stantonhicks, ٢٠٠٩)***.

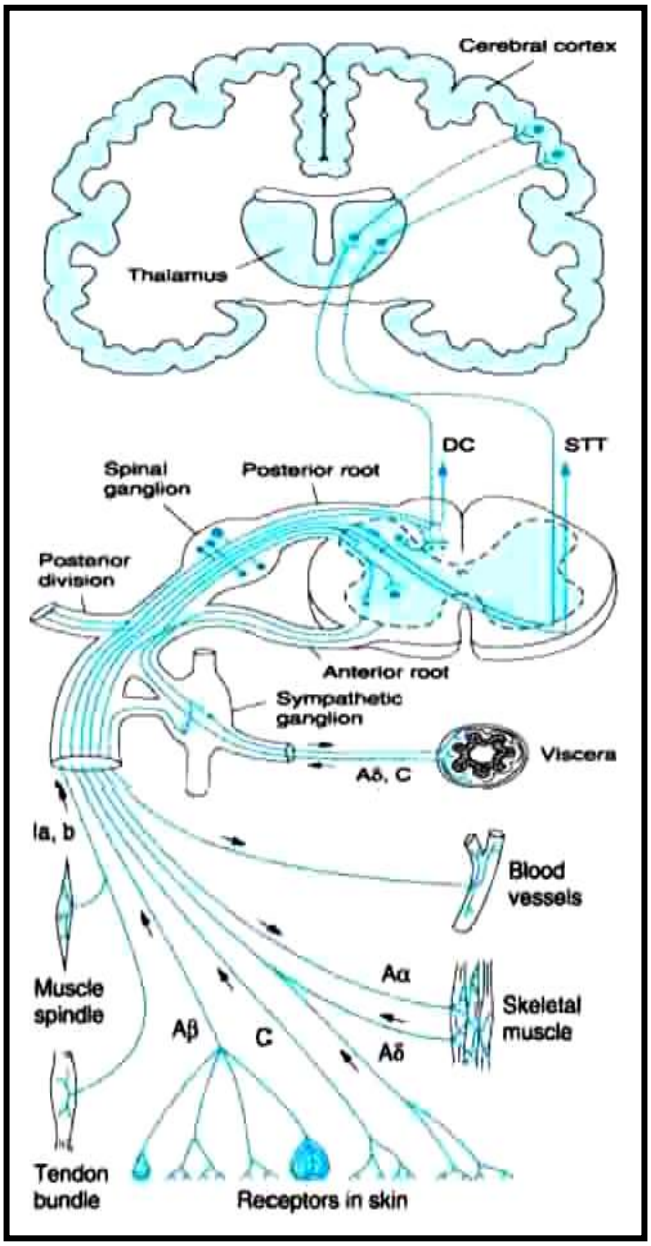

Figure ١: Pain pathway from ***Stantonhicks (٢٠٠٩).***