ACUTE POSTOPERATIVE PAIN MANAGEMENT IN CHRONIC CANCER PATIENTS RECEIVING OPIOIDS FOR CHRONIC CANCER PAIN

Thesis

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By

Rasha Ahmed Fouad Negm

M.B., B.Ch.
Faculty of Medicine – Ain Shams University

Supervised by

PROF. DR. NEHAL GAMAL ELDIN NOOH

Professor of Anesthesia, Intensive Care and Pain Management
Faculty of Medicine - Ain Shams University

PROF. DR. SHERIF FAROUK IBRAHIM

Professor of Anesthesia, Intensive Care and Pain Management
Faculty of Medicine- Ain Shams University

DR. HODA SHOKRI ABD ELSAMIE

Lecturer of anesthesia, intensive care and pain management
Faculty of Medicine- Ain Shams University

Faculty of Medicine
Ain Shams University
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مقدمة من

طبيبة/ رشا أحمد فؤاد نـجم
بكالوريوس الطب والجراحة العامة
كلية الطب – جامعة عين شمس

تحت إشراف

أ.د/ نهـال جمـال الدين نـوح
أستاذ التخدير والرعاية المركزة وعلاج الألم
كلية الطب- جامعة عين شمس

أ.د/ شريـف فـاروق إبراهيـم
أستاذ التخدير والرعاية المركزة وعلاج الألم
كلية الطب – جامعة عين شمس

د/ هدى شكري عبد السميع
مدرس التخدير والرعاية المركزة وعلاج الألم
كلية الطب – جامعة عين شمس

كلية الطب
جامعة عين شمس
2013

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LIST OF ABBREVIATIONS

- **ACTH:** Adrenocorticotropin.
- **BPN:** Brachial Plexus Neuropathy.
- **CIPN:** Chemotherapy-Induced Peripheral Neuropathy.
- **CR:** Continous Release.
- **CRH:** Corticotropin Releasing Hormone.
- **CNS:** Central Nervous System.
- **C-6-G:** Codeine-6-glucuronide.
- **DRG:** Dorsal Root Ganglia.
- **DHC:** Dihydrocodeine.
- **EMLA:** Eutectic Mixture of Lidocaine.
- **GABA:** Gamma-Aminobutyric Acid.
- **HDL:** High Density Lipoproteins.
- **HIV:** Human Immunodeficiency Virus.
- **IR:** Immediate Release.
- **IASP:** International Association for the Study of Pain.
- **IV:** Intravascular.
- **Mg:** Milligram.
- **Mm:** Millimeter.
- **MRI:** Magnetic Resonance Imaging.
- **M1:** Muscarinic Acetylcholine Receptor M1.
- **M-3-G:** Morphine-3-glucuronide.
- **M-6-G:** Morphine-6-glucuronide.
- **NCCN:** National Comprehensive Cancer Network.

- **NMDA:** N-Methyl-D-Aspartate.
- **NSAID:** Non-Steroidal Anti-Inflammatory Drugs.
- **NORC:** Norcodeine.
- **OTFC:** Oral Transmucosal Fentanyl Citrate.
- **PAG:** Periaqueductal Grey.
- **PBCSP:** Post-Breast Cancer Surgery Pain.
- **QST:** Quantitative Sensory Testing.
- **SC:** Subcutanous.
- **SSRI:** Selective Serotonin Reuptake Inhibitor.
- **TF:** Transdermal Fentanyl.
- **TRP:** Transient Receptor Potential.
- **TRPV1:** Transient Receptor Potential Cation Channel, Subfamily V , Member 1.
- **VATS:** Video-Assisted Thoracoscopic Lung Surgery.
- **VPL nucleas:** Ventroposterolateral Nucleus.
- **WHO:** World Health Organization.

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INTRODUCTION

Pain is unpleasant sensory and emotional experience associated with actual or potential tissue damage. Pain has both physical and emotional component. The International association for the study of pain classified pain according to specific characteristics: site, duration, intensity and etiology. ***(Chelly JE et al; 2011)***

Pain is transmitted from pain receptors along nerve fibers to the pain centers in the brain. One of the most important tracts that carry pain is the spinothalmic tract. ***(Waldman SD, 2011)***

Persistent unremitting pain exerts profound impact on the body's endocrine, cardiovascular, neurologic and musclo-skeletal systems. Pain also affects the patient psychologically. So, understanding the pathophysiology of pain, proper pain diagnosis and assessment together with expecting the possible complications will help in performing a proper pain management plan. ***(Block KI, 2011)***

Chronic cancer patients on high doses of opioids, who present for surgery, are a heterogenous group with a number of complex perioperative problems including management of acute, breakthrough and chronic pain. Chemotherapy is frequently given

to decrease the tumor size before surgery which also has its side effects and affects the mortality rate. In addition, the surgery itself will have variable effect on the patient's pain as it may lead to its increase or its decrease. ***(AL Parslan T et al.,2012)***

Acute pain management in these patientsis problematic because regular opioid intake is associated with tolerance and dependence. More recently, opioid induced hyperalgesia has been brought to light. As a rule, the regular opioid dose should be given with the appropriate conversions. Additional doses should be anticipated according to the planned surgery and breakthrough pain. Multimodal analgesia using opioid and non opioid drugs, local and regional anesthesia are highly indicated. Patient controlled analgesia should be used in tolerant patients. ***(Richebe P and Beaulieu P, 2009)***

So, a proper pain management perioperative plan should be made to achieve effective analgesia to avoid complications of persistent unremitting pain. ***(British Pain Society, 2010)***

AIM OF THE WORK

To study the management of acute postoperative pain in chronic cancer patients on regular opioid therapy.

