Comparative Study between the effect of intraperitoneal injection of Bupivacaine versus Ropivacaine on postoperative pain following laparoscopic cholecystectomy

Thesis submitted for the partial fulfillment of the M.D degree in Anesthesiology

By

Tarek Mohammed Ahmed Ashoor
M.B.B.CH., M.Sc., Anesthesiology
Faculty of Medicine- Ain Shams University

Under supervision of

Professor Doctor. Mohammed AbdElgalil Sallam
Professor of Anesthesiology and Intensive Care
Faculty of Medicine-Ain Shams University

Professor Doctor. Sohair Abbas Sadek
Professor of Anesthesiology and Intensive Care
Faculty of Medicine-Ain Shams University

Professor Doctor. Amr Esam AbdElhameed
Professor of Anesthesiology and Intensive Care
Faculty of Medicine-Ain Shams University

Faculty of Medicine
Ain Shams University
٢٠٠٨

Introduction

Given the expanding role of ambulatory surgery and the need to facilitate an earlier hospital discharge, improving postoperative pain control has become an increasingly important issue for all anesthesiologist (**Paul F., ٢٠٠٥).**

In common with all other types of pain, acute postoperative pain is an extraordinarily complex sensation which may be described as an interpretation of these signals by higher centers (involving memory experiences of painful situation, and an affective component which generally comprises anxiety and /or depression.

Uncontrolled postoperative pain has an adverse sequel of delayed resumption of normal pulmonary function, restriction of mobility (thus contributing to thrombo-embolic complications), nausea and vomiting, increase in the systemic vascular resistance, cardiac work, and myocardial oxygen consumption through an increase in the catecholamine release induced by the stress response.**(Rawal etal., ٢٠٠١).**

Control of acute postoperative pain and the timing, duration (e.g., preemptive analgesia), and fashion in which, it is implemented (e.g., multimode analgesia management) is important in facilitating short and long-term patient convalescence. **(Miller's etal., ٢٠٠٥).**

Adequacy of postoperative pain control is one of the most important factors in determining when a patient can be safely discharged from surgical

facility and has a major influence on the patient's ability to resume their normal activities of daily living**.(Kehlet H, Dahl J.B, ٢٠٠٣).**

Perioperative analgesia has traditionally been provided by opioid analgesics. However, extensive use of opioids is associated with a variety of perioperative side effects, such as ventilatory depression, drowsiness and sedation, postoperative nausea and vomiting, pruritus, urinary retention, ileus and constipation, thus can delay hospital discharge. In addition, it has been suggested by the Joint Commission on Accreditation of Health Organizations that excessive use of postoperative opioids analgesics leads to decrease patient satisfaction. **(White P.F, ٢٠٠٢).**

In addition the use of conventional method of administration of intramuscular opioids in standard prescribed doses, may be too large (causing side effects), or too small (causing inadequate analgesia).Therefore, anesthesiologist and surgeons are increasingly turning to non-conventional techniques as adjuvant for managing pain during perioperative period to minimize the adverse effect of analgesic medications. **(Palvin D.J etal., ٢٠٠٣).**

From the non-conventional methods, the infiltration of long-acting local anesthetics as an adjuvant for regional or local anesthetic techniques, improve postoperative pain management, furthermore, when administrated before surgery, these simple techniques can also decrease anesthetic and analgesic requirement during surgery as well as reduce the need for

opioid-containing analgesic postoperatively. **(Palvin D.J etal., ٢٠٠٣).**

Intraperitoneal infiltration of local anesthetic in combination with general anesthesia has been investigated in several interventional studies during laparoscopic cholecystectomy. Approximately half of these studies showed reduce in the postoperative pain significantly, but without a clear relation between the dose, application sites or the nature of the local anesthetic that has been used.

Definition of pain

Pain is not just a sensory modality but an experience .The International Association for the Study of Pain defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage.” This definition recognizes the interplay between the objective, physiologic sensory aspects of pain and its subjective, emotional and psychological components. **(Morgan’s etal., ٢٠٠٢).**

Pain is clinically divided into, acute pain which is primarily due to nociception and chronic pain, which may also be due to nociception, but in which psychological and behavioral factors often play a major role. Postoperative pain is one of the types of acute pain and can be further differentiated based on the origin and feature into somatic and visceral pain. Somatic pain is due to nociceptive input arising from skin, subcutaneous tissues, and mucous membranes. It is characterized by being well-localized and described as sharp, pricking, throbbing or burning sensation. Visceral pain –on the other hand- is due to nocceptive input arising from internal organ or one of its covering. It is usually dull diffuse pain which is frequently associated with abnormal sympathetic or parasympathetic activity causing nausea, vomiting, sweating and /or changes in blood pressure or heart rate. **(Macintyre, Ready, ٢٠٠١).**

Magnitude of the problem:

Many factors influence the occurrence intensity quality and duration of postoperative pain like the site, nature and duration of operation, type of incision (thoracic and upper abdominal operations are associated with the most severe pain), the preoperative psychological, physical and pharmacological preparation of the patient, added to this the anesthetic management and the quality of post operative care (the attitude of the ward staff). **(Macintyre, Ready, ٢٠٠١).**

So, in order to achieve good quality of postoperative analgesia, careful history should be taken from the patients about any coexisting medical conditions such as substance abuse or withdrawal, anxiety disorder, affective disorder, hepatic or renal impairment, and any past history of poor pain management. In addition, preoperative patient education should be done to the patients to improve expectations, compliance and ability to effectively interact with pain management techniques. **(Chris Thompson, ٢٠٠٣).**

Neuro-physiology of pain

Nociceptors:

Sensation is often described as either protopathic (noxious) or epicritic (non-noxious). Epicritic sensation (light touch, pressure, proprioception, and temperature discrimination) is characterized by low-threashold receptors (specialized end-organs on the afferent neurons) and conducted by large myelinated nerve fibers while; protopathic sensation (pain) is sub served by high-threshold receptors (free nerve endings). **(Morgan etal., ٢٠٠٦).**

Noxious sensations can often be broken down into two components: a fast, sharp, and well-localized sensation "first pain" which is conducted by Ad fibers; and a duller, slower onset, and poorly localized sensation "second pain" which is conducted by C fibers. This protopathic pain is transmitted mainly by free nerve endings that sense mechanical or chemical tissue damage. Several types of this pain is recognized; (١) mechano-nociceptors, which respond to pinprick, (٢) silent nociceptors, which respond only on the presence of inflammation, (٣) polymodal mechano-heat receptors which is more prevalent and respond to excessive pressure, extreme of temperature, and pain producing substances. Nociceptors are either somatic that include those in skin and deep tissues (muscle, tendons, joints), or visceral nociceptors that include those in internal organs. **(Julius and Basbaum, ٢٠٠١).**

Pain pathway:

Pain is conducted along three neuron pathways; from the periphery to the cerebral cortex.

First order neuron:
Cells of these neurons are located in the dorsal root ganglia (for the body) and specific cranial nerve ganglia (for the head and neck) e.g Gasserian ganglion for trigeminal nerve. The Proximal end of their axons reach spinal cord via the dorsal sensory root of cervical, thoracic, lumbar, and sacral level (for the body) and through the cranial nerves (for head and neck). **(Julius and Basbaum, ٢٠٠١).**

Second order neurons:
Pain fibers may ascend or descend three spinal cord segments in the Lissauer's tract before synapsing with the second order neuron in the gray matter of the ipsilateral dorsal horn, this synapsing may be through interneurons. Second order neurons are either; neciceptive specific which serves only noxious stimuli and are normally silent or wide dynamic range (WDR) neurons that can receive also non-noxious afferent input. WDR neurons are more prevalent in the dorsal horn and are responsible for the increased intensity of firing in response to same stimulus "wind-up".
Lamina II of the gray matter of the dorsal horn of the spinal cord, (also called the substantia gelatenosa) contains many interneurons and is believed to play a role in the processing and modulating nociceptive input.
Axons of most of the second order neurons cross the midline to the contra-lateral side of the spinal

cord forming the lateral spinothalamic tract that send its fibers to the thalamus, the reticular formation, nucleus raphy and periaquidactal gray. **(Carr and Goudas, ١٩٩٩).**

Third order neurons:
Those are located in the thalamus and send their fibers to the somato-sensory area I and II in the cerebral cortex. **(Carr and Goudas, ١٩٩٩).**

Physiology of pain:

There are four distinct processes in the sensory pathway: transduction, transmission, modulation and perception **Figure ١.**

(a) Transduction:
Nociceptors; terminal branches of A-delta and C fibers, respond selectively to noxious stimuli resulting from tissue damage or inflammation and convert chemical, mechanical, or thermal energy at the site of stimulus into neural impulses.Prostanoids (prostaglandins, leukotrienes, an hdroxyacids) are products of the arachidonic acid pathway and are major mediators of the hyperalgesia that accompanies inflammation.