CHAPTER ONE

PATHOPHYSIOLOGY OF PAIN AND ITS PATHWAYS

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage according to the International Association for the Study of Pain (IASP) definition. Pain is always subjective. Each individual learns the application of the word through experiences related to injury in early life. ***(IASP, 2012)***

Many people report pain in the absence of tissue damage or any likely pathophysiological cause; usually this happens due to psychological reasons. There is usually no way to distinguish their experience from that due to tissue damage if we take the subjective report. If they regard their experience as pain, and if they report it in the same ways as pain caused by tissue damage, it should be accepted as pain. This definition avoids tying pain to the stimulus. ***(Merskey H and Bogduk N, 2012)***

The American Academy of Pain Medicine defines pain as *"An unpleasant sensation and emotional response to that sensation"*. Pain is the commonest symptom for which a person approaches medical care. The definition of pain that is most appropriate for use in clinical practice was given by Margo McCaffrey in1968. He defined pain as *"whatever the experiencing*

person says it is, existing whenever he says it does". ***(The American Academy of Pain Medicine, 2011)***

The Web version of the Encyclopedia Britannica defines pain as "*A complex experience consisting of a physiological (bodily) response to a noxious stimulus followed by an affective (emotional) response to that event. Pain is a warning mechanism that helps to protect an organism by influencing it to withdraw from harmful stimuli. It is primarily associated with injury or the threat of injury, to bodily tissues".* ***(The American Academy of Pain Medicine, 2011)***

Dr. Don Ranney, in his book "Anatomy of Pain" defines pain as –"*A perception, not really a sensation, in the same way that vision and hearing are. It involves sensitivity to chemical changes in the tissues and then interpretation that such changes are harmful. This perception is real, whether or not harm has occurred or is occurring. Cognition is involved in the formulation of this perception. There are emotional consequences and behavioral responses to the cognitive and emotional aspects of pain"* Even though the experience of pain varies from one person to the next, it is possible to categorize the different types of pain. ***(Ranney D, 2011)***

CLASSIFICATION OF PAIN

Here's an overview of the different types of pain and what distinguishes them from one another. Pain is generally classified according to its location, duration, frequency, underlying cause, and intensity. Classification of pain is thus complicated and can be a source of confusion for many clinicians. As a result, many practitioners now commonly use several different classification systems. Clear distinctions between these systems are not always possible. To successfully manage pain, practitioners must be able to work with pain classifications that encompass all considerations (ie, time course, involved anatomy, intensity, type of patient, and specific pathology) and be able to switch from model to model, depending on a patient's individual circumstances. ***(Waldman SD, 2009)***

1-Location of Pain:

Pain is often classified by body location. Two overlapping schemes relate the pain to the specific anatomy and/or body system thought to be involved. The anatomic pain classification system identifies sites of pain as viewed from a regional perspective (eg, lower back pain, headache, pelvic pain). In contrast, the body system pain classification method focuses on classical body systems (eg, musculoskeletal, neurologic, vascular). Yet, both classification systems address only a single dimension (ie, where or why does the patient hurt) and thus may ultimately

fail to adequately define the underlying neurophysiology of the problem**.** ***(Waldman SD, 2009)***

2-Duration of Pain

The duration of the pain process is the most obvious distinction that can be made when classifying pain symptoms. Acute pain is limited to pain of less than 30 days' duration, whereas chronic pain persists for more than 6 months. Sub-acute pain comprises the interval from the end of the first month to the beginning of the seventh month of continued pain. Recurrent acute pain describes a pain pattern that persists over an extended period of time but occurs mainly as isolated episodes of pain. **(Nazario B, 2011).**

Chronic pain is further divided by its underlying etiology into non–cancer related pain (benign or nonmalignant pain) and cancer-related pain (malignant pain). About 70% of people with chronic pain treated with pain medication experience episodes of what's called breakthrough pain.

Breakthrough pain refers to flares of pain that occur even when pain medication is being used regularly. ***(Nazario B, 2011)***

The primary distinction between acute and chronic pain, regardless of its etiology, is crucial. Acute pain is useful and serves a protective purpose. It warns of danger, limits use of injured or diseased body parts, and signals the departure of pathology. Without acute pain, it is doubtful that human survival would be possible at all. **(Waldmann SD, 2009).**

Chronic pain, on the other hand, has little protective significance, persists despite normalization after injury or disease, and ultimately interferes with productive activity. Pain after surgery (ie, postoperative pain) is a specific type of acute pain. No matter how successful or well performed, operations cause tissue trauma and release potent mediators of inflammation and pain.

This type of pain is often poorly managed. Patients often receive significantly fewer opioid analgesic agents than ordered, either because the nursing staff may be overly concerned about opioid addiction or because analgesic agents are irrationally selected by physicians, many of whom have little knowledge about the pharmacology of such agents**.** ***(Waldmann SD, 2009)***

Although postoperative pain is experienced by millions of patients through the world, it is rarely recognized as producing harmful physiologic or psychological effects. The axiom "No one ever died from pain" is clearly incorrect, given the modern recognition that unrelieved pain increases cardiac work, increases metabolic rate, interferes with blood clotting, leads to water retention, lowers oxygen levels, impairs wound healing, alters immune function, interferes with sleep, and creates negative emotions. Unrelieved pain can, for example, delay the return of normal gastric and bowel function in postoperative patients. Recognition of the widespread inadequacy of acute pain management prompted the United States Department of Health and