The activity and sensitivity of sensory neurons is profoundly altered by the mediators released as a result of tissue injury and inflammation, those mediators produce and increase nociceptor sensitivity, neurogenic oedema and hyperalgesia of tissues in the vicinity of the injury.The complex changes in the peripheral signal processing result in increased pain

sensation, alteration in the quality and duration of pain and may lead to altered central pain processing with the development of chronic pain. **(Kelly's, etal., ٢٠٠١).**

(b) Transmission:

When signal transduction has occurred, impulses are transmitted via A-delta and C fibers to the dorsal horn of the spinal cord. A variety of neurotramitters are released by the incoming first order nociceptive neuron; one of those is substance P, a neurokinin, and calcitonin gene-related peptide (CGRP) which extends the spinal cord zone from which substance P is released, thereby contributing to increase the excitability. Enhanced synaptic transmissions due to the release of excitatory amino acids (EAA) (secondary to the release of substance P) induce a prolonged enhancement of response by the dorsal horn neurons; this is termed "wind up". **(Kelly's, etal., ٢٠٠١).**

(c) Perception:

Impulses transmitted in the spinal cord via the spinothalamic tract are delivered to the thalamus from which it is transmitted to somato-sensory cortex where sensory discrimination of pain and its emotional component is done. While the reticular formation (that receive projections from the spinothalamic tract) is probably responsible for the increased arousal component of pain. **(Kelly's, etal., ٢٠٠١).**

(d) Modulation of pain:

Modulation of pain occurs peripherally at the nociceptor, in the spinal cord or in supra-spinal structures. This modulation can either inhibit or facilitate pain transmission.

(i) Peripheral modulation:

Nociceptors and their neurons display sensitization following repeated stimulation, causing hyperalgesia that is either primary or secondary. Primary hyperalgesia is due to decrease in threshold, and increase in the frequency response to the same stimulus intensity, a decrease in response latency and spontaneous firing after cessation of stimulus. Those responses are produced due to the release of allogens (e.g. histamine) from tissue damage. Secondary hyperalgesia on the other hand is manifested by the triple response of fare, local tissue oedema and sensitization to noxious stimuli, this is mediated through the release of substance P by antidromic afferent neurons. **(Hollmann and Durieux, ٢٠٠٠).**

(ii) Central modulation:

This is either in the form of facilitation or inhibition.

(-) Facilitation:

Central sensitization is mediated by the following mechanisms: (١) Wind-up which is mediaed by increase in the frequency of discharge of WDR neurons to repeated stimuli. (٢) Receptor field expansion: where dorsal horn neurons increase their receptive field so as adjacent neurons become responsive to stimuli. (٣) Hyperexcitability of flexion reflexes both

ipsilaterally and contralaterally. (٤) Marked increase in the sympathetic tone with subsequent increase in the heart rate, blood pressure, and cardiac output.

(-) Inhibition:

Segmental inhibition: where the massive nociceptive input generated by the operation inhibits WDR neurons and spinothalamic tract activity.

Supra spinal inhibition: This is mediated by the descending tracts from higher centers like periaqueductal gray, reticular formation and nucleus raphe magnus. Axons from these tracts act pre-synptically, in primary afferent neurons and post-synaptically, in second order neuron (interneurons). These pathways mediate their antinociceptive actions via $\alpha^{٢}$- adrenergic, seratonergic, and opiate receptor mechanisms. **(Grubb , ١٩٩٨).**

Preemptive Analgesia:

Development of central sensitization and hyperexcitability occurs after surgical incision and results in the amplification of postoperative pain. *Preemptive analgesia* is defined as what is administered before surgical incision that prevent the development of central sensitization from incisional injury and inflammatory injuries (i.e., intraoperative and postoperative periods).the combination of experimental data and positive clinical trials strongly suggests that preemptive analgesia is a clinically relevant

phenomenon. Maximum benefit is observed when there is complete blockade of noxious stimuli. **(Moiniche's, etal., ٢٠٠٢).**

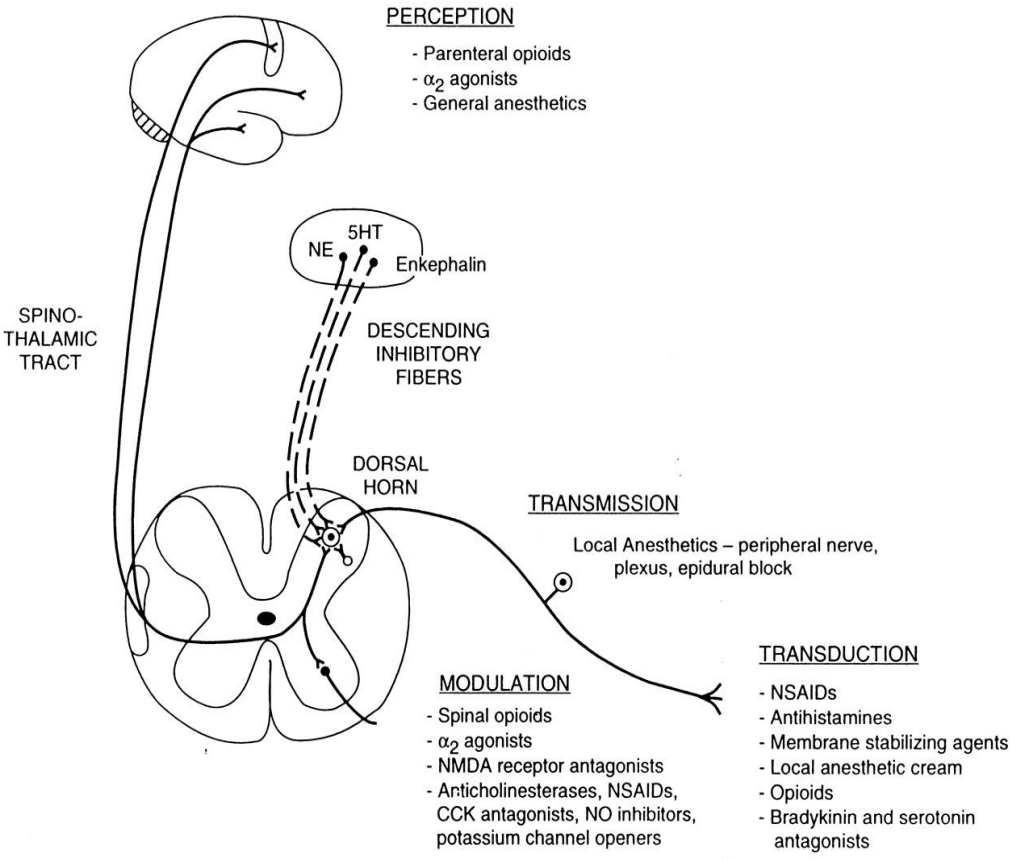

FIGURE ١ Diagrammatic representation of the four processes involved in the sensory pathway: transduction, transmission, perception, and modulation. Primary afferent neurons transmit information from the periphery to the dorsal horn of the spinal cord. Afferent information is then transmitted via the spinothalamic tracts by second-order neurons to the thalamus and to the sensory cortex. The descending inhibitory fibres (interrupted lines) modulate the afferent input at the dorsal horn. Also represented are the agents that can modify the sensory input of eachofthe four processes. **(Kelly's, etal., ٢٠٠١).**

Pain after laparoscopy:

Pain occur after laparoscopy, but is usually less and shorter than that caused by the same surgical procedure made possible by laparotomy. The reduction in pain has made possible earlier discharge from the hospital provided that the control of the residual pain is adequate and that the drugs or techniques used for analgesia are safe enough. **(Joris's etal., ١٩٩٥).**

Pain may occur in the upper abdomen, lower abdomen, back, or shoulders. The incidence of pain is not altered if suxamethonium is used to facilitate tracheal intubation. The greatest incidence of pain is in the upper abdomen. **(Joris's etal., ١٩٩٥).**

Pain after laparoscopy may be transient or it may persist of at least ٣ days. Reporting of pain is greatest just after operation, and then decreases to a low level within ٢٤ hours, but it may increase to a second or even a third peak later. After laparoscopic cholecystectomy, visceral pain was found to predominate in the first ٢٤ hours, whereas shoulder pain, minor on the first day, increased and becomes significant on the following day. **(Alexander's, ١٩٩٧).**

Mechanism of pain in laparoscopy:

In addition to the trauma caused to the abdominal wall and the visceral organs by the enoscope and the surgical instruments, there are

other mechanisms responsible for pain after laparoscopy. Rapid distension of the peritoneum may be associated with tearing of blood vessels, traumatic traction of the nerves and release of inflammatory mediators. Peritoneal inflammation is probably also the origin of the upper abdominal pain after lower abdominal surgery or after diagnostic laparoscopy. This can persist for at least ٣ days. Peritoneal biopsy performed ٢-٣ days after laparoscopy showed peritoneal inflammation and neuronal rupture, and there was a linear inverse relationship between abdominal compliance at the time of laparoscopy and severity of postoperative pain. Therefore, abdominal distention should better be slow with adequate muscle relaxation to ensure suitable abdominal compliance. The prolonged presence of shoulder tip pain suggests excitation of the phrenic nerve that is caused by the persistence of gas in the abdomen (pneumoperitoneum). There is statistically significant correlation between the width of the gas bubble and pain score, and this pain can be reduced by the aspiration of the gas under the diaphragm. **(Alexander's, ١٩٩٧).**